TECHBRIEF

HORIZON SCANNING REPORT

MRI-GUIDED LASER INTERSTITIAL THERMAL THERAPY (LITT) FOR BRAIN TUMOUR

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MRI-GUIDED, LASER INTERSTITIAL THERMAL THERAPY (LITT) FOR BRAIN TUMOUR

INTRODUCTION

Tumour or neoplasm is a new growth of tissue in which cell multiplication is uncontrolled and progressive. It may exist in forms of solid or fluid-filled. A brain tumour is abnormal and uncontrollable multiplication of cells grows in the brain. It can either be cancerous or non-cancerous. According to Ministry of Health Malaysia, cancer was listed as the sixth of the overall burden of disease and was responsible for 6.6% of the total DALYs (disability-adjusted life year).[1-4]

Brain tumour is relatively rare compared to other tumours. It accounts for 1.95% of all cancers in Malaysia. The brain and other nervous system tumours occurred in all age groups and the highest incidence was in the 60-69 year age group with ASR (Aged-standardized rate) per 100,000 population of Malaysian was 2.9 and 2.4 in male and female respectively between 2003-2005.[5-6]

In United States, cancer is a significant cause of morbidity and mortality for adolescents and young adults (age between 15-39 years) and was reported as the fourth most common cause of death in this group with 8.78 deaths per 100,000 person annually between 2008 and 2012. Central Brain Tumor Registry of the United States (CBTRUS) also reported that the brain and CNS tumours ranked the third most common cause of cancer death with approximately 10,600 brain and CNS tumours diagnosed in adolescents and young adults per year and approximately 450 deaths reported annually in this age group.[7]

Neurosurgeons encounter difficulty to treat brain tumours without causing long term neurological complications from surgery when location of tumours are either in or near areas of eloquence.

Craniotomy procedure performed on high-grade gliomas in or near areas of eloquence has been reported to have risk of neurological complications such as functional or cognitive deficits on neurological basis.[8]

Recently, new MRI guided laser interstitial thermal therapy (LITT) systems which function at wavelength of 980 nm has been discovered to treat primary and recurrent gliomas especially the gliomas which are located in areas of eloquence.[8]

THE TECHNOLOGY

Laser interstitial thermal therapy (LITT) is a new minimally invasive technique for treating intracranial tumours. Focused laser energy was used to ablate tumour tissues from inside the brain. This system is equipped with real time MRI thermometry, and could lessen damages of surrounding healthy tissues as surgeons could concentrate and selectively ablate the tumours and lesions in the brain which are unreachable by surgical procedure.[8-9]

This LITT system is an integrated and MRI-guided which operates at wavelength of 980 nm. It comprised of:[9-10]

a) Laser energy generator
b) Cooling catheter with fiberoptic applicator
c) Pump for circulating coolant through the applicator
d) Computer workstation with magnetic resonance imaging (MRI) analysis software for determination and visualization of relative changes in tissue temperature during therapy.

Software application running on the workstation allows the workstation user to control the laser output by displaying the real-time thermographic at the treatment location, and also to operate the coolant pump from the workstation interface.

PATIENT GROUP AND INDICATION

The LITT systems are meant for treatment of neurosurgical lesions including difficult-to-access malignant gliomas and radiosurgery-resistant metastases as well as the ablation of lesions such as epileptogenic foci and radiation necrosis.[11]

CURRENT PRACTICE

Current practices available are as follows.[10]

a) Surgery, radiotherapy and chemotherapy are the standard of care in patients diagnosed with intracranial neoplasms. Maximal surgical resection is the preferred treatment and is associated with an increased long-term survival compared with no treatment. 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.

b) Radiotherapy and chemotherapy both increase survival in patients with intracranial neoplasms, but they have limited applicability. 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.

c) NeuroBlate® System (operates at 1064 nm). It takes 73 minutes to ablate 2.5 cm metastatic tumour compared to the new LITT which only takes 6 minutes.

d) New therapies currently under investigation include dendritic cell vaccination, oncolytic viral infection, radiolabeled antibody conjugates and signal pathway inhibitors.

EFFICACY & SAFETY

There were seven studies on LITT for intracranial tumours treatment identified. All these studies were case series with small number of patients.

