AN APPROACH TO THE MANAGEMENT OF PATIENTS WITH UVEAL MELANOMA

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It may be difficult for an ophthalmologist to decide upon the best course of management for a patient with uveal melanoma, especially in view of the rarity and the lethal nature of the disease and because of the complexity of various forms of treatment. The aim of this article is to provide a guide to the selection of treatment for intraocular melanoma and it is directed at the general ophthalmologist who is likely to encounter the problem only occasionally. The published literature is still incomplete so that subjective opinions cannot be avoided where statistical comparative data are not available.

INDICATIONS FOR TREATMENT

There is no doubt about the fundamental need to destroy the primary tumour completely before lethal extraocular dissemination has occurred. At present, however, the efficacy of treatment in preventing metastatic death remains uncertain. This situation exists firstly because metastases can be detected only at a late stage, when death is imminent, and secondly because the shortest possible latent period between the time of tumour seeding and the onset of clinical metastatic disease is not known. Workers such as Zimmerman, who believe that this latent period can be as short as 1 year, have suggested that treatment can accelerate metastatic death.[1] An opposing view, held by workers such as Manschot, is that the minimum latent period is about 7 years, so that any metastatic deaths occurring less than 7 years after treatment are the result of tumour dissemination before treatment.[2] Pre-enucleation radiotherapy and various modifications of enucleation aimed at reducing tumour seeding do not seem to have reduced the risk of metastatic disease,[3–7] but it is perhaps too soon to draw valid conclusions from such studies. Improved methods of detecting tumour cells in the general circulation[8] may provide insights into the process of metastatic disease. In the meantime, as long as it remains impossible to establish whether or not a patient is already doomed because of sub-clinical micrometastases, all patients with a definitive diagnosis of uveal melanoma who are not obviously moribund must be treated without undue delay, especially in view of the incurable and lethal nature of metastatic disease.

It must be remembered that there are other reasons for treating uveal melanomas, apart from the prevention of metastatic disease. The tumour is likely to cause visual loss as a result of secondary retinal detachment, macular invasion, lens opacification or subluxation, and vitreous haemorrhage. Intolerable pain and an unsightly eye can eventually occur as a result of extraocular tumour extension, glaucoma or inflammation.

Several conditions must be met for an intraocular melanoma to be left untreated. Firstly, there should be sufficient doubt about the diagnosis of melanoma. Secondly, it should be possible to monitor the ocular status adequately, by means of regular ultrasonography and colour photography. Thirdly, the size of the tumour and the patient's life expectancy should indicate a low risk of metastatic disease in the event of the tumour being a melanoma. Finally, observation of the tumour is easier to justify if any 'prophylactic' treatment would inevitably reduce vision because of proximity of the tumour to the optic disc or fovea.

INDICATIONS FOR CONSERVATIVE TREATMENT

A variety of methods for destroying uveal melanomas have been developed with the aim of conserving a useful eye, but these can be justified only if and when they do not increase the risk of metastatic disease as compared with enucleation.

With the exception of one small study,[9] which as the authors acknowledge is biased because of poor matching of the tumours in the two treatment groups, the published data suggest that survival after radiotherapy is not significantly different from that after enucleation.[10–13] These studies have been questioned because of their short follow-up times and because they were not performed in a randomised prospective manner.[2] At present, a large multicentre investigation called the Collaborative Ocular Melanoma Study (COMS) is under way in the United

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States and Canada and this may establish whether or not plaque radiotherapy reduces the chances of survival as compared with enucleation.[14] Two investigations suggest that local surgical resection does not significantly increase the risk of metastatic disease as compared with enucleation,[15,16] but as with radiotherapy further long-term studies are required.

It is not the physical manipulation of the globe at the time of the primary treatment that is likely to alter the prognosis, but the presence of residual tumour. Tumour regrowth after radiotherapy is rare. After iodine plaque radiotherapy, for example, the recurrence rate was 7.8% in 64 patients with a mean follow-up of 65 months,[17] and after proton beam radiotherapy the recurrence rate was 1.9% in 1077 patients with a mean follow-up of 48 months.[18] However, a large proportion of tumours remain bulky after radiotherapy, and histological examination of eyes which were not necessarily enucleated for tumour regrowth has shown viable tumour cells in nearly all cases, although the metastatic potential of these cells is not known.[2] Visible residual tumour at the end of a local resection is very unusual when the operation is performed by a surgeon experienced in the technique, and the main problem is that of tumour recurrence from invisible microscopic deposits located either in the sclera or retina within the surgical coloboma[19] or, more commonly, in apparently normal choroid at the margins of the coloboma. The overall incidence of residual tumour after local resection is approximately 20%, but the problem has diminished as a result of ocular decompression during the local resection and prophylactic post-operative laser photocoagulation of the margins of the coloboma (B. E. Damato, J. Paul and W. S. Foulds, unpublished data). Furthermore, with proper follow-up, any recurrences are usually detected when they are still minute and treatable by photocoagulation or plaque radiotherapy.

