

# Recent Advances in Radiofrequency Ablation in the Treatment of Hepatocellular Carcinoma and Metastatic Liver Cancers

Shi-Ming Lin, MD

Hepatocellular carcinoma (HCC) and liver metastases are common cancers worldwide. Recent imaging modalities have been able to detect HCC and liver metastases at an early stage, with surgical resection as the choice of management. However, because of poor liver reserve, co-existing liver cirrhosis and multiplicity of tumors, resection is only feasible in 10-30% of HCC or liver metastases on presentation. Thus, various local tumor ablation modalities are being developed to effectively ablate small liver tumors. Of these, percutaneous ethanol injection and radiofrequency (RF) ablation (RFA) are the two best options because of their high effectiveness and minimal invasiveness. RFA has the particular advantage of more predictable ablation areas and fewer treatment sessions required. It has been applied for local ablation of liver malignancy since 1990 and is currently widely accepted as an alternative to resection in small, un-resectable or even resectable liver malignancies. Because current RF devices can only effectively ablate 3 cm tumors in a single RF electrode introduction, recent advances have focused exclusively on improving RF devices, including the design of electrodes and the algorithm to magnify the ablation zone in a single session or over a short duration. This review article updates results of RFA for HCC and liver metastasis in terms of complete ablation, local recurrence, overall survival, and recent advances in RFA for liver malignancy. (*Chang Gung Med J* 2009;32:22-32)



Dr. Shi-Ming Lin

**Key words:** radiofrequency ablation, hepatocellular carcinoma, liver metastases, complete ablation, local recurrence, survival

Hepatocellular carcinoma (HCC) is the 4<sup>th</sup> most common malignancy in the world. It is particularly prevalent in Asia and some south European and African countries where hepatitis B virus (HBV) infection is hyper-endemic.<sup>(1)</sup> Similarly, colorectal cancer (CRC) is common in the West and liver metastasis develops in approximately 40% of these patients, accounting for most deaths.<sup>(2)</sup> Therefore,

HCC, CRC liver metastases, and other liver metastases are very common malignancies that require effective therapies when detected at an early stage. Although there are multiple modalities in the treatment of HCC, resection or orthotopic liver transplantation (OLT) remains the treatment of choice for small HCC, which is generally defined as a solitary tumor  $\leq 5$  cm or a tumor number  $\leq 3$  with each tumor

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From the Liver Research Unit, Chang Gung Memorial Hospital, Taipei, Chang Gung University College of Medicine, Taoyuan, Taiwan.

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Correspondence to: Dr. Shi-Ming Lin, Liver Research Unit, Chang Gung Memorial Hospital, 5, Fusing St., Gueishan Township, Taoyuan County 333, Taiwan (R.O.C.) Tel.: 886-3-3281200 ext. 8102; Fax: 886-3-3272236; E-mail: lsmpaicyto@cgmh.org.tw, lsmpaicyto@gmail.com

≤ 3 cm in diameter.<sup>(3, 4)</sup> Most clinicians restrict the indications for resection to patients with a single tumor in a suitable location for resection.<sup>(3-10)</sup> However, resection remains feasible for a large single tumor with no evidence of vascular invasion.<sup>(5-10)</sup> Moreover, the risk of recurrence is not significantly increased in these large tumors compared to small ones.<sup>(5-10)</sup>

Similarly, resection is also primarily considered for CRC liver metastases if there is no unresectable hepatic and extra-hepatic disease.<sup>(2,11-13)</sup> However, 70-80% of HCC and 80-90% of CRC or other liver metastasis on diagnosis are unsuitable for resection due to advanced tumor stage or poor liver reserve.<sup>(5-12)</sup> As a result, percutaneous tumor ablation (PTA) has been developed for un-resectable HCC or liver metastases with a limited number and size, or for those that are un-resectable due to concomitant major systemic disease or poor hepatic reserve.<sup>(13)</sup> Fortunately, the majority of reports on PTA in HCC and liver metastasis have shown effective results, with comparable survival for PTA and resection in small HCC.<sup>(3,4,14-18)</sup>

