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Abbreviation:

LITT = laser-induced interstitial
 thermotherapy

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Colorectal Carcinoma Metastases in Liver: Laser-induced Interstitial Thermotherapy—Local Tumor Control Rate and Survival Data¹

PURPOSE: To evaluate the local tumor control and survival data for magnetic resonance (MR) imaging-guided laser-induced interstitial thermotherapy (LITT) of colorectal liver metastases.

MATERIALS AND METHODS: MR imaging-guided LITT was performed in 603 patients (mean age, 61.2 years) with 1,801 liver metastases of colorectal cancer. Survival rates were calculated by means of the Kaplan-Meier method. Local tumor control and tumor volume were evaluated with nonenhanced and contrast material-enhanced MR imaging. Indications for the procedure were defined for patients with five or fewer metastases, none of which were larger than 5 cm in diameter. The indications included recurrent liver metastases after partial liver resection in 37.6% of study patients, metastases in both liver lobes in 32.5%, locally nonresectable lesions in 11.3%, general contraindications for surgery in 4.6%, and refusal to undergo surgical resection in 13.9%.

RESULTS: Local recurrence rate at 6-month follow-up was 1.9% (nine of 474) for metastases up to 2 cm in diameter, 2.4% (13 of 539) for metastases 2.1–3.0 cm in diameter, 1.2% (four of 327) for metastases 3.1–4.0 cm in diameter, and 4.4% (13 of 294) for metastases larger than 4 cm in diameter. The mean survival rate for all treated patients, with calculation started on the date of diagnosis of the metastases (which were treated with LITT) was 4.4 years (95% CI: 4.0, 4.8) (1-year survival, 94%; 2-year survival, 77%; 3-year survival, 56%; 5-year survival, 37%). Median survival was 3.5 years (95% CI: 3.0, 3.9). Mean survival after the first LITT treatment was 3.8 years (95% CI: 3.4, 4.2). Median survival was 2.9 years (95% CI: 2.4, 3.3).

CONCLUSION: MR imaging-guided LITT yields high local tumor control and survival rates in well-selected patients with limited liver metastases of colorectal carcinoma.

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Surgical resection, which is well established in the treatment of liver metastases of colorectal carcinoma, typically yields 5-year survival rates of 25%–38% (1–8). Two-thirds of patients experience recurrent metastases, and many patients do not benefit from surgery. Data in studies to investigate the effectiveness of surgical resection of liver metastases include 1-year survival rates of 71%–88%, 3-year survival rates of 21%–46%, and mean survival times of 25–35 months. Perioperative mortality data range from 4.4% to 10.0% (1–8).

The high incidence of new liver metastases following successful resection of metastases—60%–80%—has spurred interest in therapeutic alternatives, the goal of which should be achievement of survival statistics similar to those attained with surgery (6,9,10). Ideally, such therapeutic alternatives should be less invasive than liver resection, have a low

complication rate, be performed with local anesthesia (for patients with general contraindications for surgery), and be less expensive.

Findings in several studies prove the effectiveness of local therapies (ie, percutaneous ethanol injection, radiofrequency ablation, and microwave or ultrasound ablation) for the treatment of primary liver carcinoma (11–14). Results of several studies indicate that effective local treatment is far more difficult for liver metastases (15, 16). Radiofrequency ablation is effective in ablation of liver metastases with respect to survival rates (17,18); however, a high local recurrence rate of 21.6%–68.4% is reported (19). Besides, findings in several other studies show that laser-induced interstitial thermotherapy (LITT) is capable of destroying not only liver metastases locally, which results in improved survival data (20,21), but also other abdominal tumors (22).

The purpose of our study was to evaluate the local tumor control and survival data for MR-guided LITT of colorectal liver metastases.

MATERIALS AND METHODS

Patients and Lesions

Between June 1993 and February 2002, LITT was performed in 603 patients with 1,801 colorectal liver metastases that were treated in 1,555 treatment sessions. Inclusion criteria for the 603 patients were the five major indications for LITT: recurrent liver metastases after partial liver resection ($n = 227$, 37.6%), metastases in both liver lobes ($n = 196$, 32.5%), locally nonresectable lesions ($n = 68$, 11.3%), general contraindications for surgery ($n = 28$, 4.6%), or refusal to undergo surgical resection ($n = 84$, 13.9%). Patients were excluded who initially had more than five lesions larger than 5 cm in greatest diameter or who had known extrahepatic tumor spread. Lymph node metastases that were resected during resection of the primary colorectal tumor were not considered to be extrahepatic tumor spread. Our institutional review board approved our study. Informed consent was obtained from all patients.

