Malignant Liver Tumors Treated with MR Imaging–guided Laser-induced Thermotherapy: Experience with Complications in 899 Patients (2,520 lesions)[1]

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Abbreviation:
LITT = laser-induced thermotherapy

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PURPOSE: To evaluate the complications from laser-induced thermotherapy (LITT) of malignant liver tumors and demonstrate that LITT is safe as an outpatient procedure.

MATERIALS AND METHODS: During 8 years, 899 patients with malignant liver tumors were treated with magnetic resonance (MR) imaging–guided LITT. A total of 2,132 LITT procedures were performed to treat 2,520 lesions. To account for the technical evolution of LITT during this time and the change from performing the procedure on an inpatient basis to performing it on an outpatient basis, patients were assigned to four groups. Overall complication rates and major and minor complications in the inpatient versus outpatient groups were evaluated. Multidimensional contingency table analysis with the χ^2 test was performed.

RESULTS: On the basis of a total of 2,132 LITT procedures performed, complications were divided into major and minor categories and detected at clinical or imaging studies. Major complications included three deaths (0.1%) within 30 days after LITT, pleural effusion requiring thoracentesis in 16 (0.8%) cases, hepatic abscess requiring drainage in 15 (0.7%) cases, bile duct injury in four (0.2%) cases, segmental infarction in three (0.1%) cases, and hemorrhage requiring transfusion in one (0.05%) case. Minor complications included postprocedural fever in 710 (33.3%), pleural effusion not requiring thoracentesis in 155 (7.3%), subcapsular hematoma in 69 (3.2%), subcutaneous hematoma in 24 (1.1%), pneumothorax in seven (0.3%), and hemorrhage in two (0.1%) cases. Outpatient management did not significantly affect pleural effusion ($P = .96$) or subcapsular hematoma ($P = .33$) rate.

CONCLUSION: MR imaging–guided LITT with local anesthesia is safe and yields an acceptably low rate of major complications.

Minimally invasive techniques involving lasers, radio-frequency energy, or cryotherapy for percutaneous destruction of hepatic tumors are increasing in importance, and the survival results with these procedures seem to compare favorably with those of conventional hepatic surgery. For example, in a single-center study of laser therapy in 222 patients with hepatic metastases from colorectal cancer and 12 patients with hepatocellular carcinoma, all of whom were treated with magnetic resonance (MR) imaging–guided laser-induced thermotherapy (LITT), local tumor control rates of 98% after 3 months and 97% after 6 months and mean survival times of 42 and 32 months, respectively, were reported (1). In a laser study conducted by Gillams and Lees (2), patients with lesions smaller than 5 cm had a mean survival time of 33 months, and major and minor complication rates of 3.2% and 12.0%, respectively, were observed in 69 patients. In a study performed by

Reither et al (3), 25 patients were treated with MR imaging–guided LITT and an open system without clinically relevant complications. The follow-up time was too short to obtain meaningful survival data, however (3).

Nolsoe et al (4) performed basic investigations of laser and applicator techniques. More recently, Pacella et al (5) reported 1-, 2-, and 3-year cumulative survival rates of 92%, 68%, and 40%, respectively, for patients with hepatocellular carcinoma treated with laser thermal ablation combined with transcatheter arterial chemoembolization (5). Improved overall results were obtained with the use of liquid-cooled applicator systems and improved application techniques, and rapid enlargement of areas of coagulation necrosis, to 6–8 cm (6–8), that was achievable with multiple applications in a single session followed.

In contrast to the high morbidity and mortality associated with conventional surgery, improved patient acceptance and outpatient management possibilities have been achieved with percutaneous ablation methods, especially in the treatment of liver metastases. With a continuously increasing number of patients being treated and increasing volumes of necrosis being achieved, special attention must be focused on the potential complications of LITT and the appropriate management of them. The radiologist must recognize the typical imaging findings following such ablative procedures and be able to assess the range between normal and abnormal findings. When combined with clinical findings, imaging results are helpful in determining the necessity of further therapy. The purpose of this study was to evaluate MR imaging–guided LITT of malignant liver tumors and demonstrate that in patients with these cancers, local tumor ablation performed by using minimally invasive percutaneous MR imaging–guided LITT with local anesthesia is a safe therapy. Herein, we report our experiences with this therapy.

MATERIALS AND METHODS

Laser Equipment

Laser coagulation was accomplished by using neodymium–yttrium aluminum garnet laser (Dornier mediLas 5060, Dornier mediLas 5100; Dornier Medizintechnik, Germering, Germany) light with a wavelength of 1,064 nm. The light is delivered through fiberoptic bundles that are terminated by a specially developed diffuser. The diffuser, a protective glass dome with a diameter of 1.4 mm, is mounted at the end of a 400-mm-long silica fiber core to emit laser light to an effective distance of up to 12–15 mm. Microdome applicators that are 0.9 mm in diameter and flexible diffuser tips that are 1.0 mm in diameter were used in the internally cooled laser systems.

Laser Radiation Application

The laser application kit (SOMATEX, Berlin, Germany) consists of a cannulation needle with a tetragonal tip, a guide wire, a sheath system that contains a 15-cm mandril, and a 43-cm special protective catheter closed at the distal end. The protective catheter is flexible, transparent to near-infrared radiation, and made of polytetrafluoroethylene. Conventional laser applicators are 7 F in diameter, whereas power applicators are 9 F in diameter and internally cooled with a room-temperature sodium chloride solution that circulates within a double-lumen catheter. Cooling the surface of the laser applicator modifies the radial temperature distribution so that the maximum temperature shifts in deeper tissue layers. Furthermore, the cooling effect enables one to avoid the carbonization that results from the subsequent vaporization and thus allows the use of higher laser power, up to 35 watts. These parameters result in a more homogeneous tissue penetration of laser radiation (4,9,10).

The pull-back technique involves the retraction of the fiberoptic bundle at the end of the first laser cycle by a distance of 2 cm, followed by a second laser cycle, to enlarge the area of coagulation necrosis. The multiple-application technique involves the treatment of one lesion with multiple (up to five) laser applicators simultaneously.

The laser systems are fully compatible with MR imaging units. Magnetic markers on the laser applicator enable MR imaging visualization during the positioning procedure. Similar marks on the sheath and protective catheter enable exact positioning of the emitter within the lesion.

Patients

Between June 1993 and May 2001, the authors performed a total of 2,132 LITT sessions in the Department of Diagnostic and Interventional Radiology to treat 2,520 malignant hepatic lesions in 899 consecutive patients. Five hundred seventeen patients (57.5%) had metastases from colorectal cancer; 163 patients (18.1%), metastases from breast cancer; 42 patients (4.7%), hepatocellular carcinoma; and 177 patients (19.7%), metastases from various other primary tumors. Mean patient age was 59.9 years (age range, 24.6–88.6 years); 406 (45.2%) patients were women and 493 (54.8%) men. Our study had institutional review board approval, and all patients gave informed consent.

