# Preliminary Experience of Cyberknife® Fractionated Stereotactic Radiotherapy in Management of an Orbital Pseudotumor: Case Report

## Orbital Psödotümör Tedavisinde Cyberknife® Fraksiyone Stereotaktik Radyoterapi Deneyiminin Ön Sonuçları

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**ABSTRACT** Orbital pseudotumor is a rare tumor of orbit which concerns a benign inflammatory process with an unknown etiology. They account for up to 10% of orbital masses and can involve any part of the orbit. Systemic steroids are the accepted as first line treatment modality. External beam radiation therapy has a well defined role in cases of failure, recurrences, persistent disease or medical contraindications for administration steroids. Management of orbital pseudotumors with stereotactic robotic radiotherapy was evaluated in a few studies. We aimed to describe a case involving the management of an orbital pseudotumor with the use of fractionated stereotactic radiotherapy using the CyberKnife® (Accuray Inc., Sunnyvale, CA).

**Key Words:** Orbital pseudotumor; corticosteroid; radiosurgery; adrenal cortex hormones

**ÖZET** Orbital psödotümör, bilinmeyen etyoloji ile benign inflamatuar proçeslerden kaynaklanan orbitanın nadir görülen tümörlerindendir. Orbital kitlelerin % 10' unu oluşturur ve orbitanın herhangi bir bölümünü tutabilir. Sistemik steroidler kabul görmüş ilk tedavi seçeneğidir. Başarısızlık, tekrarlama, dirençli hastalık durumunda ya da steroid kullanımı için tıbbi kontrendikasyonu olan hastalarda radyoterapinin iyi tanımlanmış rolü vardır. Stereotaktik robotik radyoterapi ile orbital psödotümör tedavisi çok az sayıda çalışmada değerlendirilmiştir. Biz bir orbital psödotümör olgusunda CyberKnife® (Accuray Inc., Sunnyvale, CA) fraksiyone stereotaktik radyoterapi yaklaşımımızı sunmayı amaçladık.

**Anahtar Kelimeler:** Orbita yalancı tümorü; kortikosteroid; radyocerrahi; adrenal korteks hormonları

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Orbital pseudotumor (OP) or idiopathic orbital inflammatory syndrome is a rare tumor of orbit which concerns a benign inflammatory processes with an unknown etiology. They account for up to 10% of orbital masses and can involve any part of the orbit.[1,2] Clinically, OP presents at a median age of 40-50 years with unilateral and occasionally bilateral involvement.[1,2] Proptosis, soft tissue swelling, orbital pain and exophtalmos are diagnostic symptoms and signs. It appears as an orbital mass and/or extraocular muscle enlargement on radiologic imagining.[3]

High dose corticosteroids are established as the initial most common form of treatment and are administered for several months to provide re-

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mission, for pseudotumor of the orbit.[4-7] External beam radiation therapy (EBRT) has a well defined role in cases of failure, recurrences, persistent disease or medical contraindications to use steroids.[5-10] Complete response rates with steroid therapy and radiotherapy are %50 and %66-%100, respectively.[4,5,8-10] The other treatment options are immunotherapy, chemotherapy and surgery.[11] Management of orbital pseudotumors with stereotactic robotic radiotherapy was evaluated in a few studies.[12-15] Herein, we present a young patient with an orbital pseudotumor, who was treated with fractionated stereotactic radiotherapy (FSRT) using the CyberKnife® (Accuray Inc., Sunnyvale, CA). Close proximity of critical structures to the target lead us to choose CyberKnife as an efficient and safe treatment option to avoid adverse affects.

## CASE REPORT

A 29-year-old man presented with a 9-month history of right sided eyelid soft tissue swelling, exophthalmus and ptosis. Magnetic resonance imaging (MRI) showed an enhancing lesion on superior-lateral side of the right orbit. Orbital biopsy revealed a chronic non-infectious inflammatory reaction including vascular proliferation within the fibroadipose tissue. Te patient was initially treated with oral steroids for six months, upon discontinuation, his symptoms reappeared in two weeks and the patient was referred for radiotherapy to our department. On admission, his physical exam was unremarkable except exophtalmos and ptosis. Magnetic resonance imaging (MRI) showed thickening in retrobulbar muscles with contrast enhancement (Figure 1 a,b).

