OTHR-12. THE DEVELOPMENT OF MACHINE LEARNING ALGORITHMS FOR THE DIFFERENTIATION OF GLIOMA AND BRAIN METASTASES – A SYSTEMATIC REVIEW

Waverly Rose Brim1, Leon Jekel1, Gabriel Cassinelli Petersen1, Faryar Afshari2, Tal Zeevi1, Sam Parnes1, Khaled Boushabarah1, MingDe Lin1, Jin Cui1, Alexandria Brackett1, Ayaj Mahajan1, Michele Johnson1, Amit Mahajan1, Mariam Aboain1; 1Brain Tumor Research Group - Department of Radiology & Biomedical Imaging, Yale School of Medicine, New Haven, CT, USA; 2Visage Imaging, San Diego, CA, USA. 1Harvey Cashing/John Hay Whitney Medical Library, Yale University, New Haven, CT, USA

PURPOSE: Machine learning, surgical planning, and therapeutic decisions are significantly different for brain metastases versus gliomas. Machine learning (ML) algorithms have been developed to differentiate these pathologies. We performed a systematic review to characterize ML methods and to evaluate their accuracy. METHODS: Studies on the application of machine learning in neuro-oncology were searched in Ovid Embase, Ovid MEDLINE, Cochrane trials (CENTRAL) and Web of science core-collection. A search strategy was designed in compliance with a clinical librarian and confirmed by a second librarian. The search strategy comprised of controlled vocabulary including artificial intelligence, machine learning, deep learning, magnetic resonance imaging, and glioma. The initial search was performed in October 2020 and then updated in February 2021. Candidate articles were screened in Covidence by at least two reviewers each. A final analysis was conducted in agreement using a checklist assessment tool similar to CLAIMS. RESULTS: Twenty-nine articles were used for data extraction. Four articles specified model development for solitary brain metastases. Classical ML (cML) algorithms represented 85% of models used, with Deep Learning (DL) accounted for the ML algorithms combined with an average accuracy, sensitivity, and specificity of 82%, 78%, 88%, respectively; DL performed 84%, 79%, 81%. The support vector machine (SVM) algorithm was the most common used cML model in the literature and convolutional neural networks (CNN) were standard for DL models. We also found T1, T1 post-gadolinium and T2 sequences were most commonly used for feature extraction. Preliminary TRIPOD analysis yielded an average score of 14.25 (range 8–18). CONCLUSION: ML algorithms that can differentiate glioma from brain metastases by SVM and CNN are leading approaches with high accuracy. Standardized algorithm performance reporting is a clear limitation to be addressed in future studies.

OTHR-13. IMPACT THE BRAIN: IMPROVING METASTATIC BREAST CANCER PATIENT ACCESS TO COordinated TREATMENT.

Nicole Grogan1, Donna Pierce-Gjeldum1, Leigh Swartz2,1, Kait Verbal1, Sofia Merajver1, Christopher Fries1, Ayano Kwota1, Jason Heth1, Denise Leung1, Sean Smith1, Nicollete Gabel1, Michelle Kim1, Aki Morikawa4, 1University of Michigan, Ann Arbor, MI, USA, 2Hunter Holmes McGuire VA Medical Center, Richmond, VA, USA, 3Virginia Commonwealth University School of Medicine, Richmond, VA, USA

Central nervous system (CNS) metastases are associated with decreased survival and quality of life for patients with metastatic breast cancer (MBC). Multi-disciplinary care can optimize outcomes. This project aims to improve access to coordinated care for patients with MBC and CNS metastases. Patients with MBC and CNS metastases are referred and offered to enroll in our care coordination program. A team consisting of specialists (breast medical oncology, breast cancer genetics, radiation oncology, neurosurgery, neuro-oncology, physical medicine and rehabilitation (PM&R), neuropyschology, and palliative care) supports a dedicated program coordinator who provides navigation, education, specialty referral, and clinical trial screening. A unique intake form developed for the program creates personalized, coordinated, and expedited referrals. Patient-reported outcomes and caregiver burden assessments are collected. Since May 2020, 43 patients were referred and a total of 40 patients (93%) were enrolled – 2 (5%) declined due to perceived burden of participation and 1 (2%) died before enrollment. 85% of patients were Caucasian (n = 34) and 15% were non-Caucasian (n=6). Median time to program intake was 1 day (range: 0–8 days). Of the 43 patients referred, 17 (40%) consented to research studies in the metastatic setting, 11 were for an interventional trial (65%), while 9 consents were for non-interventional studies (53%). In addition to the initially referred specialties, 56 referrals were made across 7 subspecialties; 37 patients (66%) were subsequently seen by a subspecialty, most commonly radiation oncology (n=8), PM&R (n=8), and neuropsychology (n=8). Implementation of a care coordination program for patients with MBC and CNS metastases is feasible. Further, it allows for improved access to care across subspecialties and supports patient satisfaction. This project is ongoing. Funding: National Comprehensive Cancer Network Oncology Research Program from financial support provided by Pfizer.

