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Intraoperative Real-Time MRI Guided Stereotactic Biopsy Followed by Laser Thermal Ablation for Progressive Brain Metastases after Radiosurgery

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Abstract

Stereotactic radiosurgery is one of the treatment options for brain metastases. However, there are patients who will progress after radiosurgery. One of the potential treatments for this subset of patients is laser ablation. Image-guided stereotactic biopsy is important to determine histopathological nature of the lesion. However, this is usually based on preoperative, static images, which may affect the target accuracy during the actual procedure as a result of brain shift. We therefore performed real-time iMRI guided stereotactic aspiration and biopsies on two patients with symptomatic, progressive lesions after radiosurgery followed immediately by laser ablation. The patients tolerated the procedure well with no new neurologic deficits. Intraoperative MRI-guided stereotactic biopsy followed by laser ablation is safe and accurate by providing real time update and feedback during the procedures.

Keywords

metastasis; radiation necrosis; radiosurgery; real time iMRI biopsy; laser ablation

INTRODUCTION

The most common intracranial brain tumor in adults is brain metastases. Current treatment options for brain metastases include surgery, whole brain radiation, fractionated stereotactic radiation therapy or stereotactic radiosurgery. SRS alone has been reported to have a local average tumor control rate of 76% at 1 year and up to 82% when combined with WBRT [1]. However, a common side effect of SRS is the development of cerebral radiation necrosis, which occurs with an incidence of 5 to 32% and can be observed as early as 3 months and up to 2 years after initial treatment [2]. Diagnosis of cerebral radiation necrosis based on MRI and even metabolic imaging is difficult and inconclusive. Surgical resection can provide symptomatic relief of mass effect and histopathologic confirmation [3]. Patients

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with lesions unamenable to safe surgical resection often undergo stereotactic biopsy and radiation. For these patients, it will be difficult to exclude tumor recurrence or radiation necrosis because of the small tissue sample size. Treatment options for cranial radiation necrosis include steroids, anticoagulation, surgery, and bevacizumab [2]. Recently, laser interstitial thermal therapy has emerged as a potential treatment for patients with biopsies confirming cerebral radiation necrosis and has also used to treat 14 patients with brain metastases who failed prior SRS [4, 5].

Stereotactic biopsy of progressive lesions post radiosurgery before laser ablation is important to confirm the histopathology and the target site. Ideally, this procedure should be performed just before the laser ablation in the same setting to avoid brain shift. The current navigation system used for stereotactic biopsy (frame-based or frameless) relies on preoperative images which are static with no real time feedback and confirmation of the biopsy site. Therefore, it is inherently unable to account for potential inaccuracies due to brain shift during the actual procedure and may therefore compromise target accuracy and patient safety.

We report on our initial experience with intraoperative in-bore real-time MRI-guided stereotactic biopsy followed by laser ablation for 2 patients with progressive metastatic lesions post radiosurgery.

Methods

The two patients included in this study had pre-operative contrast enhanced structural MRI, functional MRI and DTI.

Case #1—An 80 year-old diabetic male patient with metastatic papillary thyroid cancer to the deep left frontal lobe treated with LINAC stereotactic radiosurgery to 18 Gy. Postoperatively, patient presented with headaches and word finding difficulty 5 months after radiosurgery. Interval MRI showed increase in the size of the lesion with associated small hemorrhage and edema. FDG-PET showed decreased tracer uptake suggestive of post treatment effects. Patient initially improved with steroids but had difficulty with taper due to recurrence of symptoms and hyperglycemia and was deemed a poor candidate for open neurosurgical resection due to advanced age, medical co-morbidities, and deep location of the lesion in the dominant hemisphere. Therefore, the neuro-oncology team elected to proceed with intraoperative MRI guided stereotactic biopsy followed immediately by laser ablation.

Case #2—A 49 year old male patient with lung cancer who was found to have a left deep frontal enhancing lesion after staging work up. This was treated with stereotactic radiosurgery to 18 Gy. Patient presented 5 months later with progressive numbness and weakness of the right side. MRI of the brain showed interval progression with cyst formation of the previously treated left frontal lesion with edema. FDG PET showed decreased uptake. Open neurosurgical resection as well as stereotactic laser ablation were discussed with the patient. The decision was made to pursue the less invasive option since the location was deep to the motor strip, within the cortico-spinal tract, and in the dominant

hemisphere. Patient was offered intraoperative MRI guided stereotactic aspiration of cyst then biopsy followed immediately by laser ablation.

