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MR-guided laser-induced thermotherapy in recurrent extrahepatic abdominal tumors

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Abstract The aim of this study was to evaluate the feasibility of MR-guided laser-induced thermotherapy (LITT) for treatment of recurrent extrahepatic abdominal tumors. In 11 patients (6 women and 5 men; mean age 53 years, age range 29–67 years) with 14 lesions the following tumors were treated in this study: paravertebral recurrence of hypernephroma (*n* = 1); recurrence of uterus carcinoma (*n* = 1); recurrence of chondrosarcoma of the pubic bone (*n* = 1); presacral recurrence of rectal carcinoma (*n* = 1); recurrent anal cancer (*n* = 1); metastases in the abdominal wall (*n* = 1); and lymph node metastases from colorectal cancer (*n* = 8). A total of 27 laser applications were performed. A fast low-angle shot 2D sequence (TR/TE/flip angle = 102 ms/8 ms/70 °) was used for nearly real-time monitoring during treatment. All patients had no other treatment option. Seventeen LITT sessions were performed using a conventional laser system with a mean laser power of 5.2 W (range 4.5–5.7 W), and 10 LITT session were performed using a power laser system with a mean laser power of 28.0 W. In 10 lesions total destruction could be achieved. In the remaining recurrent tumors, significant reduction of tumor volume by 60–80 % was obtained. All patients tolerated the procedure well under local anesthesia. No complications occurred during treatment. Laser-induced thermotherapy is a practicable, minimally invasive, well-tolerated technique that can produce large areas of necrosis within recurrent tumors, substantially reducing active tumor volume if not resulting in outright destruction of tumor.

Keywords LITT · MR-guided therapy · Lymph node metastases · Recurrent tumors · Laser ablation

Introduction

Magnetic resonance-guided minimally invasive laser-induced thermotherapy (LITT) has become a well-established procedure for local treatment of liver metastases and primary liver tumors in some European centers. Several studies using this technique have shown that local minimally invasive destruction of liver tumors improves the survival rate of patients with liver metastases [1, 2, 3].

Nd:YAG laser light, which has a wavelength of 1064 nm, is well suited for penetrating deeply into soft tissue. Photon absorption by, and heat conduction within, tissue lead to hyperthermic and coagulative effects. A specially designed laser applicator delivers the energy of the Nd:YAG laser through a thin optical fiber bundle to the target area to produce a clearly demarcated area of necrosis while minimizing damage to surrounding structures. Magnetic resonance imaging has been shown to be an ideal clinical instrument for exact positioning of the optical fibers in the tumor. For real-time monitoring of the hyperthermic process during the laser treatment, thermosensitive sequences are used to assess the progress of induced coagulation in relation to surrounding structures such as vessels or nerves [4, 5, 6, 7].

For recurrent extrahepatic tumors the value of minimally invasive treatment modalities has not been previously demonstrated. Initial clinical data obtained from laser therapy of lung cancer [8] and head and neck tumors [9] suggest that there are indications for minimal treatment of tumors in other soft tissues of the body.

The goal of this study was to evaluate the feasibility of MR-guided laser-induced thermotherapy (LITT) for the treatment of recurrent extrahepatic abdominal tumors with respect to safety, feasibility, and reproducible clinical results.

Materials and methods

Eleven patients (6 women and 5 men) with 14 lesions were included in this study. A positive vote of the ethics committee was obtained for LITT treatment and informed consent was obtained from all patients. Their mean age was 53 years (age range 29–67 years). All patients had no other treatment option. Magnetic resonance imaging was performed prior to laser treatment with a conventional 1.5-T MR unit (Siemens, Erlangen, Germany), and comprised conventional T1-weighted spin-echo [TR/TE: 500–700 ms/15 ms and 2D T1-weighted fast low-angle shot (FLASH); TR/TE: 154 ms/6 ms] sequences before and after administration of 0.1 mmol of gadopentetate dimeglumine (Magnevist, Schering, Berlin, Germany) per kilogram of body weight, and plain T2-weighted (TR/TE: 2000–2500 ms/80–90 ms) spin-echo sequences. Magnetic resonance thermometry was performed in axial and sagittal or coronal section orientations with a specially designed thermo-FLASH 2D sequence (TR/TE: 102 ms/8 ms; acquisition time of three sections per 18 s), allowing nearly real-time monitoring of laser interventions. These sequences revealed reproducible thermal effects during heating in the form of decreased signal intensity [10].

