Stereotactic Laser Ablation (SLA) followed by consolidation stereotactic radiosurgery (cSRS) as treatment for brain metastasis that recurred locally after initial radiosurgery (BMRS): a multi-institutional experience

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Abstract

Introduction The optimal treatment paradigm for brain metastasis that recurses locally after initial radiosurgery remains an area of active investigation. Here, we report outcomes for patients with BMRS treated with stereotactic laser ablation (SLA, also known as laser interstitial thermal therapy, LITT) followed by consolidation radiosurgery.

Methods Clinical outcomes of 20 patients with 21 histologically confirmed BMRS treated with SLA followed by consolidation SRS and > 6 months follow-up were collected retrospectively across three participating institutions.

Results Consolidation SRS (5 Gy × 5 or 6 Gy × 5) was carried out 16–73 days (median of 26 days) post-SLA in patients with BMRS. There were no new neurological deficits after SLA/cSRS. While 3/21 (14.3%) patients suffered temporary Karnofsky Performance Score (KPS) decline after SLA, no KPS decline was observed after cSRS. There were no 30-day mortalities or wound complications. Two patients required readmission within 30 days of cSRS (severe headache that resolved with steroid therapy (n = 1) and new onset seizure (n = 1)). With a median follow-up of 228 days (range: 178–1367 days), the local control rate at 6 and 12 months (LC6, LC12) was 100%. All showed diminished FLAIR volume surrounding the SLA/cSRS treated BMRS at the six-month follow-up; none of the patients required steroid for symptoms attributable to these BMRS. These results compare favorably to the available literature for repeat SRS or SLA-only treatment of BMRS.

Conclusions This multi-institutional experience supports further investigations of SLA/cSRS as a treatment strategy for BMRS.

Keywords Brain metastasis (BM) · Stereotactic laser ablation (SLA) · Laser interstitial thermal therapy (LITT) · Stereotactic radiosurgery (SRS)
Introduction

In independent randomized clinical trials, ~30% of brain metastases (BM) recur locally twelve months after treatment with radiosurgery [1]. The local recurrence rate is higher for BM intrinsically resistant to radiation [2, 3] or those with up-regulated DNA repair capacity [4–6]. There is currently no consensus on the optimal treatment strategy for brain metastases that recur after radiosurgery (BMRS). Repeat radiosurgery to BMRS is often employed in this context. However, such treatments are associated with an increased risk for neurologic decline secondary to adverse radiation effects, including radiation necrosis [7, 8]. These repeat radiation-associated deleterious effects can compromise the patient’s quality of life, delay systemic therapy, or necessitate surgical interventions [8, 9]. Moreover, up to 30% of repeat radiosurgery cases fail to achieve local control of BMRS [10].

Stereotactic laser ablation (SLA, also known as laser interstitial thermal therapy (LITT)) refers to a procedure whereby a fiberoptic laser probe is stereotactically inserted into a target abnormality in the brain or spine [11]. Activation of the probe induces hyperthermia within the target tissue, causing coagulative necrosis [11]. While SLA has been employed as a treatment for newly diagnosed BM, the clinical outcomes have been disappointing, with 30–50% local failure within twelve months of treatment [12–15]. Despite these results, there are reasons to consider SLA in combination with repeat radiosurgery as a treatment strategy for BMRS. First, there is sound laboratory science [16], preclinical [17], and clinical data [18–20] suggesting synergy in the anti-tumoral effects of hyperthermia and radiation. This synergy warrants consideration given the radiation resistant nature of BMRS. Second, SLA is a highly effective treatment for radiosurgery associated adverse radiation effects [14, 21, 22]. The available literature suggests that SLA inactivates immune cells and/or denatures inflammatory cytokines that mediate radiation-induced injuries [23]. Thus, the addition of SLA to repeat SRS can potentially mitigate the risk of subsequent adverse radiation effects.

In this context, we previously reported results from four BMRS patients treated with SLA followed by cSRS in 2016 [13]. Here, we report a larger multi-institutional experience examining the efficacy and safety profile of this treatment strategy for patients with >6 months of follow-up.

