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Radio-frequency thermal ablation of liver metastases with a cooled-tip electrode needle: results of a pilot clinical trial

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Abstract. The aim of this study was to evaluate feasibility, safety, and effectiveness of radio-frequency (RF) thermal ablation, performed by using a cooled-tip electrode needle, in the treatment of liver metastases. Twenty-nine patients (20 males and 9 females; age range 43–77 years) with one to four hepatic metastases 1.1–4.8 cm in diameter (mean 2.9 ± 0.8 cm) from previously resected intra-abdominal primary malignancies were treated. All patients were excluded from surgery and had partial or no response to chemotherapy. Radio-frequency ablation was performed by using a 100-W generator and 17-gauge, dual-lumen, cooled-tip electrode needles with a 2- to 3-cm exposed tip. Exposure time was 12 min for each needle insertion. Findings at spiral CT were used to assess the therapeutic response. A total of 127 insertions were performed (mean 2.4 ± 1.7 insertions/lesion) during 84 treatment sessions (mean 1.6 ± 0.7 sessions/lesion) in absence of major complications. Complete tumor response (i.e., unenhancing area of thermal necrosis larger than the treated tumor) was seen in 41 (77%) of 53 lesions, including 33 (87%) of 38 lesions 3 cm or less in diameter. After a mean follow-up period of 6.5 ± 2.1 months (range 3–9 months), recurrence of the treated lesion was seen in 5 (12%) of the 41 cases. New metastatic lesions appeared in 7 patients. Two patients died after 6 and 8 months, respectively. Of the 27 patients still in follow-up, 14 are currently free of disease. Radio-frequency thermal ablation with a cooled-tip electrode needle is a safe and effective local treatment for hepatic metastases 3 cm or less in greatest dimension.

Key words: Liver – Interventional procedure – Liver neoplasms – Therapy – Radio-frequency ablation

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Introduction

Metastatic disease of the liver is one of the most common and troublesome issues in oncology. Patients with secondary hepatic tumors rarely survive for more than 1 year following tumor detection [1]. In patients with hepatic metastases from primary malignancies developed in the gastrointestinal tract, particularly colorectal adenocarcinoma, a substantial improvement in long-term survival can be achieved with surgical removal of the metastatic burden. Follow-up studies have shown a 5-year survival rate of 20–40% in patients who have hepatic metastases from colorectal cancer resected vs 0% in those who do not [2].

Unfortunately, only approximately 5–10% of patients with colorectal metastases are suitable to undergo curative surgical resection [3]. Therefore, numerous investigators have searched for alternate means to treat liver metastases in situ. These means have involved, among other techniques, arterial embolization, intra-arterial chemotherapy, intraoperative application of cryotherapy, and percutaneous methods of treatment with ethanol injection and laser fibers [4–14].

More recently, a percutaneous technique has been developed, in which radio-frequency (RF) waves are used to induce thermal ablation of small hepatic malignancies [15–20]. With the RF technique, an alternating current flows from the uninsulated tract of the active electrode to the tissue. Ionic agitation is produced in the tissue around the electrode, as the ions attempt to follow the changes in direction of the alternating current, resulting in frictional heating. Conventional RF generators, however, are currently capable of producing cylindrical lesions no greater than 1.6 cm in diameter with a single-probe insertion [19]. The inherent limitation of these devices is that tissue temperatures exceeding 100 °C may cause charring of the tissues adjacent to the electrode. This charring leads to increased tissue impedance from gas formation and cavitation, which then limits heat dif-

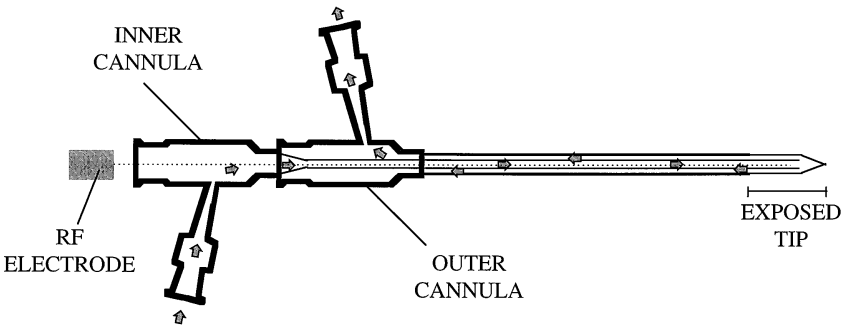


Fig. 1. Graph shows the cooled-tip electrode needle used in the current study. *Arrows* indicate the circulation of the chilled saline pushed by the peristaltic pump from the lumen of the inner cannula to the lumen of the outer cannula

fusion and therefore lesion size [20]. This limitation sharply restricts the potential use of the technique.

