Laser thermal therapy for brain metastases: Ex vivo and in-vivo validation in an ovine brain model

Verena Kn appe1, Christian Osswald2, Cristina Pantaleone3, Jimmy Johansson3, Emily Emilsson Rossander3

1Clinical Laserthermia Systems GmbH, Johann-Hittorf-Strasse 8, 12489 Berlin, Germany,
2MRI interventions Inc., 5 Musick, Irvine, California 92618, USA
3Clinical Laserthermia Systems, AB, Scheelevägen 2, 22381 Lund, Sweden

Introduction

Minimally invasive magnetic resonance (MR)-guided laser interstitial thermal therapy (LITT) is becoming an alternative to conventional surgical management or traditional radiation strategies of intracranial tumors including metastases, gliomas, radiation necrosis, and functional disorders among others (1). The technological advancement allowing the use of LITT for brain tumors is the combination of MR-thermometry with the ability of real-time image feedback of laser thermal energy delivery, making it possible to predict the thermal temperature and damage of a planned target in the brain (2,3).

In our case, this principle relies on the temperature-dependent water proton resonance frequency (PRF)-shift. Phase map subtraction is therefore necessary; Subtracting the reference phase map – acquired before the start of the heating – from the phase map of the current timeframe the PRF temperature map can be calculated (4).

Minimally invasive insertion of the laser fiber into the brain can be done with stereotactic neuro-navigation tools in the operating room or directly in the MRI suite in conjunction with real-time MR imaging (5). We aim to characterize the performance of a non-cooled 1064-nm diode laser ablation system in a large animal brain model and investigate a new MR thermometry software (pre-CE mark) for treatment monitoring.

Material & Methods

The minimally invasive TRANBERG® Thermoguide Therapy System (CLS AB, SE) consists of a laser unit (1064 nm) with non-cooled laser applicators and a new MR-thermometry software (Fig.1). For this study, the laser applicator used has a circumferential radiation length of 15 mm at the distal fiber tip.

1) For identifying reliable and efficient power and time settings, the evaluation was initially performed ex vivo in native ovine brain tissue (24°C±3°C), and subsequently in vivo in two Hampshire-breed sheep brains (37.8°C±0.7°C) (with local ethical approval in Minnesota) after craniotomy. Ovine brain was used due its large, gyrencephalic structure with relevant physical characteristics such as its optical and thermal properties. Different power settings and exposure times were tested in triplicate in the range of 6-25 W/3-5 min, ex vivo.

Each animal in vivo was treated in duplicate at 7 W/5 min. In both cases, actual temperature was measured with temperature probes placed 10 mm lateral to the laser applicator.

2) First tests with the CLS Thermoguide thermometry software was run in a 1,5T-MRI (Siemens Magnetom Avanto fit), with loop coil on the ex vivo sheep skull and was used for the temperature distribution evaluation. For acquisitions, a clinically approved segmented EPI sequence was used with TR=29ms, TE=15ms, Flip angle 10°, FOV = 190mm, voxel size 1.5x1.5x3.0mm. For temperature mapping two orthogonal planes were generated, increasing rate in thermal mapping was 4.8s. Laser parameters were 7W/3 min.

3) For a minimally invasive approach to brain lesions, the compatibility between TRANBERG® Thermoguide Therapy System and the MR-compatible ClearPoint® Neuro Navigation System (MRI Interventions Inc., CA) and an R&D prototype of SF-introducer was tested.

Results

1) Coagulative necrosis did not appear macroscopically in the native brain. Therefore, necrotic cores were determined with the lateral temperature probes placed parallel to the laser applicator. For all parameters, no charring or carbonization appeared. The tissue around the diffuser laser applicator was slightly firmer (Fig 2) and in some high-power settings, the color became slightly brown. Ex vivo, the max temperatures (at 10 mm distance) obtained on average range from 41.0°C (6W/5min.) to 103.2°C (25W/3min.). The procedure was reproducible and highly efficient.

In sheep brain in vivo, the temperatures were 42.2°C at 10mm distance and 68.4°C at 5mm distance with both at 7W/3min. These parameters generated a safe and controlled treatment with clinically relevant thermal damage.

2) The starting conditions at T0 provided by the Thermoguide software are displayed in two orthogonal sections in Fig.3. The white arrows mark the laser applicator entrance channel in the brain tissue. Fig. 4 is taken at the end of treatment at maximum heat after 3 min. of active laser. The color bar on the left side of Figs. 3 and 4 correspond to the temperature distribution. A max temperature of 76.3°C was seen close to the fiber axis.

A temperature cross-section along the blue line is displayed in the left graph of Fig.5. The right graph shows the temperature development over time at an arbitrary spot in 5 mm distance, the max temp. was 66.1°C. During the validation process the Thermoguide software deviated with ±2°C in comparison to optical temperature probes.

Conclusions

The TRANBERG® Thermoguide Therapy System is well-suited for safe and reliable ablation in ovine brain tissue used as a model for brain metastases and other pathologies.

The laser technology enables control of heat distribution. For later clinical applications it allows tailoring on tumor size and localization.

Utilizing MR thermometry will protect sensitive structures (e.g., eloquent cortex) and provide every 4.8s a refreshed temperature overview with these parameters. Based on this information, a damage calculation is provided for the user. The additional guidance during the treatment.

The intraoperative ClearPoint® MR-guided neuro-navigation system enables minimally invasive insertion of the laser fiber to intracranial pathologies.

Further in vivo evaluation for the whole system is planned on an MR-guided animal brain model and will show the potential of LITT to become a widely applied treatment in neurosurgery with demonstrated oncologic effectiveness.

Fig.1: Schematic overview of the TRANBERG® Thermoguide Therapy System. The mobile Tranberg laser is controlled by Thermoguide, which receives displays the temperature maps.

Fig.2: 15mm Diffuser laser applicator ex vivo, 8W, 5 min

Fig.3: Initial reference image before heating

Fig.4: Temperature map at the end of the treatment. The blue line marks the position of cross section.

Fig.5 Left: Temperature along the blue line

Fig.5 Right: Temporal development on a single spot, 5mm from this center

References

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