



## RETINAL TUMORS

### **Three cases of large retinal capillary hemangiomas treated with verteporfin and photodynamic therapy**

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Arch Ophthalmol. 2005 Mar;123(3):328-32.

**OBJECTIVE:** To investigate the efficacy of verteporfin and photodynamic therapy in the treatment of large retinal capillary hemangiomas.

**METHODS:** Case reports of 3 patients with large retinal capillary hemangiomas treated with photodynamic therapy using verteporfin. Standard verteporfin dosages (6 mg/m<sup>2</sup> of body surface area) were given. Both standard and modified photodynamic protocols were followed. Modified protocols included shorter verteporfin infusion times and longer light exposure times.

**RESULTS:** Pretreatment best-corrected Snellen visual acuity of the 3 affected eyes were 20/100, 20/50, and 2/200, respectively. All cases had associated exudative retinal detachments involving the macula. Cases 1 and 2 were classic endophytic retinal capillary hemangiomas. Case 3 was a reactive retinal capillary hemangioma. Case 1 had 2 photodynamic therapy treatments, and after 8 months, visual acuity improved to 20/40. Two years after initiating photodynamic therapy, the visual acuity was 20/30 and there was no reperfusion of the hemangioma. Case 2 had 3 photodynamic therapy treatments. The hemangioma was fibrotic, and 20 months after initiating photodynamic therapy visual acuity improved to 20/30. Case 3 had 1 treatment, 11 weeks later and visual acuity improved to 20/400. Four months after treatment, visual acuity returned to counting fingers because of tractional elevation of the macula as the capillary hemangioma fibrosed. Vitrectomy surgery was performed, and choroidal and retinal neovascularization was discovered. Three months after vitrectomy visual acuity was 20/400. In cases 1 and 2, the capillary hemangioma ultimately regressed, and the exudative detachment resolved.

**CONCLUSIONS:** Verteporfin and photodynamic therapy were effective in achieving closure of large retinal capillary hemangiomas. In all cases, the hemangioma underwent fibrosis with consequent macular puckering due to retinal traction. In all cases, the visual acuity improved.

### **Systemic non-hodgkin's lymphoma simulating primary intraocular lymphoma**

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Am J Ophthalmol. 2005 Mar;139(3):573-4.

**PURPOSE:** To describe a case of an unusual presentation of systemic non-Hodgkin's lymphoma with clinical and histopathologic findings closely resembling that of primary intraocular lymphoma.

**DESIGN:** Observational case report.

**METHODS:** A 58-year-old woman with a history of treated systemic non-Hodgkin's lymphoma presented 2 years later with a subretinal lesion and intraocular inflammation in her left eye.

**RESULTS:** Diagnostic enucleation and histopathologic studies revealed findings consistent with primary intraocular lymphoma including intraretinal, subretinal, and subretinal pigment epithelial tumor cells without involvement of the choroid.

**CONCLUSIONS:** We conclude that systemic non Hodgkin's lymphoma can present remotely with findings resembling primary intraocular lymphoma and should be included in the differential diagnosis of intraocular inflammation and subretinal infiltrates.

### **Systemic melanoma metastatic to the retina and vitreous**

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Ophthalmologica. 2004 Nov-Dec;218(6):424-33.

**PURPOSE:** Report of a case of retinal and vitreous metastases of a systemic melanoma, possibly arising in the lung, that responded favourably to radiotherapy.

**CASE REPORT:** Retinal and vitreous metastases were demonstrated in a 57-year-old woman during routine follow-up after surgical resection of a melanoma presumed to be a primary pulmonary melanoma. After a 7-week observation period, which confirmed the progressive nature of the intra-ocular lesions, the patient was treated by external beam radiotherapy at a dose of 35 Gy delivered in 14 fractions of 2.5 Gy. Complete disappearance of the vitreous invasion and progressive elimination of the retinal invasion were observed over a period of 9 months. Final visual function was 20/25.