In the absence of any definite evidence that enucleation is better than conservative treatment in preventing metastatic disease, enucleation is no longer the standard form of treatment for intraocular melanoma but is reserved for (1) patients who are unable or unwilling to receive regular and life-long ocular examination for tumour recurrence after treatment; (2) patients who cannot cope psychologically with the possibility of local tumour recurrence; (3) tumours which cannot be completely destroyed because of excessive involvement of the optic disc, ciliary body, angle or orbit; and (4) eyes which are unlikely to be considered useful by the patient after treatment. Whether or not the eye and vision are useful after treatment depends on the resulting visual acuity and field and the cosmetic appearance, which are judged according to the patient's own objectives. These are determined by factors such as age, gender, occupation, recreational activities, cultural background and vision in the fellow eye. When loss of central vision is inevitable, the importance of the temporal visual field should not be underestimated, especially if the patient wears spectacles.

CLINICAL METHODS

Pre-operative Management

Pre-operative ocular examination is aimed at diagnosing the tumour and defining the size and extent of the lesion and is based on biomicroscopy, indirect ophthalmoscopy, B-scan ultrasonography, and transpupillary transillumination. Full clinical examination is directed at establishing the patient's fitness for general anaesthesia and excluding the presence of extraocular malignancy.

Informed consent is obtained after discussing in detail the various treatment options available together with their respective advantages and problems. Special care is taken to ensure that the patient understands the need for life-long monitoring after conservative treatment. To aid communication, each time I explain to a new patient about the tumour and its treatment, the conversation is recorded using a cassette tape-recorder, and the tape-recording given to the patient. Arrangements are made for appropriate counselling, taking due regard of what the patient wishes to know.

Plaque Radiotherapy

Plaque radiotherapy is currently the most popular form of conservative treatment for choroidal and ciliary body melanomas because of its simplicity and convenience. The plaque is sutured to the sclera directly over the tumour after disinserting any overlying extraocular muscles and localising the margins of the tumour by transpupillary transillumination. The implant usually remains in place for 5–7 days, depending on the age of the plaque, until the desired dose has been delivered. This is conventionally about 70–100 Gy at the tumour apex.

Initially, cobalt plaques were widely used, but the high incidence of radiational complications[20–22] has led to the adoption of less energetic isotopes such as ruthenium, iodine, and, recently, palladium.[23] Ruthenium-106 plaques have been extensively used in Europe for tumours of up to 5 mm in thickness.[24] Iodine-125 plaques, which have been in use in North America since the mid-1980s, have now become the standard form of implant.[17,25] They have a half-life of approximately 60 days and emit gamma-rays with sufficient energy to treat tumours with a thickness of more than 5 mm. The treatment of large tumours with iodine-125, however, is associated with a higher incidence of radiational complications.[17] Accordingly, various methods are being developed to increase the radiosensitivity of uveal melanomas by hyperthermia, using ultrasound, microwaves or other means in the hope of reducing the dose of radiation.[26–28] However, it has been suggested that ocular morbidity following radiotherapy is not necessarily due to the radiation but is caused by the presence of necrotic tumour tissue within the eye,[29] in which case such developments may be only partially successful in preventing complications.

Charged Particle Radiotherapy

Charged particle radiotherapy of uveal melanomas is

currently possible in about a dozen centres world-wide, although the number of cyclotron machines that can be used for this treatment is increasing. A highly collimated beam of protons[30] or helium ions[31] can be directed at the tumour with great precision. Because of a phenomenon known as the Bragg peak, the fall-off of the charged particles can be adjusted to within 1 mm, with the entry site receiving approximately 60–70% of the maximal dose. Prior to the treatment, four tantalum marker rings are sutured to the sclera so that the tumour can be localised radiographically. The dimensions of the tumour and the eye are measured and these data, as well as information regarding the marker locations, are computerised for treatment planning (Fig. 1). Between 50 and 70 Gy are delivered to the tumour in four fractions.

Local Resection

The surgical resection of small iris and ciliary body melanomas has been performed for many years.[32,33] Local resection of choroidal melanomas has been advocated only as a last resort, after unsuccessful radiotherapy in patients with poor vision in the fellow eye.[34] In 1972, however, Foulds started performing local resection of choroidal melanomas as a primary procedure irrespective of the vision in the fellow eye[35] and, in 1984, was joined by the author, who has performed some 250 such procedures to date. Interim results have been published[16,36,37] and, recently, other workers have adopted this type of operation.[15,38,39]

