



# Localised Therapy and Biopsies of Intraocular Tumors

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The majority of intraocular neoplasms are amenable to a variety of treatment options depending on the underlying pathology and location within the globe. Increasingly the role of diagnostic and prognostic biopsies has become an integral part of the management of these lesions. Enucleation and radiation therapy are important treatment modalities that are discussed elsewhere in this textbook. This chapter will review focal modalities including cryotherapy and laser treatment as well as incisional and excisional biopsy techniques.

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## Cryotherapy

There are many tumors amenable to cryotherapy including retinoblastoma, retinal capillary hemangioblastoma, and vasoproliferative tumors of the retina [1, 2]. Generally, anterior tumors less than 3 mm in height are preferred for this approach. Multiple applications may be necessary to ensure complete tumor regression. The

technique can be performed on an outpatient basis with a local block or alternatively under general anesthesia for children. Using indirect ophthalmoscopy and scleral depression the tumor is visualized and cryotherapy is administered trans-sclerally. The surgeon visualizes the uptake of ice through the entire extent of the tumor followed by thawing. Generally, 2–3 freeze-thaw cycles are administered per session depending on the thickness of the tumor. Care is also taken not to freeze the overlying vitreous. Complications can include serous and rhegmatogenous retinal detachment, vitreous hemorrhage and periocular edema. It is recommended not to administer cryotherapy to retinoblastoma foci associated with significant calcification due to the risk of retinal tear [3].

There are various cryotherapy models that are available, some with greater length and curvature. While the technique is best suited for anterior tumors, following a conjunctival cut down, access and administration to posterior segment lesions is possible.

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## Laser Therapy

Laser therapy plays a significant role in the treatment of various tumors managed by ocular oncologists. It can be administered as a primary or adjuvant modality and is used for both malignant and benign neoplasms including

uveal melanoma, choroidal metastasis, retinoblastoma, circumscribed choroidal hemangioma, and retinal capillary hemangiomas. There are different types of lasers each with distinct indications. These include traditional photocoagulation, thermotherapy, and photodynamic therapy.

### **Thermotherapy**

Thermotherapy is generally used to manage uveal tumors as well as retinoblastoma. Small lesions can be lasered as a primary modality. Alternatively, it can be administered in an adjuvant setting after primary radiation or chemotherapy [4–6]. The laser is painful and requires either retrobulbar or (for pediatric patients) general anesthetic. The technique utilizes an 810 nm laser administered via slit lamp or indirect attachment. Principles of therapy include continuous large spot application directly to the tumor. The clinician begins at a low energy setting and gradually increases power at small intervals until a gray uptake is appreciated. A dense white appearance and application directly to retinal vessels should be avoided. Concomitant administration of indocyanine green (ICG) can be used for amelanotic lesions such as retinoblastoma and select choroidal metastases [7]. Complications to therapy include retinal and vitreous hemorrhage, vascular occlusion, serous and rhegmatogenous retinal detachment. It is preferred to avoid direct laser over areas with calcification for retinoblastoma foci. In general, this technique requires multiple applications until an acceptable endpoint with flattening of the tumor is achieved.

### **Photocoagulation**

Photocoagulation administers therapy at higher temperatures than thermotherapy. It is commonly used for retinal tumors including capillary hemangiomas and in select cases as an adjuvant for retinoblastoma. Historically it was used to man-

age small uveal melanomas however, this has largely been abandoned. Laser can be administered with various wavelengths. A common one is 532 nm. For retinal capillary hemangioblastomas, topical anesthesia is administered and laser applied via slit lamp or indirect attachment. Spots are applied circumferentially avoiding draining vessels. Subsequently, laser is administered to the surface of the lesion. Settings employ a low power, long interval approach. Multiple sessions may be necessary to achieve complete regression [8, 9]. Complications include hemorrhage, vascular occlusion, retinal exudation, and detachment. Treating retinoblastoma lesions with this modality requires care to avoid retinal perforation, tear, and rupture of the tumor leading to seeding. Clinicians should avoid direct application to areas of calcification and maintain low power settings with a gray endpoint.

