Medical Dosimetry ■■ (2017) ■■–■■

Medical Dosimetry

journal homepage: www.meddos.org

Clinical Radiation Oncology Contribution:

Whole-brain Irradiation Field Design: A Comparison of Parotid Dose

Cheng-Chia Wu, M.D., Ph.D.,* Yen-Ruh Wuu, B.S.,* Ashish Jani, M.D.,* Anurag Saraf, B.A.,* Cheng-Hung Tai, B.A.,* Matthew E. Lapa, B.S.,* Jacquelyn I.S. Andrew, B.A.,* Akhil Tiwari, B.S.,* Heva J. Saadatmand, M.P.H.,* Steven R. Isaacson, M.D.,*,† Simon K. Cheng, M.D., Ph.D.,*,‡ and Tony J. C. Wang, M.D.*,‡

*Department of Radiation Oncology, Columbia University Medical Center, 622 West 168th Street, BNH B-11, New York, NY 10032; †Department of Neurological Surgery, Columbia University Medical Center, New York, NY 10032; and ‡Herbert Irving Comprehensive Cancer Center, Columbia University Medical Center, New York, NY 10032

ARTICLE INFO

Article history:
Received 10 November 2016
Accepted 27 February 2017

Keywords:
Whole-brain radiation
WBRT
Parotid
Xerostomia

ABSTRACT

Whole-brain radiation therapy (WBRT) plays an important role in patients with diffusely metastatic intracranial disease. Whether the extent of the radiation field design to C1 or C2 affects parotid dose and risk for developing xerostomia is unknown. The goal of this study is to examine the parotid dose based off of the inferior extent of WBRT field to either C1 or C2. Patients treated with WBRT with either 30 Gy or 37.5 Gy from 2011 to 2014 at a single institution were examined. Parotid dose constraints were compared with Radiation Therapy Oncology Group (RTOG) 0615 nasopharyngeal carcinoma for a 33-fraction treatment: mean <26 Gy, volume constraint at 20 Gy (V20) < 20 cc, and dose at 50% of the parotid volume (D50) < 30 Gy. Biologically effective dose (BED) conversions with an α/β of 3 for normal parotid were performed to compare with 10-fraction and 15-fraction treatments of WBRT. The constraints are as follows: mean < BED 32.83 Gy, V15.76 (for 10-fraction WBRT) or V17.35 (for 15-fraction WBRT) < 20 cc, and D50 < BED 39.09 Gy. Nineteen patients treated to C1 and 26 patients treated to C2 were analyzed. Comparing WBRT to C1 with WBRT to C2, the mean left, right, and both parotids' doses were lower when treated to C1. Converting mean dose to BED_3, the parotid doses were lower than BED_3 constraint of 32.83 Gy: left (30.12 Gy), right (30.69 Gy), and both parotids (30.32 Gy). V20 to combined parotids was lower in patients treated to C1. When accounting for fractionation of WBRT received, the mean corrected V20 volume was less than 20 cc when treating to C1. D50 for C1 was lower than C2 for the left parotid, right parotid, and both parotids. BED_3 conversion for the mean D50 of the left, right, and both parotids was less than 39.09 Gy. In conclusion, WBRT to C1 limits parotid dose, and parotid dose constraints are achievable compared with inferior border at C2. A possible mean parotid dose constraint with BED_3 should be less than 32.83 Gy.

Introduction

Historically, radiation therapy plays a main role in the treatment of brain metastasis. The use of palliative whole-brain radiation therapy (WBRT) in treating patients with multiple brain metastases has historically shown to improve neurologic symptoms and median overall survival from approximately 1 to 2 months to 3 to 6 months.[1] With the advancement of stereotactic radiosurgery, patients with good prognosis and limited disease in the brain are often treated with stereotactic radiosurgery. However, WBRT still plays a significant role in patients with high numbers of brain metastasis or poorer prognosis.[1,2]

The dose for WBRT ranges from 2000 cGy to 4000 cGy.[3,4] The conventional dose fractionation for WBRT is 3000 cGy in 10 fractions, but with recent publications examining the neuroprotective role of memantine, patients are also often treated with 3750 cGy in 15 fractions.[3-6] Side effects related to this treatment are often neglected given the unfavorable prognosis of metastatic disease. Given the improved systemic treatment options, surgical options, radiation treatment modalities, as well as a better understanding of the different histologic and molecular marker characteristics of brain metastasis, various prognostic indices have stratified patients with

Cheng-Chia Wu and Yen-Ruh Wuu contributed equally to this work.