Usually, only one liver lesion was treated in a single LITT session, and nearly all patients underwent repeat sessions. In the cases of multiple LITT sessions performed in a single patient, the sessions were performed a minimum of 2 weeks and as many as 4 weeks apart. We believe this allowed patients to recover from treatment and prevented them from being excessively inconvenienced. The complications of the procedure were evaluated at clinical examination, and both nonenhanced and contrast material–enhanced MR imaging examinations were performed 24–48 hours after the intervention initially and every 3 months thereafter. Inclusion criteria were fewer than five liver lesions, each smaller than 5 cm, and absence of extrahepatic spread. Patients with ascites and a prothrombin time longer than 40 seconds were excluded from the study. The findings in a portion of the patient population examined in this study were published previously to demonstrate the technical evolution of LITT (8,11,12).

As a result of the rapid technical evolution of the LITT procedure in recent years and to reflect the change from performing LITT on an inpatient basis (patient groups 1–3) to performing it on an outpatient basis (patient group 4), patients were assigned to four groups in this study: The patients in group 1, patients 1–100, were treated in 278 LITT sessions with conventional laser application systems, laser power of 4–5 W, and up to two applicators. The patients in group 2, patients 101–175, were treated in 218 LITT sessions with the improved multiple-applicator technique, up to five laser catheters in one session, and one or more pull-back maneuvers per lesion to increase the volume of coagulation necrosis. Group 3, patients 176–285, included all patients who were treated in 287 LITT sessions with one of the newly developed internally cooled power laser systems by using multiple-applicator and pull-back techniques. Laser power was increased up to 40 W per applicator, and necrosis volumes increased accordingly to a diameter of up to 7 cm. The patients in group 4, patients 286–899, were treated in 1,349 LITT sessions on an outpatient basis (from

TABLE 1
Patient Safety Parameters for Sequential Stages of LITT Treatment

Treatment Stage	Action Taken
Preprocedural, clinical	Monitoring for possible jaundice, fever, and/or common cold; complete blood count and coagulation (ie, hematocrit, prothrombin time, partial thromboplastin time) tests
Intraprocedural	Monitoring of heart rate, blood pressure, and blood oxygen level; administration of 1% mepivacaine for local anesthesia, diazepam for mild conscious sedation, single dose of antibiotics (usually, 2 g of cefotiam), and opioids (eg, piritramide and pethidine) intravenously for pain
Postprocedural	
Immediate	Administration of opioids (eg, piritramide and pethidine) intravenously for pain, antinausea medication (eg, metoclopramide), and fluids; continuous monitoring of heart rate; monitoring of blood pressure every 30 minutes for 6 hours
Delayed	After 10 days, check for possible fever, jaundice, and/or shortness of breath

1998–2001) with use of the equipment and techniques used to treat group 3.

Before the introduction of outpatient LITT, 783 LITT sessions had been performed for 5½ years (groups 1–3). In the outpatient group (group 4), 1,349 LITT sessions were performed for 2½ years.

Treatment Protocol and Setup

All patients were examined by using an MR imaging protocol that included T1- and T2-weighted spin-echo sequences to localize the target lesion and plan the interventional procedure, and nonenhanced and contrast-enhanced (with 0.1 mmol of gadopentetate dimeglumine [Magnevist; Schering, Berlin, Germany] per kilogram of body weight) gradient-echo sequences.

After all patients were informed of the potential complications of LITT, their consent was obtained and medications were administered intravenously to induce analgesia and conscious sedation. The outpatient protocol (for group 4) also included a prophylactic single dose of intravenous antibiotics (2 g of cefotiam [Spizef; Takeda Pharma, Aachen, Germany]) directly before computed tomography (CT)-guided catheter placement.

The lesions were localized on CT scans (Somatom plus 4; Siemens, Erlangen, Germany), and the injection site was infiltrated with 20 mL of 1% lidocaine. With CT guidance, a 7-F (for conventional system) or 9-F (for internally cooled system) sheath was inserted by using the Seldinger technique. A special heat-resistant protective catheter was then introduced, after which the patient was moved to the MR imaging unit. Either a conventional 1.5-T (SP 4000; Siemens) or a 0.5-T (Privileg; Elscint, Haifa, Israel) MR imaging system was used. The laser fiber was then inserted outside of the unit, and the light was transmitted through a 10-m fiberoptic bundle. After confirmation that the applicator position (with views in coronal, sagittal and transverse orientations) and laser placement were correct, the system was switched on. Gradient-echo MR imaging was performed before and during LITT.

Laser energy was applied: typically 4–5 W in groups 1 and 2 and 35–40 W in groups 3 and 4. The duration of the laser application depended on the progress of the heat distribution within the tumor and surrounding tissue and varied between 3 and 28 minutes, depending on factors such as tumor size and location and whether the tumor was a secondary or primary cancer. The effects on the tissue were monitored and seen in the form of signal intensity loss at thermosensitive gradient-echo MR imaging. Depending on the geometric features and extent of the area of signal intensity loss, the position of the laser fiberoptic bundle was readjusted within the thermostable catheter. With use of the pull-back technique, laser energy was applied so as to adapt the thermally induced changes individually to the geometric features of the given lesion.

After the laser was switched off, contrast-enhanced T1-weighted gradient-echo MR images were obtained to determine the degree of induced necrosis. At the end of the procedure, the cannulation channel was closed with fibrin glue (Tissucol Duo S 2 mL Immuno; Baxter, Vienna, Austria). Nonenhanced and contrast-enhanced follow-up MR imaging examinations were performed 2 days and every 3 months after the LITT procedure. CT was performed during the immediate follow-up period—that is, 2–12 hours after the intervention, only to rule out or confirm acute complications, such as hemorrhage or perforation.

The safety parameters before, during, and after LITT are listed in Table 1. All patients were instructed to take their body temperature (axially) twice daily for 8 days following LITT. Body temperatures of up to 38.4°C during the first 2 days after intervention were considered normal. Patients with a body temperature higher than 38.4°C for 2 days or longer took antibiotics orally for 10 days, and then ultrasonography (US) was performed 14 days after LITT. For patients who did not respond to antibiotic therapy within 2 weeks, a specific cause of the possible complications, such as abscess formation, pleuritis, or cholangitis, was sought.

Medications

Prophylactic antibiotics (cefotiam 2 g) were administered to all patients on the basis of the reported effectiveness of these agents for surgical procedures, specifically abdominal surgical procedures (13–15). For intravenous pain medication, opioids such as piritramide and pethidine were administered during and after LITT throughout the study. For all patients, local anesthesia at the puncture site was achieved with 1% mepivacaine and conscious sedation with diazepam. Antiemetic medication such as metoclopramide and posttreatment oral pain medications such as metamizol and tramadol were given as needed. For applicator channel closure, a biologic tissue glue (Tissucol Duo S 2 mL Immuno) consisting of frozen human fibrinogen and thrombin was used.

