Health Policy Advisory Committee on Technology

Technology Brief

Magnetic resonance thermometry-guided laser interstitial thermal therapy for intracranial neoplasms

August 2013
**Technology, Company and Licensing**

**Register ID**
WP166

**Technology name**
Magnetic resonance thermometry-guided laser interstitial thermal therapy for intracranial neoplasms

**Patient indication**
For use in patients with inoperable intracranial neoplasms

**Description of the technology**

Laser interstitial thermal therapy (LITT) is a minimally invasive ablative treatment for intracranial neoplasms.¹ In LITT, an applicator probe is placed within the tumour and deposits precise amounts of light energy. Light energy is converted to thermal energy within the tumour, resulting in a rise in local temperature. The heat generated damages intracellular proteins leading to coagulation and cell necrosis.² LITT potentially enables tumour resection in patients who are unable to undergo open surgery. However, the inability to monitor tissue temperature and thermal energy deposition, and to view the resulting anatomical changes in real time, has hindered the application of LITT. Consequently, LITT has often resulted in suboptimal treatment, with patients receiving under or over ablation of their tumours.³

Two systems, Visualase and the NeuroBlate® System, overcome these problems by combining LITT with magnetic resonance thermometry (MRT) imaging. MRT scans produce detailed images of internal organs and temperature patterns in real time. The Visualase and NeuroBlate® software process the MRT scan data and generate real-time, colour-coded thermal and tissue images, allowing the surgeon to precisely monitor and guide tumour ablation. The software also includes safety limits. If the surgeon exceeds the required thermal dose or strays outside the tumour zone, the laser is automatically deactivated. The safety features and real-time feedback enable the surgeon to maximise tumour ablation while avoiding critical brain areas.

The Visualase and NeuroBlate® System share many similar components, including an image-processing workstation, a laser applicator probe, a laser generator and a cooling catheter. However, the two systems differ in the efficiency of the laser. The Visualase laser functions at a wavelength of 980 nm, whereas the NeuroBlate® laser operates at 1064 nm. The smaller wavelength of the Visualase laser enables it to rapidly heat tissue and produce sharper thermal gradients at lower power than the NeuroBlate® laser.⁴ For example, ablation of a 2.5 cm metastatic tumour would take 6 minutes with the Visualase laser and 73 minutes with the NeuroBlate® System.⁵ In addition, the NeuroBlate® laser requires a larger cooling catheter than the Visualase laser. This feature is particularly relevant when trying to minimise damage to adjacent sensitive areas in the brain. A final point of contrast between the two LITT systems relates to the use of anaesthesia. Patients treated with the NeuroBlate® System require general anaesthesia, whereas patients undergoing treatment

---

¹ Laser interstiti... the tumour and deposits precise amounts of light energy. Light energy is converted to thermal energy within the tumour, resulting in a rise in local temperature. The heat generated damages intracellular proteins leading to coagulation and cell necrosis.² LITT potentially enables tumour resection in patients who are unable to undergo open surgery. However, the inability to monitor tissue temperature and thermal energy deposition, and to view the resulting anatomical changes in real time, has hindered the application of LITT. Consequently, LITT has often resulted in suboptimal treatment, with patients receiving under or over ablation of their tumours.³

Two systems, Visualase and the NeuroBlate® System, overcome these problems by combining LITT with magnetic resonance thermometry (MRT) imaging. MRT scans produce detailed images of internal organs and temperature patterns in real time. The Visualase and NeuroBlate® software process the MRT scan data and generate real-time, colour-coded thermal and tissue images, allowing the surgeon to precisely monitor and guide tumour ablation. The software also includes safety limits. If the surgeon exceeds the required thermal dose or strays outside the tumour zone, the laser is automatically deactivated. The safety features and real-time feedback enable the surgeon to maximise tumour ablation while avoiding critical brain areas.

