Noncoplanar volumetric modulated arc therapy for patient with optic nerve sheath meningioma: a case report and literature review

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Abstract: A 74-year-old female presented with progressive oculus dexter (OD) visual deterioration caused by optic nerve sheath meningioma (ONSM). The Farnsworth D-15 Dichotomous Color Blindness Test progressed from 3/15 to 1/15 in OD. The visual acuity with correction (VACC) changed from 0.4 to 0.3 in OD after 1 month of medication therapy. A total dose of 54 Gy in 30 fractions was delivered to the ONSM with the noncoplanar volumetric modulated arc therapy (VMAT) technique (Versa HD, Elekta, Crawley, West Sussex, UK). Color discrimination was improved from 1/15 to 13/15 after the patient received 27 Gy in 15 fractions. The VACC of the right eye treated with 54 Gy was improved from 0.3 to 0.6 at 9 months and to 1.0 at 15 months after radiotherapy (RT). There was no neuropathy, visual impairment, cognitive problem or retinopathy upon ophthalmologic examination during or after RT. The size of the tumor was stable, which was confirmed by radiographic studies. The fractionated noncoplanar VMAT technique provides delicate balance between dose coverage and normal tissues protection with well tumor control and improvement in visual function without treatment-induced morbidity.

Keywords: Optic nerve sheath meningioma (ONSM); volumetric modulated arc therapy (VMAT); image-guided system; orbital neoplasms; case report

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Introduction

Optic nerve sheath meningioma (ONSM) is a rare disease, accounting for 1% to 2% of all meningiomas; approximately 92% of ONSMs are intraorbital in origin, and 95% of these are unilateral (1). ONSM occurs primarily in females, with a mean age at presentation of 40 years (1,2). The optic pathway compression, proptosis, or ocular motility disorder caused by ONSM progresses slowly (2,3). Ophthalmological findings, together with magnetic resonance imaging (MRI), usually allow establishing the diagnosis of ONSM without biopsy (2,3).

The management of ONSM remains a particular challenge. The National Comprehensive Cancer Network (NCCN) guideline version 1.2019 of central nervous system (CNS) cancers (https://www.nccn.orgprofessionals/physician_gls/pdf/cns.pdf) indicates that observation is preferred for asymptomatic small meningiomas. Unfortunately, observation has historically led to poor
outcomes; for example, 86% of ONSM patients under observation experienced visual deterioration (1). In patients with one or more tumor- and/or treatment-related risk factors, such as proximity to the optic nerve, active treatment by surgery and/or radiotherapy (RT) is recommended by NCCN guidelines. However, in Dutton's reviewed report, there was a significantly increasing risk of vascular injuries through surgery, leading to 94% of patients with worsened vision and 78% with loss of light perception, and only 5% of patients demonstrated an improvement in vision (1). Resection of the tumor is associated with a high risk of blindness (4) and a high rate of local recurrence (5).

Highly conformal fractionated RT [such as three-dimensional conformal radiation therapy (3DCRT), intensity-modulated radiation therapy (IMRT), volumetric modulated arc therapy (VMAT) and proton therapy] with 45–54 Gy is also suggested by the NCCN guidelines for grade I meningioma. Recent advances in RT techniques, such as fractionated stereotactic radiotherapy (FSRT) based on three-dimensional treatment planning (6) or IMRT (7), have been recommended for patients unsuitable for surgery and the long-term control rate was 86–100% (1,8,9).

The VMAT technique could allow for IMRT delivery during gantry rotation with dynamic multi-leaf collimator motion, variable dose rates and gantry speed modulation. These characteristics significantly reduces the time and monitor units required to deliver a patient's treatment (10). However, little information is available on the impact of noncoplanar VMAT on ONSM. Herein, we present a first report of primary ONSM patient treated by a fractionated noncoplanar VMAT technique with an encouraging response including long-term efficacy and toxicity outcome. We present the following case in accordance with the CARE reporting checklist (available at http://dx.doi.org/10.21037/tro-2019-pmc-07).

