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Cancer and the eye: giant steps forward. The Cambridge Symposium 2012

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The Cambridge Ophthalmological Symposium was conceived as a 2-day intense meeting for the in-depth study of specific fields of eye disease. This noble conference, held on the grounds of St John's College in the campus of Cambridge University rings with character, educational giants, footsteps of previous Nobel Prize winners, and a taste of early autumn. The symposium began in 1971 with 'Glaucoma', headed by Professor Hans Goldman, and meandered into other topics of 'Connective Tissue Disease of the Eye' in 1974 guided by Dr Edward Maumenee and 'The Optic Nerve' in 1976 lead by Dr William Hoyt. It was 1977 when the first study of eye cancer was undertaken in a formal fashion by this esteemed symposium entitled 'Pigmented Tumours' and directed by Dr Frederick Blodi. At that time, the field of ocular oncology was in its infancy. The challenge was simple. The task was to find clinical features that typified the main intraocular tumors, namely nevus, melanoma, metastasis, and retinoblastoma. Fluorescein angiography and ultrasonography were in early development as ocular imaging techniques, potentially able to detect a mass within the eye. The radioactive phosphorus (P32) uptake test was the in-fashion method to confirm malignancy. At that time, an eye with either uveal melanoma or retinoblastoma was usually removed and techniques of laser and irradiation were being explored. With regard to uveal melanoma, a heated controversy was eminent, with proponents of observation for small melanomas versus others demanding immediate enucleation for such lesions. The challenge was simple. The prognosis was ominous. Fast forward to 35 years later.

The topic of eye cancer was revisited in 2012 at the Cambridge Ophthalmological Symposium under the title of 'Cancer and the Eye' and coordinated by Professor Bertil Damato of Liverpool, England. Huge advances have been made in this three-decade intermission.[1,2] Not only have we refined ultrasonography and fluorescein angiography but we have developed other methods for ocular imaging including magnetic resonance imaging for large tumors and extremely powerful imaging of sub-millimeter tumors, down to a few microns, with enhanced depth image optical coherence tomography (EDI-OCT). Believe it or not, we can now measure choroidal tumors in their infancy, using EDI-OCT, before they are clinically visible. The P32 test, although highly reliable in differentiating benign from malignant tumors, has been abandoned because fine needle aspiration biopsy has been introduced and perfected. Ocular oncologists have become quite proficient in recognizing intraocular tumors with slit lamp biomicroscopy, binocular indirect ophthalmoscopy, and other non-invasive methods. And there's more.

With regard to retinoblastoma, the genetics of this malignancy have since been defined and we can predict at-risk family members. We have incredible new techniques involving delivery of chemotherapy into the vein, the artery, the subTenon's space, and even into the vitreous to provide tumor control, save the eye, and often provide remarkable visual outcome. Enucleation, once the most common method of treating retinoblastoma, is performed much less often and the great majority of eyes are salvaged today.

With regard to melanoma, the past three decades have seen a revolution in conservative therapy with early detection of melanoma when the tumor is 1–2 mm in thickness rather than previously 8–10 mm. We have a better understanding of the differences between the benign choroidal nevus and malignant melanoma, using published risk factors for

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tumor growth and metastasis, and we currently are exploring the molecular pathways for the development of melanoma.

Since 1977, there have been newly defined intraocular tumors that were not widely recognized in the past. These include choroidal osteoma, uveal melanocytoma, leiomyoma, schwannoma, iris lacrimal gland choristoma, retinal lymphoma, retinocytoma, vasoproliferative tumor, combined hamartoma of the retina and retinal pigment epithelium (RPE), pigmented ocular fundus lesions with familial adenomatous polyposis, and others. Moreover, we have clarified the differentiation of the various pigmented tumors of the eye from congenital hypertrophy of the RPE to adenoma of the RPE to pigmented medulloepithelioma to choroidal nevus to choroidal melanoma and even to the 'rare birds' of congenital simple RPE hamartoma, torpedo maculopathy, and others. Looking back, out of breath, we have taken giant steps in defining tumors of the eye.

At the 2012 symposium, there were fascinating discussions on subjects not foreseen in the 1977 meeting, including the hallmarks of cancer, the molecular biology of retinoblastoma, melanoma, and lymphoma, and the immunology of cancers. Discussion of new therapies using techniques of tumor resection, lasers, photodynamic therapy, and methods of radiotherapy with plaque brachytherapy, charged particles, gamma knife, and robotic cyberknife methods. Diagnostic fine needle biopsy indications, techniques, and results were deliberated. There were overviews on the current state-of-the-art of management of retinoblastoma, lymphoma, melanoma, metastasis, and vascular tumors. Huge strides in the innovative chemotherapy methods for retinoblastoma have culminated in the highest cure rate for any pediatric malignancy. Children with retinoblastoma can expect complete eradication of the malignancy with low risk for recurrence and with the added benefit of globe salvage and decent visual acuity in most cases. Novel methods of genetically typing uveal melanoma into low-risk or high-risk tumors using DNA or RNA methods have lead to a better understanding of melanoma behavior and hopefully future targeted therapy. And there's even more.

The field of ocular oncology has matured into an esteemed and respected subspecialty of ophthalmology with centers of excellence in most developed nations. A recognized International Society of Ocular Oncology was established in 2006 and biennual meetings have had presentations of cutting edge ideas, investigations, genomics, and therapies. Ocular oncology is exploding with fast forward movement. One of us (JAS) participated in both the 1997 and the 2012 Cambridge symposia and has personally witnessed this incredibly rapid progress in the field of ocular oncology.

So in 1977, we were taking baby steps in learning the task at hand—definition of the features of intraocular tumors. Now in 2012, we are beginning to take giant steps forward in understanding, trapping, and eliminating intraocular tumors before they threaten the patient. These giant steps will hopefully help to prolong life, preserve eyes, and provide better vision for our patients.

Acknowledgements

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References

1 Shields JA, Shields CL. *Intraocular Tumors. An Atlas and Textbook*. 2nd ed. Lippincott, Williams and Wilkins: Philadelphia, 2008.
2 Damato B. *Ocular Tumors: Diagnosis and Treatment*. Butterworth Heinemann: Oxford, 2000.

The two textbooks cite many aspects of intraocular tumors and numerous references. For further reading on more recent information, the reader is advised to read selected articles of the proceedings of the 2012 Cambridge Symposium that are published in this issue of Eye.