

Radio-Frequency Ablation of Hepatocellular Carcinoma: Influence of the Anatomy on the Outcome of the Procedure

AHMAD HESHAM M. SAID, M.D.*; MOHAMAD REDA HAMZA, M.D.** and ALI GABALLA, M.D.***

Radiology Department, Beny Suef Division*, Department of Medical Oncology, National Cancer Institute** and Department of Tropical Medicine***, Cairo University.

ABSTRACT

Purpose: To study the contribution of the morphology and the anatomical relations of a hepatocellular carcinoma (HCC) lesion to the outcome of radiofrequency ablation therapy (RFA) and the expectancy of ablation extent.

Material and Methods: Twenty-five patients with thirty-seven HCC lesions had undergone RFA therapy. Of these, twenty-nine lesions were done under conscious sedation or general anesthesia, using an internally cooled electrode. Lesions were anatomically classified: A) according to size into three groups; 1) < 2.92 cm, 2) 2.92-5.1 cm and 3) >5.1 cm; B) according to margin definition into, ill-defined or well-defined; C) according to difficulty of accessing the lesion through percutaneous route into 1) difficult and 2) easily accessible; and D) anatomical relationship to nearby structures into 1) critically, < 1 cm, and non-critically, \geq 1 cm, away from nearby structures.

Results: Complete ablation was achieved in 15 patients (51.7%), 90-99% ablation in 5 patients (17.2%); 50-89% ablation in 6 patients (20.7%) and < 50% in 3 patients (10.3%). Factors that contribute to outcome are lesion diameter and anatomical relation to nearby vessels. Margin ill-definition may lead to misinterpretation of tumour diameter and subsequent sub-optimal results. Ease of accessibility of the lesion is subjective and has no true contribution. No major complications related to the procedure were encountered. One patient died of bleeding oesophageal varices, three weeks after the procedure. Minor complications (twelve patients) included persistent pain, short term fever and local electric burn at the site of the grounding pad.

Conclusion: RFA is an effective modality for treating HCC when a patient is properly selected. Best outcome is expected -in good hands- with smaller lesions, not related to a major vessels with well-defined margins.

Key Words: Radiofrequency - Ablation - RFA - Hepatocellular carcinoma - HCC.

INTRODUCTION

The use of radiofrequency ablation (RFA) is being widely accepted as an effective method

of treatment of hepatic focal lesions [11,14]. Not all patients with HCC are candidates for this modality. Selecting patients with HCC for RFA is a challenge. Size of the lesion is a significant parameter. A lot of work accessed the relation between the size of the lesion and the outcome of the procedure [4,5,7,10,13]. Local tissue perfusion may alter the volume of the ablated tissue [2].

This work aims at validation of the effect of the anatomical parameters of the lesion on the outcome of the procedure. These anatomical parameters are: a) the size of the lesion, b) the location of the lesion and relation to other hepatic structures and c) the definition of tumour margin.

MATERIAL AND METHODS

Patients:

Between January and September 2000, 29 HCC lesions in 25 patients (22 males, 3 females; mean age 54.6; age range 44 - 71 years) associated with cirrhosis were treated by RFA, in an outpatient clinic. Two patients had three lesions, while 8 patients had two lesions. Four patients had treatment for two lesions, while 21 patients received treatment for a single lesion. Some lesions were not treated with RFA either because they were shifted to another form of treatment (intra-arterial chemo-embolization), or the patient died before the 2nd lesion was attacked. All patients were not candidate for surgery because of hepatic or non-hepatic causes.

The diagnosis of HCC was based on the triad of 1) cirrhosis, 2) contrast enhancement in the arterial phase at dynamic (spiral) CT and 3) AFP

level more than 50 ng/ml. This level was considered by Cedrone et al. as the best accurate AFP threshold value for HCC diagnosis [1]. Ten patients had AFP levels below this level. These patients had undergone fine needle biopsy which confirmed the diagnosis of HCC. Based on Peng, we have classified our patients into 6 groups according to the levels of AFP (Table 7): > 5-20 ng/ml, > 20-50 ng/ml, > 50-100 ng/ml, > 100-200 ng/ml and > 200-400 ng/ml, and > 400 ng/ml [9].