OTHR-14. AN IMMUNOGENOMIC ANALYSIS OF MELANOMA BRAIN METASTASES (MBM) COMPARED TO EXTRANERIAL BRAIN METASTASES (ECM)

Lucy Boyce Kennedy1, Amanda E.D. Van Swaeringen2,1, Jeff Sheng1, Danielle Ling2,3,3, Tao Zhang2,3,4,5, Xiaoqi Qin6,7, MingDe Lin1, Jin Cui1, Alexandria Brackett1, Ayaj Mahajan1, Michele Johnson1, Amit Mahajan1, Mariam Aboain1; 1Brain Tumor Research Group - Department of Radiology & Biomedical Imaging, Yale School of Medicine, New Haven, CT, USA; 2Visage Imaging, San Diego, CA, USA, 3Harvey Cashing/John Hay Whitney Medical Library, Yale University, New Haven, CT, USA

BACKGROUND: MBM have a unique molecular profile compared to ECM. METHODS: We analyzed a previously published dataset from MD Anderson Cancer Center, including RNA-seq on surgically resected, FFPE MBM and ECM from the same patients. STAR pipeline was used to estimate mRNA abundance. DESeq2 package was used to perform differential gene expression (DGE) analyses. Pathway analysis was performed using Gene Set Enrichment Analysis (GSEA). Paired DGE and GSEA compared MBM vs. lymph node (LN) metastases (n = 16) and MBM vs. skin mets (n = 10). CIBERSORTx estimated relative abundance of immune cell types in MBM and ECM. GATK Mutect2 pipeline was used to call somatic mutations using paired normal tumor samples. Mutations were annotated using the Ensembl Variant Effect Predictor and visualized using the Maftools package in R. RNA-seq data was available on 50 patients. TRIPOD, a checklist assessment tool, was used to assess adherence. RESULTS: Assessment of TRIPOD adherence in 29 eligible studies was performed. In our systematic review, 164 reported 288 items (8/30) to 0.60 (18/30). Best overall item performance, with an ADI of 1, was achieved for item 2 (Presence of controlled vocabulary including artificial intelligence, machine learning, deep learning, magnetic resonance imaging, and glioma). This initial search was performed in October 2020 and then updated in February 2021. Candidate articles were screened in Covidence by at least two reviewers each. A final analysis was conducted in agreement using a checklist assessment tool similar to CLAIMS. RESULTS: Twenty-nine articles were used for data extraction. Four articles specified model development for solitary brain metastases. Classical ML (cML) algorithms represented 85% of models used, with Deep Learning (DL) accounted for the ML algorithms combined with an average accuracy, sensitivity, and specificity of 82%, 78%, 88%, respectively; DL performed 84%, 79%, 81%. The support vector machine (SVM) algorithm was the most common used cML model in the literature and convolutional neural networks (CNN) were standard for DL models. We also found T1, T1 post-gadolinium and T2 sequences were most commonly used for feature extraction. Preliminary TRIPOD analysis yielded an average score of 14.25 (range 8–18). CONCLUSION: ML algorithms that can differentiate glioma from brain metastases by SVM and CNN are leading approaches with high accuracy. Standardized algorithm performance reporting is a clear limitation to be addressed in future studies.