**Case presentation**

**Patient history**

A 74-year-old female with a history of hypertension and colon tubule-villous adenoma had suffered from progressive oculus dexter (OD) visual deterioration for 2 or more months without trauma or operation history. She visited the local medical department for visual deterioration, but the cause was undetermined. Therefore, she was referred to the Department of Ophthalmology, Far Eastern Memorial Hospital, Taiwan. Ophthalmological examinations showed visual acuity with correction (VA_{cc}): 0.4 OD, 0.6 over oculus sinister (OS); intraocular pressure: 18 mmHg OD, 17 mmHg OS; Farnsworth D-15 Dichotomous Color Blindness Test: 3/15 OD, 15/15 OS; obvious visual field decreased OD assessed by automated perimetry (Figure 1). The 24-2 Visual Field Test revealed generalized visual field loss over the right eye and arcuate scotoma over the left eye. The mean deviation (MD) was −27.69 dB OD and −11.73 dB OS. A relative afferent papillary defect (RAPD) was noted in the right eye with intact extraocular motion and without ptosis. MRI showed a 12x6 mm eccentric enhanced mass located on the right distal optic nerve, and right ONSM was diagnosed (Figure 2). Prednisolone (1# po q.i.d.) was used to release the nerve decompression; however, visual impairment with color perception declined progressively (VA_{cc} and color vision in OD were 0.4 to 0.3 and 3/15 to 1/15, respectively). Thereafter, the patient was transferred to the department of Radiation Oncology.

The patient was treated with Versa HD™ (Elekta, Crawley, West Sussex, UK) to 54 Gy in 30 fractions within 6 weeks with a VMAT technique. The contouring system was operated using the Pinnacle 3 Treatment Planning System (Philips Healthcare, Madison, WI, USA). The clinical target volumes (CTVs) were defined as the area encompassing the gross tumor. The CTV areas plus 3 mm were used to generate the planning target volume (PTV). The RT plan with different techniques for the patient were compared (Figure 3). The dose constraints for organs at risk (OAR) were as follows: (I) optic chiasm and optic nerve: maximum dose, 55 Gy; (II) lenses <10 Gy; and lacrimal gland <35 Gy; (III) one parotid gland was spared to a mean dose of less than 20 Gy or, if both glands are spared, to less than 25 Gy (mean dose); (IV) brainstem: maximum dose, 54 Gy; (V) spinal cord: maximum dose, 50 Gy.

**Plan evaluation**

To compare VMAT and conventional radiation therapy (2DRT), 3DRT and IMRT, the Paddick conformity index (PCI) and uniformity index (UI) were applied. The PCI was originally proposed by Paddick (11) to evaluate the tightness of fit of the PTV to the prescription isodose volume in the treatment plans and was calculated as follows: PCI = (TV_{ piv})/ (TV × PIV), in which TV is the PTV volume, PIV is the treated volume enclosed by the prescription isodose surface, and TV_{ piv} is the volume of the PTV within the prescribed isodose. A PCI value close to unity means more conformity of the dose distribution to the target volume. The UI is
defined as $D5%/D95\%$, in which $D5\%$ and $D95\%$ are the minimum doses delivered to 5% and 95% of the PTV, respectively, as previously reported (12).

A total dose of 54 Gy was delivered to the PTV in 30 fractions by the noncoplanar VMAT technique with a PCI of 0.665 and UI of 1.074. The non-coplanar plan consisted of two noncoplanar partial arcs spanned from 310–240° and 240–300° with couch rotations of 90° and 45° and collimator angles of 5° and 355°, respectively. Compared with the other techniques, noncoplanar VMAT had the best uniformity and coverage and had fewer doses in the OAR than the other RT techniques (Table 1).

Treatment was well tolerated. From September 2017 to May 2019, no visual impairment, impaired ocular mobility, trigeminal deficit, proptosis, localized alopecia, transient worsening of headache or visual deterioration during or shortly after treatment, radiation retinopathy, cerebrovascular accident, cognitive impairment or brain necrosis were recorded. The color discrimination was improved from 1/15 to 13/15 after receiving 27 Gy in 15 fractions. The VA of the right eye treated with 54 Gy improved from 0.3 to 0.6 at 9 months and to 1.0 at 15 months after RT. Significant improvement of the visual field with an MD of –11.27 dB in the right eye was noted by automated perimetry (Figure 1). The following MRI revealed a mildly altered tumor density with a stable tumor.