**REVIEW OF PUBLISHED CASES:** A review of the literature identified 28 cases of melanoma with metastases to the retina and vitreous. In almost all of these cases, the primary tumour was a cutaneous melanoma and the mean patient survival following the diagnosis of intra-ocular metastases was 22 months. Retinal metastases, as in the case reported here, present a vascular tropism and tend to develop around veins. These metastases are generally unilateral and may be either solitary or multiple. Tumour invasion of the vitreous occurred by means of isolated cells forming a suspension of aggregates or spherules. Vitreous haemorrhage and irreducible neovascular glaucoma leading to functional impairment, which requires enucleation, were both the most frequent and the most serious complications of these metastases. Treatment is always palliative and is effective in cases with limited retinal and vitreous invasion, as in the case reported here.

**CONCLUSIONS:** Metastatic melanoma in the retina and vitreous is a rare entity and can lead to functional impairment and enucleation because of neovascular glaucoma. As treatment is only effective in cases with limited invasion, systematic screening is recommended in all patients with a metastatic cutaneous melanoma presenting with suggestive ocular symptoms.

### **Aggressive retinal astrocytomas in four patients with tuberous sclerosis complex**

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Trans Am Ophthalmol Soc. 2004;102:139-47; discussion 147-8.

**OBJECTIVE:** To report the clinical and histopathologic findings of retinal astrocytic tumors that showed progressive growth in four patients with tuberous sclerosis complex (TSC).

**METHODS:** Four young children each developed an enlarging retinal neoplasm that eventually necessitated enucleation of the affected eye. The systemic findings, clinical course, and histopathologic findings were reviewed.

**RESULTS:** Each patient had a progressively enlarging retinal mass associated with a total exudative retinal detachment and neovascular glaucoma. Enucleation was necessary in each case because the affected eye became blind and painful. The mean patient age at enucleation was 7 years, and the median age was 3 years. At the time of enucleation the tumors ranged from 10 to 20 mm in basal diameter and from 10 to 25 mm in thickness. Histopathologic studies of each eye revealed a giant cell astrocytoma that had produced a total exudative retinal detachment. The tumor cells showed positive immunoreactivity to neuron-specific enolase and glial fibrillary acidic protein. The retinal neoplasms in these cases were identical histopathologically to the subependymal giant cell astrocytoma that typifies TSC in the brain. One tumor filled the entire eye and perforated the globe. Although the lesions simulated retinoblastoma clinically, each patient had ocular and systemic findings of TSC, supporting the diagnosis of astrocytic hamartoma.

**CONCLUSIONS:** Although retinal astrocytic lesions of TSC generally are stationary, they can sometimes grow relentlessly and cause severe ocular complications. Patients with retinal astrocytic hamartomas should have serial ophthalmic evaluations because of this possibility.

### **Retinal neovascularization associated with retinoblastoma**

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Am J Ophthalmol. 2005 Jan;139(1):210-2.

**PURPOSE:** To report retinal neovascularization associated with retinoblastoma in a 14-month-old infant.

**DESIGN:** Observational case report.

**METHODS:** Review of clinical and pathologic findings.

**RESULTS:** A large frond of retinal neovascularization was present posterior to the lens in the right eye, which also contained a retinoblastoma.

**CONCLUSIONS:** Retinal neovascularization is an unusual association with retinoblastoma.

### **Hereditary cancer predisposition syndromes**

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J Clin Oncol. 2005 Jan 10;23(2):276-92.

Cancer genetics is increasingly becoming integrated into the practice of modern medical oncology. The ability to distinguish a growing proportion of the 5% to 10% of all cancers that develop in individuals who have inherited a genetic mutation conferring heightened susceptibility to specific cancers may permit targeted efforts in cancer surveillance and prevention. While these individuals comprise a small proportion of the overall burden of cancer, strategies successful in reducing their remarkable cancer risks may be generalizable to the broader population. In this review, we highlight the most common hereditary cancer syndromes, most attributable to genes inherited in an autosomal dominant manner with incomplete penetrance, and a number of rare syndromes in which particular progress has been made. The prevalence, penetrance, tumor spectrum, and underlying genetic defects are discussed and summarized in a large table in which a more comprehensive enumeration of syndromes is provided.

### **Metastatic retinoblastoma of the maxilla and mandible**

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Dentomaxillofac Radiol. 2005 Mar;34(2):126-31.