The surgical techniques vary according to the size and location of the melanoma.[36] Briefly, the tumour is localised by transpupillary transillumination and the overlying extraocular muscles are disinserted. A lamellar scleral flap is prepared, and the tumour is excised together with the deep scleral lamella and a surround of normal uveal tissue, if possible without damaging the subjacent retina. Access to the posterior tumour is facilitated by ocular decompression, which is achieved by pars plana vitrectomy. Haemorrhage is minimised by hypotensive anaesthesia, which reduces the systolic blood pressure to approximately 50 mmHg.[40] After the tumour is removed, the scleral flap is sutured and the eye is reformed with gas, balanced salt solution or silicone. If a retinal defect is present, external plombage is also performed. After the operation the margins of the surgical coloboma are treated by laser photocoagulation to reduce the risk of local tumour recurrence and retinal detachment. Peyman had advocated an alternative method of performing local resection, in which the tumour is excised together with the retina and the full thickness of the adjacent sclera,[41] but he has recently abandoned this in favour of the lamellar scleral dissection technique.

Endoresection

It is possible to excise small posterior tumours transvitreally. The surface of the tumour and the surrounding retina are treated by photocoagulation, to eliminate any exudative retinal detachment and to create retino-choroidal adhesion. A few weeks later, the tumour and remnants of overlying retina are removed transvitreally using standard vitrectomy equipment. Complete removal of the tumour is followed by vitrectomy and photocoagulation of any residual pigmented tissue. At the end of the operation the eye is filled with balanced salt solution. Peyman has described a similar technique, but advocates preservation of the retina over the surgical coloboma and the use of

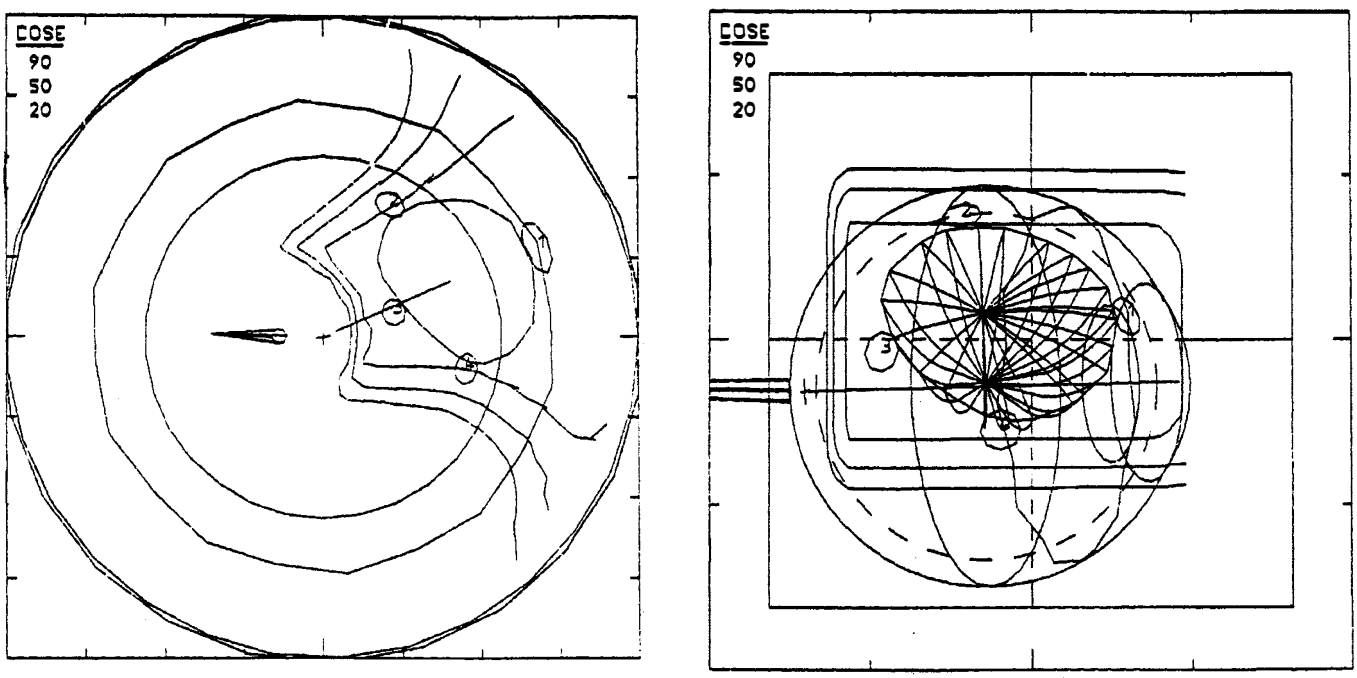

Fig. 1. *Computer-generated diagrams showing base of tumour, position of tantalum marker rings, and isodose curves of proton beam radiation. In Britain, the radiotherapy is planned and administered at the Douglas Cyclotron Unit, Clatterbridge Centre for Oncology, Bebington, Merseyside, after consultation with the ophthalmic oncologist, who is responsible for inserting the marker rings and for monitoring the response to therapy.*

silicone and panretinal ablation to prevent retinal detachment.[42]