The following tumors were treated: paravertebral recurrence of hypernephroma ($n = 1$); recurrence of uterus carcinoma ($n = 1$); recurrence of chondrosarcoma of the pubic bone ($n = 1$); presacral recurrence of rectal carcinoma ($n = 1$) and anal cancer ($n = 1$); metastases in the abdominal wall ($n = 1$); and lymph node metastases of colorectal carcinoma close to the aorta or inferior vena cava ($n = 8$). The maximum diameter of the lymph node metastases was 3.5 cm (mean 2.6 cm). The maximum diameter of the other lesion was 8.0 cm (minimum 2.5 cm). A total of 27 laser applications were performed. A FLASH 2D (TR/TE/flip angle = 102 ms/8 ms/70°) sequence were used for nearly real-time monitoring during treatment.

The first seven lesions were treated with a conventional laser application system (7 F) without cooling (Somatex, Berlin, Germany). With the improvement of the LITT technique now an internally cooled power laser application system (9 F; Somatex, Berlin, Germany), as described elsewhere [11], is available and was used for the next seven lesions.

The laser application set was positioned under CT guidance using only local anesthesia. After positioning the laser application systems, the patient was moved to the MR unit. A special position control catheter which is clearly visible on MR was first inserted into the protective catheter to verify the position of the laser application system which was placed under CT guidance in three dimensions. After that verification of the position of the laser application system, the laser fibers were inserted and treatment was performed. After finishing the LITT treatment, the puncturing canal was closed using fibrin glue (Tissucol, Baxter, Heidelberg, Germany).

Evaluation criteria

The first criterion for evaluation was the analysis of the feasibility of MR-guided LITT for the treatment of recurrent extrahepatic abdominal lesions under local anesthesia.

The second criterion for evaluation was the analysis of the induced coagulative necrosis in relation to the initial tumor size. The patients who were treated with the new internally cooled power laser application system were evaluated independently of the patients who were treated with the conventional laser system. The size of the area with decreased signal intensity correlated very well with the size of the obtained caogulative necrosis documented in the 24- to 48-h control study.

Follow-up MR imaging was performed every 3 months to evaluate local tumor control. Clinical follow-up examinations were also performed every 3 months to evaluate clinical symptoms such as pain or neural irritation. The mean follow-up was 21.6 months (median 18.7 months, range 5.8–60.8 months).

Results

All patients tolerated the procedure well under local anesthesia. No complications occurred during treatment. For the laser applications performed with the conventional laser application set, the mean laser power was 5.2 W (range 4.8–6.5 W) and the mean duration was 19.7 min. Seven lesions were treated with the internally cooled power laser application system (mean laser power 26.6 W (range 24.0–30.8 W), and mean duration of application was 11.8 min (range 7–20 min; Table 1).

The hospitalization of the patients after the first six treatments was 1–2 days after the intervention. The remaining treatments were performed on an outpatient basis.

Total destruction of lymph node metastases and recurrent anal cancer could be obtained. The follow-up examination at 3 and 6 months, using plain and contrast-enhanced MRI, confirmed the absence of active tumor tissue in these patients. This was particularly notable for the patient with the recurrent anal carcinoma who had undergone various treatment modalities for recurrence during the previous years, including multiple surgical resections, percutaneous radiotherapy, and radiotherapy using afterloading technique, and various chemotherapy protocols. For the latest recurrence (Fig. 1) no further surgical or radio-chemotherapeutic approach could be offered to the patient due to previously performed radiotherapy and extensive scar tissue in the pelvis. Magnetic resonance imaging demonstrated at-