Metastatic retinoblastoma of the jaws is very rare. We present a 4-year-old boy with metastatic retinoblastoma that involved both the maxilla and mandible simultaneously. Enhanced CT indicated bone-destructive masses with partially non-enhanced area and enhanced margin in the right maxilla and left mandible. MRI showed well-delineated masses that were isointense on T(1) weighted images and hyperintense on T(2) weighted images. Four weeks after chemotherapy and bone marrow transplantation, the size of lesions remarkably decreased. The patient died 19 months later with extensive tumour metastases despite additional chemotherapy. In this case, the dental crypt of a permanent tooth was considered the potential target through which retinoblastoma metastasized to the jaws.

### **The clinical spectrum and treatment outcome of retinoblastoma in indian children**

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J Pediatr Ophthalmol Strabismus. 2005 Mar-Apr;42(2):75-81.

**PURPOSE:** To study the clinical spectrum and treatment outcome of Retinoblastoma in Indian children.

**PATIENTS AND METHODS:** This retrospective study analyzed 488 eyes of 355 retinoblastoma patients treated at a tertiary care ophthalmic hospital in southern India during a 14-year period.

**RESULTS:** Retinoblastoma involved one eye in 177 (50%) and both eyes in 178 (50%) patients. Mean age at presentation was 23.98 +/- 23.37.

### **The retinoblastoma protein--from bench to bedside**

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The retinoblastoma tumour suppressor protein (Rb) has come a long way since its initial discovery in 1986. Encoded by the first candidate tumour suppressor gene it has emerged a versatile and context-dependent modulator of cell behaviour. Its activity is managed by signalling networks sensing intra- and extracellular cues. These cues are relayed to hold or permit inactivation of Rb by phosphorylation. Loss or mutation of the retinoblastoma gene is rare in sporadic cancers but defects in the pathways that license inactivation of Rb are found in the majority of them, suggesting that loss of Rb control is central to tumour development and arguing that its reinstatement might reverse tumour formation. Furthermore, mouse models with engineered defects in the Rb-phosphorylating kinases provide evidence that moderation of Rb inactivation may be a strategy for the prevention of tumour formation. The rationale behind these arguments, their underlying molecular concepts and strategies towards therapeutic application will be discussed.

### **Clinical implications of promoter hypermethylation in rassf1a and mgmt in retinoblastoma**

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Neoplasia. 2005 Mar;7(3):200-6.

We investigated the epigenetic silencing and genetic changes of the RAS-associated domain family 1A (RASSF1A) gene and the O6-methylguanine-DNA methyltransferase (MGMT) gene in retinoblastoma. We extracted DNA from microdissected tumor and normal retina tissues of the same patient in 68 retinoblastoma cases. Promoter methylation in RASSF1A and MGMT was analyzed by methylation-specific PCR, RASSF1A sequence alterations in all coding exons by direct DNA sequencing, and RASSF1A expression by RT-PCR. Cell cycle staging was analyzed by flow cytometry. We detected RASSF1A promoter hypermethylation in 82% of retinoblastoma, in tumor tissues only but not in adjacent normal retinal tissue cells. There was no expression of RASSF1A transcripts in all hypermethylated samples, but RASSF1A transcripts were restored after 5-aza-2'-deoxycytidine treatment with no changes in cell cycle or apoptosis. No mutation in the RASSF1A sequence was found. MGMT hypermethylation was present in 15% of the retinoblastoma samples, and the absence of MGMT hypermethylation was associated ( $P = .002$ ) with retinoblastoma at advanced Reese-Ellsworth tumor stage. Our results revealed a high RASSF1A hypermethylation frequency in retinoblastoma. The correlation of MGMT inactivation by promoter hypermethylation with lower-stage diseases indicated that MGMT hypermethylation provides useful prognostic information. Epigenetic mechanism plays an important role in the progression of retinoblastoma.

### **Evolution of a retinoma case in 21 years**

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Ophthalmic Surg Lasers Imaging. 2005 Mar-Apr;36(2):155-7.

A 35-year-old man was observed during a 21-year period with fundus color photography, fluorescein angiography, and B-scan ultrasonography for a presumed retinoma detected in his left eye during routine ophthalmoscopy in 1982. The patient was a carrier of the 13q14 retinoblastoma gene. His retinal lesion remained stable during the follow-up period without signs of malignant transformation. Retinomas are most commonly observed in patients with retinoblastoma and their relatives. In this case, none of the patient's parents, siblings, or children had evidence of a retinal tumor. Photographic documentation of the nonprogressive nature of this presumed retinoma is provided and demonstrates the absence of growth.