There were 432 (71.6%) male and 171 (28.4%) female patients (mean age, 61.2 years; range, 31–89 years). Mean tumor volume before treatment was 15 mL (range, 0.5–62.5 mL). Of the 1,801 lesions, 523 (29.0%) were smaller than 2 cm in diameter, 594 (33.0%) were 2.1–3.0 cm in diameter, 360 (20.0%) were 3.1–4.0 cm in diameter, and 324 (18.0%) were 4.1–5.0 cm

in diameter. The 1,801 lesions were located in the following hepatic segments: segment I, 158 lesions (8.8%); segment II, 167 lesions (9.3%); segment III, 111 lesions (6.2%); segment IV, 229 lesions (12.7%); segment V, 182 lesions (10.1%); segment VI, 324 lesions (18.0%); segment VII, 252 lesions (14.0%); and segment VIII, 378 lesions (21.0%). Eight hundred sixty-one (47.8%) of all lesions had contact with the liver capsule.

MR Imaging

Unenhanced and contrast material-enhanced (0.1 mmol per kilogram of body weight of gadopentetate dimeglumine [Magnevist; Schering, Berlin, Germany]) MR imaging was performed in all cases to verify the resultant necrosis. The imaging protocol included a T2-weighted breath-hold turbo spin-echo sequence (repetition time msec/echo time msec of 3,000/92, matrix of 154×256 , flip angle of 150°) in transverse section orientation, a half-Fourier rapid acquisition with relaxation enhancement sequence (1,000/60, matrix of 178×256 , flip angle of 147°) in coronal section orientation, and a T1-weighted unenhanced and contrast-enhanced fast low-angle shot two-dimensional gradient-echo sequence (110/5, matrix of 178×256 , flip angle of 90°) in transverse and sagittal section orientations. The first follow-up MR imaging study was performed the day after the LITT treatment. Further follow-up studies were performed every 3 months after the intervention for 2 years and then every 6 months. All follow-up studies were performed with a 1.5-T MR imager (Symphony Quantum; Siemens, Erlangen, Germany).

LITT

Patients treated in the initial clinical trial were evaluated together as patient group 1 ($n = 56$). In group 1, a nonirrigated laser application system was used with limited power settings up to 2 W/cm active length of the laser application. Patients treated in a second clinical trial were evaluated as group 2 ($n = 117$). These patients had already been treated with an internally cooled laser application system (Power; Somatex, Teltow, Germany). Patients treated thereafter were evaluated as group 3 ($n = 430$). The difference between group 2 and group 3 was the aggressiveness of the treatment. The mean number of applicators used to treat each lesion was higher in group 3 than in group 2 (Table 1). All laser applicators for each metastasis were used si-

TABLE 1
Mean Number of Inserted Irrigated Laser Applicators per Metastasis Size

Size of Metastases (cm)	Group 2	Group 3
0–2	1.3	1.7
2–3	1.9	2.6
3–4	2.7	3.5
>4	3.5	4.4

multaneously to achieve synergistic effects.

Internally cooled laser application systems were placed with computed tomographic (CT) guidance with local anesthesia (23) in all patients except those in group 1, who were treated with a conventional nonirrigated laser application system. A 9-F sheath was inserted. Thereafter, the patients were transferred to the MR imaging unit, where MR imaging-guided ablation was performed with a neodymium:yttrium-aluminum-garnet, or Nd:YAG, laser (MediLas 5100; Dornier MedTech, Germering, Germany) with a wavelength of 1,064 nm, while T1-weighted gradient-echo MR imaging was performed for nearly online thermometry (24). After the procedure, the puncture tract was closed with fibrin glue (Tissucol Duo S; Baxter, Unterschleissheim, Germany).

The LITT treatment (T.J.V., M.G.M., with 10 years of experience in this method) was performed with MR imaging guidance with a 0.5-T MR imager (Privilig; Escint, Frankfurt, Germany) with two T1-weighted gradient-echo MR sequences (140/12, flip angle of 80° , matrix of 128×256 , five sections, section thickness of 8 mm, intersection gap of 30%, acquisition time of 15 seconds) in transverse section orientation and parallel to the laser applicators. These sequences were repeated every minute. The entire LITT treatment was performed with local anesthesia and intravenously injected analgesics (Pethidine [10–80 mg], Aventis, Frankfurt, Germany, and/or Piritramid [5–15 mg], Janssen, Beerse, Belgium) and sedation (Midazolam [2–10 mg]; Merkle, Blaubeuren, Germany). Local anesthesia was achieved with 20–30 mL of 1% Lidocaine (Astra Zeneca, Wedel, Germany). All patients tolerated the intervention well with local anesthesia.

In all patients, T1-weighted thermal sequences were performed to monitor the LITT procedures. These sequences were used in all cases to define the duration of the ablation. The mean, median, minimum, and maximum values for applied

TABLE 2
Applied Energy per Metastases Treated with Irrigated Power Laser Applicators
(groups 2 and 3)

Size of Metastases (cm)	Mean	Median	Minimum	Maximum
0-2	54.6	45.5	8.6	198.2
2-3	95.2	87.2	11.6	361.4
3-4	146.5	134.8	29.0	452.6
>4	213.8	208.6	21.9	515.0

Note.—Data are applied energy per metastases (kilojoules).