Photocoagulation

Photocoagulation, using xenon,[43,44] argon[45] or krypton,[46] is not often performed as a primary procedure and is usually reserved for adjunctive therapy after radiotherapy or local resection. For many years the standard technique was to apply brief, high-energy flashes of light, but in 1986 Foulds and Damato described a method using low-energy laser photocoagulation.[46] After creating chorioretinal scars around the tumour and ablating the retina overlying the lesion, using an argon laser, the tumour is treated with long, low-energy krypton burns (e.g. 0.3 watts for 20 seconds). The tumour diminishes in thickness by only 0.5 mm after each treatment so that several sessions of photocoagulation are necessary to achieve a flat scar. Whilst the generally accepted view is that a flat grey scar (i.e. 'grey mouse') is an appropriate end-point, the author believes that it is important to end treatment only after the sclera has been exposed, either by creating several explosions in the tumour remnants, using high-energy laser, or by endoresection. A novel technique has been described recently in which diode laser photocoagulation is applied, using intravenous indocyanine green injection to enhance the light absorption (V. Shimoyma, *et al.*, personal communication, ARVO 1992). Experiments using an animal model have shown extensive tumour necrosis after such treatment, although whether or not the resulting inflammation would be well tolerated by the eye has yet to be established.

Photodynamic Therapy

In addition to delivering thermal energy, light can be used to activate chemotherapeutic agents such as haematoporphyrin derivatives (HPD)[47,48] and bacteriochlorin A.[49] These are injected intravenously and accumulate within the tumour, which is then treated with a sub-thermal dose of light energy. At present, the use of HPD is limited by the risk of sunburn, which lasts for several weeks after treatment, but in future such a problem may be avoided by targeting HPD or indeed other agents at the tumour using heat-labile liposomes (M. H. Rahimy, B. Khoobehi and G. A. Peyman, personal communication, ARVO 1992).

Post-operative Management

After most forms of conservative treatment, patients are usually reviewed after approximately 1 month, then 6-monthly for about 5 years, then annually. Indirect ophthalmoscopy, biomicroscopy and colour photography are performed routinely in addition to B-scan ultrasonography and transillumination. Systemic examination and special scans are performed only if symptoms suggest the presence of metastatic disease.

SELECTION BETWEEN DIFFERENT FORMS OF CONSERVATIVE TREATMENT

There is no single form of treatment which is ideal for all intraocular melanomas, so that it is important to select the most suitable method according to (1) the size and location of the tumour, (2) secondary changes in the affected eye, (3) the general health and motivation of the patient, and (4) the equipment and skills available. When selecting between treatments on the basis of the published literature, only broad comparisons are possible because of the inconsistent ways in which different workers have categorised and evaluated their data.

Choroidal Tumours

For choroidal tumours with minimal or no involvement of the pars plicata, the primary determinants of treatment type are the tumour thickness and the proximity of the posterior tumour margin to the optic disc and fovea (Fig. 2).

Tumour Thickness Less Than 6 mm. If the tumour is less than 6 mm thick and does not extend to within 3–4 mm of the optic disc or fovea, the author's first choice is ruthenium plaque radiotherapy, which is less difficult than local resection and less expensive than charged particle radiotherapy. Iodine plaques, because of their relatively short half-life, are more expensive than ruthenium plaques and have an increased risk of causing radiational complications because of the deeper penetration of radiation, although comparative studies with ruthenium have not been performed. In 28 patients treated with ruthenium plaque radiotherapy, with a tumour thickness of less than 6 mm and a posterior tumour margin more than one disc diameter of the optic disc or fovea, 27 eyes retained vision of counting fingers or better after a minimum follow-up of 3 years, with 60% of all eyes having vision of 6/12 or better (B. E. Damato, J. Paul, A. N. Harnett and W. S. Foulds, unpublished data). Other workers also report good results with such favourable tumours.[50–52]

With tumours extending close to or involving the optic disc or fovea, the probability of visual loss from radiational optic neuropathy or maculopathy after proton beam radiotherapy is about twice that of more anterior tumours.[53] The risk of visual loss after external beam radiotherapy is probably smaller than with plaques, despite the use of notched implants.[54] With tumours having a tapering posterior edge, the visual result may be improved by placing the plaque eccentrically in relation to the tumour and treating the posterior edge by photocoagulation (Fig. 3). With posterior tumours, there is a higher risk of recurrent tumour both after external beam radiotherapy[18] and after plaque radiotherapy.[54] This is because of difficulty in localising the tantalum marker rings precisely in relation to the posterior tumour margin and because the optic nerve may interfere with the correct positioning of the radioactive plaque. With small posterior tumours, it would be useful to compare the results of plaque radiotherapy with those of charged particle radiotherapy.