Methods

Patient population and data collection

This study was a multi-institutional, retrospective case series of patients who underwent SLA/cSRS between 2012 and 2020 for needle biopsy-confirmed brain metastasis recurrence after initial SRS treatment. Each of the participating institutions holds an approved IRB for this retrospective review. To characterize long-term effects of SLA/cSRS, we included only patients who had >6 months of follow-up data. All diagnoses of BMRS were made based on tissue diagnosis. Demographic and clinical data collected from the electronic record system included: sex, age at BMRS presentation, primary tumor subtype, tumor location, tumor volume, prior whole brain radiation therapy (WBRT), 30-day readmission, and SLA/cSRS associated morbidity (including radiation induced adverse effects). Baseline and post-SLA/cSRS Karnofsky Performance Status (KPS) and steroid use were collected for all patients at the time of BMRS diagnosis, one day post-SLA, one-month post-cSRS, and at subsequent follow-up visits. As per standard of care, patients were seen by the neurosurgeon ~2 weeks after SLA. Patients were seen by the radiation oncologist one month after cSRS and every 2–3 months thereafter. Follow-up duration was calculated from the time of cSRS. Overall Survival was calculated from the time of initial cancer diagnosis. Local control was calculated from the time of SLA treatment. None of the patients underwent concurrent immunotherapy treatment or received bevacizumab treatment during the course of this study.

MRI analysis

All patients underwent surveillance MRI every 2–3 months unless imaging or clinical findings warranted shorter interval follow-up. MRIs from each site were reviewed by two independent assessors. MRIs were obtained before and after treatment and imported into the Brainlab (Brainlab AG, Munich, Germany) iPlan Cranial 3.0 software or 3D Slicer (www.slicer.org) or imageJ (https://imagej.nih.gov/ij/) to determine maximal diameter and volume. The volume of contrast enhancing (CE) and FLAIR volumes surrounding the SLA/cSRS treated lesion were recorded immediately post-SLA and for each imaging follow-up. Local control (LC) was defined using modified RANO-BM criteria [24], as described below. We adopted the local failure criteria of RANO-BM (increase of >20% in the sum of the longest distance relative to nadir). However, since the SLA ablated region often shows expansion of...
contrast enhancement immediately post-procedure that resolves in the subsequent one to three months [25], we classified local failure after SLA only if RANO-BM criteria were met on two sequential MRIs that were more than three months apart (similar to immunotherapy RANO [26]). Lesions demonstrating such local failure were surgically excised for definitive tissue diagnosis.

**SLA and consolidation SRS**

BMRS patients considered for SLA/cSRS were reviewed at a multi-disciplinary board consisting of representatives from neuro-oncology, neurosurgery, radiation oncology, neuroradiology, and neuropathology. As such, the decision to treat with SLA-cSRS factored into the neuro-oncologist’s assessment of whether the patient would benefit from immunotherapy. None of the study patients were treated with immunotherapy prior to SLA/cSRS. Informed consents were obtained by neurosurgery and radiation oncology. The SLA procedures were performed as previously described [13]. For lesions treated with the NeuroBlate system (Monteris Medical Inc., Plymouth, MN, USA), extent of ablation was assessed based on CE region covered by the blue contour line (equivalent to tissue heating to 43 °C for > 10 min) [27]. For lesions treated with the Visualase system (Medtronics Inc., Minneapolis, MN), extent of ablation was assessed based on CE region covered by orange pixels (equivalent to tissue injury achieved at 60 °C).

Consolidation SRS was carried out approximately one to two months after the SLA and delivered through five consecutive fractions of 5 Gy or 6 Gy. Hypofractionated SRS was employed given that (1) the target lesions had previously been treated with > 18 Gy of SRS within the past 12 months and (2) SLA ablation cavities are typically larger than the target lesions, warranting concerns of radiation injury with single session SRS (28). SRS treatment was performed using either the Leksell Gamma Knife Icon (Elekta Instrument AB, Stockholm, Sweden) or the TrueBeam linear accelerator (Varian Medical Systems, Palo Alto, California). The planned target volume (PTV) was defined as the entirety of the ablated lesion, including regions of contrast enhancement (Fig. 1). For Icon-treated patients, PTV was prescribed to the 50% isodose. For the TrueBeam treated patients, PTV was prescribed to the 90% isodose.