### **Photodynamic Therapy**

Photodynamic therapy was initially introduced for the management of macular degeneration. It includes the intravenous infusion of a photosensitizing agent, vertoporphin, followed by laser administration. Subsequent studies demonstrated efficacy in the management of circumscribed choroidal hemangiomas [10, 11]. Recent reports have expanded its indication to include choroidal metastatic tumors [12]. Treatment involves topical anesthesia and administration of the photosensitizing agent intravenously. Similar to macular degeneration treatment is applied with a large spot over the entire neoplasm. If the lesion is too large to be encompassed with one spot, multiple spots can be applied with minimal overlap. Full fluence (50 J/cm<sup>2</sup> 600 mW/cm<sup>2</sup> 689 nm light over 83 seconds) as well as half fluence (25 J/cm<sup>2</sup> 600 mW/cm<sup>2</sup> 689 nm light over 83 seconds) has been described. One or two sessions are effective in inducing tumor regression. Following laser, patients should be instructed to avoid sunlight due to the photosensitizing agent.

## Intraocular Biopsy

Historically many clinicians deferred intraocular biopsy for concern of extraocular extension. The last two decades has seen a significant shift toward increased use of this technique. Biopsies may be excisional with the intent of tumor resection or incisional with the desire of tumor sampling. Incisional biopsies can be performed for diagnostic or prognostic purposes. Except under unique circumstances, the biopsy of an eye thought to be harboring retinoblastoma is contraindicated. The techniques differ for tumors in the anterior versus posterior segment.

### Posterior Segment Incisional Biopsy

Indications of incisional biopsy are for histopathologic diagnosis or prognostic testing for diseases such as uveal melanoma. Posterior segment lesions can be approached with either an *ab interno* or *ab externo* approach. External approaches are preferred for tumors anterior to the equator. Internal approaches work best for those located more posteriorly.

#### An Interno

Internal approaches involve sampling the eye from the pars plana through the vitreous into the retina and underlying choroid. This can be achieved with a use of an indirect ophthalmoscope and a 25- or 27-gauge needle [13, 14]. The patient is placed under general anesthesia and a conjunctival peritomy is performed. The muscles are isolated in standard fashion and indirect ophthalmoscopy is used to visualize the tumor. The biopsy is obtained from the same quadrant where the tumor is located. The needle is inserted between 3 and 4 mm posterior to the limbus and is visualized through its introduction into the eye toward the center of the tumor. The sample is aspirated under direct visualization and the needle removed through the pars plana. Cryotherapy can be administered at the biopsy site to lower the risk of extraocular extension. The same approach

can be used with a traditional three-port vitrectomy. Some surgeons prefer a two-port approach (excluding the infusion line) using a small gauge vitrector. It should be noted that biopsies requiring histopathologic assessment often require more tissue than those for prognostic testing alone. Complications include vitreous hemorrhage and retinal detachment (Video 9.1).

#### Ab Externo

For tumors anterior to the equator, an external approach is sometimes preferred and allows for larger volume tissue sampling. Following a peritomy and isolation of the extraocular muscles, the tumor is identified with a combination of transillumination and indirect ophthalmoscopy. The biopsy is directed toward thickest portion of the tumor. A 90% thickness scleral flap measuring approximately  $4 \times 4$  mm is constructed and hinged over the center of the neoplasm. Toward the base of the flap, the remaining fibers of the sclera are pierced with a blade, removing a uveal sample approximately one by one millimeters in size. Judicious application of cautery and use of systemic hypotension are helpful in minimizing bleeding. The wound is closed with nylon or silk suture. If lymphoma the tissue should be placed in liquid media (RPMI).

