SECOND-STAGE LASER ABLATION AT TUMOR MARGINS FOR TREATMENT OF GLIOBLASTOMA

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DISCLOSURES

NEITHER AUTHOR HAS ANY FINANCIAL DISCLOSURE OR CONFLICT OF INTEREST WITH THE PRESENTED MATERIAL IN THIS PRESENTATION
INTRODUCTION

GLIOBLASTOMA (GB) IS A UNIFORMLY FATAL CANCER OF GLIAL CELLS WITH AN OVERALL MEDIAN SURVIVAL OF ONLY 15 MONTHS, WITH 90% OF PATIENTS NOT LIVING BEYOND 5 YEARS.\textsuperscript{1} EVEN AFTER MANY ATTEMPTS AT OPTIMIZING THE TREATMENT OF GB, AN EFFECTIVE TREATMENT REMAINS ELUSIVE TO THIS DAY.

WE PROPOSE THAT MAXIMAL TUMOR ELIMINATION COULD BE ATTAINED BY SUPPLEMENTING STANDARD SURGICAL RESECTION WITH MRI-GUIDED LASER-INDUCED THERMOTHERAPY (LITT), A MINIMALLY-INVASIVE, HIGH-PRECISION APPROACH WHICH IS SAFE AND WELL-TOLERATED.\textsuperscript{2,3} MAXIMAL TUMOR CELL ELIMINATION USING LASER ABLATION WOULD BEST BE ATTAINED THROUGH TARGETING THE GB TUMOR MARGIN., THE SITE FROM WHICH 90% OF GB RECURRENCES ORIGINATE.\textsuperscript{4}

WE SOUGHT TO ASCERTAIN WHETHER THIS NOVEL, SECOND-STAGE ABLATION APPROACH WOULD BE SAFE AND TOLERABLE, AND WHETHER IT MAY FACILITATE MAXIMAL TUMOR ELIMINATION IN TWO TYPICAL GB CASES: ONE PATIENT WITH A LEFT FRONTAL GB LESION (PATIENT 1) AND ANOTHER PATIENT WITH A LEFT PARIETAL GB LESION (PATIENT 2).
METHODS

WITHIN TWO WEEKS OF CRANIOTOMIES FOR SUBTOTAL TUMOR RESECTION, BOTH PATIENTS UNDERWENT MRI-GUIDED LASER ABLATION OF THEIR TUMOR MARGIN USING THE MONTERIS NEUROBLATE® SYSTEM. THIS WAS FOLLOWED BY THE STUPP PROTOCOL OF RADIOTHERAPY AND CONCOMITANT AND ADJUVANT TEMOZOLOMIDE (TMZ). THE PATIENTS WERE CLOSELY MONITORED FOR ANY ADVERSE EVENTS DURING THE ABLATION, WITHIN 30 DAYS OF THE ABLATION, AND AT REGULAR FOLLOW-UP APPOINTMENTS THEREAFTER.

PATIENTS RECEIVED FOLLOW-UP APPOINTMENTS WITHIN 30 DAYS OF THE ABLATION, AND IN 2-3 MONTH INTERVALS THEREAFTER TO MONITOR FOR CLINICAL PROGRESSION OF THE DISEASE. MRIs OF THE BRAIN WITH AND WITHOUT CONTRAST WERE CONDUCTED FOR EACH PATIENT IN 2-3 MONTH INTERVALS TO MONITOR FOR RADIOGRAPHIC DISEASE RECURRENCE.

OVERALL SURVIVAL (OS) WAS MEASURED FROM THE TIME OF HISTOLOGICAL DIAGNOSIS TO THE TIME OF THE PATIENT’S DEATH. PROGRESSION-FREE SURVIVAL (PFS) WAS MEASURED FROM THE TIME OF HISTOLOGICAL DIAGNOSIS TO THE POINT AT WHICH TUMOR RECURRENCE WAS FIRST RADIOGRAPHICALLY DETECTED ON POST-ABLATION MRI.
RESULTS

PATIENT 1

PATHOLOGY RESULTS: PATHOLOGY REVEALED A LEFT-FRONTAL GB MASS CHARACTERIZED BY MGMT PROMOTER METHYLATION, AND THE ABSENCE OF AN IDH MUTATION CONSISTENT WITH "GLIOBLASTOMA, MGMT-METHYLATED, IDH WILD TYPE".