**Literature search and statistical analysis**

The literature search was performed in June 2021, reviewed by the first author (IP) and senior author (CCC). For assessment of the published literature for SLA as treatment for BMRS, we repeated a published strategy that was implemented in 2019 by Loi et al. [29]. We identified four publications bearing pertinent local control and adverse radiation effect information following repeat, hypo-fractionated radiosurgery of BMRS.

GraphPad Prism Version 9 was used for all statistical analyses (GraphPad Software, San Diego, California). Categorical and continuous data are described as frequency (percentage) and median (interquartile range), respectively. Fisher’s exact test and the Mann–Whitney U-test were used for the univariate analyses of categorical and continuous data, respectively.

**Results**

**Study population**

The study cohort consists of six male and thirteen female patients. All diagnoses of BMRS were made based on tissue diagnosis. The median age of the cohort was 64 years old (range: 34–74). The histology of the BMs treated included: lung (n = 6), breast (n = 5), gastrointestinal (n = 3), melanoma (n = 2), laryngeal (n = 1), urothelial (n = 1), ovarian (n = 1), and undifferentiated (n = 1). The median CE tumor volume at the time of BMRS presentation was 5.6 cm³ (range: 3.1–34.2 cm³). All lesions were deemed by the treating neurosurgeon to be difficult to access surgically based on the MRI findings or deemed poor candidates for craniotomy. All patients underwent stereotactic needle biopsies prior to SLA (during the same procedure), with pathology confirming BMRS. All lesions had received 18–21 Gy of single fraction SRS at the time of initial diagnosis. The location of the lesions as well as other demographic and tumor characteristics are shown in Table 1. Except for patient 11, who was treated with WBRT two years prior to the initial SRS, none of the patients had received prior WBRT. Patient 4 underwent two separate SLA/cSRS for lesions located in the frontal and parietal lobe, identified approximately six months apart. All other patients underwent a single SLA/cSRS. All patients were treated with corticosteroids following the BMRS diagnosis and prior to SLA. All patients underwent subsequent systemic therapy.

**SLA/cSRS and post-operative course**

The volume of BMRS CE ablated was as defined in the Methods section. All patients underwent a needle biopsy for definitive tissue diagnosis prior to SLA, during the same procedure. Seventy-three to 100% of the BMRS CE volume was ablated at the time of SLA (Table 2). There were...
no new neurologic deficits immediately post-SLA or at the one-month follow-up. Consistent with previously published SLA series [14, 30], the KPS of 80% (16/20) of the patients remained unchanged after SLA. Three of 20 patients (15%) suffered a temporary decline in KPS post-SLA, while 1/20 (5%) showed an improvement in KPS. All patients were discharged home within two days of SLA. There was no operative morbidity or mortality attributable to the SLA.

Consolidation SRS was performed one to two months after SLA and was performed as an outpatient procedure. The median time from SLA to cSRS was 26 days (range 16–73 days). The median BMRS CE volume for this series was 5.6 cm³. cSRS was targeted to the post-ablative region, including the rim of contrast enhancement (Fig. 1). Eighteen of 20 (90%) of the patients were treated with a 5 Gy × 5 consecutive day regimen, and 2 patients