### **A retrospective review of visual outcome and complications in the treatment of retinoblastoma**

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Ir Med J. 2005 Jan;98(1):17-20.

The aim of this study was to look at the visual outcome and treatment complications of children diagnosed with Retinoblastoma during the years 1985-2003 inclusive. A retrospective review of all patients records was performed. Patient characteristics, treatment methods and complications were recorded. Twenty eight children presented to Temple street Hospital between 1985-2003. Six of these infants had bilateral tumours. The mean age at presentation was 23.7 months. Sixty-nine percent presented with Leucocoria, of these 33% also had a squint. The mean duration of symptoms was only known in 58% and this figure was approximately 19.8 months. Enucleation was performed in 24 eyes of 24 patients. Three patients required adjuvant chemotherapy post enucleation. Two eyes was treated with

external beam radiation and one eye with plaque radiotherapy. One eye (second eye) was treated with systemic chemotherapy and radiation. Five eyes of three patients were treated with systemic chemotherapy followed by adjuvant Argon laser, cryotherapy and diode laser to each eye. The complications of each treatment group was recorded. The visual outcome in the salvaged eyes was favourable. There were no deaths recorded. Though chemotherapy with adjuvant local treatments provide adequate treatment for early tumours, enucleation still plays a major role in the treatment of Retinoblastoma. The total eye salvage rate in this study was 29% with an enucleation rate of 90% in unilateral cases and 33% in bilateral cases. Sixty-six percent of bilateral eyes affected were salvaged. Seventy-one percent of tumours were diagnosed after a parent noticed a gross abnormality of the eye. This highlights the possible need for screening for retinoblastoma in the infant population.

### **Exposure of orbital implants wrapped with polyester-urethane after enucleation for advanced retinoblastoma**

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Ophthal Plast Reconstr Surg. 2005 Mar;21(2):123-8.

**PURPOSE:** Enucleation is the main form of treatment for advanced retinoblastoma. The major complication of this procedure is orbital implant exposure. Different implants and wrapping materials are currently in use. The aim of the current study was to analyze the complications associated with the use of polyester-urethane, an artificial dura substitute, as a wrapping material for enucleation in advanced retinoblastoma.

**METHODS:** A retrospective review of 32 cases (28 patients), who were treated with enucleation for advanced retinoblastoma, was performed. The age of the patients ranged between 3 months and 6.7 years (median, 19 months). Additional chemotherapy was administered in 12 cases. The removed eyeball was replaced either with a silicone implant and polyester-urethane wrapping (13 cases) or hydroxyapatite, silicone-hydroxyapatite, or polyethylene implants without additional wrappings (19 cases). The follow-up period ranged from 7 months to 5.9 years (median, 22.4 months). Statistical analysis was performed using the Kaplan-Meier method.

**RESULTS:** Single or multiple exposures occurred in 22% of cases (7/32). There were 6 exposures (46%, 6/13) in the group with polyester-urethane wrapping compared with only 1 exposure (5%, 1/19) in the implants without wrapping. This difference was statistically significant ( $p=0.0236$ ). None of the other analyzed factors (additional chemotherapy, surgeon, age of the patient, or size of the implant) demonstrated a significant correlation to implant exposures.

**CONCLUSIONS:** Wrapping of orbital implants with polyester-urethane resulted in a high rate of implant exposures after enucleation for advanced retinoblastoma. In this series, the best results were achieved with integrated implants without additional wrapping.

### **Age at diagnosis of isolated unilateral retinoblastoma does not distinguish patients with and without a constitutional rb1 gene mutation but is influenced by a parent-of-origin effect**

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Eur J Cancer. 2005 Mar;41(5):735-40.

Patients with hereditary cancer are usually diagnosed earlier than patients with non-hereditary tumours. In children with isolated unilateral retinoblastoma, some of whom have a hereditary predisposition, this

rule has been subject to debate. We have analysed the clinical manifestation of disease in 188 children with completely resolved mutational status. In 24 (13%) of these patients, testing of blood DNA showed a constitutional RB1 mutation. The distribution of age at diagnosis was not different between patients with and without a constitutional mutation. However, patients with loss of the maternally inherited RB1 allele had an earlier age at diagnosis than patients with loss of the paternally inherited RB1 allele. Our data show that early age at diagnosis does not identify patients with isolated unilateral retinoblastoma that have a higher risk of being carriers of a RB1 gene mutation. Our findings suggest that, at least in some patients, age at diagnosis is modified by a parent-of-origin effect.