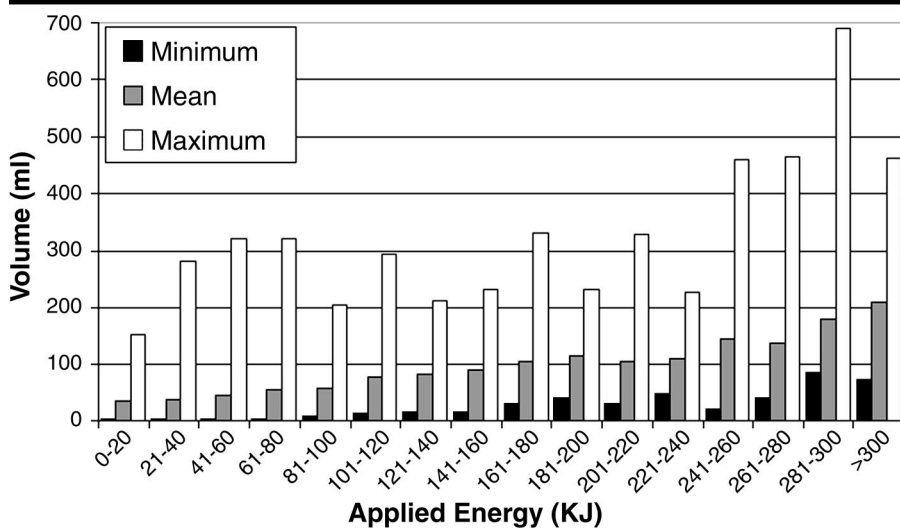


Figure 1. Bar graph shows mean, minimum, and maximum volumes of coagulation necrosis in relationship to applied energy. Findings indicate that with a certain amount of energy, completely different volumes of necrosis can be induced.

energy (in kilojoules) are shown in Table 2. The mean and median duration of ablation was 20 minutes (range, 2–55 minutes). In all patients, the use of thermal imaging resulted in an adaptation concerning the duration of ablation. Besides, the pull-back procedure with a repositioning of the laser fiber within the application system was calculated on the basis of thermal imaging. In no case was the ablation procedure performed on the basis of a predefined time or energy level. Because the heat deposition in the tissue cannot be predicted, a certain amount of energy can result in completely different volumes of coagulation necrosis (Fig 1).

Qualitative and Quantitative Evaluation

Local tumor control was evaluated for all patients ($n = 547$) in groups 2 and 3, who were treated with the irrigated power laser application system. Comparisons were made between the images of lesions and surrounding liver paren-

chyma obtained before laser treatment, at 24 hours after treatment, and at follow-up (1,634 of 1,801 metastases). At follow-up, unenhanced and contrast-enhanced MR imaging were performed with the initial technique. Areas that did not enhance with contrast medium were considered to represent necrotic tissue (25–28). Recurrent tumor at the ablation site was defined as increased lesion volume compared with that seen on MR images obtained 3 months earlier. Parts of the lesions showed a bulge that consisted of contrast-enhanced solid material. The reviewers (T.J.V., M.G.M.) made decisions by consensus.

The number of treated metastases per patient, laser applicators per metastases, and treatment sessions and the duration of laser ablation and applied energy were documented in a self-constructed database (M.G.M.).

Complications or side effects were identified at routine clinical follow-up examinations, chart evaluation, and fol-

low-up MR imaging after the laser ablation. This evaluation was performed independently by one of the authors (R.S.). We defined clinically relevant complications as those that necessitated further treatment (eg, tube drainage for pleural effusion or liver abscess). Small non-symptomatic subcapsular hematomas were not classified as clinically relevant.

Statistical Analysis

Tumor volume and coagulation necrosis volume (in milliliters) were calculated on the basis of measurements in three dimensions (in millimeters). The three greatest dimensions (x , y , and z) were then used to calculate the volume of an ellipsoid (29): $[(4\pi/3)(x/2)(y/2)(z/2)]$.

Local tumor control was determined on unenhanced and contrast-enhanced MR images obtained at 3, 6, and 12 months after LITT treatment.

Survival rates were calculated for all patients ($n = 603$ [groups 1–3]) by means of the Kaplan-Meier method (30). Subset analysis was based on indications for performing the study, such as primary lymph node stage, development of metachronous metastases, number of initial metastases, and patient group. The Breslow test, the Tarone-Ware test, and the log-rank test were used to calculate the statistical significance of differences between the groups. A P value of less than .05 was considered to indicate a statistically significant difference.

The estimated mean survival times are biased as a result of the number of censored cases. In these cases, the event in question had not been reported in the patient chart by the end of the observation period. For the purposes of calculating the mean survival time, these cases were treated as if the event had been reported by the end of the observation period. However, the median time could not be estimated in a number of groups because of the small number of occurrences of the event in the group or censoring of the longest times observed. We present both the mean and median values, if possible, to allow the reader some idea, though biased, of the trend when some of the medians were not estimated.

RESULTS

The mean volume of the zones of ablation 24 hours after LITT treatment was measured for all patients in groups 2 and 3 ($n = 547$) and was 60 mL (range, 3–460 mL). After 3 months, the mean volume of the zones of ablation was 40 mL (range,

2–230 mL) as a result of shrinkage of the lesion. The follow-up volume of the zones of ablation significantly exceeded ($P < .001$) the initial tumor volume (Fig 2). The numbers of treated metastases and laser applicators are shown in Table 3. Unenhanced and contrast-enhanced MR images depicted coagulation necrosis in all cases (Fig 3).