Therefore, recent studies have focused on the possibility of improving RF technology. In particular, a new technique has been devised, in which a dual-lumen RF electrode needle is cooled through continuous perfusion with chilled saline [22]. The hypothesis beyond this technique is that cooling of the tissue adjacent to the electrode could prevent tissue charring and vaporization. This might increase the area of thermal necrosis that can be created during a single treatment session. This pilot clinical trial, which followed ex vivo and animal studies, was undertaken to evaluate the feasibility, safety, and effectiveness of this technique.

Materials and methods

Patients

Criteria for entering this prospective study included the following findings: (a) adult patient with biopsy-proved liver metastasis from previously resected intra-abdominal primary malignancy; (b) no evidence of extrahepatic disease; (c) presence of a single hepatic lesion ≤ 5 cm in diameter or multiple (up to four) lesions ≤ 3 cm each; (d) exclusion of surgery and partial or no response to chemotherapy; and (e) prothrombin time ratio (normal time/patient's time) greater than 40% and platelet count higher than 40000/ μl.

Between November 1996 and May 1997, 29 consecutive patients who met the aforementioned criteria were included in the study after consultation with the referring oncologists, surgeons, and gastroenterologists. Informed consent was obtained from all patients after the nature of the procedure had been fully explained. The patient population was composed of 20 males and 9 females (age range 43–77 years, mean age 60.9 ± 10.3 years). Twenty-four patients had liver metastases from colorectal adenocarcinoma, four had metastases from gastric adenocarcinoma, and one had metastases from malignant glucagonoma. All patients had undergone resection of the primary tumors 7–34 months before RF treatment, and 4 patients had also undergone resection of one to four synchronous hepatic metastases. In 4 other patients, metachronous liver metastases had been resected 8–22 months after the resection of the primary tumor but before RF treatment. All patients had been excluded from surgical treatment or had refused to undergo surgery.

Pretreatment workup included full clinical and laboratory assessment, (including measurement of hepatic functional serum indexes and carcinoembryonic antigen level) chest X-ray, abdominal US, thoracic and abdominal spiral CT, and bone scintigraphy. A total of 53 hepatic nodules were detected in the 29 patients included in the study. All lesions proved to be metastases at US-guided percutaneous biopsy (44 metastases from colorectal carcinoma, seven metastases from gastric adenocarcinoma, and two metastases from malignant glucagonoma). Seventeen patients had a solitary lesion, 4 had two lesions, 4 had three lesions, and 4 had four lesions. The maximum diameter of the tumors, as measured by US, ranged between 1.1 and 4.8 cm (mean 2.9 ± 0.8 cm). In particular, 38 lesions were ≤ 3 cm, and 15 lesions were in the range 3.1–4.8 cm.

Technique

Radio-frequency ablation was performed with a commercially available generator (RFG 3D, Radionics, Burlington, Ma.) and a dedicated kit for liver tumor ablation. The generator has a maximum power output capability of 100 W and produces a 500-kHz sinusoidal waveform. The liver ablation kit included modified, dual-lumen electrode needles and a Watson-Marlow peristaltic pump. The modified electrode needle is constituted by two coaxial stainless steel cannulae and an RF electrode. The outer cannula has a caliber of 17 gauge (0.058 inches) and is completely insulated, except for an exposed tip 2–3 cm long. The inner cannula has a caliber of 22 gauge (0.028 inches) and an open terminal tip. The RF electrode is placed within the inner cannula, and the proximal parts of the two cannulae are attached, via two connecting tubes, with the peristaltic Watson-Marlow pump (Fig. 1). The pump pushes chilled saline in the lumen of the inner cannula. The chilled saline passes into the lumen of the outer cannula through its open terminal tip and is then aspirated by the pump (Fig. 1). Therefore, a continuous cooling of the electrode needle may be achieved. A temperature sensor is also embedded in the exposed tip of the electrode and attached to a calibrated digital thermometer that is built into the generator.

