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RESEARCH ARTICLE

RADIOSURGERY TREATMENT VOLUME DETERMINATION FOR BRAIN LYMPHOMAS WITH AND WITHOUT INCORPORATION OF MULTIMODALITY IMAGING

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ABSTRACT

Primary Central System Lymphoma (PCNSL) constitutes an infrequent type of extra nodal non-Hodgkin lymphoma (NHL). While RT may be included in management of brain lymphomas to improve treatment outcomes, radiation induced toxicity and deterioration of overall health has been an important concern. In this original research article, we evaluate the incorporation of Magnetic Resonance Imaging (MRI) for treatment planning of brain lymphomas. Radiation treatment volume determination based on incorporation of MRI or based on CT-simulation images only was comparatively evaluated for patients with CNS lymphoma in our study. Ground truth target volume used as reference for comparison purposes was outlined by the expert team of radiation oncologists after colleague peer review, collaboration, and consensus. Treatment volume determination by CT-only imaging and by CT-MR fusion based imaging was assessed. Ground truth target volume outlined by the expert team of radiation oncologists after thorough assessment, collaboration, colleague peer review and consensus has been found to be similar with CT-MR fusion based treatment volume determination.

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INTRODUCTION

Primary Central System Lymphoma (PCNSL) is an infrequent type of extra nodal non-Hodgkin lymphoma (NHL) accounting for approximately 3-5% of Central Nervous System (CNS) tumors and comprising about 1% of all NHLs, with its incidence in a rising trend particularly in the elderly population [1-7].

Once the diagnosis of PCNSL has been established, it is important to commence therapy early since treatment delays can lead to inferior patient outcomes. PCNSL is sensitive to both chemotherapy and Radiation Therapy (RT), however, it is common practice to offer systemic management with methotrexate initially and deferring irradiation for salvage therapy. While RT may be included in patient management to improve treatment outcomes, radiation induced toxicity and deterioration in overall health status has been an important concern. In this context, utility of less extensive RT fields and lower doses has been investigated [8-11]. Although not standard, radiosurgery can be utilized for initial management, for relapse or salvage disease settings in meticulously selected patients [12-15].

Advanced RT techniques and radiosurgery as Stereotactic Radiosurgery (SRS), Stereotactic Body Radiation Therapy (SBRT) and Fractionated Stereotactic Radiation Therapy (FSRT) can be used for focused radio therapeutic management of several CNS disorders and several other tumors throughout the human body. As for CNS lymphomas, radiosurgery may be utilized as part of multidisciplinary patient management.

Determination of radiosurgery target volume has been a very important aspect of successful patient management since relatively small volumes are treated using higher radiation doses per fraction. Planning of radio surgical treatment is traditionally based on the Computed Tomography (CT)-simulation images. In this original research article, we evaluate the incorporation of Magnetic Resonance Imaging (MRI) for radio surgical management of brain lymphoma.

MATERIALS AND METHODS

Treatment volume determination based on inclusion of MRI in planning or based on CT-simulation images only was comparatively evaluated for patients with CNS lymphoma in our study. Ground truth target volume used as reference for comparison purposes has been outlined by

expert team of radiation oncologists after colleague peer review, collaboration, and consensus. Informed consents were available prior to management, and therapy by radiosurgery has been judged after multidisciplinary assessment of experts from oncology, neurosurgery, and neuroradiology. Thorough assessment was performed for lesion location, size, and manifestation along with the contemplated treatment outcomes.

Patient simulation for planning was done at the CT-simulator in our department. Planning CT images were acquired and then transferred for delineating the treatment volumes along with surrounding normal tissues. Either images acquired at CT-simulation or CT and incorporated MR images were used in target volume determination for radiosurgery. Target determination based on CT and based on CT and MRI fusion was assessed comparatively. Definition of the reference was done by the board-certified team of radiation oncologists after detailed assessment, collaboration, colleague peer review and consensus for use in actual treatment as well as for comparison purposes.

RESULTS

Ground truth reference determined by expert radiation oncologists after thorough assessment, collaboration, colleague peer review and consensus has been found to be similar with treatment volume determination based on multimodality imaging with incorporation of both CT and MR in radio surgical planning.

Radiosurgery treatment planning was done by the available system in our tertiary cancer center. In order to secure critical organ sparing whilst maintaining target coverage, appropriate combinations of treatment arcs were utilized in planning for brain lymphoma radiosurgery. Synergy (Elekta, UK) LINAC available at our department was used for treatment delivery. Target volume definition has been improved by choosing the proper selection of visualization parameters in treatment planning. Accurate contouring of target volume and surrounding normal tissues was achieved by supplementation of axial planning CT images with the coronal and sagittal images. Figure 1 shows axial CT image and figure 2 shows the axial MR image of a patient with brain lymphoma.