Qualitative and Quantitative Evaluations

Qualitative evaluation of the laser-induced effects was performed by analyzing the lesions and surrounding liver parenchyma depicted on MR and CT images obtained during and 24 hours after the laser intervention. Pleural effusion volumes were estimated by using the formula $d2 \times l$, where d is the greatest depth of the effusion seen on a single MR image and l the greatest length of the effusion. Use of this formula yields a reliable estimation of the quantity of the liquid (16). To assess patient pain, three grades were assigned: 1 indicated no pain; 2, tolerable pain; and 3, severe pain.

In accordance with the complication definitions established by the Society of

TABLE 2
Most Frequent Major and Minor Technical Development–related Complications after LITT

Patient Group*	No. of LITT Sessions	Technical Data	Death†	Abscess†	Pleural Effusion†	Subcapsular Hematoma†	Bile Duct Injury†	Hemorrhage†	Subcutaneous Hematoma†
1: Patients 1–100, treated 1993–1996	278	Conventional laser applicator, 4–5 W	0	0	0	0	0	1 (0.4)	3 (1.1)
2: Patients 101–175, treated 1996–1997	218	Conventional laser applicator, multiple-application technique, 4–5 W	1 (0.5)	1 (0.5)	16 (7.3)	8 (3.7)	0	0	2 (0.9)
3: Patients 176–285, treated 1997–1998	287	Power laser applicator, multiple-application technique, 35–40 W	0	0	46 (16.0)	13 (4.5)	0	0	3 (1.0)
4: Patients 286–899, treated 1998–2001	1,349	Power laser applicator, multiple-application technique, 35–40 W	2 (0.2)	14 (1.0)	109 (8.1)	48 (3.6)	4 (0.3)	2 (0.2)	16 (1.2)

Note.—Complications of pain, fever, nausea, and dyspnea are excluded. The presented data are based on findings in 899 patients who underwent a total of 2,132 LITT procedures.

* Patient groups 1–3 were treated on an inpatient basis. Group 4 was treated on an outpatient basis. No statistically significant differences among groups 2, 3, and 4 were observed, but there was a highly significant difference in the number of pleural effusions and subcapsular hematomas between groups 1 and 2 ($P < .001$).

† Data are the numbers of cases of the given complication encountered during treatment of the given group. The numbers in parentheses are percentages based on the number of LITT procedures performed in the given group.

Cardiovascular and Interventional Radiology (17,18), specific complications were assigned to major and minor categories: Major complications were those that required therapy with hospitalization, an unplanned increase in the level of care, and/or prolonged hospitalization (ie, 48 hours or longer) and/or involved permanent adverse sequelae, including death. Included in this group were death, hepatic abscess, segmental infarction, hemorrhage requiring transfusion, bile duct injury, pleural effusion requiring thoracentesis, tumor cell seeding, and laser burn.

Minor complications were those that required no therapy and involved no sequelae but may have required an overnight hospital stay for observation. These complications included pain, nausea, body temperature higher than 38.4°C, dyspnea, subcapsular and subcutaneous hematomas, pneumothorax, biloma, and pleural effusion and hemorrhage that did not require treatment. The numbers of complications were measured on a procedure-by-procedure basis, and for the complication of death only, on a patient-by-patient basis.

Statistical Analysis

The patients were assigned to groups according to the technical evolution of LITT, without randomization. The study was designed retrospectively, and the groups were created ad hoc. Because the patients were European, usually no racial factors had to be considered. The age and sex distributions were similar among all groups. To investigate the effects of in- versus outpatient management, of technical developments on treatment, and of different tumor histologic features on complication rates, multidimensional contingency table analysis with the χ^2 test was performed. A P value of .05 indicated a significant difference.

RESULTS

Overall Complications

The complications were identified at clinical or imaging studies in the 899 patients after a total of 2,520 hepatic lesions were treated in a total of 2,132 LITT sessions. The percentages of complications are based on the 2,132 LITT procedures performed. There were three deaths (0.1%) within 30 days after the procedure. Pleural effusion occurred in 171 cases (8.0%); subcapsular hematoma, in 69 cases (3.2%); subcutaneous hematomas, in 24 cases (1.1%); intrahepatic abscess, in 15 cases (0.7%); cutaneous infection at the cannula puncture site, in four cases (0.2%); bile duct injury, in four cases (0.2%); and hemorrhage, in three (one intrahepatic, two abdominal) cases (0.1%). Increased body temperature and pain, along with nausea and dyspnea, were frequently encountered. In 16 cases (0.8%), symptomatic pleural effusion was treated with thoracentesis. All 15 cases of intrahepatic abscess were treated by means of percutaneous drainage. One (0.05%) abdominal hemorrhage required blood transfusion.

Complication Rates Related to Technical Development

No major complications were observed in group 1, patients 1–100, who underwent 278 LITT sessions with conventional laser application systems (Table 2). Three subcutaneous hematomas (1.1%) and one abdominal hemorrhage (0.4%), both minor complications, were seen but required no clinical treatment. No pleural effusions or subcapsular hematomas were seen at MR or CT imaging.

The following complications occurred in group 2, patients 101–175, who underwent 218 LITT sessions (Table 2): one death that may have been related to LITT (0.5%), one liver abscess (0.5%), 16 pleural effusions (7.3%), eight subcapsular hematomas (3.7%), and two subcutaneous hematomas (0.9%). Six of the pleural effusions (2.8%) and the one liver abscess (0.5%) required interventional treatment.

In group 3, patients 176–285, who underwent 287 LITT sessions, 46 pleural effusions (16.0%), 13 subcapsular hematomas (4.5%), three subcutaneous hematomas (1.0%), and two local wound infections (0.7%) were observed (Table 2). Three pleural effusions (1.0%) required drainage.

In group 4, patients 286–899, who underwent 1,349 LITT sessions, two deaths (0.2%), 14 liver abscesses (1.0%), four bile duct injuries (0.3%), 109 pleural effusions (8.1%), 48 subcapsular hematomas (3.6%), 16 subcutaneous hematomas (1.2%), one abdominal and one intrahepatic hemorrhage (0.2%), and two local wound infections (0.2%) occurred after

TABLE 3
Post-LITT Complications Related to Inpatient and Outpatient Management

Patient Group*	No. of LITT Sessions	Treatment Period	30-day Mortality†	Liver Abscess†	Bile Duct Injury†	Pleural Effusion†	Subcapsular Hematoma†	Hemorrhage†	Subcutaneous Hematoma†
Inpatient groups 1–3: patients 1–285	783	1993–1998	1 (0.1)	1 (0.1)	0	62 (7.9)	21 (2.7)	1 (0.1)	8 (1.0)
Outpatient group 4: patients 286–899	1,349	1998–2001	2 (0.2)	14 (1.0)	4 (0.2)	109 (8.1)	48 (3.6)	2 (0.2)	16 (1.2)

Note.—The presented data are based on findings in 899 patients who underwent a total of 2,132 LITT procedures.
* χ^2 test analysis revealed no statistically significant differences in the rates of pleural effusion ($P = .96$) or subcapsular hematoma ($P = .33$) between the inpatient and outpatient treatment groups.
† Data are the numbers of cases of the given complication encountered in the given group. The numbers in parentheses are percentages based on the number of LITT procedures performed in the given group.