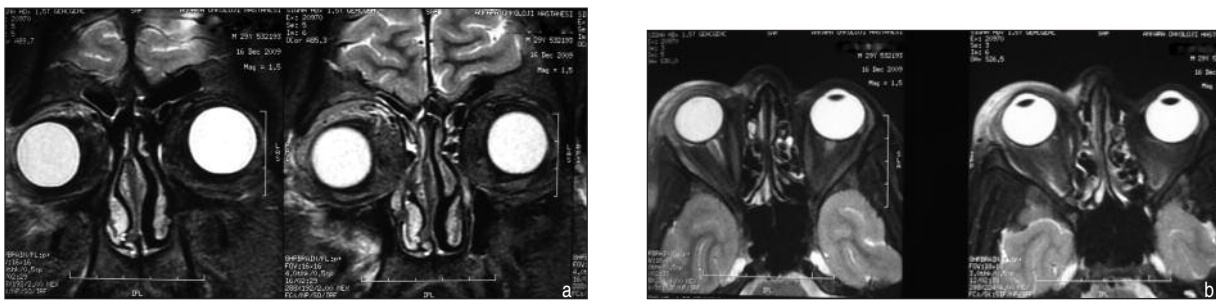


**FIGURE 1a, b:** The patient's MRI before FSRT. Orbital MRI showed thickening in retrobulber muscles and eyelid soft tissue swelling with contrast enhancement in the right orbit with proptosis of the globe.

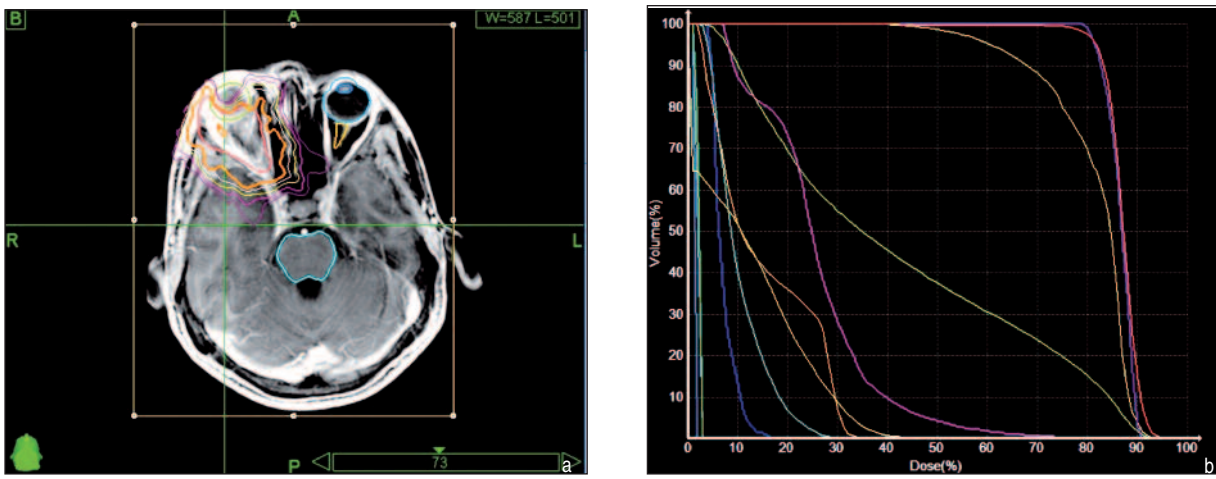



**FIGURE 2a, b:** The patient's planning image and dose volume histogram (DVH).
(See for colored form http://tipbilimleri.turkiyeklinikleri.com/)