The Visualase and NeuroBlate® System share many similar components, including an image-processing workstation, a laser applicator probe, a laser generator and a cooling catheter. However, the two systems differ in the efficiency of the laser. The Visualase laser functions at a wavelength of 980 nm, whereas the NeuroBlate® laser operates at 1064 nm. The smaller wavelength of the Visualase laser enables it to rapidly heat tissue and produce sharper thermal gradients at lower power than the NeuroBlate® laser.⁴ For example, ablation of a 2.5 cm metastatic tumour would take 6 minutes with the Visualase laser and 73 minutes with the NeuroBlate® System.⁵ In addition, the NeuroBlate® laser requires a larger cooling catheter than the Visualase laser. This feature is particularly relevant when trying to minimise damage to adjacent sensitive areas in the brain. A final point of contrast between the two LITT systems relates to the use of anaesthesia. Patients treated with the NeuroBlate® System require general anaesthesia, whereas patients undergoing treatment
with Visualase only require general anaesthesia if they are in the supine position. Consequently, the latter patient group may experience less postoperative morbidity and may be discharged earlier.

**Company or developer**

Visualase is produced by Visualase, Inc. (Texas, United States of America (USA)). The NeuroBlate® System is manufactured by Monteris Medical, Inc. (Minnesota, USA).

**Reason for assessment**

MRT-guided LITT provides a novel treatment option that enables tumour resection in patients who are unable to undergo open craniotomy.

**Stage of development in Australia**

- ☒ Yet to emerge
- ☐ Experimental
- ☐ Investigational
- ☐ Nearly established
- ☐ Established
- ☐ Established but changed indication or modification of technique
- ☐ Should be taken out of use

**Licensing, reimbursement and other approval**

Both Visualase\(^6\) and the NeuroBlate® System\(^7\) have received United States Food and Drug Administration (FDA) 510(k) clearance.\(^8,9\) NeuroBlate® has also been approved by Health Canada.\(^10\)

At present, neither of these technologies has been listed on the Australian Register of Therapeutic Goods (ARTG), or received a European CE mark.

**Australian Therapeutic Goods Administration approval**

- ☐ Yes
- ☒ No
- ☐ Not applicable

**Technology type**

- Device

**Technology use**

- Therapeutic

**Patient Indication and Setting**

**Disease description and associated mortality and morbidity**

Intracranial neoplasms, or brain tumours, are abnormal, uncontrolled proliferations of cells within the brain.\(^11\) Brain tumours are defined by their cell type, pattern of growth and
Primary tumours originate in the brain, whereas secondary tumours have metastasised to the brain from another location. Tumour growth is broadly divided into benign or malignant. Benign tumours are slow growing, are composed of non-cancerous cells, and do not metastasise from their original location. Conversely, malignant tumours are composed of cancerous cells that grow rapidly and infiltrate healthy tissue. Metastatic tumours are the most common intracranial neoplasm in adults, followed by primary malignant and benign tumours. Common examples of brain tumours are as follows:

- primary benign
  - meningioma
  - vestibular schwannoma
  - pituitary adenoma
- primary malignant
  - glioblastoma multiforme
  - astrocytoma
  - oligodendroglioma
- secondary
  - metastatic cancer.

High rates of morbidity and mortality are associated with intracranial neoplasms owing to the functional importance of the brain. For example, glioblastoma multiforme has one of the lowest 1- and 5-year survival rates for all cancers. Tumour growth within the brain often results in damage to sensitive brain regions, and symptoms of a tumour often reflect its location within the brain. General symptoms of a brain tumour can include severe recurring headaches, nausea and vomiting. More specific symptoms can include difficulty speaking and remembering; seizures; weakness or paralysis; loss of balance; change in personality; and disturbed vision, taste, hearing or smell.

At present, it is difficult to determine who will develop intracranial neoplasms. However, age, race, genetics, sex and previous cranial irradiation or neoplasm are all potential risk factors.

**Number of patients**

Between 1991 and 2012, the incidence of brain cancer in Australia has remained stable at an age-standardised rate of 7 per 100,000 people. Compared with other cancers—for example, prostate (age-standardised rate of 163 per 100,000)—the incidence of brain cancer is relatively low. However, the mortality associated with brain cancer is among the highest for all cancer types, with an age-standardised rate of 6 deaths per 100,000 people. The 5-year survival rate for patients diagnosed with a brain tumour is only 22 per cent.