Radio-frequency treatment was administered on inpatients using mild sedation. If multiple sessions were

required, they occurred once or twice a week. Before each session, serum prothrombin activity and platelet count were measured. Blood cell count and hepatic functional serum indexes (including alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyltransferase, and bilirubin levels) were evaluated before and 24 h after each treatment session. Patients were placed in either the supine or the left lateral decubitus position, depending on lesion site and planned needle track. A stainless steel grounding pad, representing the dispersive electrode, was placed on the patient's leg. Patients were then prepared and draped in the usual sterile fashion. Local anesthesia was performed from the insertion point on the skin to the peritoneum along the planned puncture line. The skin was pricked with a small lancet and the electrode was then advanced precisely to the chosen area of the tumor under US guidance using the free-hand technique. State-of-the art US equipment and a 3.5-MHz convex probe were used.

The electrode needle was then connected with the Watson-Marlow pump and the RF generator was activated. The power output of the generator was slowly increased during the first minute to reach the RF current intensity value of 950 mA, which represents the highest value achievable with this generator. To keep this value constant during each treatment session, limited adjustment of the power output of the generator was necessary to compensate for changes in tissue impedance. Maximum power outputs ranging from 70 to 85 W were used. The exposure time was 12 min for each needle insertion. During each procedure, the degree of needle cooling was adjusted by modifying the velocity of the peristaltic pump to maintain the temperature indicated by the digital thermometer of the generator in the range of 20–25 °C.

The treatment protocol was planned to produce a thermal necrosis volume covering the tumor and part of the liver parenchyma adjacent to the lesion to create a safety margin around the tumor. On the basis of data obtained by ex vivo and animal studies, in tumors 3 cm in greatest dimension, a single insertion of the electrode needle in the center of the lesion was performed in an attempt to destroy the entire lesion with a single treatment session. In tumors exceeding 3 cm, three insertions were usually performed during the same session by placing the electrode needles in a triangular arrangement.

A spiral-CT study was performed 2–4 days after each session to determine the extent of thermal necrosis and plan further treatment whenever needed. In case of incomplete tumor ablation, RF treatment was repeated for a maximum of three sessions. As US cannot enable reliable differentiation between coagulative necrosis and viable tumor tissue, combined US and spiral CT guidance were used after the first treatment session to target precisely the areas of residual viable tumor.

Therapeutic response and follow-up protocol

The therapeutic response was assessed on the basis of findings from spiral CT performed after the last treatment session. In each patient pretreatment and post-treatment spiral-CT studies were compared slice by slice. On spiral CT scans, coagulative necrosis was seen as a low-attenuating, nonenhancing area in both the arterial and portal venous phases. Complete response was considered in cases in which thermal necrosis volume was larger than the treated lesion, and there was no evidence of residual viable tumor tissue. Partial response was defined as persistence of small portions of residual viable tumor (necrotic rate greater than 70 % of tumor volume). Minor response was defined as the presence of large areas of residual viable tumor (necrotic rate of 70 % or less). Progressive disease was considered in cases in which viable tumor size increased with respect to the pretreatment evaluation.

The follow-up period ranged between 3 and 9 months (mean 6.5 ± 2.1 months). Follow-up protocol included determination of the serum carcinoembryonic antigen level, chest X-ray, abdominal US, and abdominal spiral CT performed 1 and 3 months after the end of treatment and at 3-month intervals thereafter; and thoracic spiral CT and bone scintigraphy at 6-month intervals. Patients were studied to diagnose either recurrences of the treated tumors (i. e., local recurrences) or recurrences caused by the emergence of new intrahepatic lesions or extrahepatic metastases. Patients with local recurrence or new intrahepatic metastases were considered for repeated RF treatment, provided that they still met eligibility criteria for this procedure.

Results

All 53 detected hepatic metastases in the 29 patients were treated. A total of 127 needle insertions were performed during 84 treatment sessions. The number of needle insertions perfomed on the same tumor ranged from one to six (mean 2.4 ± 1.7 insertions/tumor), and the number of treatment sessions performed on the same tumor ranged from one to three (1.6 ± 0.7 treatment sessions/tumor). Correct placement of the electrode needle in the chosen area of the tumor was feasible in all cases using US or combined US and spiral-CT guidance.