All patients had a degree of liver cirrhosis (Child A or B). HCV and HBV were positive in 18 and 5 patients respectively. Of these, 16 patients had a past history of treatment of Schistosomiasis. None of the patients was alcoholic or had ascites at the time of the procedure. For patients had subnormal prothrombin time and concentration, while three patients had low platelet count (80,000 or less/cmm) and they received platelets transfusion one day before the procedure.

In addition to those 25 patients, there were another two patients who were treated with RFA but they died before the 28 days follow up scan, and were thus excluded from the study. One of them was due to cardiac attack, not related to RFA

The sizes of the lesions were in the range of 1.5 to 12.5 cm (mean: 4.17 cm) in diameter (Table 1).

The anatomical locations of the lesions were classified according to anatomical relation to the nearby structures into critical and non-critical locations. Location was considered to be critical, when the lesion is in direct contact, or less than one cm from the portal vein (PV, 10 lesions), the inferior vena cava (IVC, 1 lesion), hepatic vein (HV, 1 lesion), the gall bladder (GB) or major bile duct (6 lesions) and/or the capsule of the liver (4 lesions). The anatomical locations were re-classified at the time of the procedure according to the ease of access to the lesion. Lesions which were clearly and fully visualized by the used guiding modality, were considered as "easily accessible". Lesions which were not fully visualized (isoechoic, or lesions masked by the pleura) were considered as "hardly accessible or difficult".

Preparatory work up:

All patients had undergone a routine pre-treatment work-up, which included the following:

1- Ultrasonography of the liver and abdomen at 3.5 MHz, (AU 530, Esaote, Genoa, Italy; or EUB 200, Hitachi, Tokyo, Japan). The liver size and texture, biliary and portal tree were evaluated. Each lesion size, definition of its borders and relation to the nearby anatomical structures were reported. The rest of the abdomen was inspected for other organ disease, ascites or lymphadenopathy.

2- Triphasic CT of the liver (Auklet, Toshiba medical systems, Tokyo, Japan), during and after the administration of a 100 cc bolus of iodinated contrast agent (Urovideo; Bracco, Milan, Italy; or Ultravist, Scherring, Berlin, Germany). Helical CT scanning was performed in the arterial and the porto-venous phases (15 and 75 sec from the onset of injection), as well as a late phase, 12-15 minutes from the onset of injection.

3- Laboratory work-up including serum AFP (Alpha-feto protein), liver enzymes (ALT, AST, Alkaline phosphatase), total and direct bilirubin, creatinine and albumin; blood count, haemoglobin, glucose, as well as prothrombin time and concentration. Immunological tests for hepatitis B and C were also included. Except for hepatitis tests, all other tests were repeated 2, 7 and 28 days after the procedure.

Technique:

In all patients, the procedure was performed under conscious sedation or light short-acting anaesthesia. Vital signs were monitored continuously during the procedure. After the procedure patients were allowed for recovery and they went home at the same day.

Ultrasonography was selected as the guiding modality, unless 1) plain CT clearly shows the lesion while US does not and/or 2) the access (path) to the lesion is easier with CT. When using US, scanning of the whole liver at the supine, semi-lateral and lateral decubitus positions were performed in order to select the easiest and most adequate approach, while avoiding important anatomical structures. When using CT, few plain cuts were performed, covering the expected area of the lesion, as depicted from the previous diagnostic study. The optimum level and the point of entry are selected. A metallic

mark was applied to this point and a confirmatory CT cut was performed, showing the mark in place. Few CT cuts were taken after insertion of the probe to show the exact position of the tip.

The entry site was cleansed with iodized alcohol. A sterilized gel was then applied to the skin as a contact medium. Sedation or anaesthesia was started at the optimum patient position. A local anaesthetic (xylocaine 2%, Astra) was injected at the entry point, both superficially and deeply into the liver capsule, in order to minimize pain after recovery.