TABLE 4
Complications after LITT and Subsequent Treatments

Complication	No. of Cases*	Therapy†	Interval‡
Major			
Death	3 (0.1)	. . .	4 wk
Liver abscess	15 (0.7)	Drainage	4 wk
Bile duct injury	4 (0.2)	Stent, oral glucocorticoids	24 h
Pleural effusion requiring treatment	16 (0.8)	Thoracentesis	24 h
Hemorrhage requiring treatment	1 (0.05)	Blood transfusion	24 h
Segmental infarction	3 (0.1)	Oral glucocorticoids	24 h
Minor			
Postprocedural fever	710 (33.3)	Analgesics	1 wk
		Antibiotics	>2 wk
Pleural effusion	155 (7.3)	None	1–14 d
Subcapsular hematoma	69 (3.2)	None	During LITT to 24 h
Subcutaneous hematoma	24 (1.1)	None	24 h
Pneumothorax	7 (0.3)	Chest tube	During LITT for 4–6 h
Hemorrhage	2 (0.1)	None	During LITT to 24 h

* The data in parentheses are percentages based on a total of 2,132 LITT procedures.
† Therapy to treat given complication.
‡ Usual time after LITT treatment that complication was observed. Some cases of subcapsular hematoma, pneumothorax, and minor hemorrhage manifested during the laser procedure.

LITT (Table 2). Seven pleural effusions (0.5%), the abdominal hemorrhage (0.1%), and the 14 liver abscesses (1.0%) were treated. The bile duct injuries (0.3%) were treated with oral glucocorticoid therapy or stent implantation to reestablish bile flow. Local infections at the cannula puncture site were managed as described herein earlier.

Complications Related to In- and Outpatient Management

Before the introduction of outpatient LITT, 783 inpatient LITT sessions had been performed for 5½ years in patient groups 1–3. The complications related to their inpatient treatment were one death (0.1%), 62 cases of pleural effusion (7.9%), one case of liver abscess (0.1%), 21 cases of subcapsular hematoma (2.7%), eight cases of subcutaneous hematoma (1.0%), and one case of abdominal hemorrhage (0.1%) (Table 3). No bile duct injuries occurred.

In group 4, who underwent 1,349 LITT sessions on an outpatient basis in 2½ years, the encountered complications were as follows: two deaths (0.2%), 109 cases of pleural effusion (8.1%), 14 cases of liver abscess (1.0%), four cases of bile duct injury (0.3%), 48 cases of subcapsular hematoma (3.6%), 16 cases of subcutaneous hematoma (1.2%), and two cases (one abdominal, one intrahepatic) of hemorrhage (0.2%).

Statistical Evaluation

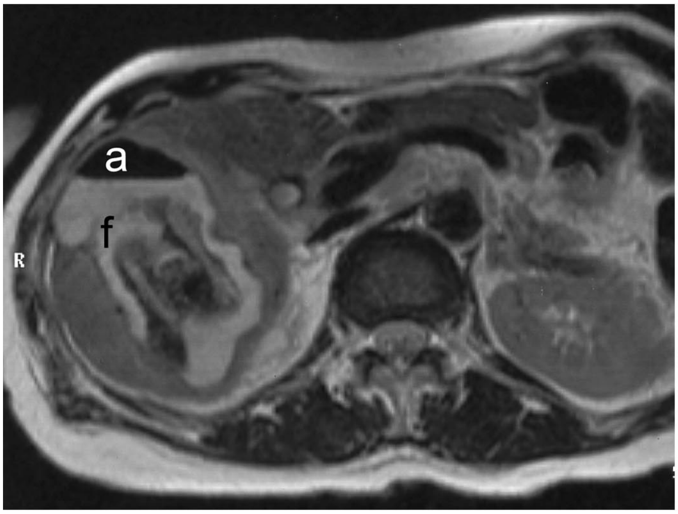
Regarding the complication rates associated with in- versus outpatient treatment, the χ^2 test revealed no statistically significant differences in pleural effusion ($P = .96$) or subcapsular hematoma ($P = .33$). Furthermore, with regard to pleural effusion and subcapsular hematoma, there were no statistically significant differences among groups 2, 3, and 4, but there were between groups 1 and 2 ($P < .001$) (Table 2).

Only those patients with liver metastases from pancreatic cancer who had undergone a Whipple procedure had more liver abscesses (after six [12%] of 50 sessions), as compared with the other groups of patients with metastases from other primary tumors (after nine [0.4%] of 2,082 sessions). This difference was statistically significant ($P < .001$). No other significant differences among the various histologic groups were seen.

Major Complications

Deaths.—Three patients died within 30 days after the procedure (Table 4). A 72-year-old patient died presumably owing to septic shock, but this could not be substantiated at autopsy. One week after the procedure, the patient developed a fever that did not respond to antibiotics; this was most likely caused by bacterial cholangitis. A 58-year-old patient died 4 weeks after treatment; extravasation from the jejunum following LITT of a liver metastasis occurred. The patient underwent surgery but succumbed to peritonitis and adult respiratory distress syndrome. This death was thought to possibly be related to LITT but more likely resulted from stress ulceration of the jejunum. One patient with hepatocellular carcinoma and a known history of severe esophageal varices died owing to hemorrhage from esophageal varices 2 weeks after LITT. This death was not considered to be related to LITT.

Liver abscess.—A diagnosis of liver abscess was verified clinically and radiologically following 15 (0.7%) LITT interventions (Table 4). At presentation, the



a.

b.

c.

