MR-guided laser induced thermotherapy (LITT) of liver metastases: Side-effects, complications and interventional treatment

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Abstract

Purpose

To demonstrate clinical findings and imaging criteria of side-effects and complications immediatly and delayed after the MR-guided LITT for the treatment of liver metastases.

Material and methods

In a time frame of 6 years 411 patients were prospectively treated with MR-guided LITT for liver metastases. Between June 1993 and March 1999 a total of 2440 laser applications were performed to treat 923 lesions in 322 consecutive patients.

Concerning to the technical development of the LITT procedure the patients were subdivided for the evaluation of the local control rate and side effects in 3 groups (group 1: patient 1-100, group 2: patient 101-175, group 3: patient 176-322). The complications of the procedure were evaluated by clinical examination and unenhanced and contrast enhanced MR imaging performed once 24 to 48 hours after the intervention and then every 3 months.

Results

All patients tolerated the procedure under local anaesthesia well. The following complications or side-effects could be visualized on clinical examination or imaging studies: pleural effusion in 7.28%, subcapsular hematoma in 2.46%, intrahepatic abscess in 0.11%, intraabdominal bleeding in 0.11% and local infection on puncturing side in 0.2%. All complications except the following were clinical not relevant and only visible on imaging studies: In 0.36% of the cases the pleural effusion had to be treated by puncture due to clinical relevant dyspnoe. Two intrahepatic abscesses have treated by percutaneous drainage. The 30 day mortality was 1,2 % with septic shock in 1 patient after an ulcer bleeding.

The 3 months MRI control demonstrated a local tumor progression in group 1 in 35.1% versus 20.3% in group 2 versus 0.8% in group 3. The 6 months control showed in group 1 a local tumor progression in 61.7% versus 32.9% in group 2 versus 2.2% in group 3.

Conclusion

In patients with liver metastases the local tumor destruction using minimally invasive percutaneous MR-guided LITT under local anesthesia is a safe therapy method and results in a reliable local tumor control and improved clinical outcomes. MR thermometry and MR imaging proved to be a non-replaceable basis for minimal invasive treatment monitoring and follow up studies.

Key words

Liver metastases, LITT, MR-thermometry, complications

Introduction

The technique of MR-guided LITT for the treatment of liver metastases and primary hepatocellular carcinoma gets rapidly spread. Due to increasing treatment numbers and increasing necrosis size a special focus has to be put on the presence and treatment of possible complications. The interventionalist has to know imaging findings post LITT and to be able to define a range between normal and abnormal. In combination with clinical findings it will be helpful to decide for the need of further therapy or wait and see.

Material and Methods

Patients:

Between June 1993 and March 1999 a total of 2440 laser applications was performed to treat 923 lesions in xxx consecutive patients. The complications of the procedure were evaluated by clinical examination and MR imaging performed once 24 to 48 hours after the intervention and then every 3 months using plain and contrast enhanced MRI.

Concerning to the development of the LITT procedure the patients were subdivided for the evaluation of the local control rate in 3 groups (group 1: patient 1-100, group 2: patient 101-175, group 3: patient 176-322). The local tumor control was also evaluated by the plain and contrast enhanced follow-up using T1 and T2 weighted SE and GRE sequences.

Laser equipment:

Laser coagulation was accomplished using a Neodymium-YAG laser light with a wavelength of 1064 nm (Dornier mediLas 5060, Dornier mediLas 5100, Dornier Medizintechnik GmbH, Germering, Germany; Martin MY 30, Martin MY 60, Martin, Tuttlingen, Germany), delivered through optic fibers terminated by a specially developed diffusor. The diffusor, a protective glass dome of 1.4 mm diameter, was mounted at the end of a 400-mm-long silica fiber core. Frosted on its inner surface, the diffusing dome emitted laser light to an effective distance of 12 to 15 mm.

Application kit:

The used laser application kits (SOMATEX, Berlin, Germany) consists of a cannulation needle with a tetragonally sharpened tip, a guide wire, a sheath system containing a 15cm mandrin, and a 43cm special protective catheter, which is closed at the distal end. Conventional laser applicators have a 7F size and the internal liquid irrigated applicator, representing a further development, a 9 F diameter.