Figure 1 The 24-2 Visual Field Test showed the following before (A) and after (B) VMAT treatment. (A) Generalized visual field loss (OD) and arcuate scotoma (OS) with a MD of –27.69 dB OD and –11.73 dB OS; (B) residual right peripheral scotoma (OD) with MD –11.27 dB and a nearly normal OS with MD –0.44 dB were observed after treatment. Visual function in the right eye significantly increased after VMAT treatment. VMAT, volumetric modulated arc therapy; OD, oculus dexter; OS, oculus sinister; MD, mean deviation.
size in the following period (Figure 2). The timeline to outline the whole process was listed in the Figure 4 to make the whole process more clear.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s)

Figure 2 The MRI study performed before and after VMAT revealed a mildly altered tumor density with a stable tumor size. MRI, magnetic resonance imaging; VMAT, volumetric modulated arc therapy.

Figure 3 Isodose distributions of the prescribed dose of 54 Gy to the PTV for different treatment techniques in the transverse, sagittal and coronal views. (A) 2DRT; (B) 3DCRT; (C) coplanar IMRT; (D) noncoplanar IMRT; (E) coplanar VMAT; (F) noncoplanar VMAT; (G) helical tomotherapy. 2DRT, conventional radiation therapy; 3DCRT, three-dimensional conformal radiation therapy; IMRT, intensity-modulated radiation therapy; VMAT, volumetric modulated arc therapy.
Table 1 Comparison of the PCI, UI and various OAR with different techniques in the patient

<table>
<thead>
<tr>
<th>Parameters</th>
<th>2DRT</th>
<th>3DCRT</th>
<th>Coplanar IMRT</th>
<th>Noncoplanar IMRT</th>
<th>Coplanar VMAT</th>
<th>Noncoplanar VMAT</th>
<th>Helical tomotherapy</th>
<th>Tolerance dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCI</td>
<td>0.251</td>
<td>0.210</td>
<td>0.535</td>
<td>0.625</td>
<td>0.621</td>
<td>0.665</td>
<td>0.754</td>
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<tr>
<td>UI</td>
<td>1.063</td>
<td>1.070</td>
<td>1.088</td>
<td>1.104</td>
<td>1.112</td>
<td>1.074</td>
<td>1.056</td>
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<tr>
<td>OAR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brain</td>
<td>45.6</td>
<td>1.7</td>
<td>45.5</td>
<td>54.1</td>
<td>5.1</td>
<td>53.4</td>
<td>3.3</td>
<td>0.6</td>
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<tr>
<td>Optic chiasm</td>
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<td>1.7</td>
<td>22.3</td>
<td>12.3</td>
<td>5.1</td>
<td>1.8</td>
<td>3.36</td>
<td>1.4</td>
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<td>Right optic nerve</td>
<td>56.6</td>
<td>48.9</td>
<td>56.6</td>
<td>50.8</td>
<td>59.0</td>
<td>59.1</td>
<td>58.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Left optic nerve</td>
<td>1.4</td>
<td>0.7</td>
<td>56.8</td>
<td>54.1</td>
<td>23.1</td>
<td>16.3</td>
<td>15.1</td>
<td>8.9</td>
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<tr>
<td>Right lens (max)</td>
<td>31.2</td>
<td>29.0</td>
<td>25.1</td>
<td>11.7</td>
<td>5.9</td>
<td>3.9</td>
<td>4.2</td>
<td>3.4</td>
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<tr>
<td>Left lens (max)</td>
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<td>1.9</td>
<td>0.5</td>
<td>0.4</td>
<td>1.1</td>
<td>0.9</td>
<td>0.3</td>
<td>0.2</td>
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<tr>
<td>Right eye</td>
<td>55.4</td>
<td>35.0</td>
<td>56.9</td>
<td>31.3</td>
<td>54.9</td>
<td>14.9</td>
<td>54.8</td>
<td>13.5</td>
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<td>Left eye</td>
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<td>9.4</td>
<td>3.8</td>
<td>0.6</td>
<td>7.7</td>
<td>1.4</td>
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<td>Right parotid gland</td>
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<td>0.3</td>
<td>1</td>
<td>0.3</td>
<td>0.5</td>
<td>0.1</td>
<td>0.6</td>
<td>0.1</td>
</tr>
<tr>
<td>Left parotid gland</td>
<td>0.3</td>
<td>0.1</td>
<td>3.4</td>
<td>0.5</td>
<td>0.5</td>
<td>0.2</td>
<td>0.7</td>
<td>0.2</td>
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<tr>
<td>Right lacrimal gland</td>
<td>38.1</td>
<td>15.4</td>
<td>39.0</td>
<td>29.3</td>
<td>37.7</td>
<td>16.3</td>
<td>37.4</td>
<td>13.8</td>
</tr>
<tr>
<td>Left lacrimal gland</td>
<td>0.6</td>
<td>0.4</td>
<td>0.5</td>
<td>0.3</td>
<td>1.5</td>
<td>0.9</td>
<td>0.2</td>
<td>0.2</td>
</tr>
</tbody>
</table>