Brain cancer occurs more frequently in men and the elderly. In 2009, 928 men and 667 women were diagnosed with brain cancer. In addition, men have a lower 5-year survival
rate than women, as well as an increased risk of being diagnosed with brain cancer before 75 years of age and of dying before the age of 85 years.\textsuperscript{17}

The Australian Institute of Health and Welfare estimates that by 2020, approximately 2,095 new cases (1,230 men and 865 women) of brain cancer will be diagnosed per year, with the highest prevalence occurring among men aged between 80 and 84 years.\textsuperscript{18}

Speciality Neurosurgery

Technology setting Specialist and General Hospitals

Impact

Alternative and/or complementary technology

MRT-guided LITT is an option for patients who have recurrent tumour growth despite undergoing maximal resection in conjunction with optimal chemotherapy and radiotherapy treatment. The procedure is considered an alternative for patients who are unable to receive standard surgical resection because of the location or type of their tumour.

Current technology

Surgery, radiotherapy and chemotherapy are the standard of care in patients diagnosed with intracranial neoplasms.\textsuperscript{19} Maximal surgical resection is the preferred treatment and is associated with an increased long-term survival compared with no treatment.\textsuperscript{20, 21} However, surgical resection is often not possible in patients who are high-risk surgical candidates or who have a tumour that is difficult to access. Radiotherapy and chemotherapy both increase survival in patients with intracranial neoplasms, but they have limited applicability.\textsuperscript{22} For example, many chemotherapeutic agents are unable to cross the blood-brain barrier, reducing their effectiveness, and radiotherapy is most effective for the treatment of small tumours less than 3 cm.

Patients with recurrent or progressive intracranial neoplasms have few therapeutic options. Consequently, approximately one-third of these patients participate in clinical trials.\textsuperscript{3} New therapies currently under investigation include dendritic cell vaccination, oncolytic viral infection, radiolabeled antibody conjugates and signal pathway inhibitors.

Diffusion of technology in Australia

The diffusion of MRT-guided LITT within Australia could not be determined through review of published literature.

International utilisation

The Visualase and NeuroBlate\textsuperscript{®} System are the subjects of completed and ongoing clinical trials in the United States. Visualase has also undergone clinical trials in France.
In April 2013, Visualase, Inc. reported that more than 250 patients with brain tumours had been successfully treated using Visualase across 20 centres in the United States.  

<table>
<thead>
<tr>
<th>Country</th>
<th>Level of Use</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Trials underway or completed</td>
</tr>
<tr>
<td>Canada</td>
<td>☑</td>
</tr>
<tr>
<td>United States of America</td>
<td>☑</td>
</tr>
<tr>
<td>France</td>
<td>☑</td>
</tr>
</tbody>
</table>

Cost infrastructure and economic consequences

Infrastructure costs associated with MRT-guided LITT include the purchase of the laser system (Visualase or NeuroBlate® System) and a compatible 1.5 T magnetic resonance imaging (MRI) scanner. Currently, MRI scanners are mainly installed in large referral hospitals. If the hospital has an existing MRI machine, an increase in demand would be expected.

Increased costs associated with the procedure include the need for specialist and support staff, staff training, consumables such as the single-use laser probes, and access to MRI.

Ethical, cultural or religious considerations

No ethical, cultural or religious considerations were identified in the published literature.

Evidence and Policy

Safety and effectiveness

Two case series (level IV Intervention evidence) evaluating MRT-guided LITT for intracranial neoplasms were included in this Technology Brief. Jethwa et al. (2012) evaluated the use of Visualase in patients with benign, malignant and metastatic intracranial neoplasms. Sloan et al. (2013) evaluated the NeuroBlate® System in patients with recurrent or progressive glioblastoma multiforme in whom radiotherapy (with or without chemotherapy) had failed. Collectively, the safety and effectiveness of MRT-guided LITT was evaluated in 30 patients. A summary of the details of the included studies is outlined in Table 1.
Table 1  Characteristics of the included studies