Of various PTA modalities, percutaneous ethanol injection (PEI) and radiofrequency ablation (RFA) are the most widely employed.<sup>(14,19)</sup> A small

number of randomized control trials and cohort studies have also shown that RFA is superior to PEI for small HCC in terms of higher complete ablation, lower local recurrence, and higher overall survival rates.<sup>(20-23)</sup> RFA has been used for treatment of liver tumors since 1990.<sup>(24)</sup> This review describes updated long-term results of RFA in terms of complete necrosis, local recurrence, and overall survival in HCC and liver metastasis, as well as recent advances. Because RFA can also be employed for tumor reduction in advanced liver metastasis before or after chemotherapy, this review can be a reference on clinical results and RFA advances in managing liver metastases for gastroenterologists, surgeons, radiologists and oncologists.<sup>(2,11,13,25-35)</sup>

**RFA for treatment of HCC**

**Complete ablation of HCC after RFA**

Long-term results in terms of local recurrence, extra-hepatic or new tumor recurrence, overall recurrence, and survival are listed in Table 1. Complete ablation (or complete coagulation, complete necrosis, complete response) was defined as persistent hypo-attenuation of the tumor on computed tomography (CT) scan one month after the last ablation therapy.<sup>(19)</sup> When the index tumor had a hypovascular

**Table 1.** Results of Studies of Radiofrequency Ablation (RFA) for Hepatocellular Carcinoma

Authors and year	No. of cases	Maximal tumor size (cm)/No.	Mean follow-up (months)	Local recurrence (%): 1/2/3/4/5 years	New hepatic or extra-hepatic recurrence (%): 1/2/3/4/5 years	Overall recurrence (%): 1/2/3/4/5 years	Survival rate (%): 1/2/3/4/5 years
Rossi et al 1996 <sup>(27)</sup>	39	≤ 3	22	0/4/4/16/16	8/31/56/56/NA	NA	94/86/68/40/40
Buscarini et al 2001 <sup>(28)</sup>	88	≤ 3.5	34	14*	NA	NA	97/NA/67/NA/41
Lencioni et al 2003 <sup>(20)</sup>	52	< 5	22	5.8*	23.8*	NA	100/98/NA/NA/NA
Guglielmi 2003 <sup>(29)</sup>	53	≤ 4	18	6.8*	28/NA/NA/NA/NA	NA	87/63/45/NA/NA
Lin et al 2004 <sup>(21)</sup>	52	≤ 4	25	12/18/18/NA/NA	24/38/47/NA/NA	NA	90/82/74/NA/NA
Shiina et al 2005 <sup>(23)</sup>	118	3/4	37 (median)	1.3/1.7/1.7/1.7/NA	NA	22/30/61/70/NA	97/95/81/74/NA
Tateishi et al 2005 <sup>(30)</sup>	87	≤ 2	27.6 (median)	1.3/2.4/2.4/2.4/NA (total cases)	NA	NA	100/93.2/90.8/90.8/83.8
Tateishi et al 2005 <sup>(30)</sup>	215	2.1-5	27.6		NA	NA	93/85.4/74.3/63/45.2
Lencioni et al 2005 <sup>(31)</sup>	206	3/3; 5/1	24	4/NA/10/NA/10	14/NA/49/NA/81	18/37/55/71/83	97/NA/67/NA/41
Camma et al 2005 <sup>(32)</sup>	202	3/3; 5/1	19	12/24/30 (30M)/NA/NA	13/24/30 (30M)/NA/NA	22/38/44 (30M)/NA/NA	80/67/49 (30M)/NA/NA

**Abbreviations:** NA: not available; \*: Non-cumulative rates only, data represents rate in the follow-up period.

appearance on dynamic CT scan, complete ablation was determined by the maximal dimension of the ablation on CT scan. When the maximal dimension of ablation was 0.5 to 1 cm larger than the original dimensions before ablation, it was considered complete ablation.<sup>(19,33)</sup> The imaging findings were equivalent to pathological findings in most of the tumors achieving complete ablation after RFA.<sup>(34,35)</sup> After RFA, the heat induced a central “white zone” of coagulation tissue surrounded by a variable red zone of hyperemia.<sup>(34,35)</sup> In some cases with equivocal results between imaging and pathological findings, specialized vital stains may have been required to confirm cellular death after RFA.<sup>(35)</sup>