Table 1 Patients treated with LITT for extrahepatic abdominal lesions. *PA* irrigated power laser application system; *CA* conventional application system

Patient no.	Gender, age (years)	Treated tumor	Application system	No. of applicators	Watts	Time (min)	Total (KJ)
1	F, 29	Recurrent uterus carcinoma	CA	2	5.2	20	12.36
					5.2	20	
2	M, 67	Recurrent paravertebral hypernephroma	CA	4	5.1	15	20.39
					5.2	15	
					5.3	18	
					5.0	18	
3	F, 58	Presacral recurrence of rectal cancer	CA	2	5.9	18	11.556
					4.8	18	
4	F, 64	Abdominal wall metastases	CA	2	6.0	22.5	15.756
					6.5	22.5	
		Lymph node met in anterior mediastinum	PA	1	25.1	20.0	30.12
5	M, 51	Lymph node met of rectal cancer (no. 1)	PA	1	24.8	8.0	11.904
		Lymph node met of rectal cancer (no. 2)	PA	2	24.3	20.0	42.12
					24.0	9.0	
6	F, 65	Lymph node met of rectal cancer	CA	2	4.8	11	7.488
					4.8	15	
7	F, 43	Recurrent chondrosarcoma	CA	4	5.0	12	30.6
					5.0	30	
					5.0	30	
					5.0	30	
8	F, 65	Recurrent anal carcinoma	PA	2	30.8	7	25.704
					30.4	7	
9	M, 65	Lymph node met of rectal cancer	CA	1	5.2	15	4.68
10	M, 57	Lymph node met of rectal cancer	PA	2	31.4	20	75.24
					31.3	20	
11	M, 63	Lymph node met of melanoma (no. 1)	PA	1	29.0	9	15.66
		Lymph node met of melanoma (no. 2)	PA	1	28.8	9	15.552

tachment of the recurrent tumor to the sciatic nerve, causing neural irritation and pain. The clinical symptoms ultimately provided the indication to perform a laser treatment. The tumor marker carcinoembryonic antigen (CEA) level decreased from 8.4 ng/dl before laser treatment to 0.8 ng/dl after treatment (normal CEA level < 4.5 ng/ml). Contrast-enhanced follow-up MRI studies demonstrated no tumor recurrence. The patient reported a significant decrease in pain. The CEA level remained under 1.0 ng/dl.

In the eight treated lymph node metastases, the abdominal wall metastases, and the recurrent anal cancer, total destruction of tumor was achieved (Fig. 2). All of these lesions had been less than 5 cm in maximum diameter and showed a well-defined tumor border. In the remaining recurrent tumors a reduction of tumor volume of between 60 and 80 % could be obtained. All of these recurrent tumors showed either a diffuse infiltration of the surrounding structures or were larger than 5 cm in diameter (maximum 8 cm in diameter). All of these patients were treated with the conventional laser application system without internal cooling due to the fact that at this time the internally cooled power application system was not yet available and we were less experienced in performing LITT treatments. In these patients, contrast-enhanced MRI scans obtained 2 days and 3 months after the treatment showed contrast enhancement in some portions of the tumors, representing active tumor bulk; however, the clinical follow-up showed a decrease of clinical symptoms, especially pain, in these patients. The medication could be changed from drugs containing opiates to drugs not containing opiates; however, the incomplete ablation of these tumors resulted in a recurrence or further growth of the tumor within 4–6 months and a return to an analgesia containing opiates again. The follow-up period in this study was between 5.8 and 60.8 months (mean 21.6 months, median 18.7 months).

The use of the internally cooled power application system allowed more reliable local tumor destruction, reduced the number of applications which were necessary for treatment of the total tumor volume, and reduced the application time.