<table>
<thead>
<tr>
<th>Study</th>
<th>Jethwa et al. 2012</th>
<th>Sloan et al. 2013</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Level of evidence</strong></td>
<td>IV (retrospective)</td>
<td>IV (prospective)</td>
</tr>
<tr>
<td><strong>Number of patients</strong></td>
<td>20</td>
<td>10</td>
</tr>
<tr>
<td><strong>Patient diagnosis</strong></td>
<td>Benign or malignant intracranial neoplasms</td>
<td>Recurrent or progressive glioblastoma multiforme despite previous radiotherapy therapy</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>Visualase</td>
<td>NeuroBlate® System</td>
</tr>
<tr>
<td><strong>Follow-up</strong></td>
<td>Not stated</td>
<td>At least 14 days; median 8 months</td>
</tr>
<tr>
<td><strong>Conflict of Interest</strong></td>
<td>Drs Godwa and Sheety, the third and fourth authors respectively, are employees of Visualase, Inc.</td>
<td>Drs Sloan, Ahluwalia, Torchia and Barnett, the first, second, fifth and last authors respectively are paid consultants for Monteris Medical, Inc.</td>
</tr>
</tbody>
</table>

Jethwa et al. 2012

A case series (level IV intervention evidence) was conducted at a single centre in the USA by Jethwa et al (2012).² Twenty consecutive patients with an intracranial neoplasm underwent MRT-guided LITT using Visualase. The decision to perform LITT was made on an individual basis according to four main factors: personal preference, disease recurrence despite previous surgical resection and maximal adjuvant therapy, the presence of surgically inaccessible tumours, and classification as high-risk surgical candidates. The tumour types were diverse and included glioblastoma multiforme (n=6), metastatic cancer (n=4), ependymoma (n=3), hemangioblastoma (n=2), meningioma (n=2), supratentorial primitive neuroectodermal tumour (n=1), chordoma (n=1) and anaplastic astrocytoma (n=1). The average age of the patients was 60.5 years (range 9-85 years). The patient selection criteria were not reported, nor were the pre-intervention tumour volume and length of follow-up.

Safety

No deaths associated with the procedure were reported. However, major complications were reported in 20 per cent of patients: an insertion-related haemorrhage (n=1), an oedema (n=1), a pituitary injury manifesting as diabetes insipidus and metabolic derangement (n=1), and a missed lesion due to an inaccurate registration (n=1). All major complications were successfully treated. No minor complications were reported. Post-ablation oedema occurred in the majority of patients and was effectively managed using steroids. It was not considered a procedural complication.

Effectiveness

Overall, MRT-guided LITT was successfully performed in 95 per cent (n=19) of patients. One patient was converted to standard surgical resection after inaccurate pre-operative registration caused the laser to miss the target tumour. Suboptimal placement of the laser probe (>5 mm from or outside of the target) occurred five times due to inaccurate patient registration.
Most patients required a single treatment of MRT-guided LITT, although three patients returned for a second laser ablation. Two of these patients repeated MRT-guided LITT two months after the initial procedure as part of a staged ablation. The third patient repeated MRT-guided LITT 17 months after the initial procedure owing to tumour recurrence. Patients were hospitalised for an average of 2.3 days following the procedure.

The volume of tumour treated using Visualase ranged from 0.4 cm$^3$ to 68.9 cm$^3$, with an average treated volume of 7 ± 9 cm$^3$. However, the percentage of tumour ablated was not reported. The area of thermal damage ranged from 0.95 cm$^2$ to 9.63 cm$^2$. The average maximal postoperative lesion diameter and area were 2.4 ± 0.85 cm and 3.99 ± 2.60 cm$^2$ respectively.

Sloan et al. 2013

A case series study (level IV intervention evidence) was conducted across two centres in the USA by Sloan et al. (2013). Ten patients were enrolled into the study following diagnosis of progressive or recurrent glioblastoma multiforme that had recurred despite radiotherapy with or without chemotherapy. One patient who was initially registered for the trial was subsequently excluded as the tumour was too deep for the laser probe. Additional exclusion criteria included: previous treatment with stereotactic radiosurgery, brachytherapy or carmustine-impregnated wafers; symptoms due to the mass effect of the tumour; uncontrolled hypertension; angina pectoris; cardiac dysrythmia; recent intracranial haemorrhage; serious infection; immunosuppression; pregnancy; abnormal neutrophil count or coagulopathy; inadequate bone marrow; impaired liver or renal function; contraindications to MRI; medical or other conditions that may reduce the patient’s safety; an inability or unwillingness to provide consent; posterior fossa neoplasms; neoplasms with treatment boundaries that were within 5 mm of critical brain regions; and multiple tumours.