The rates of complete ablation were 80-100% in HCC  $\leq$  3 cm, 50-80% in HCC 3-5 cm, and 25% in HCC  $>$  5 cm.<sup>(20-23,36,37)</sup> Predictors of a higher complete ablation rate were small size ( $\leq$  3 cm) and well-differentiated and non-infiltrative HCCs.<sup>(37)</sup> To improve the complete ablation in larger tumors ( $>$  3 cm in diameter), various additional methods were employed which yielded better results than RFA monotherapy. These included ethanol injection immediately before RFA<sup>(38-40)</sup> or chemoembolization several days before RFA,<sup>(41,42)</sup> both of which could reduce the heat-sink effect (heat dissipation during RFA when the tumor was attached to a vessel with a dimension  $>$  3 mm) by thrombosis of intra- or peritumoral vessels, diffuse hot ethanol into the area not encompassed by RF electrodes, and increased coagulation by warmed ethanol.

Another combined therapy using the Pringle maneuver to occlude the tumor blood supply prior to RFA also increased the area of necrosis but had a higher rate of complications and was more cumbersome than PEI or transcatheter arterial chemoembolization (TACE) before RFA.<sup>(43)</sup> Other methods to enhance complete necrosis included stepwise deployment of RF tines or interactive algorithms at mid-interval in the procedure, where manipulation of the electrodes could concentrate heat in a smaller central area and then dissipate the heat after full deployment of the tines of the RF electrode.<sup>(44)</sup>

**Local recurrence or local tumor progression of HCC after RFA**

Local recurrence of HCC (equivalent to persistence of the original target tumor) was defined as the presence of an enhanced tumor on CT that corre-

sponded to the initial target tumor.<sup>(19)</sup> Local recurrence rates of small HCC after RFA were 1.3%-14% at 1 year, 1.7%-24% at 2 years, and 1.7-30% at 3 years.<sup>(20-23,31,32)</sup> Multivariate analysis showed that lower local recurrence could be predicted by a single tumor,<sup>(15,21)</sup> smaller HCC ( $\leq$  2 cm or 3 cm),<sup>(16,20)</sup> tumor with encapsulation, well-differentiated HCC,<sup>(21)</sup> non-subcapsular location of the tumor, no heat-sink effect, laparoscopic or open approach (vs. percutaneous approach), creation of a 1 cm ablative margin, a serum des-gamma-carboxy-prothrombin (DCP) level  $\leq$  40 mAU/mL,<sup>(23)</sup> and a platelet count  $\geq$  100,000/mL.<sup>(20-23,32,45)</sup> Similarly, methods to enhance complete ablation described above could also reduce local recurrence. In addition, for tumors in a sub-capsular location, an open or laparoscopic approach might be considered.<sup>(43)</sup>

**Additional new tumor recurrence and overall recurrence of HCC after RFA**

Additional new tumor recurrence rates of small HCC after RFA were 13-36% at 1 year, 24-38% at 2 years, 30-49% at 3 years, and up to 81% at 4 years.<sup>(20-23,31,32)</sup> Additional new tumor recurrence was higher in patients with a lower platelet count  $\leq$  100,000/mL (RR = 2.85) by multivariate analysis in the study by Camma *et al.*<sup>(32)</sup> The rate seemed to depend on the severity of underlying liver disease, such as cirrhosis or fibrosis.

The overall tumor recurrence rates of small HCC after RFA were 18-22% at 1 year, 30-48% at 2 years, 44-61% at 3 years, up to 71% at 4 years, and 83% at 5 years.<sup>(20-23,30-32)</sup> Multivariate analysis showed that the overall recurrence was generally higher in patients with a lower platelet count ( $\leq$  100,000/mL), representing the degree of fibrosis, positive anti-hepatitis C virus (anti-HCV) antibody, cirrhotic liver, prothrombin time  $>$  80%, multiple tumors, and higher Edmondson's grade (II, III).<sup>(23,32)</sup>

