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Original paper

Comparison of the extent of hippocampal sparing according to the tilt of a patient's head during WBRT using linear accelerator-based IMRT and VMAT

Sun Young Moon [a], Myonggeun Yoon [a], Mijoo Chung [b], Weon Kuu Chung [b,*], Dong Wook Kim [b,*]

[a] Department of Bio-convergence Engineering, Korea University, Seoul, Republic of Korea
[b] Department of Radiation Oncology, Kyung Hee University Hospital at Gangdong, Seoul, Republic of Korea

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ABSTRACT

In this paper, we report the results of our investigation into whole brain radiotherapy (WBRT) using linear accelerator-based intensity-modulated radiation therapy (IMRT) and volumetric-modulated arc therapy (VMAT) in lung cancer patients with a high risk of metastasis to the brain. Specifically, we assessed the absorbed dose and the rate of adverse effects for several organs at risk (OAR), including the hippocampus, according to the tilt of a patient's head. We arbitrarily selected five cases where measurements were made with the patients' heads tilted forward and five cases without such tilt. We set the entire brain as the planning target volume (PTV), and the hippocampi, the lenses, the eyes, and the cochleae as the main OAR, and formulated new plans for IMRT (coplanar, non-coplanar) and VMAT (coplanar, non-coplanar). Using the dose-volume histogram (DVH), we calculated and compared the effective uniform dose (EUD), normal tissue complication probability (NTCP) of the OAR and the mean and the maximum doses of hippocampus. As a result, if the patient tilted the head forward when receiving the Linac-based treatment, for the same treatment effect in the PTV, we confirmed that a lower dose entered the OAR, such as the hippocampus, eye, lens, and cochlea. Moreover, the damage to the hippocampus was expected to be the least when receiving coplanar VMAT with the head tilted forward. Accordingly, if patients tilt their heads forward when undergoing Linac-based WBRT, we anticipate that a smaller dose would be transmitted to the OAR, resulting in better quality of life following treatment.

Introduction

According to studies, the percentages of cancers that metastasize to the brain are 13–39% for breast cancer, 13% for gastrointestinal cancer, 8% for renal cancer, 7% for skin cancer, and 4% for thyroid cancer. In addition, the percentage of lung cancers that metastasize to the brain is as high as 90% [1]. For patients with cancers that can metastasize, or those that have already metastasized, to the brain, whole brain radiotherapy (WBRT) is the universal treatment that, nonetheless, can incur damaging aftereffects. Of these, the clinically representative adverse effect of radiation therapy is dementia, which can cause memory loss, attention deficit disorder, and emotional regulation [2]. According to Radiation Therapy Oncology Group 0933 (RTOG 0933), of the patients who received WBRT, a large number felt that their neurocognitive ability had diminished or suffered an actual reduction. This deterioration in neurocognitive ability was reported to have continued for as long as 153 days [3]. Frequent memory loss and cognitive impairment are the result of radiation-induced damage to the hippocampus and limbic systems [4]. The hippocampus is located medially in the temporal lobe, and contributes significantly to cognitive function. Hence, if the hippocampus is damaged by WBRT, this causes a decline in learning, memory, and spatial processing abilities [5–7]. Experiments on rats have shown that when the brain is irradiated, neurogenesis in the subgranular zone is dramatically impaired [8,9]. Furthermore, Monje's research team discovered that when the rat's hippocampus is damaged by radiation, structural changes occur in the "stem cell niche" that determines the fate of precursor cells, and this causes a decline in neurogenesis [10]. According to a study by Vinai, of 1133 metastasis patients, metastasis occurred within the hippocampal avoidance region in 8.6% of the patients. Moreover, because there was not a single case

* Corresponding authors.
E-mail addresses: wkchung@khnmc.or.kr (W.K. Chung), joocheck@gmail.com (D.W. Kim).

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of metastasis within the hippocampus [5], the possibility of metastasis to the hippocampus can be excluded. For these reasons, when performing WBRT, by making treatment plans that aim to transmit the lowest possible dose to the hippocampus, patients' post-treatment quality of life can be improved over that in conventional treatment.

In comparison with three-dimensional (3D) conformal radiation therapy, intensity-modulated radiation therapy (IMRT) provides the same treatment effect without negatively affecting the prognosis [11], can reduce acute and chronic neurotoxicity, and delivers a relatively smaller dose to the organs at risk (OAR) while simultaneously giving good coverage of the planning target volume (PTV) [12]. Volumetric-modulated arc therapy (VMAT) was subsequently developed. This technique involves a method similar to that of IMRT while adding a rotation function to the gantry, which is performed on many cancer patients. Unlike IMRT, VMAT allows the optimization of the treatment plan by altering the position of the Multileaf Collimator (MLC), the dose rate, and the rotation speed of the gantry. These have become commonly used methods in radiation therapy [13]. A recent study reported that when IMRT was applied to a patient's entire brain while his/her head was tilted forward at an angle of 30°, the mean dose entering the hippocampus decreased by approximately 21% [14]. Accordingly, in this paper, we aim to determine the extent of damage to the hippocampus when performing coplanar and non-coplanar radiation using linear acceleration (Linac)-based IMRT and VMAT on patients with tilted heads.