A free-hand technique was utilized with US-guided approach. More than one type of electrode was used according to the morphology of the lesion. All were of the internally cooled tip category (Radionics, Burlington, Mass). The length of selected electrode was either 15 or 20 cm, according to the depth of the lesion. A single electrode of either 2 or 3 cm exposed tip was used for smaller lesions, 2 or 3 cm in diameter respectively. Larger lesions required the insertion of a cluster electrode, formed of three needles with 5 mm interval in between each other [4]. A special triple-holed piece of plastic was then used with the needles to keep them at fixed relation during the introduction of the electrode. In some patients, the introduction of the cluster probe was too difficult owing to narrow intercostal space, or carried a higher risk of injury to important anatomical structures like the pleura or gall bladder. In this situation, multiple attacks with single electrodes was performed, possibly on different sessions. This is because of impaired visualization of the lesion after the procedure.

Grounding was achieved by attaching 2-3 dispersive pads, with a surface area greater than 400 cm², to the patient's lower abdomen and thigh(s), fairly away from the heart. The RF electrodes were attached to a 500 kHz RF generator (series CC-1 Radionics), capable of producing 200 W of power. Local tissue temperature was continuously monitored during the procedure through a thermocouple embedded within the electrode tip. Tissue impedance was monitored using circuitry incorporated within the generator. A peristaltic pump was used to infuse 0-5°C distilled water into the lumen of the electrode, so as to keep the measured local tissue temperature at 10-20°C. The maximum volume of required water did not exceed 1.5 liters in any

patient. Automatic impedance control was generally used, to keep tissue impedance at the range of 50-70 Ohms. Whenever the impedance exceeds this limit, RF was automatically cut off.

The duration of application of RF energy was decided according to the size of the lesion. A single RF application did not exceed 15 min/session, and never less than 8 minutes. The average duration was 12 minutes, and it was extended only in larger lesions, where the needle was slightly withdrawn during the treatment, to increase the ablated volume.

Upon the application of RF energy, there was increase in echogenicity that might take one of two forms (or both at the same time): 1) Some cases showed an intensely echogenic small focus around the electrode tip, that progressed and increased in size with the continuous application of RF (Fig 1). At a certain limit, there was no further increase in size of the echogenic focus. This focus was located within the tumor and might extend into the surrounding liver tissue as well, and is thought to represent tissue vaporization. This focus persisted after the completion of the procedure for more than one hour, although it was fading, and in some cases it showed as an echogenic ring. 2) Other cases showed a sudden increase in echogenicity. This was a fairly large and irregular focus and was slightly delayed, 1-2 minutes after the onset of RF application. It was not strictly inside the lesion, and it might occur completely out of its margins. This form was always associated with a loud popping sound. As ablation progresses, the excessive echogenicity and acoustic shadowing mask the field. At the end of the procedure, US scan of the right side of the abdomen and flank was done to rule out any bleeding or other complications.

Whenever the procedure was performed under CT guidance, no real-time image was performed during the procedure. At the end, few CT cuts were acquired at the level of the lesion. A tiny area of high attenuation (70-80 HU) was noticed in one case, inside the lesion, and might be attributed to minor intra-tumoral haemorrhage (Fig 2).

On abdominal auscultation during RF application, there was a "boiling" sound, which only becomes audible when the tissue impedance start to rise. This sound is similar to the sound of

water boiling in the pot. Upon the onset of RF application, there is no sound heard until the tissue impedance starts to increase. The sound gets louder in proportion to tissue impedance until RF is cut down, then it fades rapidly.

After the procedure, the patients were allowed for recovery and kept under observation for 2-4 hours, before they were allowed to go back home.

Anatomical and Radiological Assessment:

In our study, we depended mainly and solely on contrast-enhanced CT, for the evaluation of the outcome of the procedure. We used tumour marker -AFP- assay, as a guide line for evaluating the progress of the disease, but it was useless for the assessment of a specific lesion, particularly when the tumour is multi-centric. Moreover, some patients showed normal levels, associated with larger and progressive tumours.

CT was performed using the same parameters as those of the pre-treatment scan. First scan was performed 28 days after the procedure. Whenever a patient requires more than one session, scanning was performed 28 days after the last session. Follow up scans were repeated at intervals of 4 months. The percent of necrosis was estimated after cursor delineation and area measurement of: 1) un-enhanced part of the lesion and 2) the full margin of the lesion; in every CT cut. Tumour necrosis was classified into 4 grades:

Grade (1): 100% (complete) ablation: No enhancement in the arterial phase, in the 28 days scan (Fig 3)

Grade (2): 90-99% ablation: definite residual tumoral activity, representing less than 10% of the tumor size.