No major treatment-related complication occurred. Mild abdominal discomfort during the procedure was experienced by most patients. Transient, moderate-to-severe pain was complained by 8 (27 %) of 29 patients during or immediately after treatment. In no case, however, did the pain result in shortening of the treatment time. Three patients experienced nausea, 2 patients had a transient and slight rise in temperature (37.5–38 °C) 24–72 h after the procedure, and 2 additional patients with lesions located in the right hepatic dome developed a small, asymptomatic pleural effusion detected at subsequent CT study. The effusions lasted 2 and 3 weeks, respectively. Slight, transient increases in transaminase levels were seen in 9 patients. The mean hospital stay was 1.2 ± 0.5 days (range 1–3 days).

As visualized with spiral CT performed after the last treatment session, a complete response was achieved in 41 (77 %) of 53 lesions, including 33 (87 %) of 38 le-

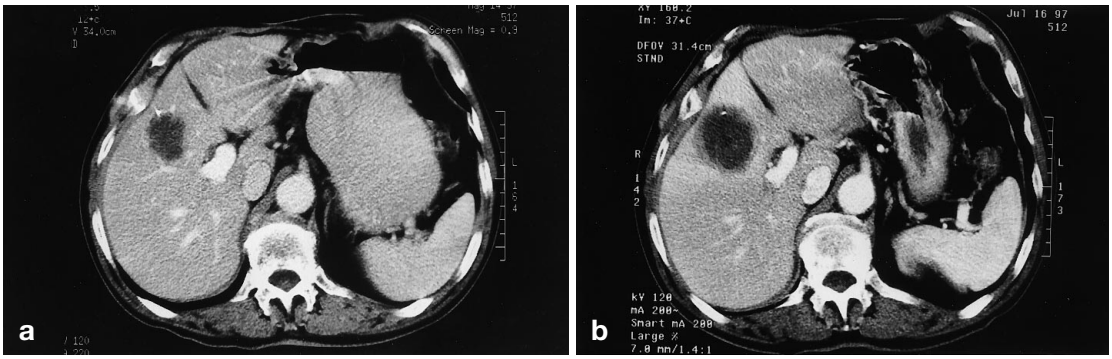


Fig. 2 a, b. Complete response of colorectal metastasis treated with RF ablation. **a** Pretreatment contrast-enhanced CT shows the lesion as a hypoattenuating nodule 3.5 cm in greatest dimension. **b** Follow-up CT obtained 1 month after RF treatment demonstrates complete tumor response by showing a thermal necrosis volume larger than the treated tumor

sions ≤ 3 cm and 8 (53 %) of 15 lesions exceeding 3 cm in greatest dimension (Fig. 2). The therapeutic efficacy of RF ablation, therefore, was significantly better ($p < 0.01$, chi-squared test) in tumors which did not exceed 3 cm in diameter than in tumors larger than 3 cm. A partial response was seen in 10 (19 %) of 53 lesions, and a minor response in 2 (4 %) of 53 (Fig. 3). No case of progressive disease was observed. Analysis of the results on a patient basis, rather than on a lesion basis, was difficult because 14 of 29 patients had multiple lesions that often responded differently to RF treatment. Nevertheless, a complete response in all lesions was observed in 19 (65 %) of 29 patients. Eight (28 %) of 29 patients had at least one lesion with partial response, and 2 (7 %) of 29 patients had at least one lesion with minor response.