Fig. 1 Representations consolidation stereotactic radiosurgery (cSRS) plans. Hypo-fractionated radiosurgery (5 Gy × 5) targeting the post-ablative region, including the rim of contrast enhancement was delivered. Radiosurgery plans for patient 8 (Fig. 2A) and 9 (Fig. 2B) are shown.
Table 1  Patient demographics and lesion characteristics

| Patient | Age  | Sex | Pre-SLA KPS | Pre-SLA corticosteroid | Primary tumor | Location | Lesion volume (cm³) | Prior WBRT | Prior SRS dose (Gy) | Time from prior SRS (d) | SRS modality |
|---------|------|-----|-------------|------------------------|---------------|----------|---------------------|------------|---------------------|--------------------------|--------------|
| 1       | 67   | F   | 90          | Y                      | Colon         | L thalamus | 3.4                 | N          | 20                  | 161                      | LINAC        |
| 2       | 58   | F   | 100         | Y                      | Melanoma      | L thalamus | 4.5                 | N          | 20                  | 113                      | LINAC        |
| 3       | 54   | F   | 90          | Y                      | Breast        | R thalamus | 5.5                 | N          | 20                  | 220                      | LINAC        |
| 4*      | 60   | F   | 80          | Y                      | Breast        | L frontal  | 3.2                 | N          | 20                  | 154                      | LINAC        |
| 4*      | 60   | F   | 80          | Y                      | Breast        | L parietal | 4.9                 | N          | 20                  | 360                      | LINAC        |
| 5       | 73   | M   | 100         | Y                      | Lung          | R temporal | 4.2                 | N          | 20                  | 274                      | LINAC        |
| 6       | 69   | F   | 100         | Y                      | Ovarian       | L cerebellar | 15.9               | N          | 18                  | 134                      | GK           |
| 7       | 73   | F   | 70          | Y                      | Urothelial    | L peri-atrial | 35                 | N          | 18                  | 275                      | GK           |
| 8       | 53   | F   | 100         | Y                      | Esophageal    | L temporal | 4.5                 | N          | 20                  | 353                      | GK           |
| 9       | 34   | M   | 70          | Y                      | Melanoma      | R peri-atrial | 34.2               | N          | 18                  | 241                      | GK           |
| 10      | 66   | F   | 80          | Y                      | Breast        | L parietal | 27.1                | N          | 18                  | 304                      | GK           |
| 11      | 66   | F   | 60          | Y                      | Lung          | L cingulate | 25.7               | Y          | 18                  | 203                      | GK           |
| 12      | 58   | F   | 90          | Y                      | SCC larynx    | R parietal | 3.6                 | N          | 20                  | 212                      | GK           |
| 13      | 74   | F   | 80          | Y                      | Lung          | L parietal | 14                  | N          | 18                  | 468                      | GK           |
| 14      | 64   | F   | 60          | Y                      | Breast        | L parietal | 5.6                 | N          | 20                  | 502                      | GK           |
| 15      | 57   | M   | 90          | Y                      | Colon         | L cerebellar | 15                | N          | 18                  | 135                      | GK           |
| 16      | 56   | F   | 80          | Y                      | Lung          | L parietal | 21                  | N          | 18                  | 110                      | GK           |
| 17      | 60   | M   | 80          | Y                      | Esophageal    | R parietal | 8.9                 | N          | 18                  | 178                      | GK           |
| 18      | 56   | F   | 80          | Y                      | Undifferentiated | L temporal | 3.1               | N          | 20                  | 200                      | GK           |
| 19      | 69   | M   | 90          | Y                      | Lung          | L parietal | 4.3                 | N          | 20                  | 624                      | GK           |
| 20      | 69   | M   | 80          | Y                      | Lung          | L occipital | 6                  | N          | 18                  | 149                      | GK           |

D Days, F Female, GK Gamma Knife, Gy Gray, KPS Karnofsky performance score prior to SLA, L Left, LINAC Linear accelerator, M Male, N No, R Right, SCC Squamous cell carcinoma, WBRT prior Whole brain radiation therapy, Y Yes