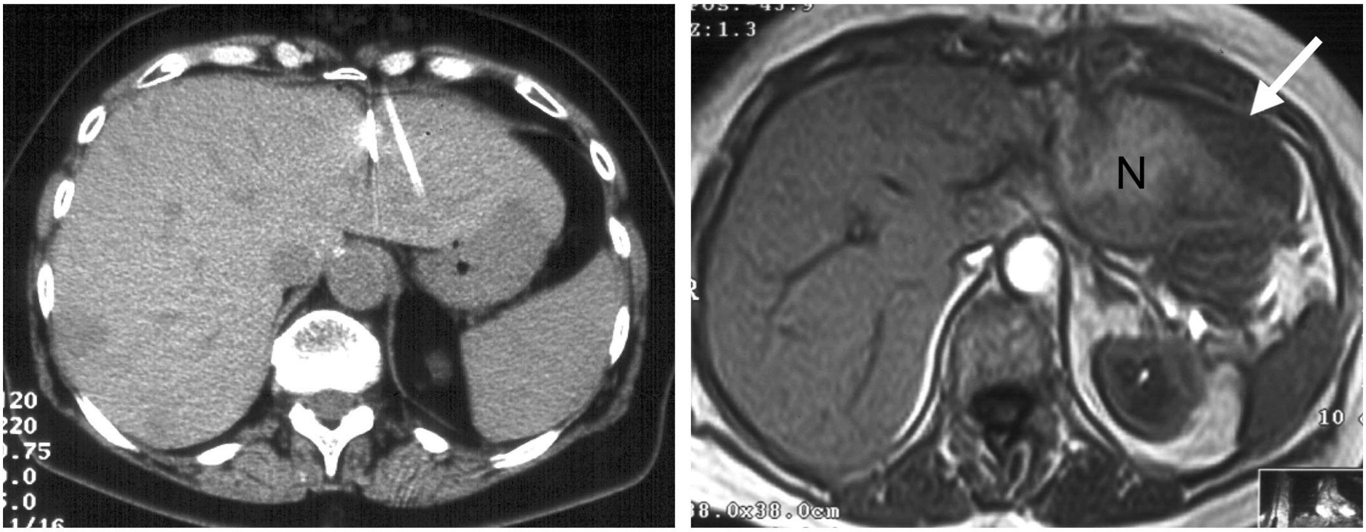
Figure 1. **(a)** Transverse T2-weighted spin-echo MR image (repetition time msec/echo time msec, 3,300/128) obtained in a 59-year-old woman shows large necrotic lesions filled with fluid *(f)* and air *(a)*. Flow artifact in the portal vein is seen, with no thrombosis. Liver abscess was confirmed by the clinical findings combined with the shown imaging findings. **(b)** Transverse contrast-enhanced CT scan (soft-tissue window) obtained 4 weeks after LITT of a segment 4 lesion in a 75-year-old man with liver metastasis from colon carcinoma. Note the large fluid-filled intrahepatic space, with air (arrow) in and compression of the normal liver parenchyma. The CT morphologic features facilitated the diagnosis of abscess formation, although no clinical or blood signs of infection were apparent. **(c)** Transverse CT scan (soft-tissue window) obtained in the patient described in **b** shows necrosis with drainage. Aspirate analysis revealed no bacterial invasion. The final microbiologic diagnosis was sterile necrosis.

patients had body temperatures higher than 38.4°C, moderate leukocytosis, and weakness of more than 3 weeks duration. CT images revealed large necrotic lesions filled with fluid and air bubbles (Fig 1). The infectious organisms included *Bacteroides fragilis, Escherichia coli, Clostridium perfringens,* and *Enterococcus* species. All patients were treated with catheters that were percutaneously implanted with CT guidance and irrigated with up to 1,500 mL of sterile isotonic sodium chloride solution. The catheters were removed after 1–4 weeks, at which time the lesion was clearly reduced and without air or fluid. The end point was the complete resolution of the fluid. Residual soft-tissue changes were considered to represent ablated residual tumor structures.

Four of the 15 patients had undergone hepatobiliary surgery and thus were more vulnerable to abscess formation. Of these patients, two had carcinoma of the head of the pancreas; one, cholangiocarcinoma; and one, an endoscopic papillotomy.

Bile duct injury.—Thermal ablation of 153 (6%) malignant lesions was performed at the liver hilus close to the portal branches and thus created a risk of injury to the central bile ducts. Therapeutic intervention was deemed necessary, however, because further tumor growth in this area would have resulted in bile duct compression and/or local invasion. Twenty-four hours after LITT, the T1-weighted MR images obtained in four patients (four [0.2%] LITT procedures) showed enlarged hypointense bile ducts in one (n = 3) or both (n = 1) liver lobes. Additionally, postinterventional edema of the treated liver parenchyma with subsequent bile duct compression was noted. Oral glucocorticoid therapy for 6 days restored the bile flow, and two patients had complete resolution of symptoms. The two other patients required percutaneous transhepatic insertion of a biliary drainage catheter followed by stent placement 5–7 days after initial treatment.

Segmental infarction.—In three patients (three [0.1%] LITT procedures), coagulation of a major arterial vessel within the liver parenchyma caused infarction of a liver segment, typically with wedge-shaped perfusion and signal intensity changes at follow-up MR imaging. An area of increased T2 signal intensity delineated the localized tissue edema. A large area of laser-induced necrosis in the central left lobe caused infarction of the entire second segment in one patient (Fig 2). Patients regularly reported having pain in the epigastric region during the following 3 weeks.



a. b.

Figure 2. **(a)** Transverse CT scan (soft-tissue window) obtained in a 66-year-old woman shows liver metastasis in segments 2–3 of the left liver lobe treated with two laser applicators in an anterior approach. **(b)** Transverse nonenhanced T1-weighted gradient-echo MR image (130/12) obtained in the same patient shows that a large area of hemorrhagic coagulation necrosis *(N)* with a reliable safety margin has been created. The area is hyperintense. Note the edema in the left lobe and the subcapsular fluid collection (arrow) in the left margin. Due to a transient increase in laboratory values, the lesion was judged to represent a local infarction of liver segments 2 and 3. No clinical or serologic signs of inflammation or abscess were identified. The scout view (box) obtained for better orientation shows the section location.

Hemorrhage requiring transfusion.—Although as many as five laser catheters were inserted for treatment of larger lesions, no patient required abdominal surgery or angiography for intractable bleeding. After three LITT sessions (0.1%), abdominal or intrahepatic bleeding was observed during MR imaging thermometry, but it was shown to have stabilized at CT control examinations. In one (0.05%) case, however, a blood transfusion was required (Table 4). MR imaging depicted perihepatic and perisplenic fluid. Active bleeding in a treated lesion during the initial CT-guided catheter placement led to rapid lesion growth. After the laser fiber was inserted and laser irradiation began, the bleeding stopped owing to the coagulative effects of the treatment. Preinterventional MR imaging studies had depicted a high degree of vascularization in these lesions, which had the histologic features of carcinoid tumors and breast cancer metastases. In one patient, intraparenchymal hematoma arising from the ablated lesion and displacing the adjacent vascular and biliary structures was depicted at MR imaging; no intervention was needed. Follow-up MR studies verified the complete resolution of this complication.

Pleural effusion.—Sixteen of the 171 pleural effusions (0.8% of 2,132 LITT procedures) required treatment with thoracentesis. The patients had effused fluid volumes that ranged from 400 to 1,000 mL and were clinically symptomatic with dyspnea.

Tumor cell seeding.—No local or general tumor cell seeding was detected.

Risk of skin burn.—No cases of skin burning were observed owing to the protective system incorporated into the laser equipment.