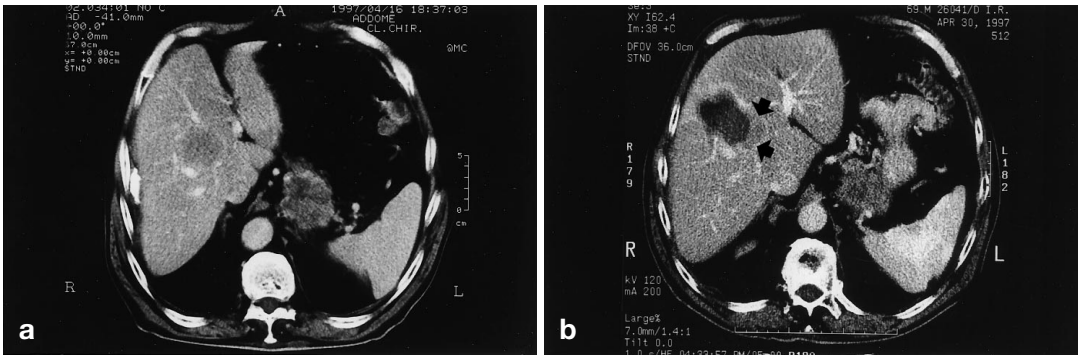
During follow-up, recurrence of the treated tumor (i. e., local recurrence) was demonstrated in 5 (12 %) of the 41 lesions that had been considered to have undergone complete response. Hence, after a mean follow-up period of 6.5 months, 36 (68 %) of 53 treated lesions had no evidence of tumor progression (Fig. 4). Three of the five lesions with local recurrence underwent repeated RF treatments. Complete response, however, was achieved in only one of three cases. The remaining two lesions (in 2 patients) were not retreated because 1 patient showed sudden size increase of the treated lesion (more than 5 cm) and the other one developed progressive multicentric disease.

During follow-up, new metastatic lesions appeared in 7 of 29 patients. In particular, 5 patients developed new intrahepatic lesions, 1 patient developed extrahepatic (pulmonary) lesions, and 1 patient developed both intrahepatic and extrahepatic (pulmonary) lesions. Three of the 5 patients with recurrence limited to the liver underwent repeated RF treatment. Complete response was seen in two of three cases. The remaining 2 patients with intrahepatic recurrences were not retreated because also the initially treated lesions had been incompletely ablated by RF treatment and had undergone tumor progression.

In 14 of 19 patients with elevated serum levels of carcinoembryonic antigen before RF ablation, a marked decrease to within the normal levels was observed 1–3 months after treatment. The significance of measurement of carcinoembryonic antigen level, however, was negligible and not taken into account during judging of the final result, since it was affected by mixed results in patients with multiple lesions.

At the time of the preparation of the present report, 27 of the 29 patients were still alive. Two patients died 6 months and 8 months, respectively, after the initial treatment. The two deaths were due to tumor progression with both intrahepatic and extrahepatic recurrence in 1 patient and to an unrelated cause (heart failure) in

Fig. 3 a, b. Partial response of colorectal metastasis after RF treatment. **a** Contrast-enhanced CT performed before treatment shows a 4-cm hypoattenuating lesion. **b** CT scan performed after three treatment sessions shows partial tumor response with residual enhancing viable tumor tissue in the medial aspect of the treated lesion *(arrows)*