OTHR-15. ASSESSMENT OF TRIPOD ADHERENCE IN ARTICLES DEVELOPING MACHINE LEARNING MODELS FOR THE DIFFERENTIATION OF GLIOMA FROM BRAIN METASTASIS

Leon Jekel1, Waverly Rose Brim1, Gabriel Cassinelli Petersen1, Subramanian Har, Tal Zeevi1, Seyyedeh Payabvash1, Khaled Boushabarah1, MingDe Lin1, Jin Cui1, Alexandria Brackett1, Michele Johnson1, Ajay Malhotra1, Mariam Aboain1, 1Brain Tumor Research Group, Department of Radiology & Biomedical Imaging, Yale School of Medicine, New Haven, CT, USA, 2Visage Imaging GmbH, Berlin, Germany, 3Harvey Cashing/John Hay Whitney Medical Library, Yale University, New Haven, CT, USA

PURPOSE: Machine learning (ML) applications in predictive models in neuro-oncology have become an increasingly investigated subject of research. For their incorporation into clinical practice, rigorous assessment is needed to reduce bias. Several reports have indicated utility of ML applications in differentiation of glioma from brain metastasis. However, a systematic assessment of quality of methodology and reporting in these studies has not been done yet. We examined the adherence of 29 published reports in this field to the TRIPOD statement, which is similar to CLAIM checklist. MATERIALS AND METHODS: Our systematic review was conducted in accordance with PRISMA guidelines. Ovid Embase, Ovid MEDLINE, Cochrane trials (CENTRAL) and Web of science core-collection were searched. Keywords included artificial intelligence, machine learning, deep learning, radiomics, magnetic resonance imaging, glioma, and glioblastoma. Assessment of TRIPOD adherence in 29 eligible studies was performed. Individual item performance was assessed by adherence index (ADI). The ratio of mean achieved score to maximum score per TRIPOD item. RESULTS: In a preliminary analysis of 8 studies, the average TRIPOD adherence score was 0.48 (14.25/30 items fulfilled) with individual scores ranging from 0.27 (8/30) to 0.62 (18/30). Best overall item performance, with an ADI of 1, was seen in item 3 (Background/Objectives), 16 (Model performance) and 19 (Interpretation). Poorest performance was detected in item 1 (Title) and 2 (Abstract), followed by item 9 (Missing Data) with ADI of 0, 0 and 0.13, respectively. CONCLUSION: Preliminary results underline the lack of reproducibility in ML studies on distinction between glioma and brain metastasis. An average TRIPOD adherence score of 0.48 indicates insufficient quality of reporting and outlines the need for increased utilization of quality scoring.
Abstracts

systems in study documentation. Systematic evaluation of quality score adherence will allow us to identify common flaws in this field for enabling translation of models into clinical workflow.

RADIATION

RADI-01. CYSTIC BRAIN METASTASES MANAGED WITH RESERVOIR PLACEMENT AND STEREOTACTIC RADIOTHERAPY

David Park, Michael Schuder; North Shore University Hospital, Manhasset, NY, USA

BACKGROUND: Stereotactic radiosurgery (SRS) has become a mainstay of treatment for patients with metastatic brain tumors. However, metastatic tumors with a large cystic component often exceed the size limit for safe and effective SRS. In such cases, surgical resection may not be the preferred first method of treatment, due to tumor location, patient co-morbidities, and patient preference. In such cases volume reduction by cyst aspiration followed by SRS may be a preferred option. METHODS: Seven patients were treated with this method. We performed reservoir insertion for the aspiration of cystic component in each patient and followed that with outpatient SRS. RESULTS: Mean overall volume reduction from this treatment method was 80% (range 46.5–94.9). Mean volume reduction from the cyst aspiration alone was 60.7% (range 3.5–90.9), and after SRS a further 71.6% (range 34.6–94.4), accounting for some cyst reaccumulation between the time of surgery and SRS. The interval between these two procedures were 24 days on average (range 11–58 days). Repeat reservoir aspiration was done a total of 10 times in 5 patients. CONCLUSION: Cyst aspiration with reservoir placement followed by SRS is a good option for patients with large cystic brain metastases. The reservoir allows for repeat aspiration if needed. Cystic placement at the center of the cyst, and SRS within 2–3 weeks of surgery, can maximize the likelihood of a successful outcome.

RADI-02. HIPPOCAMPAL-SPARING WHOLE BRAIN VOLUMETRIC MODULATED ARC THERAPY (VMAT) PLANNING IN MONACO: A “HOW-TO” NOT PULL YOUR HAIR OUT.