*Two lesions treated in the same patient
were treated with a 6 Gy × 5 consecutive day regimen. By the time of cSRS, the three patients who suffered a KPS decline after SLA had recovered to their baseline KPS. All KPS remained stable at one-month post-cSRS. There were no procedural morbidities related to SLA. There were two 30-day post-SLA readmissions. Patient 7 presented with an incapacitating headache in the context of corticosteroid dose tapering. The headache resolved after a temporary re-escalation of corticosteroid treatment. Patient 11 presented with a new-onset seizure and was placed on levetiracetam and a short course of corticosteroid. Of note, patient 11 is the only patient in this series who received WBRT prior to initial SRS. Head CT’s for both patients ruled out intra-tumoral hemorrhage but showed increased peri-BMRS hypodensity. Both patients were discharged by hospital day 2. Of note, both admitted patients harbored BMRS that were larger than the median volume of the tumors treated in this series. The median BMRS CE volume for this series was 5.6 cm³; the BMRS CE volumes for patients 7 and 11 were 35 cm³ and 25.7 cm³, respectively.

### Imaging and clinical follow-up

Follow-up duration and local control was calculated from the time of cSRS. The median follow-up for this cohort was 228 days (range: 183–1367 days). Local control was calculated from the time of SLA. We did not detect notable changes in the ablation volume between the time of the SLA and the subsequent SRS. There were two treatment failures that occurred 899 and 649 days after SLA/cSRS (patients 13 and 14, Fig. 2A). Overall survival was calculated from the time of the cancer diagnosis. The median survival for this study cohort was 378 days (Fig. 2B). Six-month follow-up was available for all patients (Table 3). At six months, the CE volumes for all SLA/cSRS treated lesions were decreased relative to the time of SLA. Similarly, the peri-CE FLAIR volumes for all treated lesions decreased relative to the initial BMRS presentation. Six months after SLA/cSRS, live out of 20 (25%) patients continued to be treated with corticosteroid. Based on both clinical documentation and surveillance MR imaging, the corticosteroid was used to treat symptoms related to other

#### Table 2: Stereotactic Laser Ablation and consolidation stereotactic radiosurgery (SLA/cSRS)

| Patient | % Of lesion ablated | Days to cSRS | Laser system | cSRS | cSRS modality |
|---------|---------------------|-------------|--------------|------|--------------|
| 1       | 77.4                | 30          | Monteris     | 5 Gy × 5 | LINAC        |
| 2       | 74.6                | 23          | Monteris     | 5 Gy × 5 | LINAC        |
| 3       | 98.2                | 23          | Monteris     | 5 Gy × 5 | LINAC        |
| 4*      | 92.4                | 30          | Monteris     | 5 Gy × 5 | LINAC        |
| 4*      | 100                 | 37          | Monteris     | 5 Gy × 5 | LINAC        |
| 5       | 100                 | 23          | Monteris     | 5 Gy × 5 | LINAC        |
| 6       | 100                 | 26          | Visualase    | 5 Gy × 5 | GK           |
| 7       | 73                  | 16          | Visualase    | 5 Gy × 5 | GK           |
| 8       | 100                 | 19          | Visualase    | 5 Gy × 5 | GK           |
| 9       | 97                  | 30          | Visualase    | 5 Gy × 5 | GK           |
| 10      | 100                 | 40          | Visualase    | 5 Gy × 5 | GK           |
| 11      | 100                 | 27          | Visualase    | 5 Gy × 5 | GK           |
| 12      | 100                 | 35          | Monteris     | 5 Gy × 5 | GK           |
| 13      | 92.4                | 27          | Monteris     | 6 Gy × 5 | GK           |
| 14      | 97.8                | 24          | Monteris     | 5 Gy × 5 | GK           |
| 15      | 99.2                | 20          | Monteris     | 5 Gy × 5 | GK           |
| 16      | 100                 | 25          | Monteris     | 6 Gy × 5 | GK           |
| 17      | 99.3                | 20          | Monteris     | 5 Gy × 5 | GK           |
| 18      | 100                 | 73          | Monteris     | 5 Gy × 5 | GK           |
| 19      | 90                  | 24          | Monteris     | 5 Gy × 5 | GK           |
| 20      | 98                  | 36          | Monteris     | 5 Gy × 5 | GK           |

