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**Review Article**

# Novel diagnostic and therapeutic measures in the field of ocular oncology: Current advances and future directions

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## Abstract

Personalized treatments and sophisticated diagnostics have led to significant advancements in ocular oncology.
Reviewing modern diagnostic and treatment approaches that are revolutionizing the treatment of ocular cancers.
Databases like PubMed, Scopus, and ClinicalTrials.gov were used to perform a narrative review.
OCTA, AI-based imaging, ctDNA analysis, and gene expression profiling are examples of new diagnostic techniques. These days, treatments include immunotherapy, gene therapy, nanomedicine, and plaque brachytherapy.
The developments mark a paradigm shift in patient care and improve accuracy and prognosis in ocular oncology.

**Keywords:** Gene therapy, AI imaging, nanomedicine, uveal melanoma, retinablastoma, liquid biopsy, ocular oncology, and personalized oncology.

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## 1. Introduction

Significant progress has been made recently in the specialized field of ocular oncology, which focuses on tumours of the eye and adnexa. Early detection and individualized treatment plans have been completely transformed by the development of high-resolution imaging, liquid biopsies, molecular diagnostics, and precision-targeted therapies. This article offers a thorough review of the most recent advancements in gene therapy, immunotherapy, targeted radiotherapy, and drug delivery using nanoparticles, as well as new therapeutic techniques like circulating tumor DNA (ctDNA) analysis, optical coherence tomography angiography (OCTA), and AI-assisted imaging. The prognosis and quality of life for patients with ocular cancers such as conjunctival melanoma, retinoblastoma, and uveal melanoma are changing because of these advancements. The article also looks at current clinical trials and future directions that could improve ocular oncology's therapeutic results and diagnostic accuracy. A broad range of primary and secondary neoplasms that impact the eye and periocular structures are included in ocular oncology. The most prevalent cancers are uveal melanoma in adults and retinoblastoma in children.[1] Reducing morbidity, protecting vision, and increasing survival all depend on early detection and prompt treatment. Despite their effectiveness, traditional diagnostic techniques are frequently invasive or insensitive to tumours in their early stages. Furthermore, organ-preserving and molecularly targeted therapies have replaced enucleation and external beam radiation as the main therapeutic approaches. The most recent and developing technologies that are changing the paradigms of diagnosis and treatment in ocular oncology are covered in this review.

## 2. Materials and Methods

A comprehensive literature search of peer-reviewed journals, clinical trials, and meta-analyses published between 2012 and 2024 served as the foundation for this article's narrative review. Keywords like *"ocular oncology," "uveal melanoma," "retinoblastoma," "novel diagnostics," "gene therapy," "liquid biopsy," "nanoparticles in ocular cancer,"*

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*and "ocular immunotherapy"* were used to search databases such as PubMed, Scopus, Web of Science, and ClinicalTrials.gov.

### *2.1. Criteria for inclusion*

1. Studies with human participants and/or verified experimental models are required for inclusion.
2. English-language publications.
3. January 2012–Dec 2024 publications.

### *2.2. Criteria for exclusion*

1. Opinion pieces, editorials, and reports without peer review are excluded.
2. Studies with no information on new therapeutic or diagnostic advancements.

Innovations in imaging, genetic profiling, molecular diagnostics, drug delivery systems, and new therapeutics were the main topics of data extraction. To forecast future directions, additional information was obtained from clinical trial registries, both completed and ongoing.