Grade (3): 50-89% ablation: the ablated area represents more than one half of the tumor size (Fig 4).

Grade (4): < 50% ablation: the ablated area represents less than one half of the tumor size (Fig 5).

RESULTS

The results of RF treatment, are summarize in tables (2-5) according to 1) tumour size, 2) definition of margin, 3) accessibility of the lesion and 4) relation to nearby vital structures.

Table (2) shows that complete ablation was achieved in 15 of 29 lesions (51.7%), ranging between 15-50 mm in diameter, (mean = 2.92 cm). Among 10 lesions below this mean diameter, 8 lesions were completely ablated (80%), while the remaining 2 showed 90-99% necrosis. Among 10 lesions ranging between 2.92-5.1 cm, 7 lesions were completely ablated (70%), while 2 lesions (20%) showed 50-89% necrosis, one lesion (10%) showed < 50% necrosis. None of the 9 lesions > 5.1 cm could be ablated completely. 3 lesions (33.3%) showed 90-99% necrosis, 4 lesions (44.4%) showed 50-89% necrosis and 2 lesions (22.2%) showed < 50% necrosis.

Table (3) shows that 23 out of 29 lesions (79.3%) had well-defined margins. Of these, only 13 lesions could be ablated completely (i.e. 56.5%), 3 lesions (13%) showed 90-99% necrosis, 5 lesions (17.2%) showed 50-89% necrosis, while 2 lesions (6.5%) showed < 50% necrosis. Six lesions (20.7%) had ill-defined margins. Only 2 of them (33.3%) were completely ablated, and another 2 lesions (33.3%) showed 90-99% necrosis. One lesion (16.7%) showed 50-89% necrosis, and another one (16.7%) showed < 50% necrosis.

Table (4) shows that 22 of 29 lesions (75.9%) were easily accessible. Of these, 11 lesions (50%) were fully ablated, three lesions (13.6%) showed 90-99% necrosis, 5 lesions (22.7%) showed 50-89% necrosis, while another three lesions (13.6%) showed less than 50% necrosis. Seven lesions out of 29, 22.6% had a hardly accessible location. Of these, 4 lesions (57.1%) were ablated completely, Two lesions (28.6%) showed 90-99% necrosis, and only one lesion (14.3%) showed 50-89% necrosis. None of them showed less than 50% necrosis.

Table (5) shows that 24 of 29 lesions (82.8%) had a critical location. Of these, 11 lesions (45.5%) were completely ablated, 5 lesions (20.8%) showed 90-99% necrosis, 5 lesions (20.8%) showed 50-89% necrosis, and three lesions (12.5%) showed less than 50% necrosis. Five lesions out of 29, 24.1% had a non-critical location. Of these, 4 lesions (80.0%) were completely ablated, none (0.0%) showed 90-99% necrosis and one lesion (20.0%) showed 50-89% necrosis. None of these lesions showed less than 50% necrosis.

The term "critical" was redefined to include

only those lesions close to a large vascular structure (portal vein, hepatic vein and/or IVC) Table (6). With this definition, there were only 11 critically located lesions (37.9%) and of these only 3 (27.3%) were fully ablated, 3 lesions (27.3%) showed 90-99% necrosis, 2 lesions (18.2%) showed 50-89% necrosis and three lesions (27.3%) showed less than 50% necrosis. Eighteen lesions out of 29, 62.1% had a non-critical location. Of these, 12 lesions (66.7%) were completely ablated, 2 lesions (11.1%) showed 90-99% necrosis and 4 lesions (44.4%) showed 50-89% necrosis. None of these lesions showed less than 50% necrosis.

As regard tumour size, all lesions < 2.92 cm (10 lesions), showed complete ablation except for two lesions. These showed 90-99% necrosis and were ill-defined, critically and hardly accessible, just beneath the diaphragm. All lesions 2.92-5.1 cm (11 lesions), were also completely ablated, except for three lesions. One of them had an ill-defined margin and showed 50-89% ablation. The other two lesions were closely related to major vessels and showed 50-89% and < 50% ablation. Both showed well-defined margins.