Reprint requests to Simon K. Cheng, M.D., Ph.D., Department of Radiation Oncology, Columbia University Medical Center, 622 West 168th Street, BNH B-11, New York, NY 10032.
E-mail: sc3225@cumc.columbia.edu
Reprint requests to Tony J.C. Wang, M.D., Department of Radiation Oncology, Columbia University Medical Center, 622 West 168th Street, BNH B-11, New York, NY 10032.
E-mail: tjw2117@cumc.columbia.edu

http://dx.doi.org/10.1016/j.meddos.2017.02.006
0958-3947/Copyright © 2017 American Association of Medical Dosimetrists

brain metastasis with a median overall survival ranging from approximately 3 months to 1 year.[1]

With improved survival, there is a need to better understand the potential side effects related to WBRT. Efforts have been made to examine neurocognitive effects of WBRT as well as potential interventions to mitigate these toxicities, including *N*-methyl-D-aspartate receptor blockers used in Alzheimer disease and hippocampal-sparing field design.[5-7] Very little is known about the effects of WBRT on xerostomia and parotid dose. Furthermore, parotid glands are not routinely delineated as organs at risk (OARs) for treatment planning. Treatment field design for WBRT involves 2 opposed lateral beams, with the inferior field border ending at the inferior border of the cervical spine C1 or C2. It is unclear as to how the difference in the inferior beam edge will affect parotid dose. This study examines and compares the parotid dose when planning WBRT to C1 *vs* WBRT to C2, as well as radiation dose of 3000 cGy in 10 fractions *vs* 3750 cGy in 15 fractions.

Methods and Materials

Patients treated with WBRT from 2011 to 2014 were retrospectively examined. Patients with a medical history of leptomeningeal disease were selected to screen for WBRT with treatment field ending at C2. All WBRT radiation treatment plans were established with 3-dimensional-computed tomography (3D-CT) planning with a multileaflet collimator (MLC) block. Radiation treatment plans were limited to patients who received 3000 cGy in 10 fractions or 3750 cGy in 15 fractions. No prior parotid contours were delineated. Patients who had radiation treatment fields that ended in the middle of the vertebral body, typically C2, were excluded. Bilateral parotid volumes were contoured, and a dose-volume histogram was used to evaluate parotid dose. Parotid dose constraints were compared with that of the Radiation Therapy Oncology Group (RTOG) 0615 study of nasopharyngeal carcinoma for a 33-fraction treatment: mean parotid dose less than 26 Gy, volume constraint at 20 Gy (V20) less than 20 cc, and dose at 50% of the parotid volume (D50) less than 30 Gy. Biologically effective dose (BED) conversion of the dose constraints was performed using an α/β of 3 for normal parotid to compare with 10-fraction and 15-fraction treatments of WBRT.[8] Mean dose less than 32.83 Gy was assessed (BED_3 of 26 Gy). A corrected V20 was determined based on fractionation of WBRT received (10 fractions *vs* 15 fractions). V15.76 (total dose of BED_3 conversion of 20 Gy assuming 10 fractions) less than 20 cc or V17.35 (total dose of BED_3 conversion of 20 Gy assuming 15 fractions) less than 20 cc was assessed depending on the WBRT dose received (3000 cGy/10 fractions or 3750 cGy/15 fractions, respectively). D50 less than 39.09 Gy was assessed (BED_3 of 30 Gy). Statistical analysis was performed using χ^2 test and Student t-test.

Results

Forty-five patients were analyzed, with 19 patients receiving WBRT to C1 and 26 patients receiving WBRT to C2. Twenty-four patients received 3750 cGy in 15 fractions and 21 patients received 3000 cGy in 10 fractions. There were no differences in patients who received WBRT to C1 or C2 receiving 3000 cGy or 3750 cGy, indicated by $p = 0.936$ (Table 1). For patients treated with 3000 cGy in 10 fractions, treating to C2 increased the mean parotid dose by approximately 8 Gy (Table 2). Similarly, in patients treated with 3750 cGy in 15 fractions to C2, the mean parotid dose increased by approximately 5 Gy (Table 3).