## 3. Novel Diagnostic Measures in Ocular Oncology

1. Advanced Imaging Techniques
   a. Optical Coherence Tomography Angiography (OCTA): OCTA provides high-resolution, non-invasive imaging of retinal and choroidal vasculature, crucial in assessing tumor vascularity and neovascularization.[2] OCTA can detect microvascular abnormalities associated with tumor aggressiveness in uveal melanoma.
   b. Enhanced Depth Imaging-OCT (EDI-OCT) and Ultrasound Bio-microscopy (UBM): EDI-OCT provides accurate choroidal tumour mapping, while UBM aids in defining anterior segment tumours such as iris melanoma.[3]
   c. Artificial Intelligence in Imaging: When combined with fundus photos and OCT, AI algorithms can accurately distinguish between benign and malignant lesions.[4] In the detection of retinoblastoma, deep learning models have demonstrated sensitivity rates of over 90%.
2. Molecular and Genetic Biomarkers
   a. Circulating Tumour DNA (ctDNA): Liquid biopsies that measure ctDNA in blood or aqueous humour have the potential to monitor the metastases of uveal melanoma and identify early retinoblastoma.[5]
   b. Gene Expression Profiling (GEP): To guide adjuvant therapy and surveillance, the 15-gene panel (DecisionDx-UM) categorizes uveal melanoma into prognostic classes.[6]
   c. MicroRNA Signatures: In ocular cancers, microRNAs such as miR-21 and miR-34a have been found to be putative biomarkers for tumour growth and treatment response.[7]
   d. Intraocular Fluid Analysis: Aqueous and vitreous humour analyses for protein biomarkers, exosomes, and cell-free DNA are becoming more and more popular for minimally invasive diagnosis, especially in paediatric retinoblastoma.[8]

### *3.1. Novel therapeutic approaches*

A variety of new diagnostic tools have been developed recently in ocular oncology (Table 1) that greatly improve the precision, early identification, and surveillance of ocular tumours like retinoblastoma, uveal melanoma, and conjunctival melanoma. High-resolution imaging methods that enable detailed visualization of tumor anatomical structures and vasculature include Ultrasound Bio-microscopy (UBM) and Optical Coherence Tomography Angiography (OCTA). Through machine learning algorithms trained on fundus and OCT images, artificial intelligence (AI) is being used more to automate the classification of tumours. Liquid biopsy techniques, specifically the analysis of cell-free DNA in aqueous humour and circulating tumour DNA (ctDNA) in blood, offer a non-invasive way to identify mutations specific to a tumour and track the course of the disease or its response to treatment. Particularly for uveal melanoma, molecular diagnostics such as Gene Expression Profiling (GEP) and microRNA signature analysis allow for risk stratification and individualized treatment. Furthermore, the analysis of protein biomarkers and exosomes in intraocular fluid provides important prognostic and diagnostic information. When combined, these developments are making ocular oncology a more accurate, individualized, and minimally invasive field that improves patient outcomes and quality of life.

**Table 1:** Summary of novel therapeutic approaches

| Therapy Type | Technique/ Agent | Application | Benefit |
|---|---|---|---|
| Local Radiotherapy | Plaque Brachytherapy, Proton Beam | Uveal melanoma | Tissue-sparing, effective local control |
| Chemotherapy | Intra-arterial, Intravitreal | Retinoblastoma | High globe salvage, low systemic toxicity |
| Immunotherapy | ICIs (Nivolumab), Tebentafusp | Metastatic Uveal Melanoma | Improved survival in trials |
| Targeted Therapy | MEK Inhibitors (Selumetinib) | GNAQ/GNA11 mutations | Targeted tumour growth inhibition |
| Gene Therapy | AAV2-RB1 Vector | Retinoblastoma | Preclinical success in RB1 repair |
| Nanomedicine | Liposomes, polymeric nanoparticles | Uveal melanoma, Retinoblastoma | Controlled delivery, reduced toxicity |