IMAGING- MRI RESULTS (T2 FLAIR- AXIAL)

1A- MRI AT TIME OF DIAGNOSIS- Heterogeneous, unifocal, ring-enhancing mass centered in the left basal ganglia was detected, with intrinsic T1 hyperintensity, gradient echo blooming, and prominent enhancing vessels traversing the mass.

1B- MRI POST-SURGICAL RESECTION- decreased size of a large necrotic hemorrhagic lesion in the left basal ganglia region with irregular rim enhancement, with moderate surrounding edema.

1C- MRI 1 MONTH POST-ABLACTION
Interval decrease in size of the left frontal lobe/basal ganglia lesion with some extension to the left medial temporal lobe. There is interval improvement in the midline shift to the right in degree of mass effect upon the adjacent sulci within the left frontal lobe.

FOLLOW-UP MRIs DONE AT OUTSIDE INSTITUTION (NOT SHOWN)
POST-OPERATIVE CLINICAL COURSE- PATIENT 1

- The patient recovered well from the ablation procedure, with favorable wound healing, and grossly normal cranial nerve, sensory and motor function at his first follow-up appointment 23 days post-ablation. The patient was noted to have a stitch abscess the day before his appointment. At this point, this patient had already commenced therapy as per the Stupp protocol.

- On follow-up appointments at 3 months, 5 months, and 7 months post-ablation, the patient maintained normal cranial nerve, cognitive, and motor function, complaining mainly of intermittent headaches and nausea, which eventually resolved.

- During the patient’s most recent follow-up 15-months post-ablation, the patient was still asymptomatic, with the exception of endorsing some short-term memory issues. Imaging done at an outside institution (not shown) exhibited no signs of radiographic GB recurrence. To this point, the patient’s disease still has not recurred, with no adverse events, indicating that this patient has tolerated the procedure well, and has surpassed the PFS and OS associated with standard care for his subtype of GBM.
PATIENT 2

PATHOLOGY RESULTS: PATHOLOGICAL ANALYSIS DETERMINED THE TISSUE MASS TO BE IDH1 WILD-TYPE BY IMMUNOHISTOCHEMISTRY, WITH MGMT PROMOTER NOT METHYLATED, AND A 1P19Q CO-DELETION WAS NOT PRESENT (IDH1 WILD TYPE, MGMT-UNMETHYLATED)

IMAGING- MRI RESULTS (T2 FLAIR- AXIAL)

2A- MRI AT TIME OF DIAGNOSIS- Large contrast enhancing intra-axial mass in the left parietal lobe with associated mass effect
2B- MRI POST-SURGICAL RESECTION- persistent enhancement along the inferolateral margin of the surgical cavity, with extensive peritumoral edema, suspicious for residual neoplasm.
2C- MRI 1 MONTH POST-ABLATION - Stable surrounding restricted diffusion representing evolving postoperative ischemic changes. No signs of tumor recurrence
2D- MRI 7.5 MONTHS POST ABLATION INDICATING FIRST SIGN OF TUMOR RECURRENCE- There is increase in nodular contrast enhancement in the left parasagittal parietal lobe at the site of the known tumor, consistent with tumor recurrence
(ALL PRIOR MRIs BETWEEN 1-7.5 MONTHS (NOT SHOWN) SHOWED NO SIGN OF RADIOGRAPHIC DISEASE)
POST-OPERATIVE CLINICAL COURSE- PATIENT 2

- THIS PATIENT’S POSTOPERATIVE COURSE 1 MONTH POST-ABLATION WAS NOTABLE ONLY FOR FOOT DROP (SUCCESSFULLY ADDRESSED WITH PHYSICAL THERAPY) AND PERSISTENT RIGHT LOWER EXTREMITY WEAKNESS, WHICH IMPROVED IN SUBSEQUENT FOLLOW-UP APPOINTMENTS, AT 2.5, 4.5, AND 5.5 MONTHS FOLLOWING THE ABLATION. ALL CRANIAL NERVE AND COGNITIVE, AND SENSORY FUNCTION WERE GROSSLY NORMAL POST-ABLATION.

- THE PATIENT EXHIBITED RADIOGRAPHIC EVIDENCE OF SUBTLE TUMOR PROGRESSION ON MRI DONE 7.5 MONTHS POST-ABLATION (IMAGE 2D). AT THAT TIME, THE PATIENT HAD JUST COMPLETED HIS 5TH CYCLE OF CHEMOTHERAPY. THE PATIENT WAS CLINICALLY STABLE, WITH GROSSLY NORMAL COGNITIVE, MOTOR, CRANIAL NERVE FUNCTION, AND GAIT. GIVEN THE RADIOGRAPHIC RECURRENCE OF HIS GB, HE UNDERWENT A LEFT-PARIETAL CRANIOTOMY FOR GROSS-TOTAL RESECTION OF THE RECURRENT NEOPLASM, WITH NO COMPLICATIONS NOTED DURING THE PROCEDURE.