In contrast, serum alpha-fetoprotein (AFP) level, serum AFP-L3 level, and tumor stain on CT were not significantly correlated with overall recurrence in the study by Shiina *et al.*<sup>(23)</sup> Therefore, the factors of overall HCC recurrence might be associated with those related to local recurrence and new tumor recurrence. To increase complete necrosis, reduction of local recurrence and prevention of progression of underlying liver disease using treatments such as antiviral therapies for hepatitis B or C might

reduce overall tumor recurrence.<sup>(3,4)</sup>

**Overall survival of HCC after RFA**

Data on long-term survival were very limited. A limited number of studies reported overall survival rates of 80-100% at one year, 63-98% at 2 years, 45-67% at 3 years, 74% at 4 years,<sup>(23)</sup> and 41% at 5 years.<sup>(31)</sup> Longer survival was commonly observed in sub-groups with an early Child-Pugh class, small tumor size, low AFP level, low DCP level, well-differentiated tumor, and single tumor. Factors which were not significantly related included age, gender, or etiology of underlying liver disease. Multivariate analysis showed that factors which significantly predicted longer survival included a smaller tumor ( $\leq 2$  or 3 cm), higher albumin level ( $\geq 3.5$  gm/dL), higher platelet count ( $\geq 100,000$ /mmc), Barcelona-Clinic Liver Cancer (BCLC) stage A1, complete ablation at 1 month,<sup>(32)</sup> and serum lectin-reactive alpha-fetoprotein (AFP-L3) level ( $\leq 10\%$ ).<sup>(23)</sup> Age ( $> 65$  years), underlying cirrhosis, serum AFP level, tumor number, and tumor stain on enhanced CT (absent vs. present) did not significantly predict survival.<sup>(23)</sup>

**RFA versus hepatic resection for small HCC**

Since RFA and resection are categorized as curative treatments for small HCC according to

European Association for the Study of Liver (EASL) 2001 and American Association for the Study of Liver Disease (AASLD) 2005 HCC management guidelines,<sup>(3,4)</sup> comparing these 2 methods is crucial to determine the choice of treatment (Table 2). Comparison between these two methods in terms of survival has only been reported in a number of cohort studies and one randomized controlled trial (RCT).<sup>(15-17,46,47)</sup> The results in general showed no significant difference in overall survival, but resection achieved 0% local tumor progression and slightly higher disease-free survival. Resection was intrinsically superior to RFA because of eradication of the target tumor and its surrounding area, or even 1-2 segments that might contain satellite nodules or microscopic metastases. Thus, there was no issue of local tumor progression such as that occurring in HCC after RFA, even though RFA can also create a 1 cm ablative margin surrounding the target tumor.<sup>(3,4,18)</sup>

No single imaging modality so far has been able to ensure the complete ablation of tumor after RFA.<sup>(34)</sup> Nevertheless, patients enrolled for hepatic resection usually had better liver function (Child-Pugh A) and their tumors were at an earlier stage than those who received RFA in most retrospective studies.<sup>(15,18,46,48,49)</sup> However, resection might carry risks of post-operative mortality and morbidity, especially

**Table 2.** Studies Comparing Radiofrequency Ablation and Hepatic Resection for Hepatocellular Carcinoma and Liver Metastasis

Authors and year	Study design/tumor type	Treatment methods	No. of patients	Max size (cm) / no. of tumor	Overall Survival Rate (%)				p value
					1-year	2-year	3-year	4-year	
Vivarelli et al 2004 <sup>(46)</sup>	Cohort/ HCC	RFA	C-P A: 43	NA	82	NA	43	NA	0.02
		HR	C-P A: 70	NA	88	NA	71	NA	
		RFA	C-P B: 36	NA	74	NA	25	NA	NS
		HR	C-P B: 9	NA	52	NA	19	NA	
Hong et al 2005 <sup>(47)</sup>	Cohort/ HCC	RFA	C-P A:55	4/1	100	NA	72.7	NA	0.24
		HR	C-P A:93	4/1	97.9	NA	83.0	NA	
Chen et al 2006 <sup>(17)</sup>	RCT/ HCC	RFA*	C-P A: 71	5/1	95.8	82.1	71.4	67.9	NS
		HR	C-P A: 90	5/1	93.3	82.3	73.4	64.0	
Oshowo et al 2003 <sup>(60)</sup>	Cohort/ liver metastases	RFA	25	NA	NA	55.4	NA	NS	
		HR	20	NA	NA	52.6	NA		
Abdalla et al 2004 <sup>(67)</sup>	Cohort/ liver metastases	RFA	57	NA	NA	43	36		
		HR	190	NA	NA	73	65		