Carpentier et al. conducted a study on 15 metastatic brain tumours in seven patients. Total coverage of the lesion by laser emission was possible in nine treatments while in the remaining six treatments only partial coverage was possible due to complex tumour geometry. After the treatment, all patients were discharged within 24 hours, and the mean total hospital stay was 26 hours. Based on Kaplan-Meier analysis, mean overall survival (OS) at the time of analysis was 17.4±3.5 months which exceeded the prognosis survival at the time of enrollment.[13]

A clinical study on focal metastatic intracranial tumours has been conducted to explore the safety and feasibility of the real-time MRI-guided LITT. The results showed that laser ablation of small focal metastatic lesions was effective for tumour control with no signs of recurrence or regrowth in all treated patients (six cases in four patients). This thermal therapy was reported to be technically feasible and safe for the lesions treated and may be an effective treatment option for up to 20% of patients who failed the radiation therapy.[14]

A case study using thermal therapy to treat four patients with recurrent glioblastomas was conducted and the results showed that all were successfully managed with no complication, satisfying treatment volume, and decreased in size of the treated tumour. The recurrence of all patients was observed with a mean/median progression free survival of 37/30 days. After LITT, mean/median overall survival was 10.5/10

months which was not higher than regular survival (The overall survival of patients was 26 months after diagnosis and 11 months after laser treatment). Researchers has recommended that study in a larger group of patients should be done to confirm the results.[15]

Another study was conducted among six patients who had previously undergone gamma knife stereotactic radiosurgery for brain metastases and 14 patients with recurrent metastatic intracranial tumours or radiation necrosis. All these patients underwent LITT and tolerated the procedure well. Thermal therapy also carries minimal morbidity and showed some effectiveness in symptomatic relief of oedema and neurological symptoms which was paralleled with radiographic lesional control.[12,16]

In another study, 20 intracranial neoplasm patients were treated consecutively using LITT whereby about 17 patients previously had treatment for their tumours. About 31 laser applicators were inserted in patients and the laser insertion was accurate in about 83.9% which indicated that LITT therapy was suitable for treating tumours in or near areas of eloquence.[17]

Schwarzmaier et al. investigated the survival after LITT in patients who experienced radiologically documented recurrence of a histologically confirmed glioblastoma of WHO grade IV. Result of the study showed a reduction in volume of the tumours at 17 months after LITT with the median overall survival time of 6.9±1.7 months. This median overall survival time was lower than the median overall survival time after patients were diagnosed with first recurrent (9.4±1.3 months). This is because the patients were divided into two distinct periods where patients in group A started the treatment after two months while group B started the treatment after 0.3 months. Furthermore, the KPS (Karnofsky Performance Status) score was higher in group B. These two groups of patients have generated different median survival time (Group A: 5.2±0.6 months; Group B: 11.2±2.0 months) where the median survival time for group B was higher when compared with the median overall survival time after patients were diagnosed with first relapse.[18]

ESTIMATED COST

A cost-effectiveness analysis from a societal perspective was carried out by *Voigt JD and Barnett G* and they reported that the overall survival improved with brain LITT when compared with current treatments by 3.07 months at an additional cost of $7,508 which is equivalent to ICER (incremental cost-effectiveness ratio) of $29,340/LYG. The ICER was less than the current international threshold value ($32,575/LYG) and the US threshold value ($50,000/LYG).[8]

The actual cost of the device is not known yet. According to the manufacturer, the device can be customized according to clients requirement. However, the incurred cost will include purchasing of the LITT system and a compatible 1.5 T magnetic resonance imaging (MRI) scanner. In hospital with existing MRI machine, an increase in demand using the MRI machine would be expected.

Extra costs should be considered for staff training and consumables such as single-use laser probes.

ORGANIZATIONAL ISSUES

Staff training on how to operate the LITT system and MRI should be provided for the team that is going to operate the device which include specialist and support staff.

POTENTIAL IMPACT

Using MRI-guided LITT procedure for brain tumours seems to be beneficial in term of decreasing length of hospital stay where the patients did not require postoperative intensive care; subsequently lead to reduction of overall costs. Compared with open surgery, this laser procedure has

potential benefit for patients to recover more quickly and reduce the incidence of venous throboembolism (VTE) which can be high in brain cancer and whose risk is further increased post craniotomy.[8,18,20]

MRI guided LITT is a minimally invasive method of treating neoplasm that may have potential impact in treatment of intracranial tumours. The addition of MRI to LITT allows the use of realtime MRI for planning, guidance and thermal monitoring by surgeons during the ablation.[9,19]

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