PCI, Paddick conformity index; UI, uniformity index; OAR, organs at risk; 2DRT, conventional radiation therapy; 3DCRT, three-dimensional conformal radiation therapy; IMRT, intensity-modulated radiation therapy; VMAT, volumetric modulated arc therapy.
and with the Helsinki Declaration (as revised in 2013). The need for informed consent was waived by the Institutional Review Board of the Far Eastern Memorial Hospital (FEMH-IRB-108081-C) due to the research involves no more than minimal risk to subject. The retrospective data were collected after receiving approval from the Institutional Review Board of the Far Eastern Memorial Hospital.

Discussion

This is the first report of a patient with ONSM treated by a noncoplanar VMAT technique with an encouraging response. The treatment was noninvasive and well tolerated. A benefit of vision recovery to normal was observed at 15 months after the VMAT technique. Additionally, no severe complications were noted during or after RT in the following period.

The annual respective incidence of meningioma for males and females reported by the Central Brain Tumor Registry of the United States (CBTRUS) is 1.8 and 3.4 per 100,000 people, respectively, and most cases are often discovered in middle-to late adult life (13). ONSMs can be categorized among grade I meningiomas using the WHO grading scale (14). The first effective results using RT to treat ONSM were reported by Smith et al. (15). In studies with case numbers larger than 20 patients, the efficacy with visual function and a visual field that remained stable or improved was 92–100% (8,9,16). Additionally, the radiologically stable disease rate was 92–95% and the rate of acute or late treatment-related toxicity was 2–33% (9,16). However, these data mentioned above mostly resulted from treatment with 3DCRT or FSRT. Recently, patients with ONSM were treated by IMRT (7,17) or image-guided RT (18) with promising results. IMRT improves the dose distributions achieved using 3DCRT. Nevertheless, IMRT treatment techniques (step-and-shoot and sliding window) are fixed-gantry techniques. Recently, the University of Texas MD Anderson Cancer Center compared the plans between proton therapy and coplanar VMAT for ONSM treatment and favored VMAT after considering the conformity and uniformity (19). In a previous report, the noncoplanar IMRT technique reduced the off-target dose to normal organs at a statistically significant level compared to IMRT and helical tomotherapy (20).

In our case, treatment planning with different techniques including 2DRT, 3DCRT, coplanar IMRT, noncoplanar IMRT, coplanar VMAT, noncoplanar VMAT, and helical tomotherapy were compared (Table 1). PCI of noncoplanar IMRT, coplanar VMAT, noncoplanar VMAT, and helical tomotherapy were above 0.6 which was better than PCI of 2DRT, 3DCRT, and coplanar IMRT. However, UI of noncoplanar IMRT and coplanar VMAT were higher than 1.1 which was higher than other techniques. Considering normal tissue sparing, noncoplanar VMAT provided significant better protection of vision associated organ and structure including optic chiasm, left optic nerve, bilateral lens, and left eye than other treatment techniques.
Moreover, in the evaluation for isodose distribution, noncoplanar-VMAT provided the best conformal isodose line than other techniques in axial image (Figure 3). Comparing with helical tomotherapy, isodose distribution of noncoplanar-VMAT tends to be more perpendicular to optic nerve pathway and leading less dose deposits to optic nerve track. Helical tomotherapy, however, causing dose spreading more parallel along with optic nerve track leading to higher dose effect on vision associated organs. After evaluated the balances between optimal tumor coverage and critical organs sparing with minimal off-target irradiation, noncoplanar VMAT plan was decided.

Treatment was well tolerated without comorbidity. Additionally, the color discrimination and VA of the right eye were recovered as normal. Although the study of Al Feghali et al. (19), along with our current observation, suggests that the VMAT technique can efficiently treat ONSM, the number of patients is limited, and a longer follow-up is needed.

Here, we describe the first successful treatment of an ONSM using a noncoplanar VMAT technique, which appears to be promising for the management of such tumors. The tolerance and safety were excellent, and further investigation is warranted to assess potential late effects.

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