\(c\text{SRS}\) Consolidation stereotactic radiosurgery (dose × fractionation), \textit{Days to cSRS} Days between stereotactic laser ablation and cSRS, \textit{Gy} Gray, \textit{GK} Gamma Knife, \textit{LINAC} Linear Accelerator, \textit{SLA} Stereotactic laser ablation, % Of lesion ablated: Percentage of contrast enhancing region of BMRS covered by blue contour line (Monteris) or orange pixel (Visualase)

*Two lesions treated in the same patient
BM and unrelated to the SLA/cSRS treated BMRS. For instance, corticosteroid was used to treat left sided hemiparesis secondary to a BM located in the right motor strip for patient 7. Given that the SLA-cSRS treated lesion was located in the left peri-atrial region, we believe that corticosteroid was used to treat symptoms related to the right motor strip lesion rather than the SLA-cSRS treated lesion.

Twelve-month follow-up was available for five patients. Local control at twelve months (LC₁₂) was 100%, and the peri-CE FLAIR volumes remained decreased for the treated lesions relative to the time of SLA. None of the patients required corticosteroid treatment. Two illustrative cases are shown in Figs. 3 and 4. Figure 3 shows the evolution of CE and FLAIR after SLA/cSRS in the longest surviving patient (patient 8) whose BMRS remained controlled 19 months after SLA/cSRS. Figure 4 shows the evolution of CE and FLAIR after SLA/cSRS in a patient (patient 14) whose BMRS recurred 649 days (~21 months) after SLA/cSRS.

**Literature of efficacy of repeat radiosurgery and stereotactic laser ablation (SLA)**

We wished to compare our case series to the published literature for salvage monotherapy using either SLA or repeat SRS for BMRS. The literature search for SLA treated BMRS (see Methods for the search algorithm) yielded one study that reported a local control of 61% at 4.6 months [13]. Broadening our search to include case series that include a mixture of pathology confirmed BMRS, newly diagnosed BMRS, and radiation necrosis, we identified two additional studies. The study by Ahluwalia et al. consisted of 22 pathology-confirmed BMRS and 22 radiation necrosis. Only three-month local control was reported (LC₃), and the reported LC₃ was 37% [14]. The second study by Bastos et al. consisted of 46 BMRS and 5 newly diagnosed BM. The reported LC₁₂ was 69.6% for this series [15] (Table 4a).

Since our cSRS used a hypo-fractionated regimen, we focused our literature search to identify articles that studied the efficacy and safety of hypo-fractionated repeat SRS as a treatment for BMRS. We identified four such articles (Table 4b) [10, 31–33]. The reported local control at 12 months ranged 70–83%, with 13–19% of the patients suffering from symptomatic adverse radiation effects after repeat radiation. Similar results were reported for single session SRS (Supplemental Table 1) [7, 8, 34–40].

The LC₁₂ of 100% and 0% adverse radiation effects at 6 and 12 months after SLA/cSRS treatment of BMRS in our series compares favorably to these reported results.

**Discussion**

Our literature search suggests that the treatment of BMRS remains an understudied area in neuro-oncology. The overall poor survival of BM patients [41] likely contributes to this limited literature. Many BM patients die before developing recurrence. However, as newer classes of systemic therapies emerge and improve cancer survival, there will be a greater need for meaningful therapeutic interventions in the treatment of BMRS [42]. Here, we retrospectively analyzed a multi-institutional experience that employed SLA/cSRS as a treatment strategy for BMRS. This study builds on and expands on the clinical outcome of the four patients reported in our 2016 study [13]. By expanding the number of patients treated as well as lengthening the follow-up duration (to >6 months), we provide data to support the safety profile and durable efficacy of SLA/cSRS as treatment for BMRS.