External beam radiotherapy of nasal juxtapapillary tumours may result in epiphora caused by damage to the lacrimal canaliculi.[55,56] Such nasal and juxtapapillary

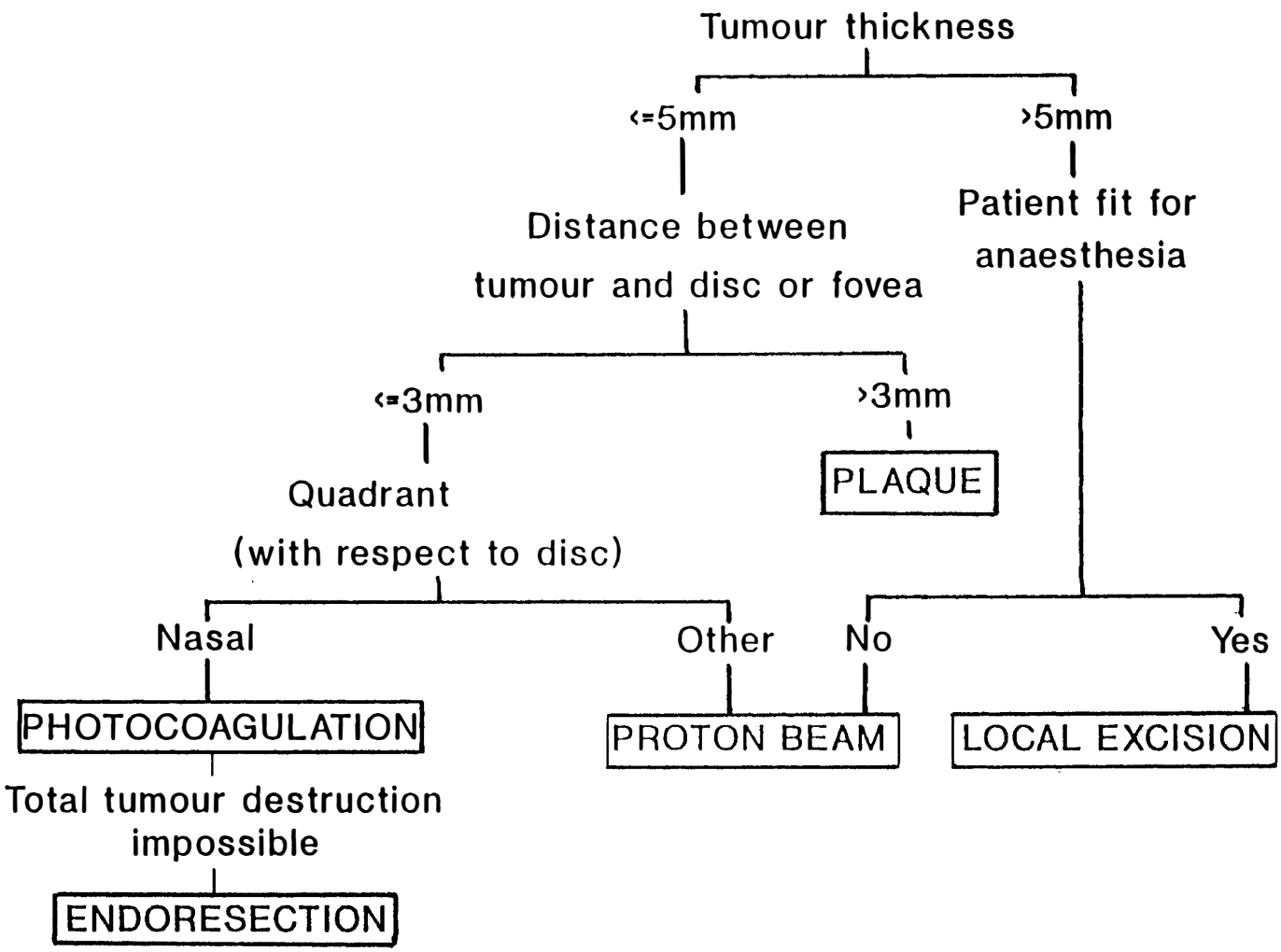

Fig. 2. *Treatment of choroidal melanomas.*

tumours, if less than 4 mm in thickness, may be treated by photocoagulation, which can be followed by endoresection if the patient cannot attend for repeated treatment or if total tumour destruction cannot be achieved (Fig. 4). Photocoagulation of macular and juxtapapillary tumours has a high risk of choroidal neovascularisation and vitreous haemorrhage, particularly if the major retinal vessels are occluded (Fig. 5), so that external beam radiotherapy is preferable for such cases.

Tumour Thickness More Than 5 mm. With tumours greater than 5 mm in thickness, ruthenium plaque radiotherapy, photocoagulation and endoresection are not possible and the choice is between local resection, iodine plaque or external beam radiotherapy.