Matthew Goss1, Rowelle Rochelle1, Lisa Spanovich1,2, Rodney Wegner1, Shaakir Hassan1, Zachary Horne2, Allegheh Health Network Cancer Institute, Pittsburgh, PA, USA, 3New York Proton Center, New York, NY, USA

PURPOSE: NRG-CC001 recently reported positive results on hippocampal-sparing IMRT (HS-IMRT) in conjunction with memantine for the reduction in cognitive decline compared to conventional whole brain radiation therapy. Herein, we report our experience in planning volumetric modulated arc therapy (VMAT) cases in Monaco® with the anticipation of increased utilization of the planning technique for delivery on Elekta linear accelerators. METHODS AND MATERIALS: Twelve patients previously treated with whole brain radiation therapy who would have been eligible for NRG-CC001 were replanned with VMAT HS-IMRT for to a dose of 30Gy/10fx using constraints from the trial. RESULTS: All twelve patients were able to be planned with VMAT and achieved NRG-CC001 dose constraints. Median maximum and D100% to the right and left hippocampi were: 13.37Gy and 13.43Gy, respectively and 8.76Gy and 8.86Gy, respectively. Median coverage of the brain minus the hippocampi with 30Gy was 96.53%. All cases passed quality assurance testing with 3%/3mm and 2%/2mm criterion. CONCLUSIONS: Hippocampal-sparing IMRT whole brain radiation therapy can be feasibly planned with VMAT technique in Monaco® and delivered on Elekta linear accelerators.

RADI-03. A STRATEGY TO PERSONALIZE THE USE OF RADIATION IN PATIENTS WITH BRAIN METASTASIS BASED ON S100A9- MEDIATED RESISTANCE

Lauritz Miarka1, Catia Moteiro1, Celine Dalmaso1, Coral Fostero-Torre1, Natalia Yebra1, Aisling Hegarty1, Stephen Keelan1, Yvonne GOY1, Michel Mothe1, Elena Miarka1, Vareslava Dumit1, Leonie Young1, Riccardo Soffetti1, Jose Fernandez-Alen1, Guillermo Blasco1, Lucia Alcazar1, Juan Manuel Sepulveda1, Angel Perez1, Aurelio Lain2, AurorSiegfried2, Harriet Wikman2, Elisabeth Cohen-Jonathan Moyal1, Manuel Valiente1, 1Brain Metastasis Group, CNIO, Madrid, Spain, 2Radiation Oncology Department, Institut Claudiu Regaud, IUCT-Oncopele, Toulouse, France, 3Bioinformatics Unit, CNIO, Madrid, Spain, 4Endocrine Oncology Research Group, RCSI University of Medicine and Health Sciences, Dublin, Dublin, Ireland, 5Radiation Oncology Department, UKE, Hamburg, Germany, 6Neurosurgery Department, UKE, Hamburg, Germany, 7Histopathology Unit, CNIO, Madrid, Spain, 8Department of Neuro-Oncology, University and City of Health and Sciences, Istituto Superiore di Sanita, Turin, Italy, 9Department of Neuro-Oncology, Hospital La Princesa, Madrid, Spain, 10Neuro-Oncology Unit, Hospital Universitario 12 de Octubre, Madrid, Spain, 11Neurosurgery Unit, Hospital Universitario 12 de Octubre, Madrid, Spain, 12Neuropathology Unit, Hospital Universitario 12 de Octubre, Madrid, Spain, 13Anatomopathology Department, CHU Toulouse, INCA Oncopole, Toulouse, France, 14Department of Tumor Biology, UKE, Hamburg, Germany

