Medical Dosimetry ■■ (2017) ■■–■■

Medical Dosimetry

journal homepage: www.meddos.org

Clinical Radiation Oncology Contribution:

Volumetric-modulated arc therapy (VMAT) for whole brain radiotherapy: not only for hippocampal sparing, but also for reduction of dose to organs at risk

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ARTICLE INFO

Article history:
Received 3 December 2016
Received in revised form 8 March 2017
Accepted 10 July 2017

Keywords:
Volumetric-modulated arc therapy
Whole brain radiotherapy
Hippocampal sparing
Dose reduction
Organs at risk
Parotid
Scalp
Auditory canal

ABSTRACT

A prospective clinical trial, Radiation Therapy Oncology Group (RTOG) 0933, has demonstrated that whole brain radiotherapy (WBRT) using conformal radiation delivery technique with hippocampal avoidance is associated with less memory complications. Further sparing of other organs at risk (OARs) including the scalp, ear canals, cochleae, and parotid glands could be associated with reductions in additional toxicities for patients treated with WBRT. We investigated the feasibility of WBRT using volumetric-modulated arc therapy (VMAT) to spare the hippocampi and the aforementioned OARs. Ten patients previously treated with nonconformal WBRT (NC-WBRT) using opposed lateral beams were retrospectively re-planned using VMAT with hippocampal sparing according to the RTOG 0933 protocol. The OARs (scalp, auditory canals, cochleae, and parotid glands) were considered as dose-constrained structures. VMAT plans were generated for a prescription dose of 30 Gy in 10 fractions. Comparison of the dosimetric parameters achieved by VMAT and NC-WBRT plans was performed using paired t-tests using upper bound p-value of < 0.001. Average beam on time and monitor units (MUs) delivered to the patients on VMAT were compared with those obtained with NC-WBRT. All VMAT plans met RTOG 0933 dosimetric criteria including the dose to hippocampi of 100% of the volume ($D_{100\%}$) of 8.4 ± 0.3 Gy and maximum dose of 15.6 ± 0.4 Gy, respectively. A statistically significant dose reduction ($p < 0.001$) to all OARs was achieved. The mean and maximum scalp doses were reduced by an average of 9 Gy (32%) and 2 Gy (6%), respectively. The mean and maximum doses to the auditory canals were reduced from 29.5 ± 0.5 Gy and 31.0 ± 0.4 Gy with NC-WBRT, to 21.8 ± 1.6 Gy (26%) and 27.4 ± 1.4 Gy (12%) with VMAT. VMAT also reduced mean and maximum doses to the cochlea by an average of 4 Gy (13%) and 2 Gy (6%), respectively. The parotid glands mean and maximum doses with VMAT were 4.4 ± 1.9 Gy and 15.7 ± 5.0 Gy, compared to 12.8 ± 4.9 Gy and 30.6 ± 0.5 Gy with NC-WBRT, respectively. The average dose reduction of mean and maximum of parotid glands from VMAT were 65% and 50%, respectively. The average beam on time and MUs were 2.3

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http://dx.doi.org/10.1016/j.meddos.2017.07.005

minutes and 719 on VMAT, and 0.7 minutes and 350 on NC-WBRT. This study demonstrated the feasibility of WBRT using VMAT to not only spare the hippocampi, but also significantly reduce dose to OARs. These advantages of VMAT could potentially decrease the toxicities associated with NC-WBRT and improve patients' quality of life, especially for patients with favorable prognosis receiving WBRT or patients receiving prophylactic cranial irradiation (PCI).

Published by Elsevier Inc. on behalf of American Association of Medical Dosimetrists.

Introduction

Brain metastases are a common problem and carry poor prognosis in cancer patients. In 2013, in the United States, an estimated 1.66 million new cancer cases were diagnosed, and more than 580,000 cancer deaths occurred.[1] An estimated 15% to 30% (250,000 to 500,000) of these cancer patients will develop brain metastases (BM) during the course of their illness.[2-4] Aggressive multimodality treatment for intracranial disease has resulted in improvement in disease local control, neurologic symptoms, quality of life (QOL), and survival particularly in favorable groups of patients.[5-7] The multimodality treatment strategy incorporates the use of surgery, whole brain radiotherapy (WBRT) and/or stereotactic radiosurgery (SRS), or a combination of all.

SRS has become an increasingly available treatment option for management of intracranial disease. Commonly, SRS alone without WBRT as initial treatment has been utilized to control limited intracranial disease (1 to 4 brain metastases or even more than 4 lesions) to reduce the adverse effects of WBRT on neurocognitive functioning and QOL scores without compromising survival benefit with the WBRT.[8-14] However, WBRT still plays a significant role in management of brain metastasis to provide higher progression-free survival rates, lower neurologic death rates (intracranial failure as a component of cause of death), lower intracranial relapse rates, lower rates of leptomeningeal dissemination, and lower salvage cranial treatment rates demonstrated in several randomized trials.[8-14] In prognostically favorable patients, SRS boost after WBRT has been associated with survival benefit.[15] In addition, the secondary analysis of the Japanese Radiation Oncology Study Group data suggests that adjuvant WBRT may improve survival in selected patients with more favorable prognosis according to disease-specific Graded Prognostic Assessment 2.5 to 4.0.[10] To reduce neurotoxicity associated with WBRT, attempts have been made, including concomitantly taking memantine during WBRT and hippocamopal sparing WBRT.[16,17] Recent Radiation Therapy Oncology Group (RTOG) 0933 demonstrated a considerable improvement in QOL and preservation of memory compared to historic controls when hippocampal sparing WBRT was used.[16] Therefore, hippocampal sparing WBRT with and without SRS should still be considered as a principal strategy in the treatment of patients with brain metastasis.

With advanced radiation technology such as helical tomotherapy and linear accelerator-based intensity-modulated radiation therapy (IMRT) techniques, it is possible to perform WBRT with hippocampal sparing and reduce neurocognitive toxicity.[18-20] In addition to the neurocognitive effects of WBRT, toxicity to the other organs at risk (OARs), including the scalp, auditory canals, inner ear structures, and parotid glands with negative impact on patients' QOL have been described.[21-33] Because of factors including relatively low total prescription dose and poor prognosis associated with WBRT in patients in multiple brain metastases, potential radiation-induced toxicity to these OARs have been overlooked and underestimated.

Herein, we present a feasibility study to explore the clinical potential for a new treatment technology of volumetric-modulated arc therapy (VMAT) to not only provide hippocampal sparing following RTOG 0933 dosimetric compliance criteria, but to also significantly reduce dose to other OARs, including the scalp, auditory canals, cochleae, and parotid glands.[16]

Methods and Materials

Patients, simulation, organ delineation

In this Institutional Review Board-approved retrospective study, we selected 10 patients who had been previously treated with nonconformal whole brain radiotherapy (NC-WBRT) for brain metastases at the University of Kansas Hospital. Patients were simulated in the supine position using face mask for immobilization on a 16-slice Phillips Brilliance Big Bore CT Scanner. The 2D-computed tomography (CT) images were acquired with 512×512 pixels at 2.5-mm slice thickness and 2.5-mm slice spacing, and the Digital Imaging and Communications in Medicine images were electronically transferred to the Eclipse treatment planning system (TPS) (Varian Medical System, Palo Alto, CA) for WBRT planning. The selected 10 NC-WBRT plans were retrieved and re-planned for this retrospective VMAT planning study. The T1-weighted cranial magnetic resonance imaging scans were rigidly registered to the bony anatomy on the planning CT