Intraoperative Real-Time MRI-Guided Stereotactic Biopsy

The intraoperative MRI guided (in bore) stereotactic biopsies were done using ClearPoint system. It is a novel, second generation platform for performing MRI guided biopsy with real-time MR imaging [6]. It has a fixed or adjustable head frame that can be mounted directly to the scanner bed [6]. The system also has a skull mounted trajectory guide called Smartframe, which provides 4 degrees of freedom allowing for angular and linear adjustment [6]. The SmartFrame has a central MRI-visible targeting cannula for passage of ceramic stylet or MR conditional biopsy needle [6]. The software is an intuitive menu driven neuronavigational work station that can be used by the neurosurgeon for target selection, entry, and trajectory [6].

Laser Thermal Ablation System

The laser thermal treatment was performed using the Visualase MRI Guided Laser Ablation (Medtronic, Minneapolis, MN). The system includes a 15 W 980 nm diode laser, cooling pump, MRI compatible laser applicator and a workstation that is connected to the MRI scanner for real time laser ablation treatment. The software provides information on the temperature (thermometry) and an estimate of the irreversible damage during the ablation process. This is calculated by the Arrhenius rate model using time and temperature as primary variables. The monitor displays the estimated irreversible zone in orange which is then superimposed on the reference image[7].

Operative Technique

Case #1

Preparation: The patient was induced with general endotracheal anesthesia outside the MRI room. After induction, the patient was then transferred to the MR room and positioned supine with the head immobilized with the MR (ClearPoint) compatible 4 point head fixation device. The patient was then moved through the magnet bore with the head positioned initially with the head out of the bore then subsequently moved to the isocenter. The area was prepped and the in-bore accordion type draping system that attaches by elastic cords at each end of the bore.

Planning: The MRI compatible scalp matrix localizing grid was then placed on the scalp. The patient was then moved to isocenter and a targeting volumetric MR sequence was performed and loaded into the ClearPoint software. The anterior commissure, posterior commissure and mid sagittal planes were identified. Based upon this landmarks and the ClearPoint software, the entry point, target and trajectory were chosen. The entry site was marked after SmartGrid coordinates were obtained. The adjustable scalp-mounted aiming device is secured to the outer table of the skull. The miniature arc system was then attached to the SmartFrame. Volumetric images were then taken for trajectory planning.

Biopsy and Laser Ablation

Case#1—The guide frame was then aligned with the anatomical target with adjustments to the pitch and roll as provided by the information from the MRI. The fine adjustments were done with the use of a hand controller while the patient's head was at isocenter. Sequential scans were obtained after each adjustment until alignment of the guide frame with the anatomical target was obtained. A stab incision was made at the point of entry followed by a twist drill hole through the guide cannula using an MRI compatible hand drill. The dura was then punctured and the ceramic stylet was initially inserted just above the superficial border of the tumor. MRI was done to confirm location and correct trajectory of the stylet in place. The stylet was removed and replaced with the MR compatible brain biopsy needle in the same trajectory. Biopsy was performed using suction aspiration technique with real time MRI confirmation of the biopsy needle inside the lesion. The biopsy needle was removed and replaced with the laser cooling catheter. The laser fiber was then inserted into the cooling catheter. The patient was positioned at isocenter and imaging was performed to confirm the location of the catheter followed by a thermal test of lesion using continuous MR thermometry. Real-time gradient echo MR thermometry was then used to constantly monitor the temperature during the actual treatment. Each lesion was treated with laser ablation in three different depths with auto shut off once the limit points were reached. Post-ablation MRI was done to confirm the target, extent of ablation and to rule out any hemorrhage.

Case#2—The patient in the second case example was positioned prone and aspiration of the cyst contents was performed after biopsy of the wall of the tumor (Figure 1).

Postoperative Course and Imaging

Both patients tolerated the procedure well without postoperative events. They were monitored in the neurosurgery ICU overnight and discharged 24 to 48 hours after the procedure.