After radiotherapy, the risks of complications such as radiation retinopathy, persistent retinal detachment and neovascular glaucoma are related to tumour thickness and diameter. For example, after proton beam radiotherapy the incidence of persistent retinal detachment is approximately 40% with tumours 4–10 mm in thickness and is almost 80% with tumours more than 10 mm in thickness.[57] Persistent retinal detachment after radiotherapy is untreatable and increases the risk of neovascular glaucoma from approximately 3% to 35%.[57] After external beam radiotherapy, large tumour size also increases the risk of local tumour recurrence[18] and enucleation.[68] Irradiation of large tumours with iodine plaques is also associated with significant morbidity. In 64 patients followed up for a mean of 65 months 10.9% developed neovascular glaucoma and 23.4% developed radiation retinopathy, with 17.2% of all eyes eventually requiring enucleation and 45% of all eyes retaining vision of 6/36 or better; however, this series included both small and large tumours as well as those extending close to the disc or fovea.[17] For tumours of equivalent size, external beam radiotherapy is more likely to cause neovascular glaucoma whereas the probability of radiation retinopathy is greater with iodine plaque radiotherapy.[29]

In contrast to radiotherapy, increasing tumour bulk (up to a diameter of about 16 mm) and the presence of subretinal fluid facilitate local resection. The main complications after this procedure are residual tumour, as mentioned above, and retinal detachment. The overall incidence of rhegmatogenous retinal detachment after local resection is approximately 20%. This complication is most likely to occur (1) after irido-cyclo-choroidectomy, which inevitably results in a large retinal dialysis,

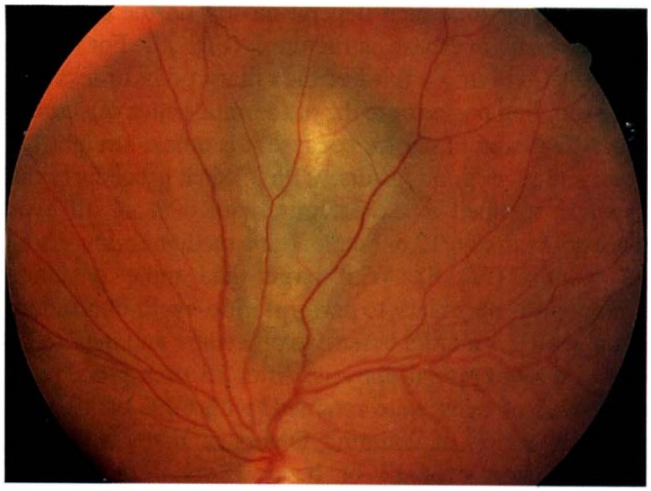

Fig. 3a.

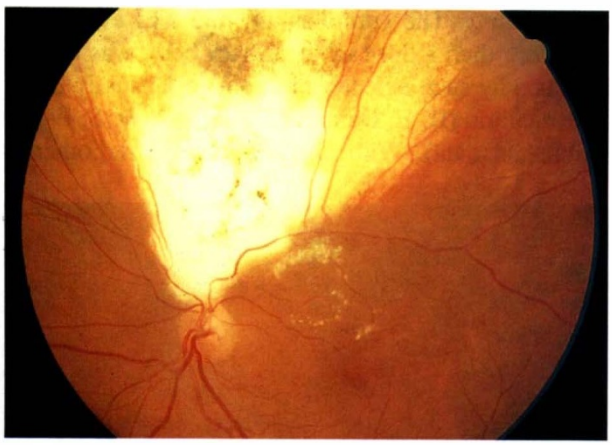

Fig 3b.

Fig. 3. *Fundus photographs of the left eye showing a choroidal melanoma extending close to the superior margin of the optic disc (a) before treatment, and (b) 6 years after ruthenium plaque radiotherapy and krypton laser photocoagulation to the posterior tumour margin. Despite the appearance of a few cotton wool spots and telangiectasia, a visual acuity of 6/6 was maintained until the patient's latest visit, almost 7 years after the radiotherapy.*

(2) when the tumour has invaded the retina, and (3) with small and posterior tumours, which are now treated by proton beam radiotherapy. The application of external plombage, internal tamponade and retinopexy at the time of the local resection seem to have reduced the incidence of retinal detachment. The results of local resection have been compared with those after cobalt plaque radiotherapy,[15] but the study was performed by workers with relatively little experience in local resection at the time, so the results are not representative of current techniques. There is scope for further studies comparing outcome in matched patients treated either by local resection, iodine plaque radiotherapy or charged particle radiotherapy.