Side Effects and Complications

All patients (groups 1–3) were included in the evaluation. Clinically relevant complications ($n = 29$) such as bleeding, infection, or pleural effusion were observed at the following rates (based on 1,555 treatment sessions): pleural effusion, 1.1% ($n = 17$); intraabdominal bleeding, 0.1% ($n = 2$); liver abscess, 0.4% ($n = 6$); 30-day mortality, 0.1% ($n = 1$); pneumothorax, 0.1% ($n = 1$); injury to bile duct, 0.1% ($n = 1$); and bronchial-biliary fistula, 0.1% ($n = 1$). The overall complication rate was 1.5%. Except for the two patients who died within 30 days after the procedure, however, complications were not severe and could be treated with either drainage or aspiration (pleural effusion, abscess) or percutaneous bile duct reconstruction by inserting a stent. One 66-year-old patient died 4 weeks after treatment. This patient had developed leakage in the jejunum following LITT of a liver metastasis in segment IVa. The patient underwent surgery but succumbed to peritonitis and acute respiratory distress syndrome. The death was considered to be possibly related to LITT, most likely as a result of stress ulceration of the jejunum. An additional 72-year-old male patient died within 30 days after laser treatment, probably as a result of sepsis. Unfortunately, this could not be proved because autopsy was not performed. In another 54-year-old female patient, intraabdominal bleeding was self-limiting, and no treatment was necessary. MR imaging during LITT revealed a small nonsymptomatic subcapsular hematoma in 1.9% of cases ($n = 30$). Local infection at the puncture site after LITT in two patients was treated with intravenous antibiotics. No seeding of metastases along the cannulation tract was found in our patients.

Local Tumor Control and Survival Data

Detailed local tumor control data were based on the evaluation of groups 2 and 3 together and are shown in Table 4 for the different sizes of metastases at 3 and 6

TABLE 3
Distribution of Metastases and Laser Applicators in Patients with Colorectal Liver Metastases

Finding	Mean	Median	Minimum	Maximum
No. of metastases	3.20	2.0	1.0	21.0
No. of laser applicators per metastases	2.28	2.0	1.0	6.0
No. of laser applicators per patient	7.60	6.0	1.0	34.0
No. of treatment sessions per patient	2.70	2.0	1.0	13.0

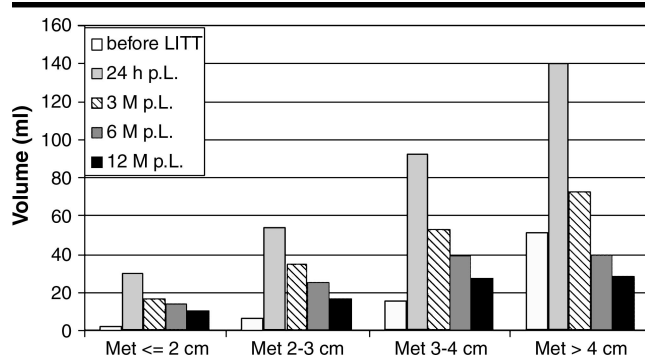


Figure 2. Bar graph shows mean values for tumor volume before LITT and necrosis volume at 24 hours (24 h p.L.), 3 months (3 M p.L.), 6 months (6 M p.L.), and 12 months (12 M p.L.) after LITT treatment. Met = metastases.

months after LITT. During the further follow-up period up to 7.6 years after LITT, unenhanced and contrast-enhanced MR images revealed no additional local recurrences after 6 months.

Survival curves were evaluated by means of the Kaplan-Meier method. All patients (groups 1–3) were included in the calculation of survival data. The mean survival rate for all patients, with calculation started on the date of diagnosis of the metastasis (which was treated with LITT) was 4.4 years (95% CI: 4.0, 4.8 [1-year survival, 94%; 2-year survival, 77%; 3-year survival, 56%; 5-year survival, 37%]) (Fig 4a). Median survival was 3.5 years (95% CI: 3.0, 3.9). Mean survival after the first LITT treatment was 3.8 years (95% CI: 3.4, 4.2 [1-year survival, 86%; 2-year survival, 64%; 3-year survival, 49%; 5-year survival, 33%]) (Fig 4b). Median survival was 2.9 years (95% CI: 2.4, 3.3).

There was a trend for patients ($n = 342$) with one or two initial metastases (mean survival, 4.7 years [95% CI: 4.2, 5.1], median survival, 4.0 years [95% CI: 3.2, 4.8]) to have improved survival compared with that for patients ($n = 167$) with three or four initial metastases (mean survival, 3.6 years [95% CI: 3.2, 4.0]; median survival, 3.0 years [95% CI: 2.6, 3.3]) or those ($n = 94$) with five ini-

tial metastases (mean survival, 3.5 years [95% CI: 2.9, 4.0]); median survival, 2.8 years [95% CI, 1.9, 3.8]). However, the differences were not statistically significant ($P > .05$) when assessed with the log-rank, Tarone-Ware, and Breslow tests for equality of survival distribution (Fig 4c).