Minor Complications

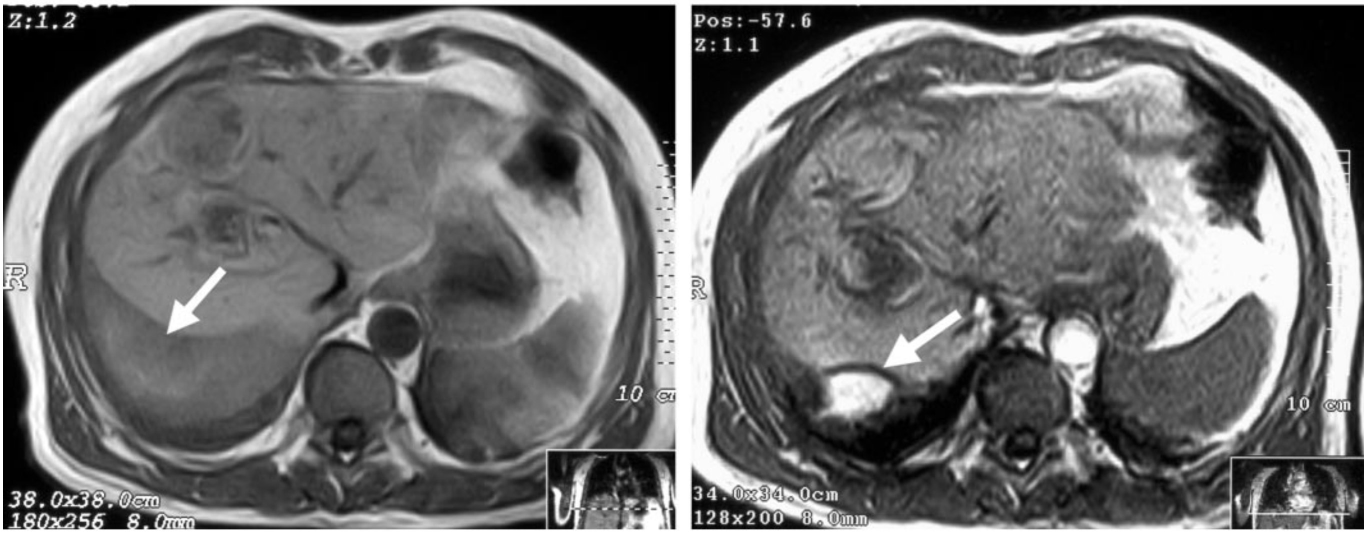
Pain.—All patients tolerated the procedure well with local anesthesia; in no patient did general anesthesia have to be induced during or immediately following LITT.

The most frequent minor complication during or after LITT was pain at the local site of catheter insertion, which occurred in 1,215 treatment sessions (57%), and pain projected to the upper part of the abdomen, thorax, or shoulder. The pain was managed with analgesic agents that were administered intravenously during the procedure or in the immediate follow-up period. Eight hours after LITT, the patients received oral pain medication as needed. In 917 treatment sessions (43%), patients felt no pain during the insertion of the laser catheter, the actual laser ablation, or the retrieval of the catheters. Regarding the LITT sessions in which severe pain occurred (n = 160 [7.5%]), follow-up MR imaging revealed localized or subcapsular hematoma in four (0.2%), and the hematoma presumably caused the local pain symptoms. In the remaining patients, a puncture in the area of the falciform ligament had occurred. No patient refused repeat treatment because of symptoms experienced during a previous treatment procedure.

Nausea.—Nausea during or immediately following LITT was the second most frequently encountered clinical symptom during 448 (21%) treatment sessions. The nausea was most likely caused by the pain medication and was effectively treated with intravenously or orally administered antinausea medications (described in Materials and Methods).

Fever.—After 710 LITT sessions (33.3%), body temperatures elevated up to 38.4°C were observed in the first 2 days after intervention (Table 4). In 320 sessions (15%), body temperatures that exceeded 38.4°C for 2 or more days were treated with antibiotics (described in Materials and Methods).

Dyspnea.—In 75 LITT sessions (3.5%), dyspnea was noted; it usually developed 24–48 hours after LITT as a result of varying degrees of atelectasis and/or pleural effusion. All patients were instructed to perform intensive breathing exercises during the first week after LITT, especially following treatment of lesions in the subphrenic liver segments.



a. c.

b.

Figure 3. **(a)** Transverse nonenhanced T1-weighted spin-echo MR image (450/13) obtained in a 60-year-old man shows a subcapsular hematoma that developed during the LITT intervention. The hematoma appears as a hypointense, concave mass (arrow) around the liver. The hematoma developed after treatment of a subcapsular liver metastasis, which was hypervascular at pretreatment MR imaging. **(b)** Sagittal T1-weighted gradient-echo MR image (140/12) obtained in the same patient shows a hypointense hematoma *(h)* and compression of the liver parenchyma anteriorly. **(c)** Transverse nonenhanced T1-weighted gradient-echo MR image (130/12) obtained in the same patient 3 months after LITT shows a small area of hyperintensity (arrow) in the hematoma depicted in **b.**

Pleural effusion.—Pleural effusion volumes of up to 400 mL were observed in 155 LITT sessions (7.3%). Patients were asymptomatic and required no treatment (Table 4).

Hemorrhage.—Of the three cases (0.14%) of hemorrhage that occurred, two (0.1%) required no treatment and were therefore considered minor complications.

Subcapsular hematoma.—The MR imaging findings of subcapsular hematoma, which were seen in 69 (3.2%) patients, included a concave mass around the liver that compressed the liver parenchyma and had clearly delineated borders and signal intensity that was dependent on the age of the oxygenated blood components. With immediate T1-weighted MR imaging sequences, hypointense to isointense signals were observed. At 3-month follow-up, high signal intensity in the affected liver section, as well as a smaller hematoma, was seen (Fig 3).

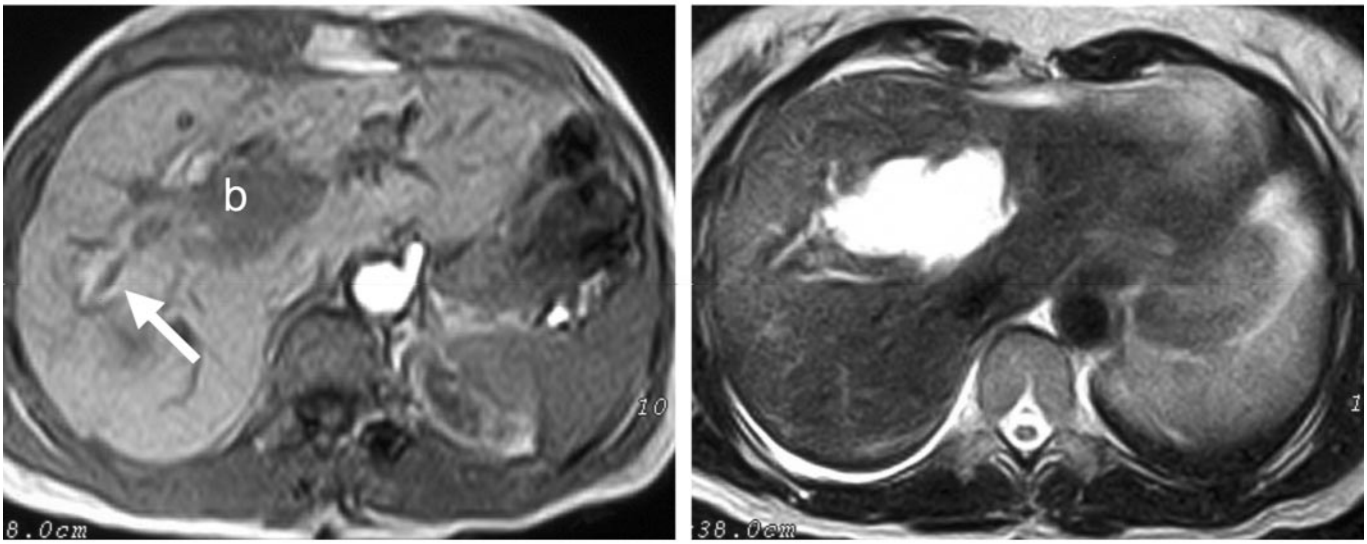
The postinterventional clinical findings were primarily pain in the upper part of the abdomen that lasted 5–10 days. Patients received oral analgesic agents (described in Materials and Methods) according to the severity of pain.