1. Local Treatments and Targeted Radiation
    a. Proton Beam Therapy: This type of charged particle therapy preserves surrounding tissues while precisely targeting uveal melanomas.[9]
    b. Plaque Brachytherapy: In small and medium tumours, radioactive plaques (Iodine-125 or Ruthenium-106) applied episclerally have demonstrated good local control rates while maintaining vision.[10]
2. Targeted and Systemic Treatments
    a. Immune Checkpoint Inhibitors (ICIs): Despite their historical lack of efficacy, ICIs such as nivolumab and ipilimumab are being used in trials to treat uveal melanoma, with new combinations being investigated.[11]
    b. Targeted Therapy for Uveal Melanoma: MEK inhibitors, such as selumetinib, have been studied for tumors with GNAQ/GNA11 mutations.[12] Bispecific T-cell engager tebentafusp is one of the novel agents that has demonstrated encouraging survival benefits.
3. Gene Therapy: Research is being done on gene therapy approaches for retinoblastoma that use adeno-associated virus (AAV) vectors to deliver the RB1 gene.[13] In early lesions, these seek to restore tumour suppressor function.
4. Nanomedicine and Drug Delivery Systems: In intraocular tumours, nanoparticles containing chemotherapeutic agents provide localized, prolonged drug release with low systemic toxicity.[14] For intravitreal and periocular administration, liposomal formulations are being investigated. Novel ocular medication administration systems are being developed because of developments in nanotechnology and non-invasive drug delivery methods. Drug bioavailability in anterior tissues can be enhanced by nano formulations such as nanomicelles, nanoparticles, liposomes, dendrimers, nanowafers, and microneedles. For the treatment of skin and eye conditions, non-invasive continuous drug administration is essential. Compared to nonfunctionalized nanoparticles, surface-functionalized nanoparticles containing targeting agents exhibit higher absorption. There are still issues, though, such as the complexity of the production technology, stability and safety issues, and a dearth of thorough in vivo research.[15]

## 4. Pediatric Aspects: Advances in the Treatment of Retinoblastoma

1. Intra-Arterial Chemotherapy (IAC): By delivering chemotherapy straight into the ocular artery via a catheter, intra-arterial chemotherapy (IAC) lowers systemic exposure. In certain instances, IAC has resulted in globe salvage rates of >90%.[16]
2. Intra vitreous Chemotherapy: Intra vitreous administration of Melphalan and Topotecan has been shown to be effective for vitreous seeds with few side effects.[17]
3. Genetic Counseling and Surveillance: Using non-invasive techniques such as handheld OCT, germline RB1 mutation testing allows for risk stratification and surveillance of at-risk siblings.[18]

## 5. Future Directions and Clinical Trials

Precision medicine, minimally invasive diagnostics, and immune-oncology-based treatments are all having a significant impact on the future of ocular oncology. Current advancements include:

1. Personalized and Genomic Medicine: Individualized tumor profiling is anticipated to be possible through whole-genome and epigenomic sequencing, allowing for the development of treatment plans tailored to each patient.[7] Intra-tumoral heterogeneity is being uncovered by advances in single-cell RNA sequencing, which will help determine drug resistance and the likelihood of metastasis in uveal and conjunctival melanoma. Increasingly, the selection of treatments is based on the distinct molecular or genetic characteristics of the patient and the tumour. Gene editing, immunotherapies, and targeted medications limit exposure to treatments that are unlikely to be beneficial, saving patients' eyesight and preventing needless side effects. With the help of localized drug systems and nanomedicine, treatments can more effectively reach the target tissue, reducing damage to healthy systemic and ocular tissues and providing patients with advanced or refractory disease with hope.
2. Integration of Artificial Intelligence and Machine Learning: Several models are getting close to clinical translation, and AI-based platforms like deep convolutional neural networks are being developed for the automated, real-time classification of ocular tumours from multimodal imaging.[4] To forecast the course of a disease and the effectiveness of treatment, ongoing projects seek to integrate AI with longitudinal patient data.
3. Liquid Biopsy Expansion: Exosomal RNA and cell-free DNA (cfDNA) from peripheral blood or aqueous humour are being studied to confirm their use as biomarkers for minimal residual disease detection and treatment monitoring. Continuous use of digital biomarkers and liquid biopsies will give doctors real-time information about patient response and tumour genetics, enabling them to modify treatments for the greatest possible benefit and the least amount of side effects.
4. Novel Therapeutics Clinical Trials: Important ongoing trials consist of:
    a. Tebentafusp for uveal melanoma (NCT04524269): Research has demonstrated that this bispecific T-cell engager increases survival in patients who test positive for HLA-A*02:01.

b. Combination immunotherapies for metastatic ocular tumors that include oncolytic viruses and checkpoint inhibitors.
c. AAV2-RB1 gene therapy trial for retinoblastoma (NCT05367206): Early intravitreal injection is used to target unilateral germline mutations.
d. Nanoparticle-based delivery systems for gene editing, chemotherapy, and siRNA in ocular tumors (preclinical studies underway).