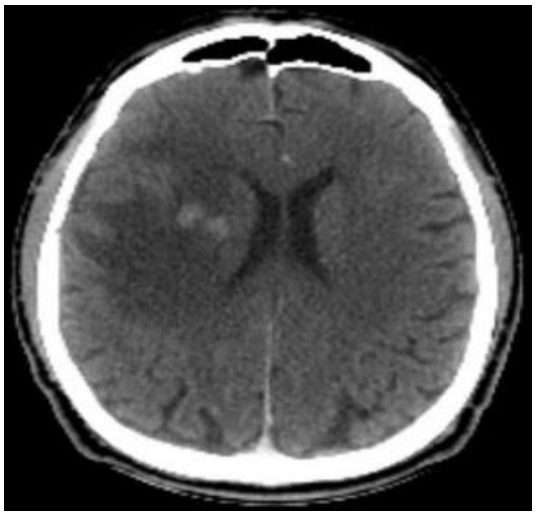

Figure 1- Axial CT image of a patient with brain lymphoma

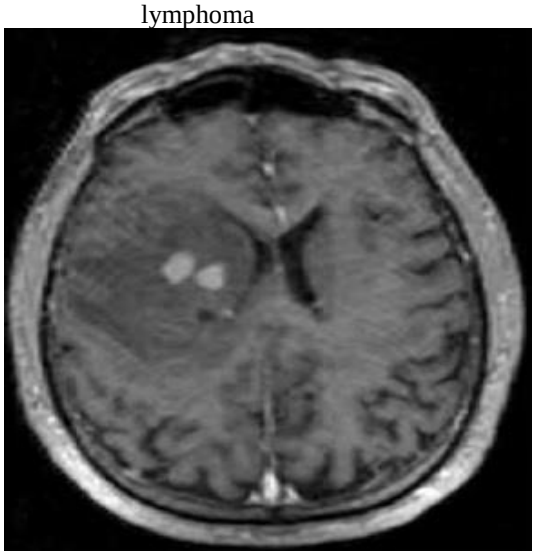

Figure 2- Axial MR image of a patient with brain lymphoma

DISCUSSION

PCNSL typically presents as a large B cell lymphoma confined within the CNS, which may infiltrate the eyes, spinal cord, brain and its coverings with no evidence of systemic disease. PCNSL is more common in males compared to females. Distinction of PCNSL from its systemic form may not be possible by histopathological assessment. Immuno compromised populations such as transplant recipients, patients with autoimmune diseases, congenital immunity disorders or Acquired Immunodeficiency Syndrome (AIDS) are at higher risk for PCNSL. Epstein - Barr virus (EBV) infections may play a role in its pathogenesis.

Patient symptomatology is typically associated with disease localization. Typical localization includes periventricular region with few lesions occurring in the supra tentorial brain. Basal ganglia, thalamus, corpus callosum are frequent locations for PCNSL while the brain lobes such as the occipital lobe, temporal lobe, parietal lobe and frontal lobe can get involved in some patients. Patients may present with headache, visual disturbances, impaired motor functions, cranial neuropathies and related symptoms.

MRI is the imaging modality of choice for PCNSL. Thorough examination of disease extent is warranted before commencing therapy for PCNSL. Cerebrospinal fluid (CSF) cytology, bone marrow aspiration, detailed neurological evaluation with ophthalmologic examination and cognitive function assessment may be performed along with staging workup based on CT imaging of the chest and abdominal pelvic

region. Stereotactic needle biopsy may be adequate for establishing the diagnosis given the lack of benefit from extensive surgical resection which may also cause excessive treatment-related toxicity particularly in the setting of deeply seated lesion localization. Establishing the diagnosis is critical for patients with PCNSL since imaging may occasionally fail to differentiate some other conditions such as sarcoidosis, multiple sclerosis, and gliomas.

Given the sensitivity of brain lymphomas to ionizing radiation, RT can be utilized as part of multidisciplinary patient management. However, RT induced toxicity has been an important concern over the years. Thus, deferring RT and usefulness of less extensive RT fields and lower doses has been the subject of several studies [8-11]. Radio surgical management can be considered as an option for brain lymphoma treatment as initial therapy or in the setting of recurrence as salvage therapy [12-15].

Advances in radiation oncology including adaptive treatment strategies and contemporary treatment delivery techniques such as Image Guided Radiotherapy, Breathing Adapted and Adaptive Radiotherapy, and stereotactic irradiation with SRS, HFSRT, and SBRT have resulted in improved radio therapeutic management of patients.

Rationale of radiosurgery is focused irradiation of the target whilst sparing surrounding critical structures. In this context, well-defined and small lesions are amenable to radiosurgery. Due to the steep dose gradients around the treatment volume, target definition comprises a critical component of radio surgical management to avoid geographical miss or excessive treatment related toxicity.

Determining of larger target volumes may lead to severe radiation induced toxicity, and defining smaller than actual target volumes may result in geographical miss and consequent disease progression. Incorporation of multimodality imaging may assist in improved target localization, and combined use of multimodality imaging may secure improved precision in target volume contouring for radiosurgery. There is scant data assessing the utility of multimodality imaging in radio surgical management of brain lymphomas in the literature. Thus, the current results enrich existing literature and suggest the incorporation of MRI to achieve improved radiosurgery treatment planning for brain lymphomas.

In conclusion, radiosurgery treatment planning for brain lymphomas may be improved by incorporation of MRI into the target definition process despite the need for further supporting evidence.