Local wound infection.—Local infection at the puncture site coupled with pain and local swelling was apparent with four (0.2%) LITT procedures. These infections were successfully treated with an iodine emulsion and frequent dressing changes.

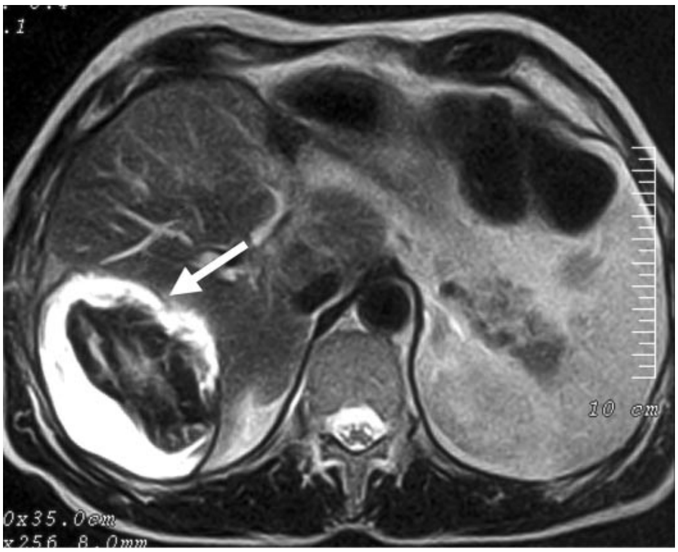
Biloma.—In 24 LITT sessions (1.1%), the area of laser-induced necrosis became enlarged 24 hours to 3 months after the procedure, as indicated by an area of low signal intensity on T1-weighted and gradient-echo MR images and an area of homogeneous, very high signal intensity on T2-weighted MR images. The spherical shape and distinct borders indicated that the necrotic area was filled with bile fluid (Fig 4). In all cases, this asymptomatic finding had disappeared by the time of the 6–12-month MR imaging follow-up studies. These imaging findings were seen after liver surgery and were judged to be characteristic findings after this intervention, so diagnostic fluid aspiration was not required.

Subcutaneous hematoma.—With 24 LITT sessions (1.1%), local subcutaneous hematoma was observed at the catheter insertion site, but treatment was not necessary because the lesion stabilized within the following 24 hours.

Pneumothorax.—In seven LITT interventions (0.3%), a pneumothorax was observed during the CT-guided positioning of the laser applicators in metastases located beneath the diaphragm; there were no clinical symptoms in four of these cases and dyspnea in three. To prevent a pneumothorax from developing during further treatment, a catheter system (Neo-Pneumocath, 500.0 × 3.2 mm; Intra Special Catheters, Rehlingen-Siersburg, Germany) was used in six (85.7%) of the seven procedures. With CT guidance, this one-step catheter system was placed and the air completely removed. Success was verified on postinterventional CT scans. After insertion of the catheter system with CT guidance, we continued to perform MR imaging thermometry with the catheter system in place. Thereafter, the patients showed no respiratory impairment and had no problems performing the 15-second breath holds for MR imaging thermometric measurements. The catheter system was removed 4–6 hours after LITT. No residual air or lesions in the pleural space were seen on follow-up CT scans or radio-



a. b.



c.

Figure 4. **(a)** Transverse nonenhanced T1-weighted gradient-echo MR image (130/12) obtained in a 56-year-old woman shows a biloma *(b)* within a laser-induced area of necrosis (arrow). The lesion resolved completely within 2 years, as verified on the follow-up MR images. There were no clinical symptoms of inflammation. **(b)** Corresponding transverse T2-weighted spin-echo MR image (3,300/128) obtained in the same patient. **(c)** Transverse T2-weighted spin-echo MR image (3,300/128) obtained in a 56-year-old man shows biloma (arrow) with homogeneous, greatly increased signal intensity. The spherical and sharply delineated shape is typical of a necrotic area filled with bile fluid.

graphs obtained 20 hours after the procedure (Fig 5).

DISCUSSION

Surgical procedures such as liver resection and hemihepatectomy for treatment of metastatic liver tumors have been associated with morbidity and mortality rates of approximately 16% and 5%, respectively (19–25). Subphrenic and liver abscesses, hematoma, and bile duct injury are considered specific major complications of these interventions, and pulmonary embolism, deep venous thrombosis, renal failure, and acute cardiac failure are considered general health complications (19–25). Liver failure alone or in combination with renal failure, intra- and postoperative hemorrhage, and pulmonary embolism are the main causes of death following these resections (23,26). To establish the safety and usefulness of the interventional radiologic techniques that are promoted as being minimally invasive, analysis to determine the true incidence of complications associated with interventional treatments for malignant liver tumors is essential.

Improved application techniques have yielded increased volumes of induced coagulation necrosis, up to 8 cm, by enabling multiple applications in a single session of laser therapy and radio-frequency ablation. In our study patients, these larger necrosis volumes were associated with increased complication rates during only the first period of the development of the LITT procedure (treatment period for groups 1 and 2). A low rate of complications has been observed during the remaining periods of procedural development until now (treatment period for groups 2–4); in our opinion, the lower complication rates reflect the learning curve for LITT. Many of these complications are asymptomatic imaging findings or minor complications, such as subcutaneous hematoma, biloma, and local wound infection.

Pleural effusions were frequently observed after LITT, and large effusion volumes, of more than 1,000 mL, that caused clinical symptoms were indications for thoracentesis. Therapy for affected patients included intensive breathing exercises. Daily monitoring of body temperature for early detection of infection is recommended. On the basis of our experience, tumors in the upper liver segments, especially those lesions adjacent to the diaphragm, are predisposed to such complications. Careful pretreatment planning, preparation of the interventional access route, and avoiding penetration or thermal damage to the pleural spaces may reduce the severity of complications such as effusion. Owing to the deep inferior position of the costodiaphragmatic pleural spaces at maximal inspiration (ie, the usual breath hold at diagnostic CT), we prefer to perform CT-

Radiology

guided catheter positioning with a breath hold at expiration. CT-guided catheter placement performed with a deep caudocranial approach without invasion of the pleural spaces is very helpful for localization of liver lesions, especially in segment 8.