Methods

Patient selection

We collected computed tomography (CT) data from patients who had previously received partial or whole brain radiation therapy. Of these, we extracted at random data from five patients who had tilted their heads forward by 30° during the radiotherapy and five patients who had not done so. We selected patients who had tilted their heads by 30° because this was found to be the optimal tilting angle for sparing effect in hippocampus in a past study [14]. For patients with tilted heads, their heads were kept by placing a wedge with a 30° slope under the pillow while CT data was recorded. (Figure 1) In the CT images of all patients, the brain, hippocampus, eye, lenses, cochleae, optic nerves, optic chiasm, and brain stem were all contoured.

LINAC-based treatment planning

Treatment planning for all patients was carried out using Eclipse™ (ECLIPSE™ version 8.9, Varian Medical System, Inc., Palo Alto, CA, USA), a software for radiation therapy planning that uses the Varian 2liX linear accelerator. The entire brain was designated as the PTV, and the hippocampi, eyes, lenses, cochleae, optic nerves, optic chiasm, and brainstem were set as the OAR. When selecting the avoidance regions, in accordance with a past study reporting that if avoidance regions were generated, a smaller dose was transmitted to the OAR [15], we demarcated the hippocampal avoidance region as 5 mm surrounding the hippocampus [16], and set the avoidance regions for the lenses and cochleae at 3 mm surrounding the organs, prior to formulating the treatment plan. We planned IMRT and VMAT for all patients, and performed both coplanar and non-coplanar irradiation for each. The number of fields was 15 in most of IMRT except two a non-coplanar IMRT cases which has 12 fields. For coplanar IMRT, beam angle distribution is symmetric and an interval of gantry angle between each field is about same as 24 degree for 15 fields, since we intended to deliver the prescription dose uniformly to the entire brain. The number of arcs is 3 in coplanar VMAT and 3–4 in non-coplanar VMAT. The exposing angle of each arc in coplanar VMAT is 360 degree so called as 'full arc'. For non-coplanar VMAT, the rotation angle of each arc is 360 degree with zero degree of couch angle or 180 degree with rotated couch. The point here is that since the planning target volume (PTV) was the entire brain rather than a part of it, we accordingly planned to irradiate the prescription dose to the entire brain. Rotation angles in VMAT consisted of 180° and 360°. The ratio of rotated couch beam on average was 43.2 ± 21.0% ranged from 27% to 100% in non-coplanar IMRT, and 70.82 ± 21.0% ranged from 50% to 100% in non-coplanar VMAT. We performed radiotherapy for a total prescribed dose of 3000 cGy for the PTV. For treatment planning, we restricted the absorbed dose for major organs according to region-specific tolerance dose table (or protocol) of study by Emami's team, such that it was less than 700 cGy for the lenses, 1500 cGy for the eyes, 1800 cGy for the cochleae, and 3000 cGy for the brainstem, optic nerves, and optic chiasm [17].

Evaluation of treatment plans

We assessed our treatment plans for the PTV and the OAR. In order to ensure an identical treatment effect in the PTV, we used the homogeneity index (HI), the coverage index (CVI), and the

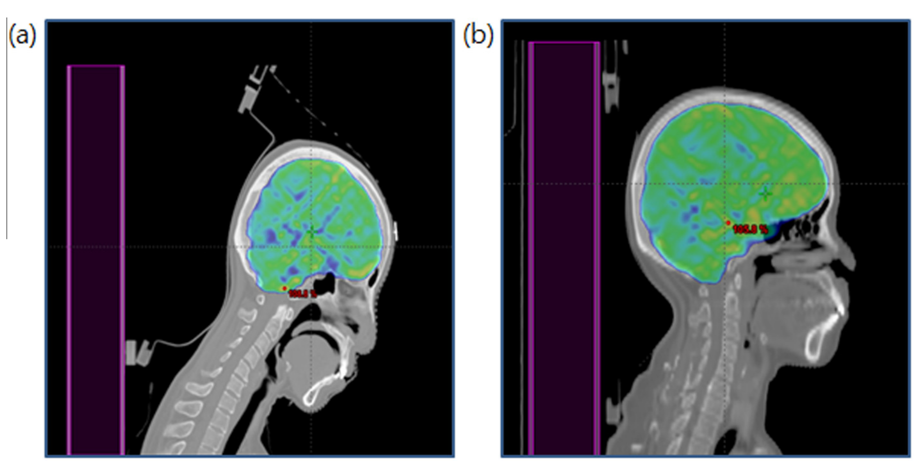

Figure 1. A CT image from a randomly selected patient. (a) is an image of the patient when a wedge was placed under the head to effect tilting; (b) is an image of a patient receiving treatment in a standard supine position.