In the group of the larger lesions > 5.1 cm (10 lesions), all were easily accessible. < 50% necrosis was achieved in one ill defined and one well-defined lesions. Both were located close to the PV. 50-89% necrosis was achieved in 4 lesions. Only one of them was located close to a major vessel (PV). All were well-defined. 90-99% necrosis was achieved in three lesions, all were well-defined and located close to the PV.

Side Effects and Follow up:

Patients had their treatment under conscious sedation or light anaesthesia. Pain during the procedure was the most common undesirable complaint. The peak of the pain corresponded constantly to RF power application, and it decreased immediately upon cessation of RF. After the procedure, there was a persistent sense of “burning” -which varied among patients- in the right hypochondrium, and it tended to be accentuated with deep inspiration. Some patients felt pain in the right shoulder, particularly those whose lesions were close to the diaphragm. Generally, this sense of pain tended to improve within few days.

Fever was encountered only in 2 patients, 24-48 hours after the procedure and responded adequately to antipyretics. Electric burn occurred in one patient, at the site of the grounding pad, following a 12 min session using a cluster probe and two grounding pads. This was treated with silver preparation and showed complete healing after 5-6 weeks.

Bleeding was not encountered in the immediate post-procedure period. One patient had an attack of oesophageal variceal bleeding and died 3 weeks after 2nd session of RFA. The high attenuation areas seen within the lesion at the immediate post-procedure CT were not seen upon follow up.

Table (1): Distribution of lesions according to their sizes.

Size	< 2.92	<= 5.1	> 5.1
Total No.	10	11	10
%	32.3	35.4	32.3

Table (2): Relationship of tumour size to the outcome of RFA.

	Size < 2.92	% of this group	% of total	Size = 2.92-5.1	% of this group	% of total	Size > 5.1	% of this group	% of total
Total No.	10		32.3	10		34.5	9		31.0
100 % ablation.	8	80.0	27.6	7	70	24.1	0	0.0	0.0
90-99% ablation	2	20.0	6.9	0	0.0	0.0	3	33.3	10.3
50-89% ablation	0	0.0	0.0	2	20	6.9	4	44.4	13.8
< 50% ablation	0	0.0	0.0	1	10	3.4	2	22.2	6.9

Table (3): Relationship between margin definition and the outcome of RFA.

	Ill-Definition	% of this group	% of total	Well- Definition	% of this group	% of total
Total No.	6		20.7	23		79.3
100 % ablation	2	33.3	6.9	13	56.5	44.8
90-99% ablation	2	33.3%	6.9	3	13.0	10.3
50-89% ablation	1	16.7%	3.4	5	21.7	17.2
< 50% ablation	1	16.7%	3.4	2	6.9	6.5

Table (4): Relationship of accessibility of the lesion to the outcome of RFA.

	Difficult loc	% of this group	% of total	Easy location	% of this group	% of total
Total No.	7		24.1	22		75.9
100% ablation	4	57.1	31.8	11	50.0	37.9
90-99% ablation	2	28.6	6.9	3	13.6	10.3
50-89% ablation	1	14.3	3.4	5	22.7	17.2
< 50% ablation	0	0.0	0.0	3	13.6	10.3

Table (5): Relationship of anatomical relations of the lesion to the outcome of RFA.

	Critical location	% of this group	% of total	Non-Critical location	% of this group	% of total
Total No.	24		28.8	5		17.2
100% ablation	11	45.5	37.9	4	57.1	17.2
90-99% ablation	5	20.8	17.2	0	14.3	3.4
50-89% ablation	5	20.8	17.2	1	14.3	3.4
< 50% ablation	3	12.5	10.3	0	0.0	0.0

Table (6): Anatomical relation to big vessels (PV or IVC) and its contribution to the outcome of RFA.

	Vascular (PV or IVC)	% of this group	% of total	Non-vascular	% of this group	% of total
Total No.	11		37.9	18		62.1
100% ablation	3	27.3	10.3	12	66	41.4
90-99% ablation	3	27.3	10.3	2	11.1	6.9
50-89% ablation	2	18.2	6.9	4	44.4	13.8
< 50% ablation	3	27.3	10.3	0	0.0	0.0

Table (7): Distribution of AFP levels among patients.