Discussion

Palliative treatment options for recurrent extrahepatic abdominal tumors are limited by the proximity of vital vascular and neural structures, especially in the pelvis, and by the aggressive nature of these tumors. Further conventional tumor resections are very difficult, if not

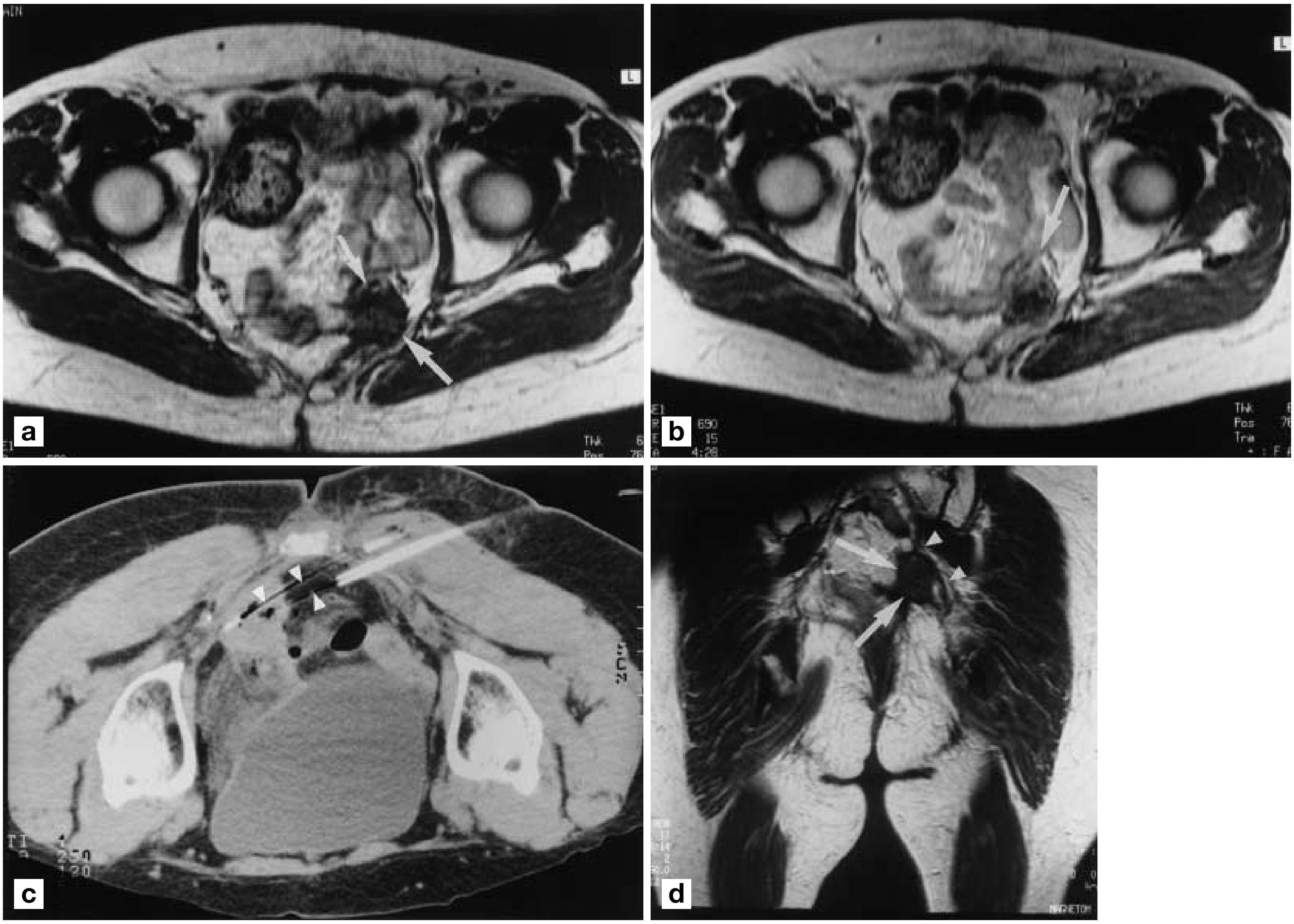

Fig. 1 a–d Recurrence of an anal carcinoma. **a** The T2-weighted axial image demonstrates recurrence of an anal carcinoma *(arrows)*. **b** Contrast-enhanced T1-weighted transverse image shows contrast enhancement in the recurrence of the anal carcinoma *(arrow)*. **c** A CT-guided puncture of the lesion and insertion of two laser application systems *(arrowheads)* after displacing the intestines and the bladder away from the tumor by injection of physiological saline solution. **d** Contrast-enhanced T1-weighted coronal image performed 2 days after CT and MR-guided laser-induced thermotherapy (LITT) shows no residual pathologic contrast enhancement of the tumor *(arrows)*. Note the faint enhancement along the ischiadic nerve, presumably due to inflammatory changes *(arrowheads)*