Posterior tumour extension, to within one or two disc diameters of the disc or fovea, increases the probability of radiational optic neuropathy and maculopathy after plaque or external beam radiotherapy[53] and also increases

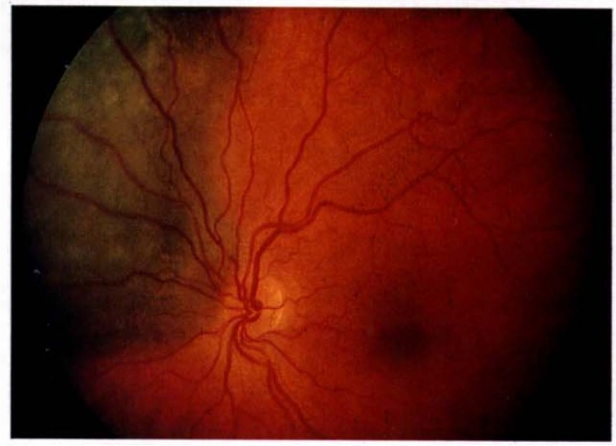

Fig. 4a.

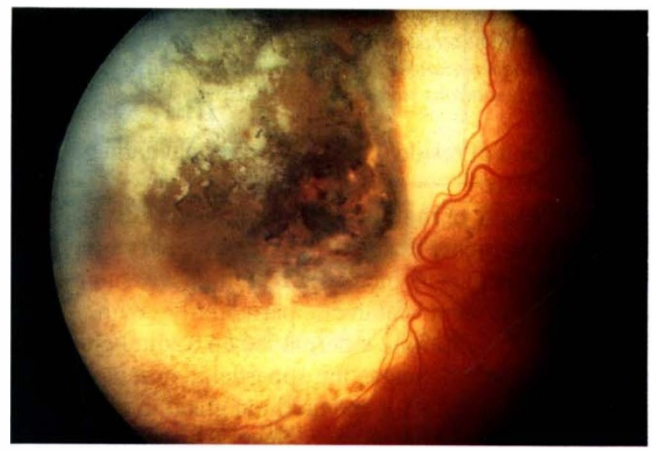

Fig 4b.

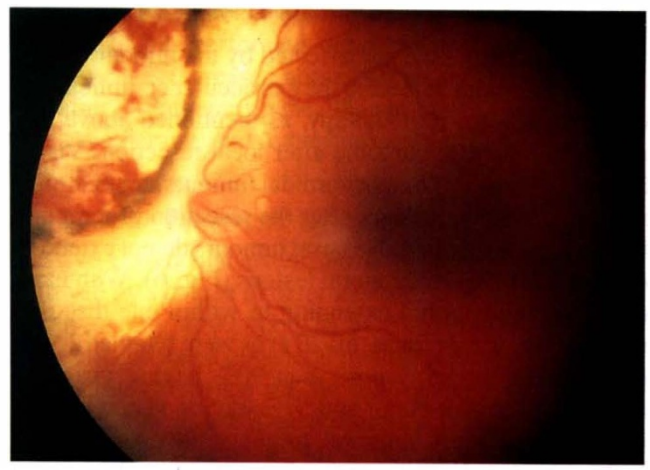

Fig 4c.

Fig. 4. *Fundus photographs of the left eye showing a 12 mm diameter melanoma extending to the nasal margin of the optic disc (a) before treatment, (b) at the end of a course of laser photocoagulation, when an excessive amount of residual tumour was present, and (c) 1 day after transvitreal resection of the tumour, which was performed after a course of photocoagulation.*

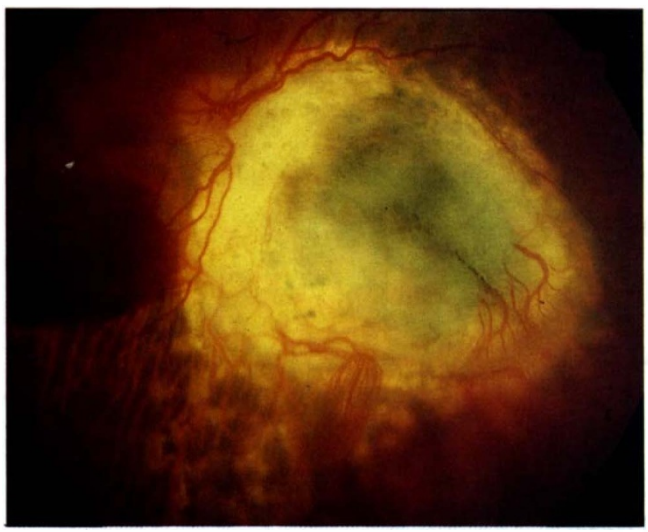

Fig. 5. *Fundus photograph of the left eye showing a macular choroidal melanoma after photocoagulation, when the treatment was complicated by choroidal neovascularisation and subhyaloid haemorrhage. The new vessels were ablated by direct photocoagulation and the haemorrhage resolved spontaneously without sequelae.*

the likelihood of residual tumour and retinal damage after local resection.[36]

Radiotherapy of tumours that extend anteriorly is associated with a higher dose of radiation to ciliary body and lens so that there is an increased risk of neovascular glaucoma, uveitis and cataract, particularly with bulky tumours.[58] In addition, external beam radiotherapy of anterior tumours damages the superficial structures such as the eyelids, canaliculi and lacrimal gland to cause eyelid scarring, loss of lashes, keratopathy, epiphora and dry eye according to whether the tumour is nasal, superior or superotemporal respectively.[55,56] In contrast to radiotherapy, local resection does not affect these extraocular structures.