AFP level	Incidence
> 400	40%
200-400	4 %
100-200	8 %
50-100	8 %
20-50	16%
5-20	24%
< 5	0 %

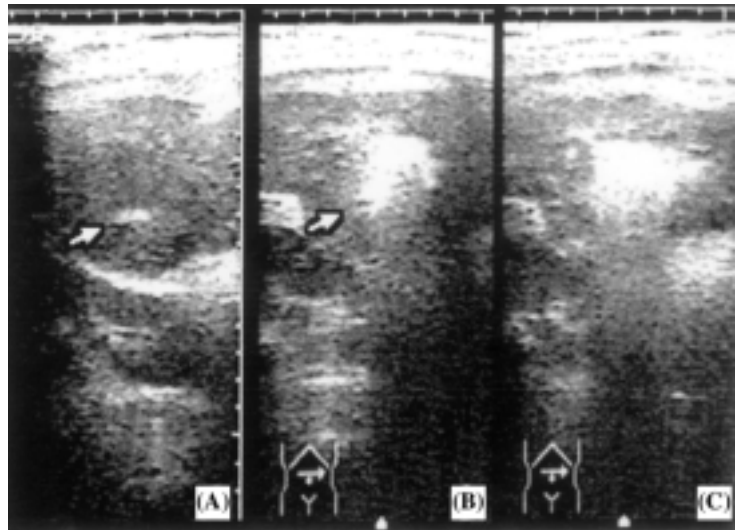
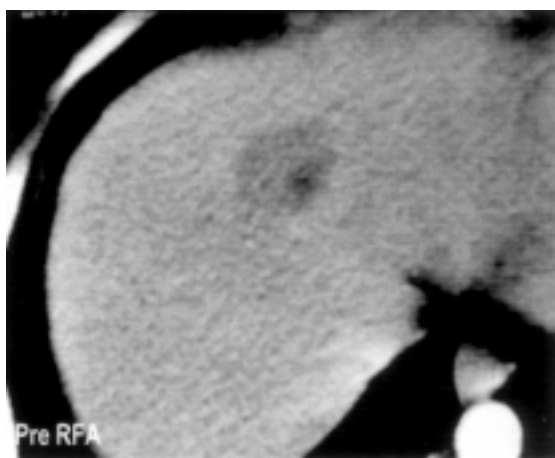


Fig. (1): Change in echogenicity during RFA:

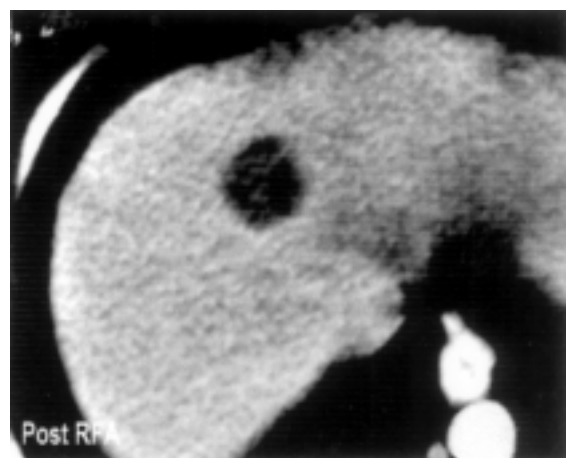
- A- The needle tip within the lesion (arrow).
- B- An echogenic focus is seen superficial to the needle, casting an acoustic shadow.
- C- Increased size of the echogenic focus, the acoustic shadow masks the needle.



Fig. (2): Plain CT cut of a focal lesion, one hour after RFA session. Notice the dense area within the low attenuation lesion (arrows).



(A)



(B)

Fig. (3): A- Before RFA, B- after RFA. Complete ablation of a well-defined tumour < 5 cm. The whole lesion shows very low attenuation and clear-cut margins in the arterial phase.



Fig. (4): Less than 90% ablation after first session RFA of a critically subcapsular tumour < 5 cm warranting another session.