The included patients had a mean age of 55 years and 20 per cent were female. The size of the tumours ranged from 22 x 15 mm to 36 x 34 mm, with an average size of 27.5 x 22.5 mm. The average tumour volume was 6.8 cm$^3$, ranging from 2.6 cm$^3$ to 19 cm$^3$. Although the location of each tumour varied, the majority were on the left side of the brain. Further investigation revealed that two tumours were near the non-eloquent cortex, five were near the eloquent cortex and three were within the eloquent cortex. The median pre-operative Karnofsky performance status (KPS) score, which measures patients’ general well-being and activities of daily living (range 0 [death]–100 [perfect health]), was 80 (range 70–90).

At the time of the procedure, an average of 614 days (standard deviation (SD) 482.0) had passed since the initial diagnosis of glioblastoma multiforme and an average of 539 days (SD 496.8) had elapsed since initial radiotherapy. On average, each patient had undergone two (SD 0.9) rounds of chemotherapy 210 days (SD 249.0) before the current treatment. Recurrence was first recorded, on average, 58 days (SD 61.2) prior to MRT-guided LITT.
Prior to the procedure, patients were assigned to one of three treatment groups corresponding to a low (n=3), medium (n=2) or high (n=5) thermal dose. Patients were followed for a minimum of six months or until death, with the first follow-up scheduled for 14 days after the procedure.

Two patients died before the six month follow-up due to the progression of the underlying disease.

Safety

No deaths associated with the NeuroBlate® System occurred. All patients were alert and responsive one to two hours post-operatively. Nine patients were ambulatory 12 hours post-operatively. An MRI scan conducted 48 hours after the procedure indicated the presence of treatment-related oedema in nearly all patients. The oedemas were effectively managed using steroids.

Temporary neurological deficits (impaired ability to communicate together with mild upper limb weakness and mild weakness with visual field loss) occurred in two patients several days after the procedure. In both cases, deficits presented contralateral to the ablated area and were successfully treated. Fourteen severe adverse events were observed, including neutropenia (n=1), a cerebral cyst (n=1), brain abscess (n=1), dysphasia (n=1), partial seizure (n=1), post-operative wound infection (n=1), hemiparesis (n=1), haematoma (n=2), glioma (n=1), vascular pseudoaneurysm rupture (n=1), pulmonary embolism (n=1) and deep vein thrombosis (n=2). Less serious adverse events included a mild balance disorder (n=1), dizziness (n=1), partial seizure (n=2), speech disorders (n=1), hemiparesis (n=1), blurred vision (n=2), confused state (n=1), partial seizures (n=2) and headaches (n=5).

Long-term severe complications included a white matter tract injury, an intracerebral haemorrhage six weeks after treatment and an epicranial gliosarcoma at the probe entry site nine months post-treatment. All severe complications were successfully managed.

Effectiveness

MRT-guided LITT was successfully performed in all patients. MRI scans taken 24 and 48 hours after the NeuroBlate® procedure demonstrated necrosis at the tumour site in all patients. The NeuroBlate® System M•Vision™ software accurately predicted the region of cell death at medium and high thermal doses. The volume of tumour ablated ranged from 1.98 cm$^3$ to 11.03 cm$^3$, with an average ablated volume of 5 cm$^3$ (SD 3.2). Thus, on average, 78 per cent (range 57–90%) of the total tumour volume was treated.

At the 14-day follow-up, one patient who received a medium thermal dose and two patients receiving high thermal doses had increased KPS scores. One patient who received the highest thermal dose reported a decreased KPS score. The remaining patients did not report any change.
The median survival of patients after MRT-guided LITT was 316 days (range 62–767 days). Thirty per cent of patients had a median progression-free survival time of six months.

**Economic evaluation**

No cost effectiveness studies of MRT-guided LITT were identified in the literature.

**Ongoing research**

Two trials were identified from ClinicalTrials.gov and the Australian and New Zealand Clinical Trials Register (Table 2).