There was statistically significant better survival for patients in group 3 ($n = 430$) than in those in group 1 ($n = 56$) and group 2 ($n = 117$) (Fig 4d).

Survival was significantly better in patients ($n = 84$) who refused surgery (mean survival, 5.8 years [95% CI: 5.3, 6.6], 1-year survival, 99%; 3-year survival, 91%; 5-year survival, 59%) compared with that in patients who were not candidates for surgery (Fig 4e).

After evaluation of the effect of the primary lymph node stage, we found that patients with N0 or N1 primary lymph nodes (387 of 603 patients [64.2%]) have a trend toward improved survival in comparison to those with N2 and N3 nodes (216 of 603 patients [35.8%]). The mean survival in patients with N0 and N1 nodes was 4.7 years (95% CI: 4.2, 5.2). The mean survival in patients with N2 and N3 nodes was 4.3 years (95% CI: 3.6, 4.9). The difference, however, was not significant (log-rank test, $P = .2$; Breslow test, $P = .08$; Tarone-Ware test, $P = .1$).

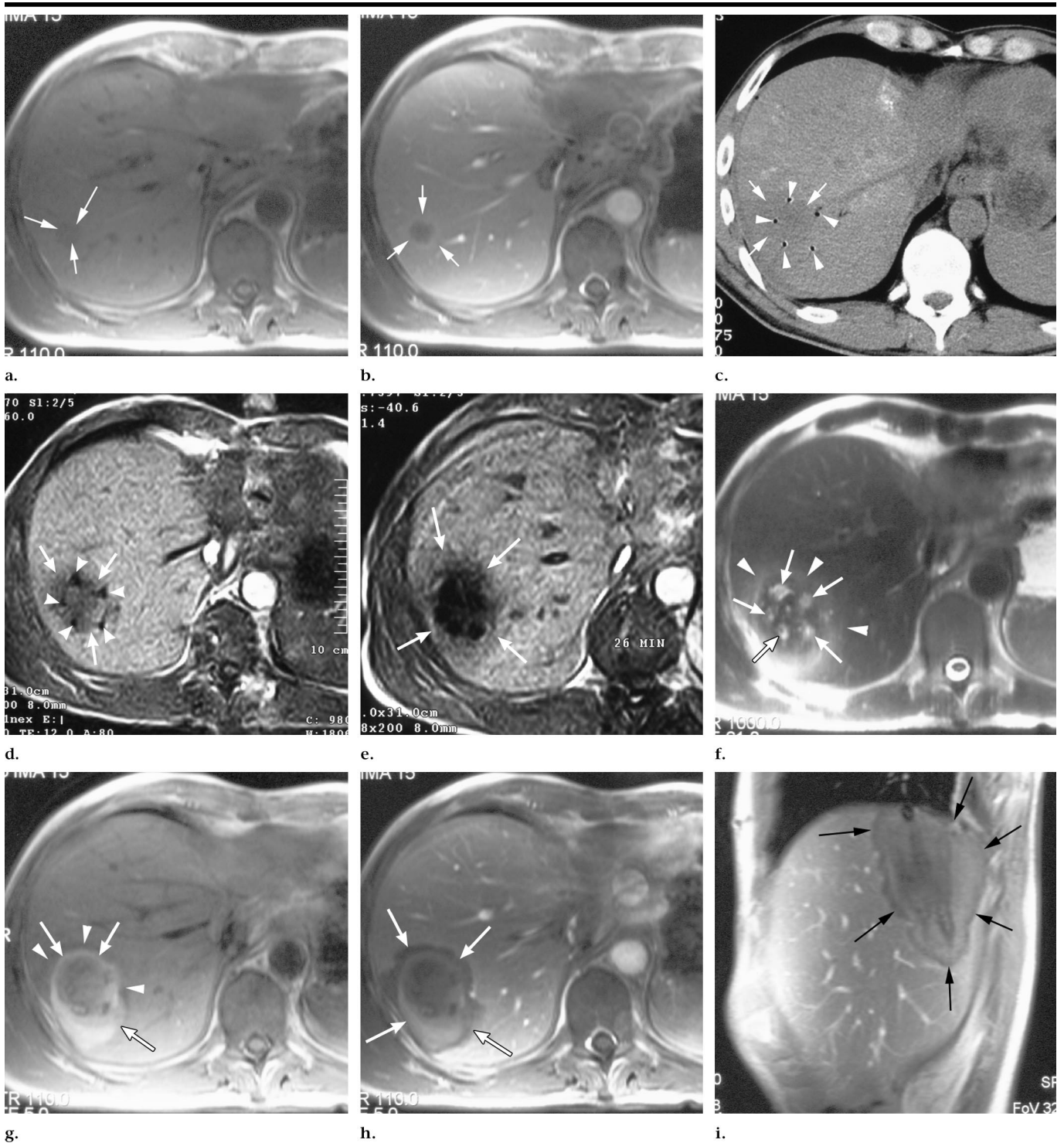


Figure 3. Transverse Images of liver metastasis of colorectal cancer in 40-year-old man. (a) Unenhanced T1-weighted gradient-echo MR image (110/5) obtained 3 weeks before LITT shows liver metastasis (arrows) in segments VII and VIII with maximum diameter of 2.5 cm. (b) Contrast-enhanced T1-weighted gradient-echo MR image (110/5) obtained 3 weeks before LITT shows enhancement in periphery of metastasis (arrows). (c) CT image obtained on day of treatment shows obvious progression of lesion (arrows) in segments VII and VIII with maximum diameter of 4.5 cm (compare with a and b). Note placement of five laser fibers (arrowheads) in periphery of metastasis. (d) Unenhanced MR image (140/12) obtained immediately before LITT shows metastasis (arrows) and laser fibers (arrowheads). (e) Unenhanced T1-weighted MR image (140/12) obtained 26 minutes into LITT demonstrates signal intensity decrease in lesion (arrows) and surrounding tissue as result of increase in tissue temperature (compare with d). Lesion temperature is approximately 110°C in the center and 60°–70°C in the peripheral zone. (f) Unenhanced T2-weighted MR image (3,000/92) obtained 24 hours after LITT shows coagulation area (arrows) with surrounding reactive changes and edema (arrowheads). (g) Unenhanced T1-weighted gradient-echo MR image (110/5) obtained 24 hours after LITT demonstrates typical pattern of coagulation area after LITT with hyperintense pattern (arrows) in periphery, probably a result of slight hemorrhage into the lesion. Corresponding to the hyperintense area in f, lesion is surrounded by a hypointense rim (arrowheads) as a result of edema and reactive changes. (h) Contrast-enhanced T1-weighted MR image obtained 24 hours after LITT shows induced coagulation area (arrows). (i) Sagittal contrast-enhanced T1-weighted gradient-echo MR image obtained 24 hours after LITT demonstrates volume of necrosis (arrows), which exceeds initial tumor size by a factor of 4.