Comparing WBRT to C1 with WBRT to C2, the combined mean left parotid dose (19.53 Gy *vs* 26.35 Gy, $p < 0.001$), right parotid dose (19.67 Gy *vs* 25.07 Gy, $p = 0.003$), and both parotids' dose (19.63 Gy *vs* 25.71 Gy, $p < 0.001$) were lower when treated to C1 *vs* C2, respectively (Table 4). Given that some patients received 3000 cGy in 10 fractions or 3750 cGy in 15 fractions, mean dose was converted to BED with an α/β of 3 for normal parotid. Converting mean dose to BED_3, the doses were as follows: left parotid (30.12 Gy *vs* 45.40 Gy, $p < 0.001$), right parotid (30.69 Gy *vs* 42.47 Gy, $p = 0.002$), and both parotids (30.32 Gy *vs* 43.85 Gy, $p < 0.001$). Using the RTOG 0615 dose constraint for parotid dose of mean dose less than 26 Gy over 33 fractions, BED_3 was calculated with a mean parotid dose constraint of BED_3 less than 32.83 Gy. The mean BED_3 dose to the left, right, or both parotids in patients treated to C1 was less than 32.83 Gy (Table 4).

In addition to a mean dose constraint, the V20 to the combined parotids was examined. V20 to the combined parotids was lower in patients treated to C1 than in patients treated to C2 (17.50 cc *vs* 26.82 cc, $p = 0.002$). When accounting for fractionation of WBRT received, the corrected V20 volumes were determined at equivalent dose at 10 fractions (V15.76 at 15.76 Gy) and at 15 fractions (V17.35 at 17.35 Gy). The average volumes for the corrected V20 of the combined parotids were 18.95 cc to C1 *vs* 28.22 cc to C2 ($p = 0.003$) (Table 5).

Lastly, the D50 for C1 was lower than C2 for the left parotid (21.46 Gy *vs* 30.16 Gy, $p = 0.006$), right parotid (21.73 Gy *vs* 28.30 Gy, $p = 0.002$), and both parotids (21.05 Gy *vs* 29.60 Gy, $p = 0.011$). BED_3 conversions for the left parotid, right parotid, and both parotids were 35.12 Gy *vs* 55.22 Gy ($p = 0.007$), 36.47 Gy *vs* 50.60 Gy ($p = 0.005$), and 34.40 Gy *vs* 53.78 Gy ($p = 0.016$), respectively. As compared with the RTOG constraint of D50 < 30 Gy (BED_3 conversion to 39.09 Gy), the mean D50 dose to the left, right, and both parotids was less than 39.09 Gy when treated to C1 (Table 6).

Discussion

WBRT remains the standard of care for patients with a large number of brain metastases. The treatment of WBRT is associated with multiple toxicities including neurocognitive deficits such as memory loss, fatigue and somnolence, nausea, vomiting, alopecia, and dermatitis.[9] Very little is known about the risk to the parotid gland in the setting of WBRT. Radiation-induced xerostomia is well documented in patients receiving higher fractionation treatments in the setting of head and neck cancers.[10,11] Although limited information is known about xerostomia in the setting of WBRT, in which patients are treated with 10 to 15 fractions, there is sufficient evidence that low-dose radiation delivered to major salivary glands over a course of low fractionation can lower saliva production. Radiotherapy to the salivary glands is clinically used in the setting of sialorrhea in patients with Parkinson disease or amyo-

Table 1
Patient demographic

	3750 cGy	3000 cGy	Total
C1 spine	10	9	19
C2 spine	14	12	26
Total	24	21	45

Table 2
Unadjusted mean parotid dose for patients treated with 30 Gy in 10 fractions

		N	Mean	Std. deviation	Std. error mean	*p*
Mean left parotid (3000 cGy)	C1	9	15.77	5.05	1.68	< 0.001
	C2	12	24.60	3.53	1.02	
Mean right parotid (3000 cGy)	C1	9	16.12	5.72	1.91	0.007
	C2	12	23.22	4.96	1.43	
Mean both parotids (3000 cGy)	C1	9	15.99	5.00	1.67	0.001
	C2	12	23.89	4.09	1.18	