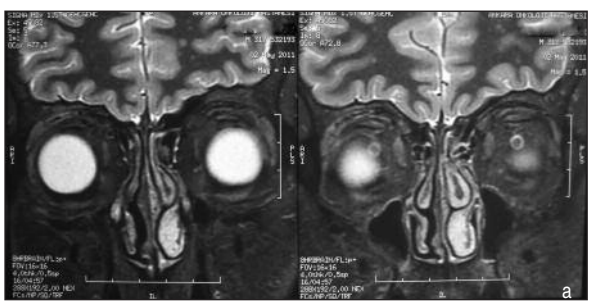
External beam radiation therapy was considered an inferior option compared to CyberKnife due to the inability to limit the dose to adjacent critical structures with increased risk of orbital and optic pathway toxicities. The potential risks and benefits of CyberKnife FSRT were explained to the patient and informed consent was obtained. Target and critical structures were delineated using fusion images of MRI with computerized tomography (CT) scanning with 3 mm slice-width. Prescribed dose of 1200 cGy to the 80% isodose line weas applied in three consecutive days (Figure 2a,b). The IRIS colimator and the sequential technique were used for treatment planning. Degree of tumor coverage was 97.76%, and, conformality index, new conformality index and homogeneity index were 1.60, 1.64 and 1.25, respectively. Intravenous steroids were used to decrease edema due to irradiation only before fractions. Doses received by adjacent critical structures are listed in Table 1. Complete resolution of symptoms was experienced within one month following FSRT. Acute side effects due to treatment were negligible, fractionated stereotactic radiotherapy was well tolerated without complications. Minimal thickness in right lacrimal gland and minimal contrast enhancement on the right preseptal area were observed on orbital MRI obtained three monthsafter the therapy, fter the therapy, which was interpreted as partial response with 80% decrease in contrast enhanced region according to Response Evaluation Criteria in Solid Tumors (RECIST version 1.1).[16] On the last follow-up at 18 months, he was symptom- and steroid-free with a normal ophthalmological examination, and orbital MRI revealed complete absence of the previously noted mass (Figure 3 a,b). Schirmer's test was applied to assess the function of the lacrimal gland, the result was within the normal limits. There was no late toxicities.

## DISCUSSION

Orbital pseudotumors are rare benign processes of orbit and may resolve spontaneously.[16] Corticosteroids are the mainstay of initial treatment; daily doses of prednisone 60-100 mg in two or three weeks followed by slow tapering is recommended.[4,17-19] Management of orbital pseudotumors with corticosteroids resulted in moderate responses, and high recurrence rates were found.[20,21]

Radiotherapy has a well defined role in cases of failure, recurrences, persistent disease or medical contraindications to steroids.[5-10] Orbital pseudotumor was found to be radioresponsive and external beam radiotherapy was as an effective treatment approach with a complete response rate of 66-100%, in previously reported series.[5-10] Different EBRT schemes were used ranging from 1400 to 3600 cGy over 10 to 18 fractions, however currently accepted dose is 2000 cGy in 10 fractions (Table 2).[5,8,9,19,22,23]

Several studies evaluated the factors affecting the response to radiotherapy. The lesions which included lymphocytes with germinal centers in the biopsy specimen had adequate responses to radiotherapy. In addition, small, discrete masses had better results with radiotherapy compared to large diffuse lesions.[22] Short interval between diagnosis and radiotherapy, erythema as a presenting symptom are other associated factors for better outcomes.[21,23] Resolution of symptoms took 3 to 8



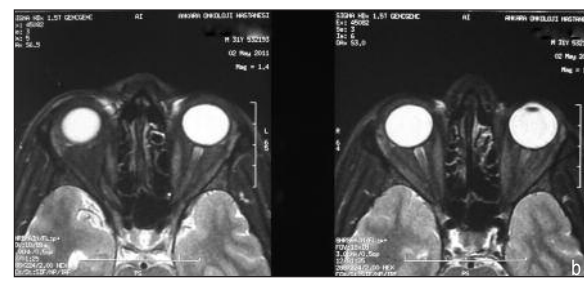


**FIGURE 3a, b:** The patient's orbital MRI at eighteen months follow-up.

**TABLE 1:** Dose statistics table.

| Volume of Interest | Minimum (cGy) | Mean(cGy) | Maximum(cGy) |
|---|---|---|---|
| Ipsilateral Structures | | | |
| Lens (Right) | 62.42 | 106.35 | 289.68 |
| Globe(Right) | 59.33 | 630.68 | 1406.68 |
| Optic nerve (Right) | 604.88 | 1215.43 | 1401.42 |
| Lacrimal Gland (Right) | 1189.27 | 1297.97 | 1365.19 |
| Contralateral Structures | | | |
| Lens (Left) | 28.02 | 28.56 | 29.18 |
| Globe(Left) | 27.24 | 31.09 | 41.27 |
| Optic nerve (Left) | 38.04 | 225.72 | 529.55 |
| Lacrimal Gland (Left) | 29.37 | 108.95 | 31.06 |
| Optic chiasm | 385.32 | 34.08 | 1194.09 |
| GTV | 644.24 | 1305.47 | 1500 |

GTV: Gross Tumor Volume.

months in previous reports.[19] In our case, we obtained symptomatic improvement within one month after FSRT.