impossible, due to previously performed resections. Further chemotherapy is often refused by the patients who have experienced further growth of recurrent tumor during chemotherapy. Therefore, a minimally invasive management modality, such as interventional MR-guided laser-induced thermotherapy, offers several potential management benefits. Firstly, MRI provides unparalleled topographic accuracy because of its excellent soft tissue contrast and high spatial resolution. Secondly, the temperature sensitivity of the thermo-FLASH 2D sequences can be used to monitor the temperature elevation in the tumor and surrounding healthy tissues, thus increasing safety and accuracy of treatment. Nearly real-time MRI monitoring during LITT therefore allows early detection of local complications and treatment effects. Thirdly, recovery times, length of hospital stay, and the risk of infection and other complications can be reduced compared with conventional palliative surgery. This minimally invasive laser therapy can be performed under local anesthesia and, under appropriate conditions, even on an outpatient basis. In the beginning of our series the patients had to stay in the hospital for 1–2 days. Since 1998 all procedures have been carried out on an outpatient basis.

The use of an internally cooled power laser application system results in larger coagulative necrosis in comparison with the conventional application system. For lesions larger than 2.5–3 cm diameter, the insertion of two or more laser application systems (multi-applicator technique) and simultaneous heating is recommended to achieve optimal coagulative necrosis with a reliable safety margin and to reduce local recurrence rate.