The system is fully compatible with MR-imaging systems. Magnetite markers on the laser applicator allow easier visualization in MR imaging during the positioning procedure; similar marks on the sheath and the protective catheter allow exact positioning of the emitter within the lesion.

Treatment protocol and set up:

All patients were examined using an MR imaging protocol including FLASH-2D plain and contrast-enhanced GD-DTPA 0.1 mmol/kg body weight (b.w). T2-and T1-weighted sequences are obtained for localizing the target lesion and planning the interventional procedure.

After informing patients about potential complications, benefits, and disadvantages of LITT, consent was obtained and pethidine (20-80 mg) was administered intravenously. The metastasis was localized on computed tomographic scans (Somatom plus 4, Siemens, Erlangen) and the injection site was infiltrated with 20 ml of 1% lidocaine. Under CT-guidance, a 7-French sheath was inserted using Seldinger technique. A special heat-resistant protective catheter was then introduced. Subsequent the patient was moved to the MRI unit. The scanner was a conventional 1.5-T magnet system (Siemens SP 4000, Siemens, Erlangen, Germany) and a 0,5-T magnet system (Elscint). The laser itself is installed outside of the examination unit, and the light is transmitted through a 10 m long optical fiber. After checking the applicator position in three slice orientations and introducing the laser fibers the laser were switched on. GRE- sequences were performed before and during LITT.

Laser energy was applied – typically 30 to 35 W over approximately 20 minutes – and its effects on tissue were monitored, seen in the form of signal loss in [?] sequences. Depending on the geometry and intensity of the signal loss, the position of the laser fibers was readjusted within the thermostable catheter. Using a pull-back technique, the laser energy was applied so as to adapt thermally induced changes individually to the geometry of the given lesion.

After switching off the laser, T1-weighted and contrast-enhanced FLASH-2D images contrast enhanced were obtained for determining the degree of induced necrosis. At the end of the procedure the cannulation channel was closed with fibrin glue. Follow-up examinations using plain and contrast-enhanced sequences were carried out 2 days, 1 month, and every 3 months after the LITT procedure. Quantitative and qualitative parameters, including size, morphology signal behavior, and contrast enhancement were evaluated for deciding whether treatment is terminated, or subsequent treatment sessions were required.

Imaging during therapy:

MR-thermometry is performed using specially designed GRE-sequence (TR/TE/flip angle = 102/8/15°), which is sensitive for the detection of thermal changes in signal intensity. During laser application of 20 to 25 W over 20 minutes ellipsoid hypointense areas are visualizing the actual heat distribution in the obtained MR-images (figure 1c). MR-thermometry is obtained in intervals of 30 seconds after starting the laser and already in the first images we observe an obvious decrease in signal intensity in the lesion area. This techique provides additional verification of the position of the laser applicator and documents that the entire laser system is working well without hot-spots (carbonization or vaporization due to failure of the cooling or laser system and resulting in a damage of the laser fiber and protective catheter). Visual control of the heat induced changes of tumor tissue, liver parenchym and vascular structures directly influences the treatment performance.

Qualitative and quantitative evaluation/ survival:

The qualitative evaluation of laser-induced effects was based on an analysis of lesions and surrounding liver parenchyma before and after evaluation periods. It also included documentation of the morphology of lesions as seen in T2- and T1-weighted SE and GRE sequences. Quantitative data were obtained by volumetric calculation of tumor and necrosis volumes before and after intervention using region of interest (ROI) assessment.

Spontaneous or therapeutically induced necrosis was defined as a hypointense area with no contrast enhancement after i.v. application of 0.1 mmol/kg b. w. Gd-DTPA. Areas with enhancement in postinterventional sequences were interpreted as residual tumor tissue, if the lesions were topographically identified in the area of the previous tumor. Surrounding structures with a high degree of contrast enhancement and hyperintense T2 behavior were defined as reactive hypervascular changes, induced by the therapy itself.