Results

Case #1—The patient did well post biopsy and laser ablation but appears to have clinical decline with word finding difficulty 16 days after the procedure while on steroid taper. MRI showed slight increase in the edema most likely related to treatment. Patient was instructed to increase dexamethasone to 2 mg TID with a slower taper schedule.

Patient was seen at 12 weeks follow-up with improving speech. However, MRI showed increase in size of the treated lesion with stable edema. Patient was instructed to further lower his steroid dose.

Patient was seen again at 15 weeks follow-up with worsening speech following a lower steroid dose. MRI showed stable lesion size but with increased in the perilesional T2/Flair signal. PET/CT was done which showed decreased FDG uptake consistent with post treatment change. Symptoms improved with a slightly higher dose of steroids.

Interval MRI at 22 weeks post laser ablation showed decreased in size of the target lesion and edema (Figure 2). Patient was also noted to have further neurological improvement with successful steroid taper.

Case #2—The patient's postoperative course was unremarkable and was successfully tapered off steroids. Patient also underwent stereotactic radiosurgery to 2 new brain metastases in the right frontal and temporal lobe close to 4 weeks after the biopsy and laser ablation of the left frontal progressive lesion.

Patient was seen at 8 weeks post laser ablation with slight weakness of the right leg. MRI at this time showed interval increased in the treated lesion with edema suggestive of treatment related effect. He was started on low dose dexamethasone (Figure 3,4)

Discussion

Stereotactic biopsy utilizing a frame-based or frameless approach is a very helpful modality for small lesions deep in the brain [8]. It is imperative to ensure accuracy and recent advances in the acquisition of high quality images and sophisticated registration softwares help further minimize intraoperative errors [8]. However, the trajectory and execution are usually based on the preoperative images on the assumption that the brain does not move with reference to the external coordinate system [8]. This becomes a problem when there is movement and deformation of the brain after the images were obtained [8]. This so called tissue deformation during surgery or brain shift can be due to a number of processes that occur during craniotomy such as intraoperative shift of intracranial structures from CSF drainage, tumor resection, patient repositioning, brain swelling or the effects of brain relaxation agents [8]. The phenomenon of cortical and subcortical brain shift is also evident in burr-hole stereotactic procedures like implantation of DBS and is mainly due to CSF loss [9]. Ivan *et al.* reported brain shift involving cortical and deep brain structures of up to 10 mm for DBS procedures implanted using interventional, serial MR images[8]. They further mentioned that brain shift was a continuous and unpredictable process, which can lead to inaccurate results if procedure was done relying only on preoperative neuronavigation data [8].

Intraoperative MRI was conceptualized more than a decade ago to improve accuracy, eliminate errors and more importantly for intraoperative feedback by providing real or near-real time images during procedures[6]. Later “prospective stereotaxy” was used to perform brain biopsies and insert deep brain stimulation (DBS) electrodes with sub-millimeter accuracy [10]. The current intraoperative MRI platform was developed to provide accurate 3D targets utilizing intraoperative images to progressively obtain accurate alignment of the guide frame with targets and subsequent confirmation of the position of the biopsy needle or leads [10]. It has been used to safely implant DBS leads with accuracy of 0.6 mm [11, 12]. More recently, it was reported to be accurate in the placement of CED convection-enhanced delivery cannulae for infusion of IL13-PE and AAV2-GDNF in 2 patients with diffuse infiltrating pontine glioma and parkinson's disease [10].

The development of cerebral radiation necrosis and/or local tumor progression are the two consequences of stereotactic radiosurgery for brain metastases[5]. Cerebral radiation

necrosis can present as early as 3 months and up to 2 years in some cases [2, 5]. On the other hand, local tumor recurrence after radiosurgery has been reported to be approximately 18% and 31% at 1 and 2 years after SRS respectively[5]. Additional imaging to differentiate between the 2 processes such as MRS, MR perfusion, SPECT or dual-phase PEC/CT are often inconclusive [5]. Biopsy of the lesion is the gold standard but the results may be confounded by sampling errors leading to under-representation of the tumor biology and in some cases mixed cell population of tumor cells and radiation necrosis [5]. Treatment options for cerebral radiation necrosis will include steroids, anticoagulation, bevacizumab or neurosurgical resection. For true tumor recurrences, surgery and/or repeat radiation may be offered with increased risk of radiation necrosis.