<table>
<thead>
<tr>
<th>Trial Identifier/ Location</th>
<th>Trial Status</th>
<th>Intervention</th>
<th>N</th>
<th>Study Design</th>
<th>Interventions</th>
<th>Estimated completion date</th>
</tr>
</thead>
<tbody>
<tr>
<td>NCT01651078 USA</td>
<td>Recruiting</td>
<td>MRT-guided LITT with the NeuroBlate® System</td>
<td>40</td>
<td>Case-series</td>
<td>MRT-guided LITT for metastatic brain tumours</td>
<td>December 2013</td>
</tr>
<tr>
<td>NCT01736722 USA</td>
<td>Recruiting</td>
<td>MRT-guided LITT with Visualase</td>
<td>22</td>
<td>Case-series</td>
<td>MRT-guided LITT for 1-3 metastatic brain tumours</td>
<td>January 2015</td>
</tr>
</tbody>
</table>

**NCT01651078 - Laser Ablation After Stereotactic Radiosurgery for Patients With Metastatic Brain Tumors (LAASR)**

The study aims to recruit participants across multiple sites within the USA. The primary endpoints are the patient’s quality of life before and after the NeuroBlate® procedure, and the progression of the tumour or radionecrosis as measured using MRI. Secondary outcomes include adverse events and utilisation of healthcare resources.

**NCT01736722 - MRT-Guided LITT for Treatment Metastatic Brain Tumors**

The study’s primary outcome is to determine the safety and feasibility of the Visualase system by examining morbidity and mortality at 30, 90, and 180 days post-operatively, as well as the rate of technical success or failure. Secondary outcomes include the survival of patients, concordance between Visualase software predicted and postoperative MRI lesions, duration of the procedure, required facilities, personnel and costs for the procedure, and the local control of the lesion at 30, 90 and 180 days postoperative.

**Other issues**

**Study Issues**

- At least three patients enrolled in Sloan et al. (2013) entered subsequent clinical trials. It is unclear whether this influenced mean survival time. 3
● Jethwa et al. (2012) noted that the response to Visualase thermal ablation was different among each tumour type and showed variability within the same tumour category. It is, therefore, unclear which tumour type responds best to thermal ablation, and whether it is appropriate for all tumour types.\textsuperscript{5}

● Sloan et al. noted that those who had poor health pre-operatively were more likely to develop complications.\textsuperscript{3}

● Sloan et al. noted that the favourable survival results may be due to the selection bias in the enrolled patients. Patients were required to have single tumours no bigger than 4 cm in diameter.\textsuperscript{3}

\textit{MRT-guided LITT issues}

● A significant problem of MRT-guided LITT is the survival of neoplastic cells at the margin of the lesion leading to secondary tumour growth.

● At present, the laser probe is of limited length, which potentially limits its application in patients with deep intracranial neoplasms.

● Unexpected patterns of thermal energy deposition were observed in both studies. This led to severe complications such as a white matter tract injury.

\textit{Additional studies}

Two studies were conducted at the same institution in Germany by Schwarzmaier et al.\textsuperscript{24, 25} However, these studies used Dornier Medizintechnik 4060N 1064(nm) lasers.

In Schwarzmaier et al. (2005), two patients with recurrent glioblastoma multiforme received partial ablation treatment due to the irregular shape of their tumours.\textsuperscript{24} The patients died 13 and 15 months after the procedure corresponding to 16 and 20 months survival since their initial diagnosis respectively.

In Schwarzmaier et al. (2006)\textsuperscript{25}, 16 patients with recurrent glioblastoma multiforme were treated with MRT-guided LITT and chemotherapy. The mean follow-up period was 9.1 months (SD 6.3). Twenty-six MRT-guided LITT procedures were performed in 16 patients. There were no deaths or serious adverse events associated with the procedure. However, there were six minor complications: temporary weakness of the right arm (n=1), neutropenia (n=3), thrombocytopenia (n=1) and increased transaminases (n=1). At the 30-day follow up, one patient had died, and at the end of the study, 12 of the 16 patients had died. The median overall survival time after LITT was 6.9 months (1.7 SD). However, the authors note a substantial learning curve. The first ten and the last six cases exhibited a survival of 5.2 (SD 0.6) and 11.2 (SD 2.0) months following LITT respectively (p=0.0267).