**Abbreviations:** HCC: hepatocellular carcinoma; RFA: radiofrequency ablation; HR: hepatic resection; RCT: randomized control trial; NA: not available; C-P: Child-Pugh class; NS: not significant; \*: Additional treatment with ethanol injection or chemoembolization.

in patients with poor reserve. RFA, on the other hand, has the benefits of safety, lower co-morbidity, lower complication rates and shorter hospital stay. However, RFA may need to be repeated within weeks if the tumor can not be completely ablated in the initial treatment course. As a result, the long-term outcomes of HCC after resection or RFA might be comparable.<sup>(17,18,46,47)</sup> Therefore, there is still disagreement about the best treatment modality for small HCC.<sup>(15-18,46-49)</sup> Based on recent guidelines, the choice of treatment has to be individualized according to liver function reserve (Child-Pugh class) and tumor stage.<sup>(3,4)</sup>

#### ***RFA for HCC in high-risk or difficult-to-treat locations***

Because of potential thermal injury to adjacent vital structures such as the gastrointestinal tract, gall bladder, bile duct and lung during the procedure, RFA was assumed to be unsuitable for around 15% of HCC in so-called high-risk or difficult-to-treat locations.<sup>(50,51)</sup> These locations were generally defined as tumors within 5 mm of a vital structure or a major vein >3 mm in diameter,<sup>(40,52,53)</sup> due to the heat sink effect, which could be overcome by ethanol injection or TACE before RFA, balloon occlusion to the vein near the tumor, or the Pringle maneuver during open RFA.

For the tumors in high-risk locations, recent studies have reported on ethanol injection into the tumor within 5 mm of a vital structure. RFA can immediately be undertaken after creation of 0.5-1 cm safety distance by introducing artificial ascites or pleural effusion.<sup>(54-56)</sup> The results in terms of complete ablation and local recurrence after RFA combined with PEI in HCC at high-risk locations were nearly comparable to HCC in non-high risk locations after RFA alone.<sup>(40)</sup> The creation of artificial ascites or pleural effusion significantly reduced post-RFA complications, such as bowel perforation, bile duct injury, full-layer diaphragm injury, and hemothorax in animal and human studies.<sup>(54-56)</sup>

#### **RFA for treatment of liver metastasis**

##### ***Overview of RFA for colorectal or other slow progressive liver metastases***

The liver is the second most common organ of metastasis by extra-hepatic primary cancers. Of these liver metastases, colorectal cancer or other slow pro-

gressive liver metastases such as neuroendocrine tumors or breast cancer deserve local ablative therapy due to the probability of metastasis confined to the liver only.<sup>(57,58)</sup> Only surgical resection can offer long-term survival in 25%-30% of patients with CRC metastases.<sup>(11,12,25,26)</sup> However, only 10-20% of patients with liver CRC metastases are suitable for resection because of multiple intra-hepatic nodules that are totally un-resectable due to their location.<sup>(11,13,25,26)</sup> Tumor ablation can be used alone or combined with resection, i.e. some metastases can be resected and others ablated.<sup>(11,59,60)</sup>

Another potential indication for RFA is liver metastases after hemi-hepatectomy.<sup>(61)</sup> Since no RCT or head-to-head comparisons have proven the benefit of RFA over systemic chemotherapy alone, RFA can therefore serve as adjuvant therapy before or after systemic chemotherapy.<sup>(25)</sup> Although RFA has been developed in recent years for the treatment of liver metastasis, its effectiveness has not been tested in RCTs in the same way as its employment in HCC. At present, the use of RFA should be restricted to the treatment of un-resectable liver metastases. The efficacy of PEI for liver metastasis has not been as satisfying as for HCC.<sup>(11,59,60)</sup>

##### ***Complete ablation of liver metastases after RFA***

The rate of complete ablation in liver metastasis was reported to be up to 98% in the Solibati study, which was similar to that in HCC.<sup>(62)</sup> In general, complete ablation could be achieved in 90% of metastases with a diameter  $\leq 3$  cm. A 0.5-1 cm ablative margin would still be required because small metastases might be present around the visible target tumor.