Our current study suggests that the procedural safety profile of SLA/cSRS is comparable to that reported for SLA alone [13, 14, 43]. Because of the limited BMRS literature and the small cohort in our study, we were unable to perform a meaningful, quantitative comparison between
the results of this study to the available literature. Qualitatively, the LC₆₆ and LC₁₂ of 100% after SLA/cSRS for tissue confirmed BMRS in our series compares favorably to the reported LC₁₂ of 69.6% [15] for SLA alone. Of note, this SLA study included a mixed population of BMRS and newly diagnosed BM, with the latter presumably more radiation sensitive than the former. The local control of BMRS by SLA/cSRS also compares favorably to the 70–83% reported for repeat hypo-fractionated SRS. These results should be interpreted with the following consideration. While it is unlikely that any practitioner would purposely treat non-recurrent BM with repeat radiosurgery, the imaging methods available for assessing recurrent BM versus adverse radiation effects following radiosurgery remain imperfect [44]. As such, it is possible that a subset of the lesions thought to be BMRS on imaging may represent post-radiosurgery radiation effects. If so, the published study of BMRS without tissue diagnosis reports local control rates that may be artificially inflated [45]. In this context, it is notable that all BMRS in this series were confirmed by tissue. Another advantage of the SLA/cSRS treatment paradigm is highlighted by the absence of adverse radiation effects in our series compared to the 13–19% reported with repeat radiosurgery of BMRS. The neurologic sequelae of these adverse effects compromise the patient’s quality of life, requiring corticosteroid therapy, surgical therapy, or both. Additionally, immune suppression secondary to corticosteroid administration may compromise the efficacy of systemic therapies [46]. Moreover, the advent of immunotherapy and targeted therapy has increased the risk for SRS-associated adverse radiation effects [47, 48]. As many as one in five melanoma BM patients treated with nivolumab and ipilimumab suffers adverse radiation effects after SRS, requiring cessation of systemic therapy [48]. Minimizing the risk of such cessation has the potential to improve therapeutic efficacy of systemic therapy. In this context, the absence of adverse radiation effects in our SLA/cSRS series despite
Fig. 3 Sequential evolution of contrast enhancement and FLAIR volume (axial T1, axial FLAIR, coronal T1, sagittal T1, respectively from top to bottom) for representative SLA/cSRS treated lesion in patient 8. This patient’s BMRS remain controlled 19 months after SLA/cSRS. SRSi: initial SRS. BMRS was diagnosed one-year after the initial SRS. 3 m f/u: 3 months follow-up, 6 m f/u: 6 months follow-up, 19 m f/u: 19 months follow-up.

Fig. 4 Sequential evolution of local recurrence for patient 14. Contrast enhancement and FLAIR volume (axial T1, axial FLAIR, coronal T1, sagittal T1, respectively from top to bottom) demonstrate increase in contrast enhancement size and FLAIR volume at 22 months post SLA/cSRS. SRSi: Initial SRS. BMRS was diagnosed 32 months after the initial SRS. 3 m f/u: 3 months follow-up, 6 m f/u: 6 months follow-up, recurrence (22 m): tumor recurrence 22 months after SLA/cSRS.
repeat radiosurgery to the same lesion suggests that SLA may minimize the risk of adverse radiation effects, rendering the treatment strategy attractive.

The imaging findings after SLA-cSRS are complex and worth noting. MRIs performed immediately post-SLA typically show an expansion in CE volume, accompanied by an enlargement of the surrounding FLAIR [27, 43]. While many SLA-treated lesions show egg-shell contrast enhancement (Figs. 3 and 4), others exhibit more heterogeneous enhancement patterns [12, 13, 49]. These SLA-associated MR changes typically resolve one to three months post-SLA [12, 13, 43, 49]. As such, assessment of MRI at any single time after SLA, such as that described by RANO-BM [50], is inadequate for assessing tumor control after SLA. In this context, we modified the RANO-BM criteria to include the sequential surveillance MRIs, similar to that proposed for immunotherapy RANO (iRANO) [26]. We considered local failure only if the criteria for RANO-BM progression persisted on two MRIs > three months apart. The pilot data presented in our series support the utility of this proposed modification. Of the two cases (patient 13 and 14) that showed tumor progression at later time points based on the above proposed criteria, both underwent surgical resection, with specimens confirming tumor progression.