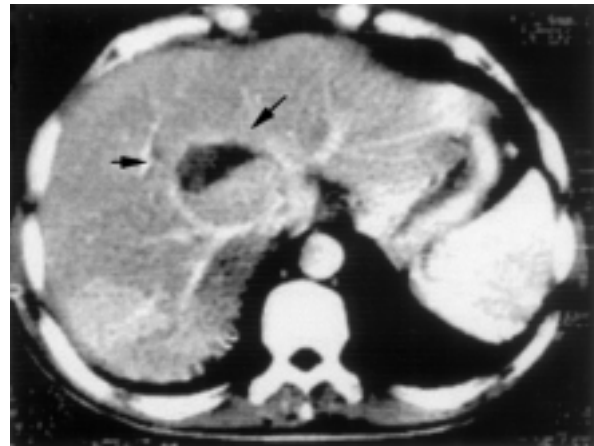


Fig. (5): Less than 50% ablation in a tumour >5 cm. The ablated area (arrows) is less than half of the tumour size. Notice the long contact with IVC and two hepatic veins.

DISCUSSION

Radiofrequency ablation is a recent modality, that showed good results as regards the ability to induce local tissue ablation, with minimal side effects. Although surgery is the definitive treatment of HCC, many patients are unfit either due to poor hepatic reserve and/or extensive disease [12,13,15]. RFA is potentially valuable in treating patients who are generally unfit for surgery [3,6,13,16].

During the period of the study, we've examined 39 patients with HCC. Eight patients were not treated with RFA for one or more reasons which include multiple tumours (more than 3), exophytic tumour, patients with advanced cirrhosis and/or ascites. Another two patients died shortly after the procedure, before completing their follow up CT scan. These were excluded from the study, as there were no documented results.

As a general rule, US was preferable to CT guidance. This is because of the inherent advantages of US, namely: 1) The high sensitivity of US in the liver without the need to I.V. contrast injection, 2) the multi-planar capability of US, which facilitates the access to the lesion especially when multiple sessions are required for treatment; 3) the real time capability of US that allows for monitoring the process of ablation. We preferred to utilize US free hand technique. This technique allows for monitoring the needle

position from different angles. In all difficult cases, we were able to reach the lesion in a satisfactory way. We may assume that 3D US would have been even more advantageous in this respect. Unfortunately, it was not available to us.

While CT may be efficient in visualizing lesions that are high up underneath the diaphragm, direct approach under CT guidance may result in pleural injury. We didn't prefer the trans-pleural approach, for fear of injury upon excessive movement of the diaphragm, particularly with the use of conscious sedation or light anaesthesia. We did not utilize CT as a guiding modality except in two specific conditions: 1) When the lesion is well visualized at CT but not US; and/or 2) the access (path) to the lesion is easier and/or safer with CT.

The boiling sound heard on auscultation can be explained on the basis of tissue evaporation and gas formation, with subsequent rise in tissue impedance. The clinical value of this sign is unclear and may need further observation with pathological entities other than HCC, before a definite conclusion is reached.

We postulated that certain anatomical criteria may contribute to the outcome of the procedure. These criteria are: 1) size of the lesion, 2) margin definition, 3) anatomical relations and 4) ease of access to the lesion.

The efficacy of treatment has been shown by some authors to correlate well with the size of the tumour [3,7,8]. Our results show a definite relationship between the size of the lesion and the extent of ablation. The relation is inversely proportional. Our classification of the mean percentage of ablation (MPA) is based on Livraghi et al. [7], with the addition of a fourth grade: < 50% ablation, which was not encountered during their work.

Fifteen lesions had complete ablation, with a mean diameter of 2.92 cm. The MPA for the 10 tumours below this diameter is 98%. Some authors [5,7] had defined the 3 cm limit for best outcome. Our study agrees with these works in establishing this limiting diameter for best expectation of outcome. Our largest lesion that was fully ablated was 5 cm in diameter. MPA for tumours below 5.1 cm was 71%, but it drops to 47% if we consider only those above 2.92 cm.

The definition of margin also contributes to the outcome of the procedure [5,7]. The MPA for well-defined tumours (n=23, mean diameter = 4.63 cm) was 86.1%, compared to 80.0% for ill-defined tumours (n = 6, mean diameter = 4.12 cm). Among these 23 well-defined tumours, the MPA for those > 5.1 cm in diameter = 72.5%, compared to 88.89% for those ≤ 5.1 cm and 100% for those < 2.92 cm. This may point to partial contribution of the size of the tumour to these results. Furthermore, the MPA for all tumours ≤ 5.1 = 87%. This is very close to that of well-defined tumours of the same diameter group. This would raise questions about the significance of this factor. In our opinion, its significance is that an ill-defined margin of a tumour may lead to underestimation of its actual diameter, leading -finally- to sub-optimal outcome.