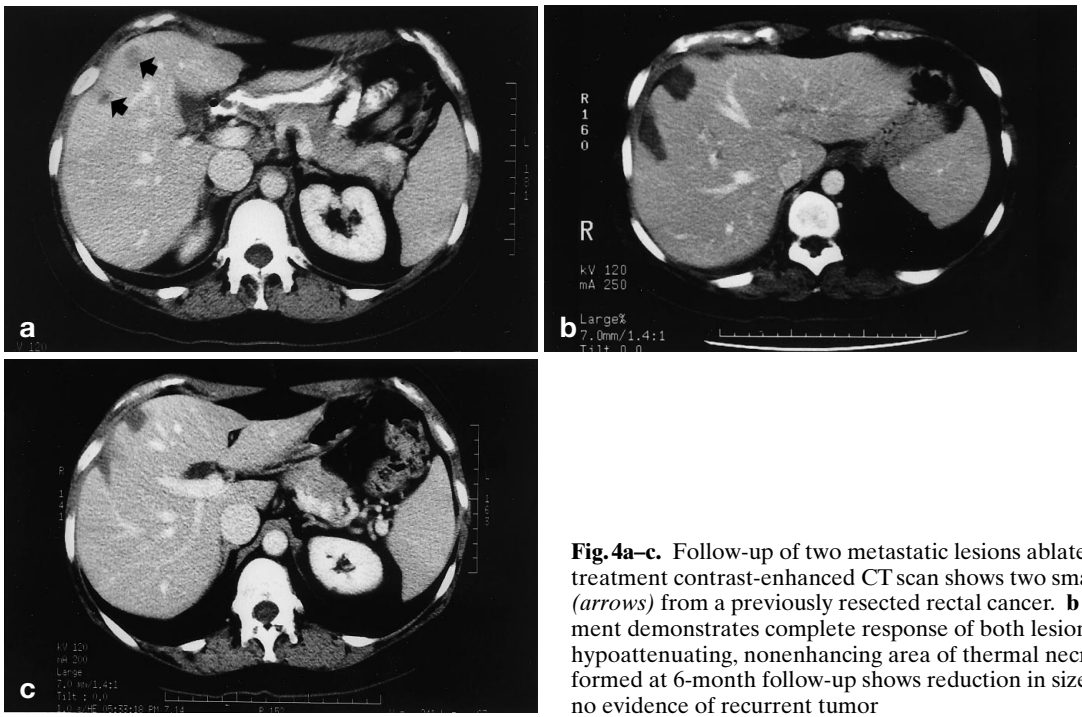


Fig. 4a–c. Follow-up of two metastatic lesions ablated by RF treatment. **a** Pretreatment contrast-enhanced CT scan shows two small metastatic nodules *(arrows)* from a previously resected rectal cancer. **b** CT obtained after RF treatment demonstrates complete response of both lesions, which are replaced by a hypoattenuating, nonenhancing area of thermal necrosis. **c** Follow-up CT performed at 6-month follow-up shows reduction in size of the treated lesions with no evidence of recurrent tumor

the other patient. Of the 27 patients still in follow-up, 14 have no evidence of tumor growth and are currently considered to be free of disease, whereas 13 have at least one lesion showing evidence of continued tumor growth and are considered not to be appropriate for further RF treatment.

Discussion

The results obtained in this pilot clinical trial confirm the feasibility of RF thermal ablation of liver metastases performed by using dual-lumen, cooled-tip electrode needles. Proper percutaneous placement of the 17-gauge electrode needle into the chosen area of the tumor was achieved in all cases using US or combined US and spiral-CT guidance. Despite the use of high-power outputs (up to 85 W), the temperature of the electrode needle was always easily maintained in the range of 20–25 °C during the procedures by adjusting the velocity of the Watson-Marlow peristaltic pump that pushes chilled saline into the needle lumina.

The treatment did not require general anesthesia and was well tolerated by most patients using mild sedation and local anesthesia. No major complications were observed in 84 treatment sessions during which 127 needle insertions were performed. In particular, no case of venous thrombosis at the border of thermal lesions, as experimentally shown, was observed, despite the fact that some lesions were adjacent to hepatic or portal vein branches. This may be explained with the fact that moderate- or large-sized perilesional vessels act as a heat sink. Importantly, no cases of tumor seeding were observed, despite the fact that repeated needle insertions were used to treat large metastatic lesions. In this regard, however, no definite conclusion can be drawn on the basis of the current study, as the follow-up period might not have been sufficient to detect tumor growth along the needle track.

Minor complications were seen in some patients. Transient, moderate-to-severe pain localized at the shoulder or the abdomen was reported by 8 of 29 patients during or immediately after treatment. Shoulder pain was thought to be due to diaphragmatic irritation, whereas abdominal pain was thought to be due to heat conduction to nearby peritoneum. In no case, however, did pain result in interruption of the procedure or shortening of the treatment time. Fever occurred in 2 patients 24–48 h after RF therapy, probably as a consequence of necrotic phenomena induced by treatment. Two patients with subdiaphragmatic lesions showed limited pleural effusions at CT studies performed after RF ablation. These patients, however, had no respiratory symptoms and the effusions resolved spontaneously in 3 weeks or less. The mean hospital stay was 1.2 days (maximum 3 days).