Results

The following complications or side effects could be visualized on clinical examination or imaging studies: pleural effusion in 7.28%, subcapsular hematoma in 2.46%, intrahepatic abscess in 0.11%, intraabdominal bleeding in 0.11% and local infection on puncturing side in 0.2%. All complications except the following were clinical not relevant and only visible on imaging studies: In 0.36% of the cases the pleural effusion had to be treated by puncture due to clinical relevant dyspnoe. The intrahepatic abscess was treated by percutaneous drainage.

1. Pleural effusion

The post interventional development of a pleural effusion is so far due to our experience the most common imaging finding post MR-guided LITT of the liver.

Main clinical symptoms were dyspnoe, fever, jaundice and pain.

Effusion volumes were estimated using the formula d2 x 1(d=greatest depth of the effusion on a single CT or MRI image, 1=greatest length of the effusion), which revealed reliable estimation for quantification of a pleural effusion in the literature (Mergo et. al., J Thorac Imaging 1999). We observed a pleura effusion of more than 300 ml in 7,28% of our patients with an effusion of more than 1000 ml in x %. ..... clinically relevant symptoms werde found in x % of patients with more than 300 ml, and in all patients with more than 1000 ml. Most frequently patients were suffering from dyspnoe, which regularly recovered within two to four weeks post-intervention. A pleural puncuture was performed in x patients, the application of a chest drainage in x patients . Due to the possible risk of infections puncture of the effusion was only performed in clinically unstable condition. However we have observed a pleural effusion in a greater extent and more clinical relevant in the period up to the middle of 1998. With the improved techniques of interventional channel occlusion via a tissue clue we have been able to further reduce the amount of therapeutically induced pleural effusion. The T2 w sequence of the 24 hours control MRI examination was a very sensitive tool for detection of pleural fluid.

Therapy instructions for affected patients were intensive breath exercises and temperature controls.

2. bleeding

Considering a huge number of punctures clinically relevant vascular complications rarely were seen. Although larger lesions were treated with up to 4 insertal laser catheters, no patient had so far to undergo abdominal surgery due to an untreatable bleeding.

subcapsular bleeding

Image findings for subcapsulare hematomas are very typical. The shape is mostly concave around the liver, sometimes with compression of the liver parenchym and sharply border lines. The signal depends on age of the oxygeneous blood components, intermediatly hypo-to isointens and from increasing T1-signal in following days and weeks. In the 3 months control there are only residual changes in the affected liver part.

Clinical findings were primary post-interventional pain at the upper abdomen for 5 to 10 days. Patients recieved oral analgetica like novolaminsulfon or tramal regarding the pain severity.

intra-abdominal and intra-lesional bleeding

Intra-abdominal bleeding is characterized by fluid within the typically spaces around the liver and spleen. The active bleeding in the treated lesion during and after CT guided catheter placement leads to relative rapid increase in lesion size during the CT-intervention. After inserting the laser fiber and starting up the laser radiation the active bleeding regulary will be stoped due to coagulative effects. Lesions with intensive Gd-enhancement are predisposed for such a complication.

Postinterventional close down of the puncture channel via fibrin clue seems to be a very useful tool for avoidance of bleeding complications.

3. Liver abscess

Clinically and radiologically the diagnosis of a liver abscess was verified in x % of patients and x % of treated lesions. The correlation with underlying histopathology and clinical outcome documented that 80 % of the observed liver abscesses were most likely due to previous hepatobiliary surgery like whipple´s surgery for pancreatic cancer. All these patients presented with biliary air and a possible infection of the bile due to a liver abscess developed. All patients were treated via percutaneously implanted catheters, all under CT-guidance. The catheters were removed after 3 to 4 weeks when the lesion appears smaller and without air and fluid. The follow up MRI demonstrated a circumscriped hypointense area with homogenous contrast enhancement.

Steril necrosis with mass effect – Borns disease: Large necrosis filled with fluid and air bubbles. The mass effect compressed the normal liver parenchyma.

5. Pneumothorax

During the CT application of the laser applicators we observed the development of a pneumothorax in two cases. Without any clinical findings CT lung window varifieds an increase in the size of pneumothorax during the CT-guided intervention. Regarding to the long period of the following MR thermometric measurements we decided for positioning of a pneumo-cat-system. Under CT-guidance the one step pneumo-cat-system was placed and the air was completely sucked of. The success was verified by postinterventional CT-scans. We continued with MR-thermometry with the pneumo-cat-system in place. Clinically patients showed no impairment of their breath function, there were no problems to perform the 15 s breath stops for MR-thermo measurements. Four to six hours post LITT we carefully removed pneumo-cat. Residual air or lesions to the pleural space were verified in a twenty hours follow-up CT-scan.