REFERENCES

1. Szczepanek D, Wąsik-Szczepanek E, Stoma F, Sokołowska B, Trojanowski T, 2017. Primary central nervous system lymphoma as a neurosurgical problem. Neurol Neurochir Pol. 51(4): 319-323.

2. Makino K, Nakamura H, Kino T, Takeshima H, Kuratsu J, 2006. Rising incidence of primary central nervous system lymphoma in Kumamoto, Japan. Surg Neurol. 66(5): 503-506.

3. Hoffman S, Propp JM, McCarthy BJ, 2006. Temporal trends in incidence of primary brain tumors in the United States, 1985-1999. Neuro Oncol. 8(1): 27-37.

4. Olson JE, Janney CA, Rao RD, Cerhan JR, Kurtin PJ, Schiff D, Kaplan RS, O'Neill BP, 2002. The continuing increase in the incidence of primary central nervous system non-Hodgkin lymphoma: a surveillance, epidemiology, and end results analysis. Cancer. 95(7): 1504-1510.

5. Yoo KH, Lee H, Suh C; CISL, 2018. Lymphoma epidemiology in Korea and the real clinical field including the Consortium for Improving Survival of Lymphoma (CISL) trial. Int J Hematol. 107(4): 395-404.

6. Villano JL, Koshy M, Shaikh H, Dolecek TA, McCarthy BJ, 2011. Age, gender, and racial differences in incidence and survival in primary CNS lymphoma. Br J Cancer. 105(9): 1414-1418.

7. Pulido JS, Vierkant RA, Olson JE, Abrey L, Schiff D, O'Neill BP, 2009. Racial differences in primary central nervous system lymphoma incidence and survival rates. Neuro Oncol. 11(3): 318-322.

8. Adhikari N, Biswas A, Gogia A, Sahoo RK, Garg A, Nehra A, Sharma MC, Bhasker S, Singh M, Sreenivas V, Chawla R, Joshi G, Kumar L, Chander S, 2018. A prospective phase II trial of response adapted whole brain radiotherapy after high dose methotrexate based chemotherapy in patients with newly diagnosed primary central nervous system lymphoma-analysis of acute toxicity profile and early clinical outcome. J Neurooncol. 139(1): 153-166.

9. Morris PG, Correa DD, Yahalom J, Raizer JJ, Schiff D, Grant B, Grimm S, Lai RK, Reiner AS, Panageas K, Karimi S,

Curry R, Shah G, Abrey LE, DeAngelis LM, Omuro A, 2013. Rituximab, methotrexate, procarbazine, and vincristine followed by consolidation reduced-dose whole-brain radiotherapy and cytarabine in newly diagnosed primary CNS lymphoma: final results and long-term outcome. J Clin Oncol. 31(31): 3971-3979.

10. Ferreri AJ, Verona C, Politi LS, Chiara A, Perna L, Villa E, Reni M, 2011. Consolidation radiotherapy in primary central nervous system lymphomas: impact on outcome of different fields and doses in patients in complete remission after upfront chemotherapy. Int J Radiat Oncol Biol Phys. 80(1): 169-175.

11. Shah GD, Yahalom J, Correa DD, Lai RK, Raizer JJ, Schiff D, LaRocca R, Grant B, DeAngelis LM, Abrey LE, 2007. Combined immuno chemotherapy with reduced whole-brain radiotherapy for newly diagnosed primary CNS lymphoma. Clin Oncol. 25(30): 4730-4735.

12. Sakamoto M, Oya N, Mizowaki T, Araki N, Nagata Y, Takayama K, Takahashi JA, Kano H, Katsuki T, Hashimioto N, Hiraoka M, 2006. Initial experiences of palliative stereotactic radiosurgery for recurrent brain lymphomas. J Neurooncol. 77(1): 53-58.

13. Dr. Joel Thomas, Dr. Joshin Sara Cherian, Dr. Vijay M C, 2018. Clinical study on possibility of antineoplastic agents induced adverse drug reactions in male and female cancer patients. Journal of Medical Pharmaceutical and Allied Sciences, V7-I7, 789. October 2018, 2000-2013

14. Kumar R, Laack N, Pollock BE, Link M, O'Neill BP, Parney IF, 2015. Stereotactic Radiosurgery in the Treatment of Recurrent CNS Lymphoma. World Neurosurg. 84(2): 390-397.

15. Hirono S, Iwadate Y, Higuchi Y, Serizawa T, Nagano O, Matsutani T, Saeki N, 2015. Stereotactic radiosurgery in combination with up-front high-dose methotrexate as a first-line treatment for newly diagnosed primary central nervous system lymphoma. J Neurooncol. 123(2): 237-244.

16. Shin SM, Silverman JS, Bowden G, Mathieu D, Yang HC, Lee CC, Tam M, Szelemej P, Kaufmann AM, Cohen-Inbar O, Sheehan J, Niranjan A, Lunsford LD, Kondziolka D, 2017. Relapsed or refractory primary central nervous system lymphoma radiosurgery: Report of the International Gamma Knife Research Foundation. J Radiosurg SBRT. 4(4): 247-253.