In the current study, RF treatment proved to be effective for nonsurgical ablation of metastastatic tissue. As visualized with spiral CT obtained after the last treatment session, a complete tumor necrosis was achieved in 41 of 53 lesions. Of the remaining 12 lesions, 10 had a necrosis rate of more than 70 %, and only 2 lesions showed necrosis rates lower than 70 %. Importantly, these results were obtained with a mean of only 1.6 treatment sessions/lesion, which is less than that reported in previous studies [16, 17]. This confirms experimental works that showed that the volume of thermal necrosis that can be created with a single insertion of a single probe can definitely be enlarged by using the cooled-tip electrode needle [22]. It can be argued that also in

vivo, cooling of the needle through continuous perfusion with chilled saline was effective in preventing vaporization and charring of the tissue adjacent to the electrode. These phenomena, in fact, are known to be among the most important factors in limiting heat diffusion and therefore thermal lesion size.

The therapeutic effect of RF treatment, however, was significantly dependent on tumor size: whereas 33 of the 38 lesions ≤ 3 cm in greatest dimension were presumed to have undergone complete ablation, only 8 of 15 lesions > 3 cm had a complete tumor response. In large nodules, in fact, it was difficult to create, even with multiple needle insertions, confluent thermal necrosis volumes covering the entire mass lesion. As a result, in some cases, areas of viable neoplastic tissue persisted after RF treatment, particularly along the edge of the treated nodule. Furthermore, during the follow-up, local recurrence (i.e., recurrence of a treated lesion presumed to have undergone complete response) occurred in 5 of 41 cases, probably as a result of small portions of viable persistent tumor undetected at posttreatment spiral CT. The remaining 36 lesions had no evidence of tumor growth and remained unchanged or showed gradual decrease in size over time. These lesions were considered to have been radically cured. It has to be taken into account, however, that the follow-up period in our study was relatively short and, therefore, it might not have been sufficient to detect late tumor regrowth.

Several other methods of RF ablation have been recently used in clinical settings to overcome the limitations of conventional RF therapy performed with a single, unmodified monopolar electrode [19]. Rossi et al. adopted the bipolar method, in which two active needle electrodes are inserted parallel into the tumor [17]. This was shown to result in a volume of necrosis more than twice that of a thermal lesion made by a simply monopolar needle [17]. Even with this technique, however, successful ablation was limited to lesions not exceeding 3–3.5 cm in largest diameter [17]. Solbiati et al. used multiprobe arrays after injection of saline solution into the target tumor immediately before RF application [18]. Despite the increase in the volume of necrosis that was achieved, however, targeting of the tumor with multiple electrodes was difficult and precise sculpting of the necrotic region to the size of the lesions was not always possible [18]. Livraghi et al. conducted a clinical study by performing RF ablation during continuous infusion of saline [20]. The electrode used by these authors was a modified needle for ethanol injection with three terminal side holes. This method is substantially different from the cooled-tip technique used in the present trial, as the saline solution does not circulate inside the lumina of the electrode, but spreads out into the tumorous tissue. As a result, the areas of coagulation – although usually increased in size with respect to those obtained with the conventional single-probe insertion – were often irregular, and only partial necrosis was seen even in some lesions < 3 cm in diameter [20].

Among other interventional methods of local tissue destruction, RF ablation has some inherent advantages. Compared with percutaneous ethanol injection, RF treatment produces a more predictable volume of necrosis at every insertion and is not impaired by the hard consistency of metastatic tissue, which makes ethanol injection ineffective in secondary tumors [9, 11]. With respect to laser photocoagulation, RF treatment is less expensive and seems to create a larger coagulation necrosis volume for each needle insertion, thus simplifying the procedure and shortening the treatment time. Cryosurgery, on the other hand, can be effective in the treatment of metastatic tumors of the liver, but has disadvantages in that it requires laparotomy to place the probe directly into the lesion and the larger probe size significantly increases the morbidity of the procedure [7, 8].

In conclusion, our pilot clinical trial showed that RF ablation with a cooled-tip electrode needle is a safe and effective technique for local treatment of hepatic metastases, and should be considered an important new approach for destruction of small metastatic lesions in patients without surgical prospects. This technique has the definite advantage of allowing a reliable and reproducible percutaneous ablation of metastatic lesions 3 cm or less in diameter with a single needle insertion. However, although the clinical effectiveness of this method has also been demonstrated by other investigators [23], the human application of RF ablation of liver tumors is in the early trial stage, and only with further experience will we be able to determine its full utility. In particular, current RF technology seems to still be insufficient to guarantee successful ablation of malignant lesions exceeding 3 cm in greatest dimension. The possibility of further enlarging the volume of necrosis that can be created with a single needle insertion, by using either an expandable electrode needle or high-power generators, is currently under investigation by our group and others with promising preliminary results.