5. bile duct lesions

Thermal ablation of tumor lesions in the liver hilus close to the portal branches is risky to harm greater bile ducts. However, the therapeutic intervention is necessary, because further tumor grow in this area will lead to bile duct compression or invasion too. Clinical appearances are scleral and skin jaundice and increased bilirubin blood levels. 24 hours post LITT aquired T1w images show the enlarged hypointense bile ducts in one or both liver lobes. During the first days we have to distinguish between a postinterventional edema of the treated liver parenchyma and subsequent compression to a real bile duct injury. Short term cortison therapy reestablish the bile flow in case of edema and the complete disappearance of symptoms. In the worst case a percutaneous transhepatic cholangioplasty is necessary.

6. mortality

4 patients to be described:

one lethal, one shock, one septic shock, one colonic perforation

7. postprocedural pain and fever

One to five days after LITT treatment mild temperature elevation up to 38.5 degrees may occur with or without pain at puncture side. This seem to characterize a reactive syndrom caused by the laser-induced hepatic necrosis. If the temperature increase up to 39 degrees more than one or two days systemic antibiosis will be necessary combined with a check of blood parameters. Suspect to be responsible for the temperature is a infection of a pleural effusion.

8. segmental infarction

Coagulation of a arterial or venous vessel within the liver parenchyma causes an infarction of a liver segment with typically wedge-shaped changes of perfusion and signal intensity. Predominantly increased T2 signal shows the localized tissue edema.

9. bilioma:

In some cases the laser induced necrosis enlarged over 24 h rapidly with a very low signal in the T1 and GRE sequences and a homogenous, very high signal in the T2 w sequences. The spherical shape and sharp borders are typical for the filling of the necrotic area with bile fluid. In most of the cases this finding disappeared in the 3 months follow up MRI without clinical symptoms.

Local infection at the punction site – are easily to manage with iode containing emulsion and a frequent change of wound dressing.

Discussion

In summary CT is of enormous diagnostic importance in the acute phase during or after MR guided LITT for the detection of local complications after. In the subacute phase contrast enhanced MRI depicts ...... even subtle changes. CT-guided puncture or drainage of fluid containing spaces means the technique of high therapeutic importance.

In patients with liver metastases the local tumor destruction using minimally invasive percutaneous MR-guided LITT under local anesthesia is a safe therapy method and results in a reliable local tumor control and improved clinical outcomes. MR thermometry and MR imaging proved to be a non-replaceable basis for minimal invasive treatment monitoring and follow up studies.

Mortality

Morbidity: abszess hematoma, postprocedural pain.

Conclusion:

Sideeffects and complications after minimally invasive MR-guided LITT might be fixed at a very low rate, if the interventional team is strictly following the presented guidelines. A major focus has to be put to the planning of the access-route for the placement of the laser catheters under ultrasound, CT or MRI guidance.

References

Figures

Tables

Tabelle 1 Patients management

clinical check	**intraprocedural monitoring**	**intraprocedural drug administration**	**postprocedural monitoring**	**Delayed postinterventional monitoring for 10 days**
Ikterus **Fever** **common cold** **laboratory parameters:** blood count gerinnung MRI scan	**pulse rate** **blood pressure**	**local anesthesia (cave: contraindications)** **mild sedation** **short infusion of antibiotics (regularly Spicef)**	**anti pain medication** **continous check of pulse rate and blood pressure for the first 30 minutes** **check every 30 minutes for a period of 6 hours** **antinausea medication if necessary**	**Check of fever** **Ikterus** **dyspnoe**

Tabelle 2 statistics of complications after LITT

complication	**Count (%)**			
Pleural effusion				
Intra-abd. Bleeding				
Subcapsular bleeding				
Liver abszess				
pneumothorax				
Bile duct lesions				
mortality				
Postprocedural fever and pain				
bilioma				
Segmental infarction				