Moreover, the number of ill-defined tumours is small and shows variable tumoral diameters (one lesion = 12.5 cm, one lesion = 4 cm and 4 lesions ≤ 2.5 cm in diameter), rendering it insufficient. Larger number of lesions is required in order to get more solid figures about the contribution of this factor to the final outcome.

The close relation of the lesion to a nearby large vessel interferes with complete ablation of the malignant cells, owing to the heat-sink effect, where the flowing blood acts to disperse the heat away resulting in continuous cooling [2,3]. More-

over, when the lesion lies in close contact to a vascular or non-vascular anatomical structure, there is always the fear to injure such organ. This is an important consideration when making the decision about the access to the lesion and the location of the needle tip. During this work, we've encountered a number of lesions in close relation to various anatomical structures; namely the PV, the hepatic veins, IVC, GB, liver capsule. The location of the lesion seems to alter the expectation of the outcome of treatment. The MPA in critically located tumours was 82.92%, compared to 94% in non-critical tumours. When we considered those tumours adjacent to a major vascular structure (like the PV, HV or IVC), the MPA dropped to 72.73%, compared to 91.54% in those relatively far from a major vessel. This is explained in view of the heat-sink effect, when the flowing blood acts to wash out the heat. The three lesions with < 50% ablation fell into this category. One of them lies at the bifurcation of the right PV, splaying its two branches. This seems to double the heat-sink effect. Another lesion has direct contact with the PV and the right and middle hepatic veins at segment 8, with similar effect. These findings should further support the poor contribution of the heat-sink effect to the outcome of treatment. The third lesion had single contact with the PV. This lesion was a huge one whose diameter = 12.5 cm. This may explain the poor outcome. There is minor difference in MPA between the non-critical and those lesions critically located near a non-vascular structure.

Some of the encountered lesions were not easily accessible, either because the lesion was isoechoic (too faint to see) and/or because of its location. Most of these hardly accessible tumours were located very high at the liver dome, so partly or totally hidden -at US- by the pleura. Un-expectedly, the ease of access to the lesion had no significant effect on the outcome. The MPA for difficult lesions was 92.86%, compared to 82.27% for easily accessible tumours. The mean diameters for the two groups were 2.74 cm and 5.1 cm respectively. All difficult lesions (n = 7) were located high up in segments 4A, 7 or 8. In 3 of them the procedure was performed under CT guidance, in an attempt to overcome such difficulty. The classification of tumours into difficult or easily accessible is merely subjective and did not significantly contribute to the outcome of the procedure. A more objective

parameter is the position of the probe tip within the tumour, as visualized at US or CT. This invalidates the ease of access, as a contribution factor.

Pain was always tolerable, so that it could be managed on an outpatient basis. We had no definite explanation why electric burn happened in one patient. It might be attributed to inappropriate application of the pads that was missed during the procedure and/or skin over-sensitivity in such patient. One patient died of bleeding from oesophageal varices, 3 weeks following his 2nd session of RFA. We believe that his fatal bleeding is attributed to portal hypertension not RFA.

In conclusion, we believe that-with careful patient selection-RFA is a relatively safe technique for the treatment of hepatocellular carcinoma with no "life threatening" hazards. For the expectation of the outcome of treatment, one should consider the size of the lesion, and any contact with a nearby major vessel. Best outcome is expected with small lesions (≤ 3 cm), not related to vascular structures. Less favourable results are expected with larger lesions, and/or tumours with longer contact with major vessels. Lesions > 5 cm are less likely to be fully ablated, -with the available instrument-compared to lesions below this limit.

Well-defined tumours have a slightly more favourable outcome than ill-defined ones, which are usually infiltrating into the surrounding parenchyma and their true diameter is liable to underestimation. The ease of access to the lesion is a mere subjective factor and it depends on the skill of the operator. What's important is the actual location of the probe tip within the lesion as visualized during the procedure.

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