#### Vitrectomy

Primary intraocular lymphoma often presents as a vitritis. Vitrectomy is critical in obtaining accurate diagnosis. In these cases, a three-port vitrectomy is used with a low rate of cutting on the vitrector. As much vitreous debris as possible should be removed. An initial undiluted core sample is sent to the pathologist as well as the cassette. The pathologist should be informed in advance of the possible diagnosis of intraocular lymphoma so that the specimen can be properly analyzed with ThinPrep and flow cytometry [15].

#### Biopsy of Anterior Segment Tumors

Similar to the posterior segment, the anterior segment can be biopsied via an internal or external approach. For fine-needle aspirations, a 27-gauge

or smaller-gauge needle is inserted through the limbus under direct microscopic visualization into the tumor. The surgeon or assistant performs the aspiration. Following removal of the needle, the anterior chamber may need to be reinflated with BSS. Post biopsy hyphema can occur and is often self-limited. Alternatively, an external approach can be used in which a keratome is inserted slightly behind the limbus in the quadrant of the tumor allowing the iris to present at the wound. Using forceps and iris scissors a small piece of tumor is excised and the iris positioned back into the anterior chamber. The wound is then closed with interrupted nylon suture in traditional fashion.

### **Excisional Biopsy of Intraocular Neoplasm**

Posterior scleral-uvectomy was once a common technique within the field of ocular oncology. Its use has diminished significantly in part due to its technical difficulties and numerous complications. It is more common for this approach to be used for smaller irido-ciliary neoplasms.

The patient is placed under general anesthesia preferably under hypotensive conditions. Following a peritomy and isolation of the extraocular muscles, the margins of the tumor are demarcated with an adjacent circumferential 2–3 mm margin. A nearly full-thickness scleral flap is constructed hinged toward the fornix. Cautery is applied to the peripheral edges and the tumor is then incised with a knife and circumferentially excised with scissors. As the tumor is expressed, it is gently separated from the retina. The sclera is then reapproximated with interrupted nylon suture and the eye reinflated with BSS. Some surgeons combine this approach with a posterior vitrectomy. Following excision adjuvant radiotherapy in the form of a plaque may be necessary. Common complications include hypotony, retinal detachment, and vitreous hemorrhage. Incomplete excision and expulsive hemorrhage are also possible [16, 17].

### **Excisional Biopsy of Iris Tumors**

The complete excision of an iris tumor is similar to the approach used for extracapsular cataract surgery. The patient is given general or local (retrobulbar) anesthesia. An incision is made into the anterior chamber in the same quadrant as the neoplasm. Corneal scleral scissors are used to extend the wound 1–2 mm beyond the margins of the tumor. Using iris forceps and scissors a wedge of the iris is excised and the lesion removed from the anterior segment. Care is made to avoid extension into the ciliary body region. Localized hemorrhage can occur. The wound is reapproximated with interrupted nylon suture and the anterior chamber inflated with BSS. Due to the associated defect of the iris, some surgeons suture the edges of the lesion with a nonabsorbable (prolene) suture to reconstruct the pupil. Adjuvant radiotherapy may be necessary if the margins are positive on histopathology. Complications include hyphema, incomplete excision, photophobia and polyopia.

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### **Conclusion**

Focal therapies such as laser and cryotherapy are important treatment options in the management of many intraocular neoplasms such as retinoblastoma and uveal melanoma. Similarly, excisional and incisional biopsy techniques have become increasingly important, as the role of prognostic testing for uveal melanoma has become standard of care. It is imperative that the ocular oncologist understand the advantages and complications of each technique to provide an individualized approach for tumor management.

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## Suggested Videos

- [https://www.youtube.com/watch?v=QeG\\_mqfqKMA](https://www.youtube.com/watch?v=QeG_mqfqKMA)  
<https://eyetube.net/video/23-25g-chandelier-assisted-biopsy-of-choroidal-mass>  
<https://www.aao.org/clinical-video/choroidal-tumor-biopsy>

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