MR-guided laser interstitial thermal therapy (LITT) is a minimally invasive approach to treat progressive post radiosurgery lesions by utilizing thermal energy to induce irreversible tissue necrosis at temperature above 43°C[13, 14]. The development of magnetic resonance thermography allows neurosurgeons to acquire real-time image guidance of the degree of tissue damage resulting from the delivery of laser thermal energy. Based on the temperature and damage estimate (area under the time-temperature curve), the surgeon can stop the treatment [15]. Other advantages of LITT aside from the absence of risk of radiation injury is the short recovery time allowing patient to be discharged the next day and resume systemic treatment for the primary cancer [5]. The use of laser ablation to treat gliomas, metastases, biopsy-confirmed radiation necrosis post radiosurgery has been reported to be safe and effective [15–18]. Therefore, laser ablation treatment may be a good treatment option for patients who present with radiographic progression post radiosurgery who are deemed to be poor surgical candidates since laser ablation can address both radiation necrosis and tumor progression.

The procedure was performed inside the MR suite with the head of the patient inside the bore. This is safer as there is no need to transport the patient from the main operating room after the stereotactic biopsy to the MRI suite for the laser ablation procedure. The ClearPoint system enabled us to perform the biopsy, cyst aspiration and laser ablation with real time feedback and confirmation. Furthermore, final images can be done to check for hemorrhage before closure.

Both patients did well after the procedure with uneventful postoperative course. There were no new or worsening neurologic deficits. They were observed to have mild clinical decline at 2 weeks and 8 weeks post treatment secondary to increased edema around the treated lesions. They responded quite well to low dose steroids with subsequent taper. The first patient had a longer follow up interval at 15 weeks while the second patient had the most recent clinic visit and interval imaging at 8 weeks. The radiographic appearance of the treated lesions correlate well with the reported characteristics of LITT treated lesions. We observed the probe tract with surrounding central zone that is hypointense on T1 and hyperintense on T2. There is also the peripheral zone of contrast enhancement and marginal edema beyond the peripheral zone [13]. The lesions were also observed to have expanded which is also typically seen and may enlarge up to 1.5 times the pre LITT size and can remain enlarged even up to 40 days due to thermal-induced swelling [13]. The central necrotic center will then slowly undergo resorption for at least 6 months [13].

Conclusion

The use of intraoperative real time MRI guided stereotactic biopsy followed by laser ablation with real time MR thermometry is a safe, accurate and potentially effective alternative treatment option for patients with progressive lesions after treatment with stereotactic radiosurgery.