Considering the large number of LITT procedures performed, vascular complications were rare and hemorrhagic complications, either acute or delayed, were unlikely. These results are consistent with most of the complication reports of other investigators (27–29) who studied minimally invasive or imaging-guided tumor ablation therapy. The low rate of bleeding complications with thermal ablation procedures is most likely due to the coagulation of bleeding vessels during treatment or to the displacement rather than penetration of the vasculature.

Cryosurgeons also have encountered liver abscesses, hemorrhages, and bile leakages or fistulas (30–35). In the study performed by Bilchik et al (36) involving 308 patients treated with radio-frequency ablation or cryoablation, it was concluded that radio-frequency ablation is safer than cryoablation and results in reduced blood loss and a shorter hospital stay. Wood et al (37), in a study involving 84 patients treated with intraoperative percutaneous radio-frequency ablation, reported an overall complication rate of 8% (seven patients). There were three deaths (one [1%] directly related to radio-frequency ablation). The complications included three hepatic abscesses, one liver failure, one skin burn, one postoperative myocardial infarction, and one postoperative hemorrhage (37).

With the currently available thermal procedures performed with radio-frequency and microwave ablation to treat liver lesions, more hepatocellular carcinoma nodules but also an increasing number of liver metastases are being treated. Livraghi et al (27,38,39) and Goldberg et al (40) described the "oven effect" that occurs during radio-frequency therapy for hepatocellular carcinoma owing to the different thermal properties of the surrounding cirrhotic liver tissue and hepatocellular carcinoma nodules. This effect yields a larger area of necrosis in a single treatment session; on the other hand, it has limitations in the treatment of very small lesions around the treated metastasis, and this is true of all minimally invasive ablation techniques. Although lesions with a diameter of up to 9 cm were treated, no complications involving the bile duct were observed (27,38–40). This was most likely because only one or two application systems were used, even for large lesions. We treated nearly all lesions in multiple probe sessions with two to five catheter insertions.

Curley et al (41) treated 123 patients with hepatocellular carcinoma (n = 48) or liver metastases (n = 75) by using percutaneous (n = 31) or intraoperative (n = 92) radio-frequency ablation. A complication rate of 2.4% and a local tumor recurrence rate of 1.8% were observed (41). Shimada et al (29), reporting on the complications of microwave therapy performed with US-guided access, observed that artificially created fluid accumulations enabled better visualization of subphrenic lesions. Furthermore, prophylactic transcatheter cooling of larger bile ducts during microwave coagulation with drainage tubes implanted with US guidance has been described (29). Among 68 patients with 121 hepatic metastases treated with radio-frequency ablation, de Baere et al (42) noted one bilioperitoneum and one liver abscess. A case report from Takahashi et al (43) described an intrathoracic biliary fistula after transdiaphragmatic percutaneous microwave therapy, followed by an intrathoracic abscess.

All of these studies emphasize the importance of a properly trained interventional or surgical team and demonstrate that similar complications have been encountered with other imaging-guided thermal ablation technologies. However, the variety of complications in these studies and the many parameters considered indicate a lack of uniformity and thus make it difficult to compare and measure complications and results. This lack of a systematic approach highlights the importance of clearly grouping complications into major and minor categories, as suggested in the guidelines of the Society of Cardiovascular and Interventional Radiology (17,18).

The initial results of a multicenter approach were presented by the investigator group of Livraghi et al (44); this study included 1,766 patients with hepatocellular carcinoma and 590 with liver metastases. Although more hepatocellular carcinomas were treated, the authors observed a relatively low rate of complications. The results of that study indicated specifically that the application of radio-frequency energy to lesions adjacent to bowel and bile duct structures must be performed carefully (44).

With regard to our population of 899 patients and performing more than 2,100 sessions to treat malignant liver lesions, the 0.7% rate of liver abscess seems acceptably low compared with the abscess rate with surgical resection. Treatment of this complication is relatively easy: standard percutaneous needle aspiration and drainage system placement combined with systemic antibiotics. This is a widely used therapy option (45,46). In our experience, daily irrigation prevents obstruction of the drainage system and facilitates the adequate drainage of pus. The present study data showed a significant correlation between underlying histopathologic features and clinical outcome, which indicates that the liver abscesses were frequently caused or supported by previous hepatobiliary surgeries such as the Whipple procedure for treatment of pancreatic cancer or by endoscopic maneuvers such as papillotomy.

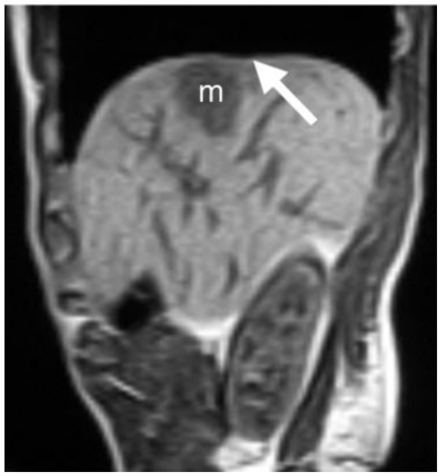


Figure 5. Sagittal T1-weighted gradient-echo MR image (140/12) obtained in a 52-year-old man. The close relationship between the metastatic liver lesion *(m)* and the diaphragm (arrow) is depicted on this pretreatment MR image because during percutaneous insertion of the laser catheter, a pneumothorax occurred.

The potential risk of the silica fiberoptic bundles being burned owing to cooling failure or damage to the active zone of the laser applicator must be prevented by using light protection systems (LPS; Dornier Medizintechnik, Germering, Germany). By using such a system, we were able to avoid injury to all of the patients. The system must immediately and automatically switch off the laser power if a light flash within the optical fiber indicates a burn at the tip. If the laser is not switched off immediately, burning along the laser fiber can arise from the point of fiber damage, spread to the laser application system, and cause severe danger to the patient in the form of skin burns. We highly recommend the use of laser systems, such as the LPS, that are equipped with a fast automatic switch-off function in case of fiber damage.

CT is substantially important in the detection of local complications in the acute phase during or after MR imaging–guided LITT and is helpful in the inter-

Radiology

ventional treatment. CT-guided thoracentesis or chest tube placement in fluid-containing spaces has high therapeutic importance. Therefore, the threshold criteria to perform CT to confirm or rule out a complication after a local ablation procedure should be very low.

In the early follow-up phase, contrast-enhanced MR imaging depicts even subtle changes in tissue. T2-weighted MR sequences performed during the 24-hour follow-up examination were very sensitive for detection of pleural effusion.

The global applicability of the results of the present study is yet to be determined. These data were obtained from a single center with much experience in performing laser ablation procedures, which helped to minimize complications. Others attempting to perform the described laser therapies presumably would have higher complication rates initially. This is especially true given the steep learning curve for all interventional procedures. Finally, the differences in patient populations between a single center and a multicenter group must be considered.

In conclusion, in patients with malignant liver tumors, local tumor ablation performed by using minimally invasive, percutaneous MR imaging–guided LITT with local anesthesia is a safe therapy. When LITT is performed as an outpatient procedure, the complications are relatively easy to treat with standard interventional drainage procedures.

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