Finding effective treatment options for patients with brain metastasis remains an unmet need. Given the limitations imposed by the blood-brain barrier and lack of systemic approaches, radiotherapy offers a superior ability to access the brain. While clinical practice recently adapted the use of stereotactic radiotherapy (SRS), Whole-Brain-Radiotherapy (WBRT) continues to be an important treatment option, since many patients present with multiple lesions and bad performance scores, rendering them ineligible for SRS. Unfortunately, overall survival of patients remains unaffected by radiotherapy. Despite this clinical data, the molecular mechanisms that allow metastatic cells to resist radiotherapy in the brain is unknown. We have applied WBRT to experimental brain metastasis from lung and breast adenocarcinoma and validated their resistance in vivo. An unbiased search to identify potential mediators of resistance identified the S100A9-RAGE-NF-kB-JUN pathway. Targeting this pathway genetically reverts the resistance to radiotherapy and increases therapeutic benefits in vivo. In two independent cohorts of brain metastasis from lung and breast adenocarcinoma patients, levels of S100A9 correlate with the response to radiotherapy, offering a novel approach to stratify patients according to their expected benefit. In order to make this biomarker also available for brain metastasis patients receiving radiotherapy surgery, we compared a specimen based approach with the less invasive detection of S100A9 from liquid biopsies. Here, serum S100A9 also correlated with a worse response to WBRT in brain metastasis patients. Furthermore, we have validated the use of a blood-borne RAGE-inhibitor to restore radiosensitivity in ex-perimental brain metastasis models in vivo and in patient-derived organotypic cultures of radio-resistant brain metastasis ex vivo. In conclusion, we identified S100A9 as a major mediator of radio-resistance in brain metastasis and offer the molecular framework to personalize radiotherapy by exploiting it as a biomarker and as a therapeutic target, thus maximizing the benefits for the patient.

RADI-04. STEREOTACTIC RADIOTHERAPY IN ALVEOLAR SOFT PART SARCOMA BRAIN METASTASIS

Jia Xu Lim1, Beng Karlsson1, Angela Pang2, Veelappan Balamurugan2, Vincent Nga1, 1National Neuroscience Institute, Singapore, 2National University of Singapore, Singapore, 3National University Hospital, Singapore

BACKGROUND: Alveolar soft part sarcoma (ASPS), although rare, has the highest incidence of brain metastasis amongst all sarcomas. Stereotactic radiotherapy (SRS) has been shown to be a well tolerated and effective treatment of intracranial sarcomatous metastasis. However, there is a paucity of published literature that guides radiation therapy in this condition. METHODS: This is a single centre retrospective review of all ASPS patients with intraparenchymal brain metastasis in our centre treated with stereotactic radiosurgery (SRS). SRS dosing is dichotomised into high and low dose (≥25 Gy and <25 Gy respectively) and outcomes such as local recurrence (LR) and radiation effects are noted. Successful treatment was defined as a lesion that regressed, is stable, or has less than 25% increase in tumour volume. Local recurrence (LR) was defined as increase in tumour volume by more than 25% during follow-up. RESULTS: There were three patients with 11 ASPS metastatic brain lesions, one of which underwent retreatment. Each lesion was followed up for a mean duration of 12 months (range: 5 – 30 months). Five lesions treated with a high dose regime and six lesions were given low dose. Lesions treated with high dose SRS experienced significantly less LR (20% vs 83.3%, OR 20.0 [95%CI 0.93 – 430], p = 0.036) with no increase in undue symptomatic radiation effects. Retreatment of lesions with LR after initial SRS using a low dose regime was successful, albeit only in the single recurrent lesion. CONCLUSIONS: We conclude that SRS can be used as a first line treatment for ASPS brain metastasis that are not surgically accessible and that using a high dose for treatment is effective and safe. Multicentre collaborative studies can be performed to validate this claim.

RADI-05. METASTATIC NEOPLASM VOLUME KINETICS FOLLOWING TWO-STAGED STEREOTACTIC RADIOTHERAPY

Ethan Damron1, Antonio Dono2, Hatim Chaft2, Magda Marrt2, Tse-Kuan Tu2, Shariq Khwaja2,3, Mark Asmaha2,4, Nitya Tandon2,3, Yoshua Esquerrazi2,4, Angel Escuredare2,4, 1Department of Neuro-Oncology, McGovern Medical School, The University of Texas Health Science Center at Houston, Houston, TX, USA, 2Memorial Hermann Hospital – Texas Medical Center, Houston, TX, USA, 3Oncology Consultants, Houston, TX, USA

INTRODUCTION: Multisession staged stereotactic radiotherapy (2-SRS) represents an alternative approach for management of large brain metastases (LBM), with potential theoretical advantages over fractionated SRS and rep-