References

1. Rajakesari S, Arvold ND, Jimenez RB, Christianson LW, Horvath MC, Claus EB, et al. Local control after fractionated stereotactic radiation therapy for brain metastases. *Journal of neuro-oncology*. 2014; 120:339–46. [PubMed: 25059451]
2. Murovic JA, Chang SD. The pathophysiology of cerebral radiation necrosis and the role of laser interstitial thermal therapy. *World neurosurgery*. 2015; 83:23–6. [PubMed: 24631912]
3. Parvez K, Parvez A, Zadeh G. The diagnosis and treatment of pseudoprogression, radiation necrosis and brain tumor recurrence. *International journal of molecular sciences*. 2014; 15:11832–46. [PubMed: 24995696]
4. Rahmathulla G, Recinos PF, Valerio JE, Chao S, Barnett GH. Laser interstitial thermal therapy for focal cerebral radiation necrosis: a case report and literature review. *Stereotactic and functional neurosurgery*. 2012; 90:192–200. [PubMed: 22678505]
5. Rao MS, Hargreaves EL, Khan AJ, Haffty BG, Danish SF. Magnetic resonance-guided laser ablation improves local control for postradiosurgery recurrence and/or radiation necrosis. *Neurosurgery*. 2014; 74:658–67. discussion 67. [PubMed: 24584138]
6. Larson PS, Starr PA, Bates G, Tansey L, Richardson RM, Martin AJ. An optimized system for interventional magnetic resonance imaging-guided stereotactic surgery: preliminary evaluation of targeting accuracy. *Neurosurgery*. 2012; 70:95–103. discussion. [PubMed: 21796000]
7. Jethwa PR, Barrese JC, Gowda A, Shetty A, Danish SF. Magnetic resonance thermometry-guided laser-induced thermal therapy for intracranial neoplasms: initial experience. *Neurosurgery*. 2012; 71:133–44. 44–5. [PubMed: 22653396]
8. Ivan ME, Yarlagadda J, Saxena AP, Martin AJ, Starr PA, Sootsman WK, et al. Brain shift during bur hole-based procedures using interventional MRI. *Journal of neurosurgery*. 2014; 121:149–60. [PubMed: 24785326]
9. Elias WJ, Fu KM, Frysinger RC. Cortical and subcortical brain shift during stereotactic procedures. *Journal of neurosurgery*. 2007; 107:983–8. [PubMed: 17977271]
10. Chittiboina P, Heiss JD, Lonser RR. Accuracy of direct magnetic resonance imaging-guided placement of drug infusion cannulae. *Journal of neurosurgery*. 2015; 1–7. [PubMed: 26473790]
11. Chabardes S, Isnard S, Castrioto A, Oddoux M, Fraix V, Carlucci L, et al. Surgical implantation of STN-DBS leads using intraoperative MRI guidance: technique, accuracy, and clinical benefit at 1-year follow-up. *Acta neurochirurgica*. 2015; 157:729–37. [PubMed: 25788414]
12. Starr PA, Markun LC, Larson PS, Volz MM, Martin AJ, Ostrem JL. Interventional MRI-guided deep brain stimulation in pediatric dystonia: first experience with the ClearPoint system. *Journal of neurosurgery Pediatrics*. 2014; 14:400–8. [PubMed: 25084088]
13. Missios S, Bekelis K, Barnett GH. Renaissance of laser interstitial thermal ablation. *Neurosurgical focus*. 2015; 38:E13. [PubMed: 25727222]
14. Rahmathulla G, Recinos PF, Kamian K, Mohammadi AM, Ahluwalia MS, Barnett GH. MRI-guided laser interstitial thermal therapy in neuro-oncology: a review of its current clinical applications. *Oncology*. 2014; 87:67–82. [PubMed: 24994550]
15. Torres-Reveron J, Tomasiewicz HC, Shetty A, Amankulor NM, Chiang VL. Stereotactic laser induced thermotherapy (LITT): a novel treatment for brain lesions regrowing after radiosurgery. *Journal of neuro-oncology*. 2013; 113:495–503. [PubMed: 23677747]
16. Fabiano AJ, Alberico RA. Laser-interstitial thermal therapy for refractory cerebral edema from post-radiosurgery metastasis. *World neurosurgery*. 2014; 81:652 e1–4. [PubMed: 24140996]

17. Carpentier A, McNichols RJ, Stafford RJ, Guichard JP, Reizine D, Delalogue S, et al. Laser thermal therapy: real-time MRI-guided and computer-controlled procedures for metastatic brain tumors. *Lasers in surgery and medicine*. 2011; 43:943–50. [PubMed: 22109661]
18. Carpentier A, Chauvet D, Reina V, Beccaria K, Leclercq D, McNichols RJ, et al. MR-guided laser-induced thermal therapy (LITT) for recurrent glioblastomas. *Lasers in surgery and medicine*. 2012; 44:361–8. [PubMed: 22488658]

Figure 1. Real-time MRI demonstrating cyst aspiration and laser ablation: a) axial T1 with ceramic stylet abutting the wall prior to cyst aspiration. b) axial T1 with biopsy needle after cyst aspiration. c) axial T1 with the needle removed demonstrating complete aspiration of cyst contents. d) Axial T1 with laser fiber inside the lesion. e) axial T1 with Gad post laser ablation

Figure 2.

Contrasted-enhanced MRI of the Case 1 lesion: a) preoperative b) 12 weeks postoperative c) 15 weeks postoperative d) 22 weeks postoperative Fluid-attenuated Inversion Recovery (FLAIR)- MRI images of Case 1: e)preoperative f) 12 weeks postoperative g) 15 weeks postoperative h) 22 weeks postoperative

Figure 3.
Contrasted-enhanced MRI of the Case 2 lesion: a) preoperative b) 2 weeks postoperative c)
8 weeks postoperative.

Figure 4. Fluid-attenuated Inversion Recovery (FLAIR)- MRI images of Case 2: a)preoperative b) 2 weeks postoperative c) 8 weeks postoperative