### **Infrared thermotherapy: from laboratory to clinic**

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Ophthalmol Clin North Am. 2005 Mar;18(1):99-110.

Thermotherapy by the transpupillary route is an effective outpatient eye-salvaging therapy for intraocular tumors. It does not require surgery, it can be repeated, and it does not affect the healthy structures of the eye. Thermotherapy by the transscleral route is under investigation and may have potential in the treatment of choroidal melanomas. The indications for chemoreduction, thermochemotherapy, and thermotherapy for retinoblastoma remain under investigation.

### **Management of advanced retinoblastoma**

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Ophthalmol Clin North Am. 2005 Mar;18(1):65-73.

This review provides an update on the current management of advanced retinoblastoma.

### **Chemotherapy for retinoblastoma**

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Ophthalmol Clin North Am. 2005 Mar;18(1):55-63.

Retinoblastoma is the most common eye cancer in children. Pilot studies of chemotherapy for intraocular retinoblastoma have been reported by several groups, using different combinations, dosages, schedules, and durations of carboplatin, etoposide, or teniposide, with or without vincristine, and with or without cyclosporine to counteract multidrug resistance. All studies of chemotherapy for intraocular retinoblastoma have included consolidation by focal therapy, with or without radiation. Chemotherapy alone reduces tumor size but does not cure retinoblastoma. Focal therapy, consisting of photocoagulation, thermotherapy, cryotherapy, or brachytherapy, is necessary to consolidate chemotherapy response.

### **Intraocular retinoblastoma: the case for a new group classification**

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Ophthalmol Clin North Am. 2005 Mar;18(1):41-53.

This article argues the case for the creation of a new group classification of intraocular retinoblastoma. The current Reese-Ellsworth group classification has not been updated since it was published 35 years ago. The proposed classification is based on the natural history of intraocular retinoblastoma and on the risk of loss of the eye following primary therapy.

### **Retinoblastoma: Animal models**

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Ophthalmol Clin North Am. 2005 Mar;18(1):25-39.

Employment of animal models in basic research has significantly advanced the understanding of fundamental processes underlying tumorigenesis in retinoblastoma, including elucidating the complex role of pRb and other related protein products in cell cycle regulation, apoptosis, DNA damage responses, and terminal differentiation. The evolution of therapy for retinoblastoma has also been facilitated through translational research using in vivo models, including xenograft and genetically engineered systems. In retinoblastoma, these models provide a valuable preclinical context for testing the efficacy and safety of conventional chemotherapy, radiotherapy, or novel agents on tumor growth, tissue invasion, and metastasis.

### **Chemoreduction for retinoblastoma: Analysis of tumor control and risks for recurrence in 457 tumors**

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Trans Am Ophthalmol Soc. 2004;102:35-44; discussion 44-5.

**PURPOSE:** To evaluate individual tumor control following chemoreduction for retinoblastoma.

**METHODS:** Prospective nonrandomized single-center case series of 457 retinoblastomas managed with six cycles of chemoreduction (vincristine, etoposide, and carboplatin). The tumors were then managed with chemoreduction alone (group A) or chemoreduction combined with thermotherapy (group B), cryotherapy (group C), or both thermotherapy and cryotherapy (group D). The main outcome measure was development of tumor recurrence.

**RESULTS:** Of 457 retinoblastomas, 63 (14%) were in group A, 256 (56%) in group B, 127 (28%) in group C, and 11 (2%) in group D. The tumor was located in the macula in 33 (52%) of group A, 109 (43%) of group B, 3 (2%) of group C, and 1 (9%) of group D. Using Kaplan-Meier analysis, recurrence of the individual retinoblastoma at 7 years was found in 45% of group A and in 18% of combined groups B, C, and D. Treatment of the 93 tumor recurrences included thermotherapy, cryotherapy, or plaque radiotherapy in 62 cases (67%) and external beam radiotherapy or enucleation in 31 cases (33%). Risk factors predictive of tumor recurrence by multivariate analysis included macular tumor location for all groups and, additionally, female sex for group A and increasing tumor thickness for groups B, C, and D.