Finally, there is a serious limitation in using RF ablation to treat malignant deposits in the liver. Radio-frequency treatment, in fact, is a local therapy, treating only macroscopic disease, compared with other regional techniques, based on hepatic arterial infusion, that treat the entire liver. In our study, in fact, new intrahepatic metastatic lesions appeared in 6 of 29 patients after a mean follow-up period of 6.5 months. Hence, further studies should be aimed at investigating the possibility of profitably combining different therapeutic approaches for any individual case. Considering the biology of metastatic disease, the combination of a systemic or regional therapy with a local treatment capable of ablating detectable tumor deposits would probably be the most appropriate treatment.

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Book review

European Radiology

Schiffer D.: Brain Tumors: Biology, Pathology and Clinical References, 2nd revised edn. Berlin, Heidelberg, New York: Springer 1997, 695 pp., 286 figures in 459 separate illustrations, (ISBN 3-540-61622-5), DM 298.00.

The second edition of this book has been published only 4 years after the first. The aim of the first edition was to provide all neuroscientists with a broad basic knowledge of brain tumors. In the preface of the second edition, the author emphasizes that the book is intended to present different aspects of neuro-oncology from the perspective of pathology and its biological and clinical correlates.

There are 26 chapters which can be divided artificially into three sections. The first 8 chapters (136 pages) are to be considered as an introduction. Chapters 9–24 (370 pages) deal with the different types of tumors. The final two chapters (30 pages) describe the relationship between the tumors and the possible therapies available.

In the introductory chapters, the reader (who is to be considered as a non-neuropathologist) gets all the information necessary to proceed with the further reading of the book. The first chapter reviews the cytogenesis of the central nervous system. In the second chapter particular attention is paid to genetics and molecular biology on the one hand and to risk factors on the other hand. The third chapter provides some principles on experimental tumors. The fourth chapter gives an overview of antigens employed in the histological diagnosis of brain tumors. The fifth chapter deals with peritumoral changes, regressive events in tumors, brain edema and calcifications. The sixth chapter gives a classification of neuroepithelial tumors. The seventh chapter deals with the concepts of malignancy. The epidemiology of central nervous system tumors is briefly discussed in the eighth chapter.

Of course, the bulk of this book, chapter 9–24, concerns the different types of tumors. In chapter 9, the authors makes a distinction between astrocytic tumors of the hemispheres, of the midline and of the spinal cord. The discussion always includes macroscopical and microscopical appearances of the tumors as well as frequency, age, site and clinical features. The neuroimaging appearances are mentioned too and occasionally an example is given. Chapters 10–12 review the other glial tumors. In chapter 13 attention is paid to tumors composed of neural cells. The pineal gland tumors are discussed in chapter 14 and the embryonal tumors in chapter 15. In this chapter most attention is paid to medulloblastoma but retinoblastoma is included in an appendix. Glomus tumors are briefly mentioned in chapter 16. Tumors of the cranial and spinal nerves are discussed in chapter 17. In chapter 18, on tumors of the meninges, most attention is paid to meningiomas. Chapters 19 and 20 are brief and deal with mesenchymal and vascular tumors. The 21st chapter is extensive and reviews dysontogenetic lesions. Chapters 22–24 are unfortunately rather too brief and only little attention is paid to primary central nervous system lymphomas.

The biological basis of therapies and the effects of treatment on brain tumors are discussed in the final two chapters: radiotherapy and chemotherapy and their effects on brain tumors are briefly reviewed.

Following the last chapter, there is an extensive list of references. More than 3800 references are provided in alphabetical order. The subject index at the end of the book is not particularly extensive but the table of contents at the beginning of the book is very detailed and therefore an excellent alternative to the index.

This hardback book is printed on high quality paper. The illustrations are excellent and the legends are very clear. The layout meets all the requirements of the reader. All chapters are subdivided into many paragraphs all with their own heading. The title of each particular paragraph is always mentioned at the top of the page.

Although the price is rather high, I do recommend this book to all neuroscientists who are regularly involved in the diagnostic work-up and therapy of brain tumors. P. Demaerel, Leuven