##### ***Local recurrence or local tumor progression of liver metastases after RFA***

Local recurrence of liver metastases after RFA approximated 3-43%.<sup>(43,62-66)</sup> The cumulative local recurrence rates were 30% at 6 months and 37% at 12 months (Table 3).<sup>(62)</sup> The local recurrence rate was also lower in liver metastasis nodules  $\leq 3$  cm. The risk of local recurrence was not related to the number of lesions ablated or the RF ablation approach (laparotomy, laparoscopy, or percutaneous).<sup>(59)</sup>

The development of new hepatic tumors or extra-hepatic disease is a crucial problem in RFA and occurs in 30-60% of patients.<sup>(59,62,64)</sup> Thus RFA may be

**Table 3.** Studies of Radiofrequency Ablation for Liver Metastasis

Authors and year	No. of patients	Tumor size (cm)	Mean follow-up (months)	Local recurrence rate of total cases (%)*	New hepatic or extra-hepatic recurrences of total cases (%)*	Survival rate (%) 1/2/3/4/5 years
Curley et al 1999 <sup>(43)</sup>	75	mean: 3.4	15	2.6	30	100*
de Baere et al 2000 <sup>(64)</sup>	68	mean: 2.5	14	9	26.4	94/NA/NA/NA/NA
Gillams et al 2000 <sup>(65)</sup>	69	mean: 4	36	10	58	90/60/34/22/NA
Solbiati et al 2001 <sup>(62)</sup>	117	mean: 2.5	18	39	66	93/69/46/NA/NA
Pawlik et al 2003 <sup>(66)</sup>	169	median: 1.8	21	4.7	40.8	98/70/50/NA/NA

**Abbreviations:** NA: not available; \*: Cumulative rates not available; †: Resection of the index tumors, followed by RFA to unresectable lesions.

not sufficient by itself and may require combined systemic chemotherapy.

**Overall recurrence of liver metastases after RFA**

The overall recurrence in CRC liver metastases following RFA monotherapy was 84%.<sup>(65-67)</sup> This further verified that RFA monotherapy might be not sufficient and might require combined systemic chemotherapy.

**Overall survival of patients with liver metastases after RFA**

The 1-, 2-, 3-, 4-, and 5-year survival rates after RFA for CRC were reported to be 93%, 69%, 46%-52.5%,<sup>(60,62)</sup> 22%,<sup>(67)</sup> and 26%, respectively (Table 3).<sup>(63)</sup> However, the majority of the reported series included chemotherapy before or after RFA. Predictors of survival in CRC liver metastases following RFA monotherapy or combined with chemotherapy were a pre-procedure carcinoembryonic antigen (CEA) level below 200 ng/ml, dominant lesion diameter ≤ 3 cm, and tumor number ≤ 3.<sup>(68)</sup>

Although RFA can effectively ablate a tumor up to 3 cm, because of the high recurrence after RFA monotherapy or combined resection, the role of RFA in liver metastasis currently remains one of the multi-modalities of therapy.

**Resection versus RFA in the treatment of liver metastases**

Since RFA and resection are still considered for eradication of small liver cancers, comparison between these two methods in terms of survival is crucial. In a limited number of reports, the overall survival in CRC liver metastases after RFA was gen-

erally inferior to hepatic resection or combined resection and RFA.<sup>(60-62,66-68)</sup> This was because resection is intrinsically superior to RFA because of eradication of the target tumor and its surrounding parts, or even 1-2 segments that might contain microscopic metastases which are not detectable on imaging.

Although the results of resection were superior to RFA in previous reports, Livraghi *et al* performed RFA during the interval before re-evaluation in patients with metastatic CRC nodules no larger than 4 cm in the greatest dimension who were being considered for hepatic resection.<sup>(69)</sup> The results showed that resection was avoided in 67 patients (76%) and none had un-resectable disease due to tumor recurrence or progression.

Unlike liver resection, there is no evidence to suggest that ablative treatments alter long term survival compared with chemotherapy alone in tumors which are otherwise considered to be beyond the scope of conventional surgical treatment.<sup>(61,62,66-69)</sup>

**Conclusions of updated results of RFA in HCC and liver metastases**

Since RFA can effectively ablate tumors up to 3 cm in diameter, it is likely that now and in the near future, patients with unresectable HCC and poor liver reserve, or even resectable HCCs and liver metastases, can benefit from tumor eradication without resection.<sup>(3,4)</sup> Most patients with liver metastases will receive multi-modality treatment, such as surgical resection, RFA, and systemic chemotherapy.<sup>(65-68)</sup>

**Recent advances in RFA for liver malignancies**

Current RF devices can only effectively ablate tumors up to 3-5 cm with a single RF electrode inser-

tion.<sup>(3,4,20-23,36,37)</sup> Therefore, new RFA devices or pre-RF administration of some agents are mainly focusing on the creation of larger ablation areas within a shorter period.