An important consideration in patient selection for SLA involves the volume of the BMRS. Post-SLA edema is a well-documented phenomenon that can lead to morbidities and mortalities [13, 43]. In this context, the larger lesions treated in this series involved patients with either cerebral atrophy or who had undergone previous surgical resections. The atrophy or previous resection reduce cerebral volume and increase capacity for tolerating post-SLA edema. Despite the cautions exercised in patient selection, two of the patients (patient 7 and 11) with larger BMRS suffered 30-day readmission after SLA/cSRS for symptoms attributable to treated BMRS. Patient 11’s prior history of WBRT further suggests that the cumulative radiation dose may compromise cerebral compliance and tolerance of post-SLA edema. As such, judicious consideration in patient selection and close follow-up of SLA/cSRS treated patients is warranted, especially for patients with larger tumor volumes or patients who have undergone multiple rounds of prior radiotherapy/SRS.

For the Visualase system, the criterion of thermal ablation is set at cumulative thermal injury that crosses the 60 °C threshold. For the Monteris system, the criterion is set at cumulative thermal injury equivalent to 43 °C exposure for 10 min. If one were to use the size of the contrast enhancing rim after laser ablation as a means to assess the extent of thermal injury, however, the Visualase and Monteris criteria seemed qualitatively comparable based on the senior author’s experience. Quantitative assessment of this observation is warranted but extends beyond the scope of the current paper. That said, we believe that our data support the main conclusion that either Visualase or Monteris ablation can be safely combined with cSRS.

As a retrospective analysis, our conclusions are subject to the influences of all forms of biases inherent within this study design [27]. Moreover, all BMRS presented in this series underwent SLA that achieved > 70% ablation of the contrast enhancing tumor volume. As such, the results reported here may not be applicable if such extent of ablation was not achieved. Additional limitations of our study include: heterogeneity in clinical practice of differing centers, the use of multiple laser ablation systems, variation in how “difficult to access” is determined

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| References | Number of patients | Local control |
|------------|--------------------|---------------|
| Ali et al. (2016) [13] | 23 | 61% at 4.6 months |
| Ahluwalia et al. (2018) [14] | 20 | 74% at 3 months |
| Bastos et al. (2020) [15] | 61 | 69.6% at 12 months |

A: Studies reporting stereotactic laser ablation as monotherapy for the treatment of brain metastasis that recurred locally after radiosurgery (BMRS). B: Studies reporting repeat hypofractionated radiosurgery as monotherapy for the treatment of BMRS. SRS Stereotactic radiosurgery, LC12 Local control at 12-month follow-up
by the surgeon, and the limited sample size. While we provide published incidence of adverse radiation effects post repeat SRS in our literature review, direct comparison of our results should be cautioned given that the criteria for adverse radiation effects differ between publications. Ultimately, a randomized control trial (RCT) will be needed to validate the results reported here. If the pilot safety and efficacy profiles reported here are recapitulated in a RCT, the results can contribute to a new standard of care for BMRS patients. While this case series focused exclusively on patients with recurrent BM, the approach should be applicable to other clinical contexts, including the treatment of BM with a high probability of SRS failure, such as larger volume melanoma BM in the upfront setting.

**Conclusion**

This multi-institutional experience provides pilot safety and efficacy data for hypo-fractionated SRS within two months of SLA treatment of BMRS and supports continued investigation of this treatment strategy. The results described here inform the design of future randomized clinical trials.

**Supplementary Information** The online version contains supplementary material available at https://doi.org/10.1007/s11060-021-03893-6.

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**Data availability** Data will be made available upon request as deemed appropriate by the corresponding author.

**Code availability** Not applicable.

**Declarations**

**Conflict of interest** The authors do not have any conflicts of interest to report.

**Ethical approval** This study was approved by the local IRB at each participating institution.

**Consent to participate** Consent for data collection was waived as this was a retrospective study.

**Consent for publication** Not applicable, no private health information is published in this manuscript.

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