Three smaller case series from a single centre in France have reported the use of Visualase in patients with intracranial neoplasms.
In Carpentier et al. (2008)\textsuperscript{26}, four patients with treatment-resistant metastatic brain tumours were treated. The procedure was successfully performed in all patients with no major or minor complications. At the 3-month follow up, peripheral tumour recurrence was slightly visible in three patients who only received partial tumour ablation.

In Carpentier et al. (2011)\textsuperscript{27}, seven patients with treatment-resistant metastatic brain tumours were treated. Patients were followed up to 30 months post-treatment. Fifteen MRT-guided LITT procedures were performed in the seven patients. Total tumour ablation was possible in 57 per cent of patients, with partial ablation occurring in the remaining 43 per cent. No salvage surgical interventions were required. Although no patients died as a result of the procedure, four complications occurred: blood suffusion without increased mass effect, a probe misplacement, a transient increase in cerebellar syndrome, and transient aphasia. Mean overall survival since diagnosis was 17.4 (SD 3.54) months. The average progression-free survival time following MRT-guided LITT was 3.8 (SD 1) months. Total tumour ablation was associated with a higher mean survival compared with partial tumour ablation (9.2 [SD 3.5] and 3.3 [SD 1.3] months respectively). However, the statistical significance of this result was not reported.

In Carpentier et al. (2012)\textsuperscript{28}, four patients with recurrent glioblastoma multiforme underwent MRT-guided LITT. Overall, the procedure was successfully performed in all patients. No significant adverse events were recorded. However, minor complications such as a transient neurological deficit, convulsive seizure, mild dysphasia and cerebrospinal leak occurred in three patients. All minor complications were successfully treated. Patients experienced a mean progression-free survival of 30 days, with an overall survival time after the procedure of 10.5 months.

Visualase has also been used to successfully ablate epileptogenic foci in children and brain lesions which have regrown after radiosurgery.\textsuperscript{29, 30}

**Summary of findings**

The treatment of recurrent or inoperable intracranial neoplasms remains a significant problem with limited successful therapeutic options. The current Technology Brief utilised two case series to assess whether MRT-guided LITT could treat intracranial neoplasms. However, there were some limitations to the current studies. For example, the average tumour volume pre-intervention and the mean percentage of the tumour ablated were not reported by Jethwa et al. (2012). In addition, the heterogeneous population of neoplasms used in this study makes determining the efficacy of MRT-guided LITT difficult to determine. Finally, patient-related outcomes were not reported across both studies; therefore, it is unclear whether MRT-guided LITT is associated with an improved quality of life.

Collectively, the literature suggests MRT-guided LITT is fairly well tolerated among patients and that unless immediate complications occur, patients can be safely discharged within 24
to 48 hours. However, 18 severe adverse events were observed across both case series, of which all were successfully managed. There were no deaths attributable to the procedure. The mean volume of tumour treated using NeuroBlate® ranged from 5 cm to 7 cm, corresponding to 78 per cent tumour ablation. While this did not meet the goal of maximal surgical resection (≥ 98%), the median survival of the patients (316 days) was longer than the 90 to 150 days observed for recurrent glioblastoma. 

Future studies should focus on patient-relevant outcomes, such as improvement in quality of life, and should define the patient and tumour type most appropriate for MRT-guided LITT, determine who is at risk for unexpected thermal energy deposition or serious adverse events, optimise the treatment dose, and compare to an appropriate comparator treatment.

HealthPACT assessment

MRT-guided LITT is an emerging therapeutic technique for patients in cases where surgical resection of an intracranial neoplasm is not possible. At present, the effectiveness of MRT-guided LITT is unknown. Consequently, the small body of evidence cannot be used to make an informed decision regarding the use of MRT-guided LITT. Therefore, it is recommended that MRT-guided LITT be monitored for 24 months, at which time the results of three larger case series will be available.

Number of studies included

All evidence included for assessment in this Technology Brief has been assessed according to the revised NHMRC levels of evidence. A document summarising these levels may be accessed via the HealthPACT web site.

| Total number of studies | 2 |
| Total number of Level IV studies | 2 |

References


Search criteria to be used (MeSH terms)

Mesh terms: Brain Neoplasm, Laser Therapy, Magnetic Resonance Imaging

Text: Visualase, NeuroBlate, AutoLITT, laser interstitial thermal therapy, laser, magnetic resonance thermometry