5. Integration of Multi-Omics and Digital Twins: To help with drug selection and outcome prediction, researchers are investigating the creation of digital twin models—virtual simulations of patient-specific tumour responses—using multi-omics platforms (genomics, transcriptomics, proteomics, and metabolomics).
6. Multidisciplinary and Holistic Care: To create integrated, all-encompassing care plans, the future standard calls for multidisciplinary teams that combine knowledge from ophthalmology, oncology, pathology, genetics, radiology, and other fields. This strategy prioritizes quality of life, optimizes vision preservation, and raises the likelihood of survival. Patients can now take a more active role in their care thanks to developments in digital health tools, remote monitoring, and data accessibility, which improves adherence and results.

Ocular oncology is a prime example of how integrating research, patient-centred care, and precision technology can transform outcomes for eye cancer as well as other uncommon and complicated cancers. The combination of molecular profiling, AI-based interpretation, and ultra-high-resolution imaging guarantees more precise and timely diagnoses, frequently before symptoms manifest or vision loss takes place. The future holds the promise of safer treatments, earlier diagnoses, and the most individualized outcomes for every patient with ocular cancer if cooperation, research funding, and an emphasis on equity are maintained.

## 6. Conclusion

Ocular oncology is on the verge of a revolutionary period characterized by precision medicine and tailored diagnosis. Early diagnosis, risk assessment, and real-time treatment monitoring have all been significantly improved by the advent of technologies like liquid biopsies, AI-assisted imaging, and genomic classifiers. At the same time, localized treatment methods such as gene therapy, plaque brachytherapy, and intra-arterial chemotherapy have contributed to the preservation of ocular structure and function without sacrificing oncological safety. Treatment algorithms are being redefined by new immunotherapies, targeted therapies, and drug delivery based on nanomedicine, especially for tumors like metastatic uveal melanoma that have poor systemic treatment responses. More efficient, less invasive, and patient-specific treatment approaches are anticipated in the future of ocular oncology thanks to ongoing multi-center clinical trials and interdisciplinary partnerships.

There is continuous research into next-generation immunotherapies, oculomic correlations, smarter drug delivery, and new biomarkers. Every development will further improve early detection, risk stratification, and treatment personalization. By incorporating these new methods, previously unsatisfactory outcomes—like metastatic ocular melanoma or recurrent retinoblastoma—are becoming better. The treatment of eye cancer is changing because of recent advancements in ocular oncology diagnostics and treatments. Increased diagnostic precision, better prognosis, and organ-preserving therapies are anticipated with the integration of high-resolution imaging, liquid biopsy technologies, artificial intelligence, and molecular therapies.

Although there are still issues with cost, accessibility, and evidence-based validation, these developments give patients suffering from these potentially fatal and blinding illnesses great hope for better outcomes. Long-term outcome data, gene-based therapy accessibility, and biomarker-based diagnostic standardization are essential for optimizing the advantages of these advancements. Predictive, preventive, personalized, and participatory oncology will be further advanced by the field's integration of AI, omics, and real-world data. Additionally, telemedicine, automated AI analysis, and portable diagnostic devices will reduce global disparities by providing underserved and rural populations with high-quality ocular oncology care. Knowledge exchange and technology transfer will help upskill providers globally and guarantee that best practices are adopted globally as more specialists receive training in cutting-edge diagnostics and therapies.

## 7. Source of Funding

None.

## 8. Conflict of Interest

None.

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