**CONCLUSIONS:** Chemoreduction alone or combined with cryotherapy and/or thermotherapy is effective for treatment of retinoblastoma, but tumor recurrence is greatest for those located in the macula and those with greater thickness. Globe salvage is usually achieved despite tumor recurrence.

### **Cyclosporin a inhibits calcineurin/nuclear factor of activated t-cells signaling and induces apoptosis in retinoblastoma cells**

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Invest Ophthalmol Vis Sci. 2005 Mar;46(3):782-90.

**PURPOSE:** Although the clinical efficacy of cyclosporin A (CSA) in Retinoblastoma (RB) has been attributed to multidrug resistance reversal activity, the authors hypothesized that CSA is also directly toxic to RB cells through inhibition of calcineurin (CN)/nuclear factor of activated T-cells (NFAT) signaling.

**METHODS:** Antiproliferative effects of CSA, PSC-833 (a CSA analogue that does not inhibit CN), and FK506 (a CN inhibitor structurally unrelated to CSA) were evaluated in Y79 and Weri-RB1 cells by WST-1 assay. Apoptosis induction by CSA and PSC-833 was measured by detection of caspase 3/7 activity and by flow cytometry, using annexin-V and 7-AAD stains. Expression of CN was assayed in RB cells by immunocytochemistry. Expression of NFAT, a CN-dependent transcription factor family, and FK506 binding protein 12/12.6 (FKBP12/12.6), effectors of CN inhibition by FK506, was assayed in RB cells by Western blot analysis. NFAT activity was assayed in CSA-treated and -untreated Y79 cells transfected with an NFAT-sensitive reporter gene.

**RESULTS:** CSA induced dose-dependent antiproliferative and proapoptotic effects at clinically achievable levels in Y79 and Weri-RB1 cells. PSC-833 induced antiproliferative effects only at nonphysiologic concentrations with minimal associated apoptosis. FK506 induced minimal antiproliferative effects in RB cell lines, probably due to trace or absent FKBP12/12.6 expression. RB cell lines expressed CN-alpha, CN-beta, NFATc1, and NFATc3. CSA treatment also potently inhibited NFAT-mediated reporter gene transcription.

**CONCLUSIONS:** These results demonstrate functional integrity of the CN/NFAT signaling cascade in RB cells and suggest that CSA is cytotoxic to RB cells through inhibition of this pathway and consequent apoptosis induction.

### **IVF and Retinoblastoma**

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Br J Ophthalmol. 2005 Mar;89(3):393.

No abstract available

### **Mothers' perceptions of children's quality of life following early diagnosis and treatment for retinoblastoma (RB)**

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Child Care Health Dev. 2005 Mar;31(2):137-42.

We describe the Quality of Life (QoL) and IQ of survivors of Retinoblastoma (Rb), both in relation to the normal population and between subgroups of Rb patients differing in relative risk (i.e. unilateral vs. bilateral disease). The sample included 54 children (28 males, age-range 8-16 years) and their mothers. Mothers completed standardized questionnaires to report their own QoL and that of their child. Children completed a brief IQ test. Compared with population norms, mothers reported lower levels of QoL for their child on total QoL and for sub-scales measuring Physical and Psychosocial function. Mothers reported their own QoL to be comparable or higher than norms on all but one of eight sub-scales (energy/vitality). Compared with population norms, children with no visual impairment scored in the normal range for tasks measuring Verbal IQ, but below the mean on tasks measuring Performance IQ. According to their mothers, survivors of Rb have excellent school attendance and take part in most school activities. However, based on standardized questionnaire, they show compromised QoL. We consider that excellent survival rates in Rb are matched with good QoL according to mothers' report.

### **Retinoblastoma: mr imaging parameters in detection of tumor extent**

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Radiology. 2005 Apr;235(1):197-207. Epub 2005 Feb 4.

**PURPOSE:** To assess diagnostic accuracy of preoperatively performed magnetic resonance (MR) imaging for detection of tumor extent in a large patient population with histopathologically proved retinoblastoma.