Patients with metachronous metastases (metastases developed more than 6 months after detection of primary tumor) showed a trend toward improved survival compared with those with synchronous metastases ($P = .11$). In our patient groups, we found a nearly equal distribution of synchronous and metachronous liver metastases. There were no statistically significant differences based on patient sex or size of treated metastases ($P > .05$).

DISCUSSION

At this time, liver resection is considered to represent the only potentially curative strategy in the treatment of colorectal liver metastases. About 40% of patients treated surgically survive 3 years, and 25% of the original patients are alive at 5 years (4,6,31–33). Repeat liver resections can be performed and result in improved survival of selected patients (34–36). Surgical treatment is contraindicated in the presence of lesions near vital structures or in both hepatic lobes and in patients with poor general clinical status.

After an analysis of a population of 1,568 patients with metastases confined to the liver that were surgically resected, there was a 5-year survival rate of 28% and a 5-year disease-free survival rate of 15% (6). Nordlinger et al (6) demonstrated that factors associated with increased risk of recurrence and death were related to the primary tumor, metastases, and surgical procedure itself. In contrast, there was no correlation with the location of the metastases or the extent of liver resection.

Liver resection can therefore be offered only to a small number of patients with a good chance of success. There is a need for alternative treatments with success rates that approach those of resection, particularly in patients for whom surgery is not an option. Alternative methods include oncologic strategies, such as systemic or local-regional chemotherapy; and interventional techniques, including radiofrequency ablation, percutaneous alcohol injection, transarterial chemoembolization, microwave ablation, and percutaneous laser treatment (14,37–41).

Until now, most patients with unresectable liver metastases of colorectal carcinoma have received either systemic or local-regional chemotherapy. The mean and median survival rates reported in these patients ranged between 12.7 and 18.7 months (42).

Findings in studies of Irinotecan com-

TABLE 4
Local Tumor Control Data at 3 and 6 Months after LITT

Size of Metastases (cm)	Local Recurrence Rate at 3 Months (%)	Local Recurrence Rate at 6 Months (%)
0–2 ($n = 474$)	1.3 ($n = 6$)	1.9 ($n = 9$)
2–3 ($n = 539$)	2.0 ($n = 11$)	2.4 ($n = 13$)
3–4 ($n = 327$)	1.2 ($n = 4$)	1.2 ($n = 4$)
>4 ($n = 294$)	3.7 ($n = 11$)	4.4 ($n = 13$)

Note.—No further local recurrence was observed after 6 months.

bined with fluorouracil as a first-line treatment (43,44) demonstrate improved survival of the patients in comparison to those treated with fluorouracil and Leucovorin alone. However, the median survival was not more than 17.4 months.