- WITH A PFS OF 7.5 MONTHS, THIS PATIENT SURPASSED THE 6.3 MONTH PFS ASSOCIATED WITH STANDARD CARE FOR GB CHARACTERIZED BY IDH WILD-TYPE AND NON-METHYLATED MGMT. MOREOVER, THIS PATIENT IS STILL ALIVE, AFTER 13 MONTHS FOLLOWING HIS GB DIAGNOSIS.
DISCUSSION

- THROUGH USING ABLATION TO BURN THE TUMOR MARGIN, FROM WHICH RESIDUAL GLIOMA CELLS INVARIABLY REPOPULATE AND MIGRATE INTO ADJACENT BRAIN PARENCHYMA, WE POSIT THAT THIS WOULD FACILITATE GREATER ELIMINATION OF TUMOR CELLS.

- IF RECEIVING STANDARD-OF-CARE, PATIENT 1 (IDH WILD-TYPE/MGMT METHYLATED), WOULD HAVE AN ESTIMATED SURVIVAL OF 15.5 MONTHS AND A PFS OF 9.4 MONTHS. PATIENT 2 (IDH WILD-TYPE/MGMT UNMETHYLATED) WOULD HAVE AN ESTIMATED SURVIVAL OF 11.1 MONTHS, AND A PFS OF 6.3 MONTHS.5

- BOTH PATIENTS TOLERATED THE ABLATION WELL, WITH NO NOTABLE LONG-TERM COMPLICATIONS OF THE PROCEDURE ITSELF. THE MRIs ABOVE INDICATED EFFECTIVE TUMOR CELL ABLATION USING SECOND-STAGE LASER ABLATION.

- MOREOVER, THEIR OS AND PFS RESULTS WERE FAVORABLE. PATIENT 1, WHEN LAST SEEN 15 MONTHS AFTER HIS DIAGNOSIS AND ABLATION, STILL HAD NO RADIOGRAPHIC SIGNS OF TUMOR RECURRENT OR ANY NOTABLE CLINICAL COMPLICATIONS. PATIENT 2 HAD A PFS OF 7.5 MONTHS, AND IS STILL ALIVE, AFTER 13 MONTHS FOLLOWING HIS GB DIAGNOSIS. BOTH PATIENTS SURPASSED THE PFS AND OS ASSOCIATED WITH STANDARD CARE BASED ON THEIR RESPECTIVE IDH/MGMT STATUS.
SUMMARY POINTS

- THE CLINICAL AND RADIOGRAPHIC RESULTS IN THESE TWO PATIENTS INDICATE THAT THE SECOND-STAGE LASER ABLATION WAS A SAFE AND WELL-TOLERATED PROCEDURE FOR GB PATIENTS.

- RADIOGRAPHIC RESULTS INDICATED EFFECTIVE TUMOR ELIMINATION VIA SECOND-STAGE LASER ABLATION.

- THE PROCEDURE YIELDED BETTER OUTCOMES FOR THESE TWO GB PATIENTS IN TERMS OF OVERALL SURVIVAL, PROGRESSION-FREE SURVIVAL, AND IMPROVEMENTS IN NEUROLOGICAL FUNCTION THAN THE STANDARD-OF-CARE TREATMENT APPROACH FOR GB.

- THERE IS THE INHERENT LIMITATION THAT THIS PROCEDURE HAS ONLY BEEN DONE IN A VERY SMALL NUMBER OF PATIENTS. FURTHER STUDIES WILL BE NEEDED TO SUBSTANTIATE THE SAFETY AND EFFECTIVENESS OF SECOND-STAGE LASER ABLATION OF TUMOR MARGINS IN TREATING GB PATIENTS.

- HOWEVER, THE RESULTS SEEN IN THE PATIENTS OF THIS CASE REPORT MAY SET THE PRECEDENT FOR A NOVEL APPROACH WHICH MAY IMPROVE TREATMENT AND OUTCOMES IN PATIENTS WHO CONTINUE TO SUFFER FROM WHAT REMAINS A LETHAL AND INCURABLE FORM OF CANCER IN GB.