**MATERIALS AND METHODS:** Local ethics committee approval and informed consent were not required for retrospective review of patients' images and records. Fifty-eight eyes in 28 girls (mean age, 21 months; range, 2-59 months) and 28 boys (mean age, 24 months; range, 2-76 months) with retinoblastoma were retrospectively reviewed by one radiologist on unenhanced T1-weighted, dual-echo T2-weighted, and gadolinium-enhanced T1-weighted MR images. MR imaging parameters such as growth pattern, anterior chamber hyperintensity, and involvement of choroid, ciliary body, optic nerve, sclera, orbital fat, and pineal gland were determined. Tumor volume was measured and correlated to metastatic risk factors. Imaging and pathologic findings were compared. Statistical analysis was performed by using logistic regression with log likelihood ratio chi(2) test or Fisher exact test.

**RESULTS:** Choroidal invasion was suspected with MR imaging in 21 eyes; findings were false-positive in 13 eyes and false-negative in three (73% sensitivity, 72% specificity, 72% accuracy). Anterior chamber hyperintensity on T1-weighted MR images obtained after contrast agent administration correlated well with clinical presence of reactive neovascular processes. MR imaging findings were true-positive in 21 of 32 eyes with proved prelaminar optic nerve invasion (66% sensitivity) and false-positive in one (96% specificity, 79% accuracy). Postlaminar optic nerve invasion was correctly detected in two eyes; in two other eyes, this metastatic risk factor was missed (50% sensitivity, 100% specificity, 97% accuracy). Scleral and extrascleral tumor invasion were correctly excluded in all eyes. Tumor volume was statistically associated with prelaminar optic nerve invasion ( $P = .001$ ) and choroidal invasion ( $P = .031$ ).

**CONCLUSION:** MR imaging is accurate for tumor staging and detection of metastatic risk factors; detection of intraocular tumor infiltration remains difficult. Tumor volume, measured with MR imaging, was associated with prelaminar optic nerve and choroidal involvement. (c) RSNA, 2005.

### **Progressive resorption of a presumed spontaneously regressed retinoblastoma over 20 years**

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Retina. 2005 Feb-Mar;25(2):230-1.  
No abstract available

### **The search for the retinoblastoma cell of origin**

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Nat Rev Cancer. 2005 Feb;5(2):91-101.

The cellular effects of the genetic defects associated with tumorigenesis are context dependent. To better understand the reasons that different cell types require distinct combinations of mutations to form tumours, it is essential to identify and characterize a tumour's 'cell of origin'. Retinoblastoma, a rare childhood cancer of the retina that is caused by RB inactivation, is a good model in which to search for a tumour cell of origin, because retinal development is well understood and the initiating genetic lesion is well characterized. Identifying the cell of origin for this tumour would advance our understanding of how cellular context affects the requirement of specific mutations for cancer initiation and progression.

### **Proton radiation therapy for retinoblastoma: Comparison of various intraocular tumor locations and beam arrangements**

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**PURPOSE:** To study the optimization of proton beam arrangements for various intraocular tumor locations; and to correlate isodose distributions with various target and nontarget structures.

**METHODS AND MATERIALS:** We considered posterior-central, nasal, and temporal tumor locations, with straight, intrarotated, or extrarotated eye positions. Doses of 46 cobalt grey equivalent (CGE) to gross tumor volume (GTV) and 40 CGE to clinical target volume (CTV) (2 CGE per fraction) were assumed. Using three-dimensional planning, we compared isodose distributions for lateral, anterolateral oblique, and anteromedial oblique beams and dose-volume histograms of CTVs, GTVs, lens, lacrimal gland, bony orbit, and soft tissues.

**RESULTS:** All beam arrangements fully covered GTVs and CTVs with optimal lens sparing. Only 15% of orbital bone received doses  $>$  or  $=$  20 CGE with a lateral beam, with 20-26 CGE delivered to two of three growth centers. The anterolateral oblique approach with an intrarotated eye resulted in additional reduction of bony volume and exposure of only one growth center. No appreciable dose was delivered to the contralateral eye, brain tissue, or pituitary gland.

**CONCLUSIONS:** Proton therapy achieved homogeneous target coverage with true lens sparing. Doses to orbit structures, including bony growth centers, were minimized with different beam arrangements and eye positions. Proton therapy could reduce the risks of second malignancy and cosmetic and functional sequelae.