The orbital fossa contains various radiosensitive structures such as the lacrimal gland, lens, optic nerve and globe. All have different tolerance doses, the most vulnerable structures to radiotherapy are the lens and the lacrimal gland.[24] Despite the recommended low doses for OP treatment, unexpected chronic complications may be observed.[23] Matthiesen et al. recently reported a review about clinical outcomes of patients diagnosed OP and treated with EBRT.[23] Twenty orbital involvement of 16 patients were evaluated retrospectively, EBRTs were applied with mean doses of 2000 cGy (range, 1400-3000 cGy). Chronic hypolacrimation was observed in three patients, and trigeminel neuralgia with unknown etiology was reported in three. Four patients received surgery after radiotherapy to correct orbital abnormalities.

Ahn et al. reported a series of 48 patients with head and neck tumors including 4 patients diagnosed with OP, treated with fractionated stereotactic radiation therapy.[25] Treatment planning was performed using Xknife-3 system with a frame. The prescribed dose was 2000 cGy in 10 fractions and the treatment was successful with symptomatic improvement and local control.

CyberKnife FSRT has been accepted widely for the treatment of benign intracranial tumors.[13] It is a 6MV linear accelerator mounted on a robotic arm which can monitor and adjust to changes in the target position in real time thus eliminating skeletal frame immobilization and allowing for convenient multi-fraction FSRT treatments.[26] Delivery of high doses to target volume, and limiting the dose exposure to the adjacent normal tissues by rapid dose fall-off, CyberKnife FSRT is a very effective and safe advanced radiotherapy technique.[26] Recent data about CyberKnife FSRT for the treatment of orbital pseudotumors is scarcy.[12-15] Brenner et al. suggested low doses in a range of 1000 to 1500 cGy in 2 to 3 fractions if the disease in inflammatory phase and relatively high doses of 1500 to 2000 cGy in 3 to 4 fractions for sclerosing subtypes. Biologically Effective Dose (BED) according to the Lineer-Quadretic model was calculated for eye ($\alpha/\beta$=1), and obtained values for EBRT and FSRT were 6000 cGy for each (for $BED_2$ and $BED_4$, respectively).[15]

Although tolerance dose of lacrimal gland changes between 3000 to 4000 cGy with conventional fractionation, it is not clearly identified for FSRT.[24] Muller et al. investigated the relation of hypolacrimation with received dose on a series of 72 uveal melonama patients who were treated with

**TABLE 2:** Radiation for treatment of orbital pseudotumor.

| Authors | Number of Patients | Follow-Up Time (month) | Prior Steroid (%) | RadiationDose (cGy) | Number of Fraction | Response Rate* (%) |
|---|---|---|---|---|---|---|
| Austin-Seymour et al.[5] | 18 | 35 | 70 | 2360 | 10-18 | 75 |
| Lanciano et al.[8] | 23 | 41 | 87 | 2000 | 10 | 66 |
| Orcutt et al.[22] | 22 | 22 | 82 | 2500 | 12 | 75 |
| Matthiesen et al.[23] | 16 | 16.5 | 93 | 2000 | 7-15 | 100 |

* Complete and partial response.

FSRT.[27] They evaluated the patients with Schirmer's test periodically. The lower Schirmer's test value was accepted as ≤10 mm after 5 minutes and the median received dose of 1000 cGy were found associated with hypolacrimation. In our case, ipsilateral lacrimal gland was delineated in tumor volume. Thereby, the lacrimal gland maximum point dose and mean dose were similarly the same as the target. In spite of receiving a significant dose to the lacrimal gland, the patient did not suffer from xerophthalmia, and this is supported by Schirmer's test which was within the normal limits at 18 months follow-up (≥15 mm after 5 minutes). In addition, contralateral orbital structures (optic nerve, lens, lacrimal gland, globe) received low dose radiation, in terms of maximal point dose and mean dose.

Currently, our knowledge about the management of orbital pseudotumors with CyberKnife® (Accuray Inc., Sunnyvale, CA) FSRT is limited. There is no report in the literature comparing efficacy and toxicity between EBRT and FSRT and due to the rarity of the disease since it is difficult to establish a randomized trial. The patient with orbital pseudotumor was treated without any complications and was seen every three months. At the 18 months follow-up, there was no recurrence and no late toxicities. Results of our case supports that CyberKnife FSRT is an effective and safe treatment modality in the management of OP. Although promising, more clinical studies and longer follow-up periods are necessary to determine effective dose per fraction and possible late sequelae of the treatment.

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