In contrast, for the patients in the current study (with a maximum of five liver metastases, none of which were more than 5 cm in diameter), MR imaging-guided LITT offers overall mean survival of 3.8 years after the first treatment and 4.4 years after diagnosis of the metastasis. Survival after LITT is clearly superior to that after systemic and local-regional chemotherapy and equal to that after surgery. The results of laser treatment of liver metastases support the surgical thesis that liver metastases should be removed or destroyed whenever possible for improved survival. These results are supported by findings in a study of patients with initially unresectable liver metastases from colorectal cancer who were treated with a three-drug chemotherapy regimen followed by surgery for liver metastases whenever possible (45).

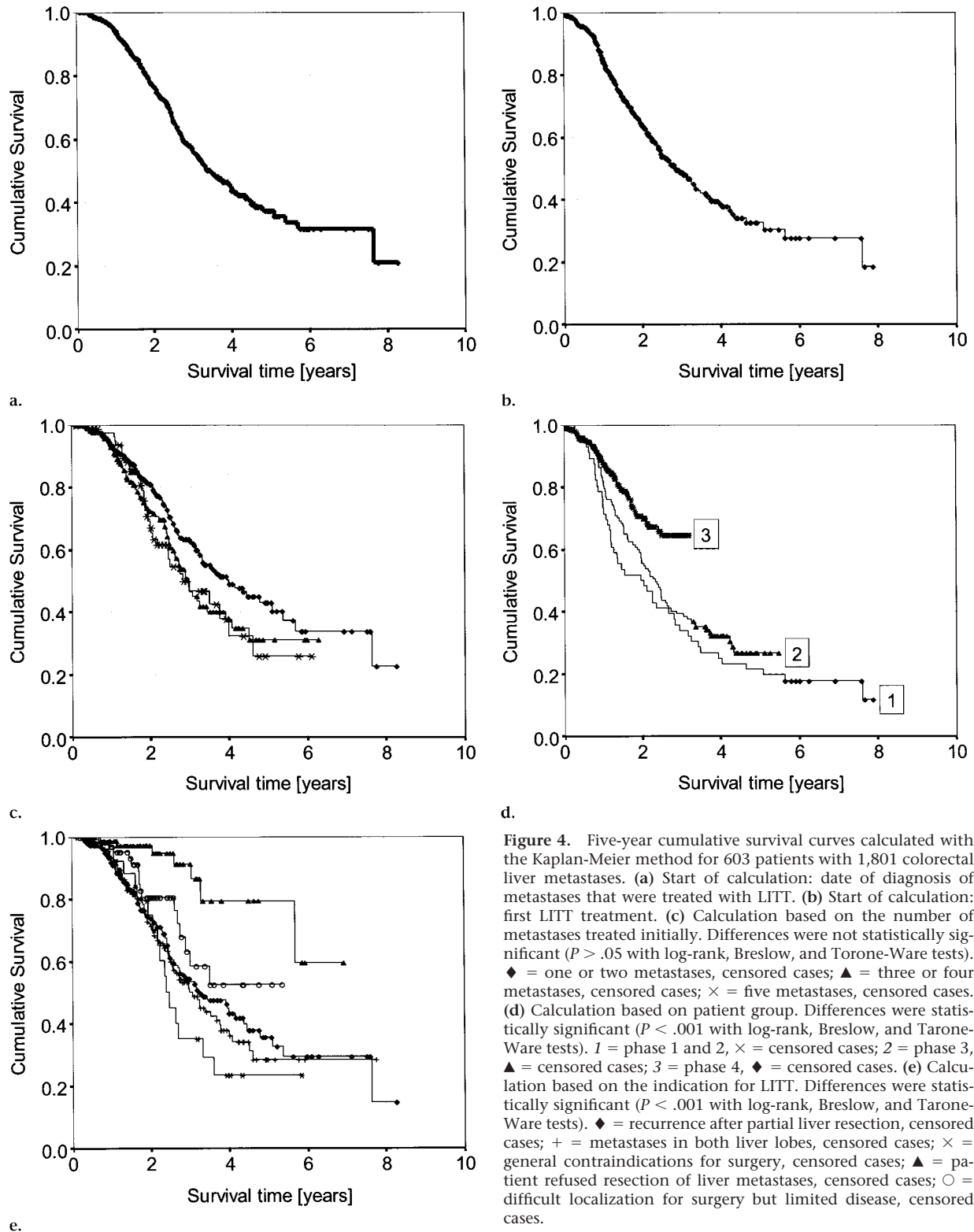
The clinical success of MR imaging-guided LITT is based on a number of factors. One imaging system serves in the planning, targeting, and monitoring of therapy and follow-up of the disease. Optimal positioning of one or more laser application systems in the lesion can be ensured in three dimensions. The main advantages of MR imaging over CT and ultrasonography include the heat sensitivity of the MR sequence and the possibility of visualizing and quantifying the degree of induced necrosis of the malignant and surrounding parenchymal structures. It allows for rapid acquisition of temperature maps, which allow near real-time documentation of LITT effects. Monitoring of these effects during ongoing therapy is advantageous for a number of reasons. The technique can be used to ensure that the entire lesion has been treated, and if there is residual tissue within the lesion that has not been treated, the applicator can be repositioned with MR imaging guidance during the same treatment session. This technique allows safe destruction of metastases and well-controlled coagulation in a safety margin surrounding the lesion.