Bipolar RF electrodes can create a larger (up to 8.4 cm) ablation in a short time ( $12 \pm 3.6$  minutes).<sup>(70)</sup> However, the ablation shape is an ellipse rather than the ideal spherical shape.<sup>(70)</sup> RF with a higher power generator (1000 W, 4000 mA) in an animal model could create a markedly larger coagulation than a 2000-mA commercial RF generator.<sup>(71)</sup> A novel high speed radiofrequency (HS-RF) bipolar ablation system (RFA Medical, Inc., Fremont California) was employed *in vitro* (explanted bovine liver), *in vivo* (ovine liver), and in fourteen patients.<sup>(72)</sup> The nominal size was achieved within  $\pm 10\%$ . In target lesions of 3.5 cm, 5 cm, and 7 cm, the ablation sizes were  $3.6 \pm 0.1$  cm,  $5.0 \pm 0.3$  cm, and  $6.9 \pm 0.3$  cm, respectively. However, the required ablation durations were only 3 min, 5 min, and 12 min, respectively.<sup>(72)</sup> Administration of liposomal doxorubicin, sorafenib or arsenic trioxide before RFA has resulted in significantly increased tumor destruction compared to RFA alone.<sup>(73-75)</sup>

In summary, recent RF devices can create larger ablation dimensions up to 7-8 cm. In addition, RFA combined with pre-RF administration of some chemical agents may enhance coagulation. However, more experience in human subjects with longer follow-up is required to draw definite conclusions on effectiveness and safety measures.

### Perspectives

RFA has been proved to be the most effective method to ablate tumors smaller than 3 cm among the various ablation modalities. Various modified algorithms or newer RF devices including RF power generators and RF electrodes may further improve the effectiveness of the procedure. In addition, a combination of various chemical agents and RFA may also enhance RF coagulation. More experience with these advanced methods and minimization of complications are warranted for optimizing RFA in the treatment of HCC and liver metastasis.

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## 以射頻燒灼治療肝細胞癌與肝轉移性癌的最新進展

林錫銘

肝細胞癌(以下簡稱肝癌)與肝轉移性癌是全世界常見的癌症之一,目前的影像學檢查已能早期發現這些癌症。在時下外科手術切除仍普遍被認為是早期肝惡性腫瘤的首選治療方式,但是因為肝功能不良、肝硬化,以及多發性腫瘤,所以只有 10% 至 30% 的肝惡性腫瘤在被診斷時可以接受手術切除。因此,已有種種能夠有效消融腫瘤的局部消融療法被加以採行,這些局部消融療法中,以經皮酒精注射治療及射頻燒灼治療(RFA)最被廣泛的使用,特別是以射頻燒灼治療能夠最準確的預估消融範圍以及最少的治療回合。射頻燒灼治療自 1990 年應用在治療人類的肝惡性腫瘤,目前已廣泛被用來治療小型肝癌及轉移性肝惡性腫瘤,但是時下的單一射頻探針引進腫瘤只能有效的消融 3 公分以下的腫瘤,因此近期針對射頻燒灼的發展主要在能夠以單一的射頻探針引進,或以更快的速度有效消融更大的腫瘤。本文將對射頻燒灼治療小型肝癌,及轉移性肝惡性腫瘤的臨床療效,包括完全消融率、局部腫瘤復發率、存活率,以及最新的進展加以陳述及探討。(長庚醫誌 2009;32:22-32)

**關鍵詞：**射頻燒灼, 肝細胞癌, 肝轉移性癌, 完全消融率, 局部腫瘤復發率, 存活率

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長庚紀念醫院 台北院區 肝臟研究中心;長庚大學 醫學院

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通訊作者:林錫銘醫師,長庚紀念醫院 肝臟研究中心。桃園縣333龜山鄉復興街5號。Tel: (03)3281200轉8102;

Fax: (03)3272236; E-mail: lsmpaicyto@cgmh.org.tw, lsmpaicyto@gmail.com