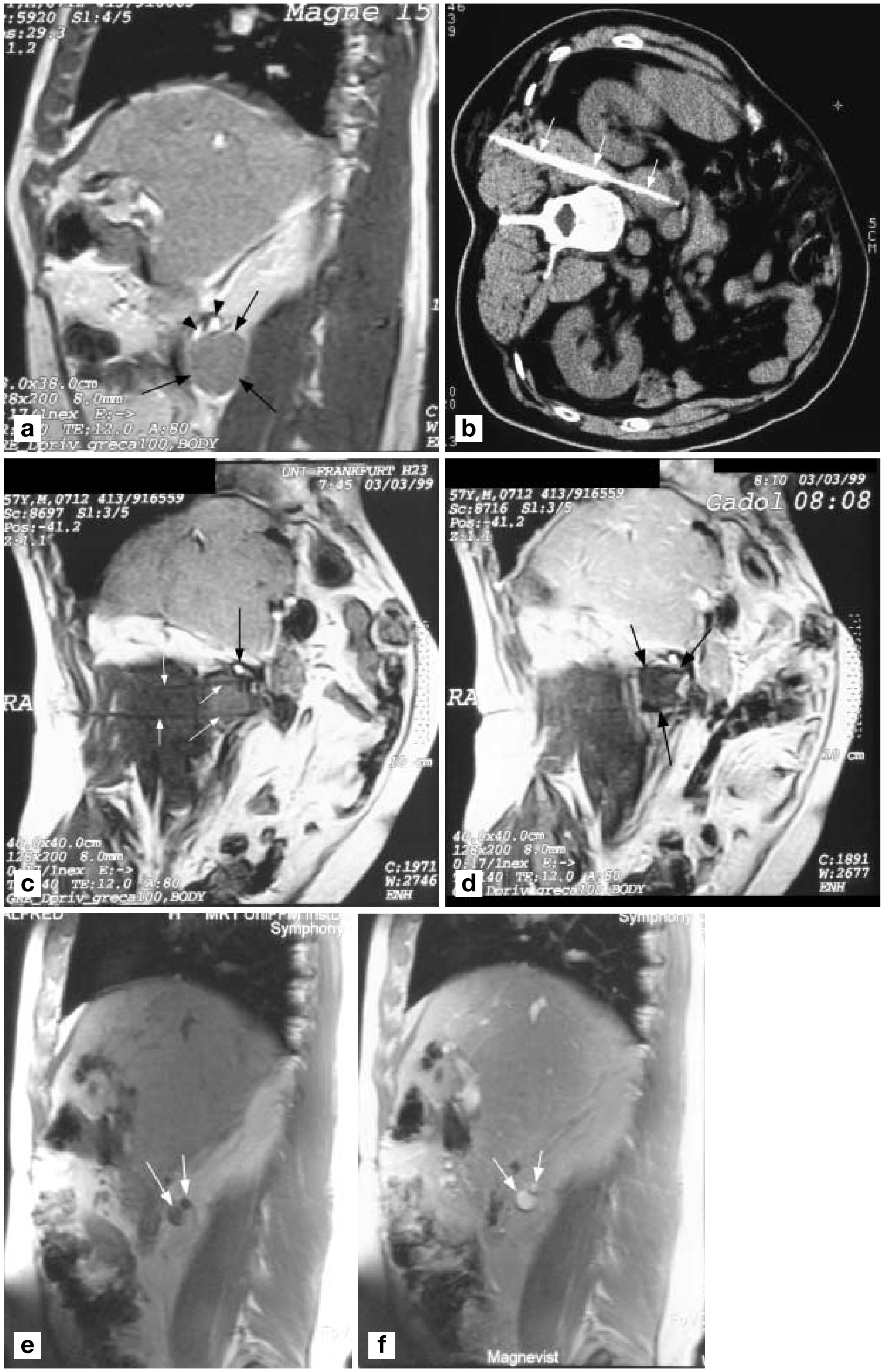

Fig. 2 a–f Para-aortal lymph node metastases. **a** The T1-weighted contrast-enhanced sagittal image demonstrates the para-aortal lymph node metastases *(arrows)* with 3.7 cm maximum diameter. Note the vessels *(arrowheads)* above the metastases representing the renal artery and vein. **b** The CT image shows one laser application system *(arrows)* which was positioned from dorsal in the lymph node metastases. **c** The fast low-angle shot (FLASH) 2D image in parasagittal slice orientation shows two laser applicators *(white arrows)* placed from dorsal in the lymph node metastases. Note again the renal artery and vein *(black arrow)* above. **d** The contrast-enhanced FLASH 2D image shows the induced coagulative necrosis as well as inflammatory changes in the border immediately after LITT. **e** The non-contrast FLASH 2D image obtained 2 years after the treatment shows a complete remission of the treated lymph node. Note again the renal artery and vein *(arrows)*. **f** The contrast enhanced FLASH 2D image obtained 2 years after the treatment demonstrates no pathologic contrast enhancement. *Arrows* indicate renal artery and vein

Indications for MR-guided LITT are the local treatment of recurrent extrahepatic abdominal tumors, the treatment of circumscribed lesions, or tumor debulking to reduce clinical symptoms such pain and neural irritation.

Due to complex anatomy, especially in patients who had extensive surgery before, MRI is the method of choice for both the monitoring of the treatment itself and the follow-up examinations. Computed tomography does not give any information regarding the heat distribution during the treatment and ultrasound is problematic due to the limited visualization of the lesion which we have treated.

In conclusion, MR has been demonstrated to be a very useful and helpful tool for guidance of minimal invasive treatment. The presented LITT protocol is a practicable, minimally invasive, well-tolerated technique that can produce large areas of necrosis within recurrent tumors, resulting in tumor inactivation and/or reduction of active tumor bulk. Reliable tumor destruction results from the internally cooled power laser application system in lesions less than 5 cm in diameter. Our experience indicates that recurrent lesions with an infiltrative growth pattern may not be well suited for minimally invasive treatment procedures such as LITT.

For extrahepatic abdominal tumors a further evaluation is necessary to verify these very promising results.

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