Monitoring with MR imaging also helps minimize destruction of healthy tissues, thus increasing the safety of the procedure, particularly in the vicinity of vital structures such as large vessels or the central bile ducts in the liver. MR imaging provides unparalleled topographic accuracy with excellent soft-tissue contrast and high spatial resolution. This allows early detection of complications (46).

The LITT treatment in our practice was performed with a conventional closed MR imager. Therefore, the needle was placed with CT guidance instead of MR imaging guidance. Another advantage of CT-guided needle placement is quicker image update and more precise visualization of the needle.

Several factors may influence the size and morphology of the areas of induced necrosis, including tumor geometry and adjacent structures such as arteries, portal and hepatic veins, and the biliary tree. The relationship of the tumor to the liver capsule is an essential factor in planning treatment of the lesion.

In our follow-up studies, the local tumor control rate depended largely on the technique used and the experience of the interventional radiologist who performed the procedure. Local tumor control in our study was better than that reported with other minimally invasive therapies. With radiofrequency ablation, the local recurrence rate was between 21.6% for metastases up to 2.5 cm and 68.4% for lesions larger than 4 cm (19); with microwave ablation, the rate was 15% (47). More data concerning survival rates and local control after radiofrequency ablation have been published for hepatocellular carcinoma (48,49). Solbiati and co-workers (19) calculated a median survival of 36 months (95% CI: 28, 52) in patients with colorectal liver metastases treated with RF ablation, al-



though repeated treatments were performed in case of local recurrence.

The high rate of intrahepatic recurrences after resection and the possibility of potentiating intrahepatic growth of metastases as a

result of release of growth factors after resection has to be discussed (50). In our opinion, these effects are less relevant for LITT because of the obviously minor loss of liver parenchyma after LITT compared with that after

liver resection. Stimulation of growth factors probably has no influence on local tumor control at the ablation or resection site but has an influence on the development of new intrahepatic metastases.

The fact that almost 80% of intrahepatic recurrences are seen in the first 2 years after resection suggests that the doubling time of colorectal liver metastases after resection is markedly shorter than has been assumed (51). Experimental animal data also show that metastatic growth after liver resection is significantly accelerated in the course of hepatic regeneration (52–55). Moreover, it is well established that surgical trauma causes transient postoperative suppression of immune function (56).

Compared with hepatic resection, in situ ablation with LITT of experimental liver metastases results in delayed and reduced residual intrahepatic tumor growth and macroscopic peritoneal tumor spread (57).

A potential limitation of the LITT procedure is that it might be difficult to introduce it in most radiology practices because of the need to use and coordinate two modalities (CT and MR imaging). With an open MR imager, however, MR imaging guidance would be possible. CT guidance alone, in our opinion, is inferior to combined CT and MR imaging guidance because thermal changes can be better visualized with temperature-sensitive sequences.

Another potential bias is the difference in mean survival calculations as a result of starting the calculation from the time of diagnosis rather than from the first LITT treatment. In some patients, up to 3 months passed after the first diagnosis of metastases before the patient was sent to our department for LITT. The delay occurred for a variety of reasons, including waiting for the patient to decide to undergo the treatment. In other patients, the gap between first diagnosis of metastases and the first LITT treatment was a result of chemotherapy that was being given by an oncologist without our knowledge and that did not stop the progression of the tumor or resulted in rapid tumor progression after initial partial remission. However, no patient was excluded during the waiting period.

Our data show that MR-guided LITT yields a local tumor control between 96.3% and 98.8% after 3 months and between 95.6% and 98.8% after 6 months. No local recurrence was observed later than 6 months after LITT. As a result of being able to place multiple application systems, we were able to induce coagulation necrosis that exceeded the volume of the tumor. All inserted laser application systems can be operated simultaneously because there is no interference between multiple inserted laser

applicators. In our opinion, this is the reason for such a low local recurrence rate in comparison to that after radiofrequency ablation. Extension of the necrosis could be exactly monitored with MR thermometry; therefore, the combination of LITT with MR thermometry is a very reliable ablation tool. The success of LITT was not influenced by the location of the lesion.

Previous studies concerning our patient material (58,59) included patients with different primary tumors, more metastases, and unresectable tumors or used a shorter observation period. In the current study, data were focused on liver metastases of colorectal cancer with a longer observation period and more detailed data analysis than were used in previously published studies.

Although the intention for LITT was originally palliative, its favorable survival rates compared with those obtained with surgical resection of liver metastases on the basis of analyses of large surgical series (1–8) with lower complication rates are encouraging. These data suggest that the indication for LITT rather than surgery can be extended to all patients with colorectal liver metastases, including surgical candidates with not more than five metastases with a maximum diameter of 5 cm.

MR imaging-guided LITT is a safe and effective treatment modality for oligonodular colorectal liver metastases. A major advantage of MR imaging-guided LITT is that it can be performed with local anesthesia in an outpatient setting; the complication rate is low.

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