The quadrant of the eye affected by the tumour is relevant not only with respect to the extraocular complications of external beam radiotherapy, as mentioned above, but also with regard to outcome after local resection. Vision after the excision of nasal choroidal tumours, for example, is significantly better than after the resection of temporal tumours, probably because nasal tumours do not extend as close to the fovea as temporal lesions (Fig. 6). With nasal choroidal tumours not extending to within one disc diameter of the disc or fovea, all 28 eyes were retained 1 year post-operatively, with more than 90% having vision of counting fingers or better and 57% having vision of 6/12 or better. With 56 temporal tumours not extending to within one disc diameter of the disc or fovea, 89% of eyes were retained at 1 year, with 82% having vision of counting fingers or better and 25% having vision of 6/12 or better (B. E. Damato, J. Paul and W. S. Foulds, unpublished data).

Ciliary Body Tumours

With tumours involving the ciliary body or angle, or both, the results of treatment depend mostly on the extent of involvement of these structures (Fig. 7). For small tumours involving a third of the ciliary body or less and not extending posterior to the ora serrata, iridocyclectomy is the treatment of choice because it is quick, straightforward and gives good results. With 33 such procedures the eye was retained in 32 patients, with 60% of all eyes having vision of 6/12 or better after a median follow-up of 43 months (Fig. 8). With larger and more posterior tumours it is necessary to perform irido-cyclo-choroidectomy, which is a more extensive procedure and inevitably causes a large retinal dialysis. After 75 such procedures only 67% of eyes were retained, with 50% of all eyes retaining vision of counting fingers or better and 12% having vision of 6/12 or better. Retinal detachment occurred in none of the patients treated by iridocyclectomy but in as many as 35% of patients after irido-cyclo-choroidectomy. The complication rate was even higher when more than a third of the ciliary body was excised, which is why such extensive tumours are usually treated by enucleation (B. E. Damato, J. Paul and W. S. Foulds, unpublished data). With charged particle radiotherapy,

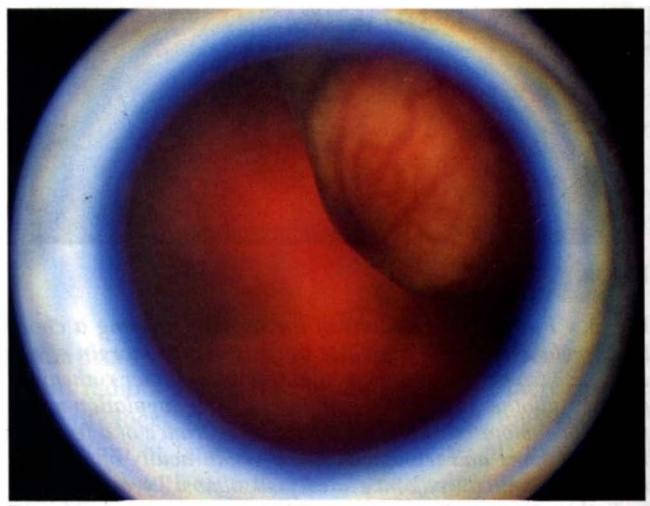

Fig. 6a.

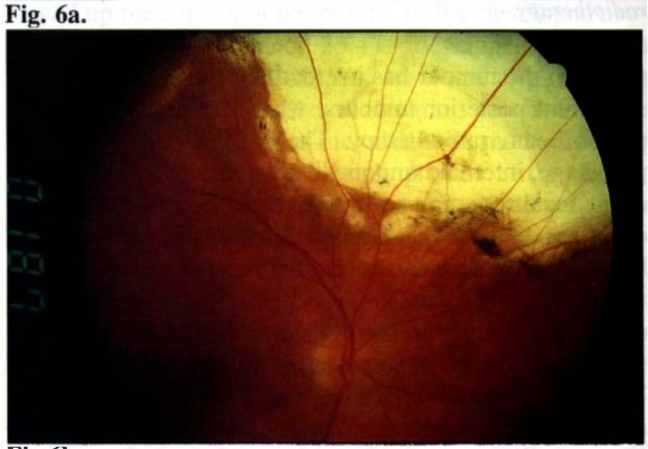

Fig 6b.

Fig. 6. *Fundus photographs of the right eye showing a supero-nasal choroidal melanoma with a diameter of 10 mm and a thickness of 8 mm (a) before local resection and (b) 17 months later when the vision was 6/12.*

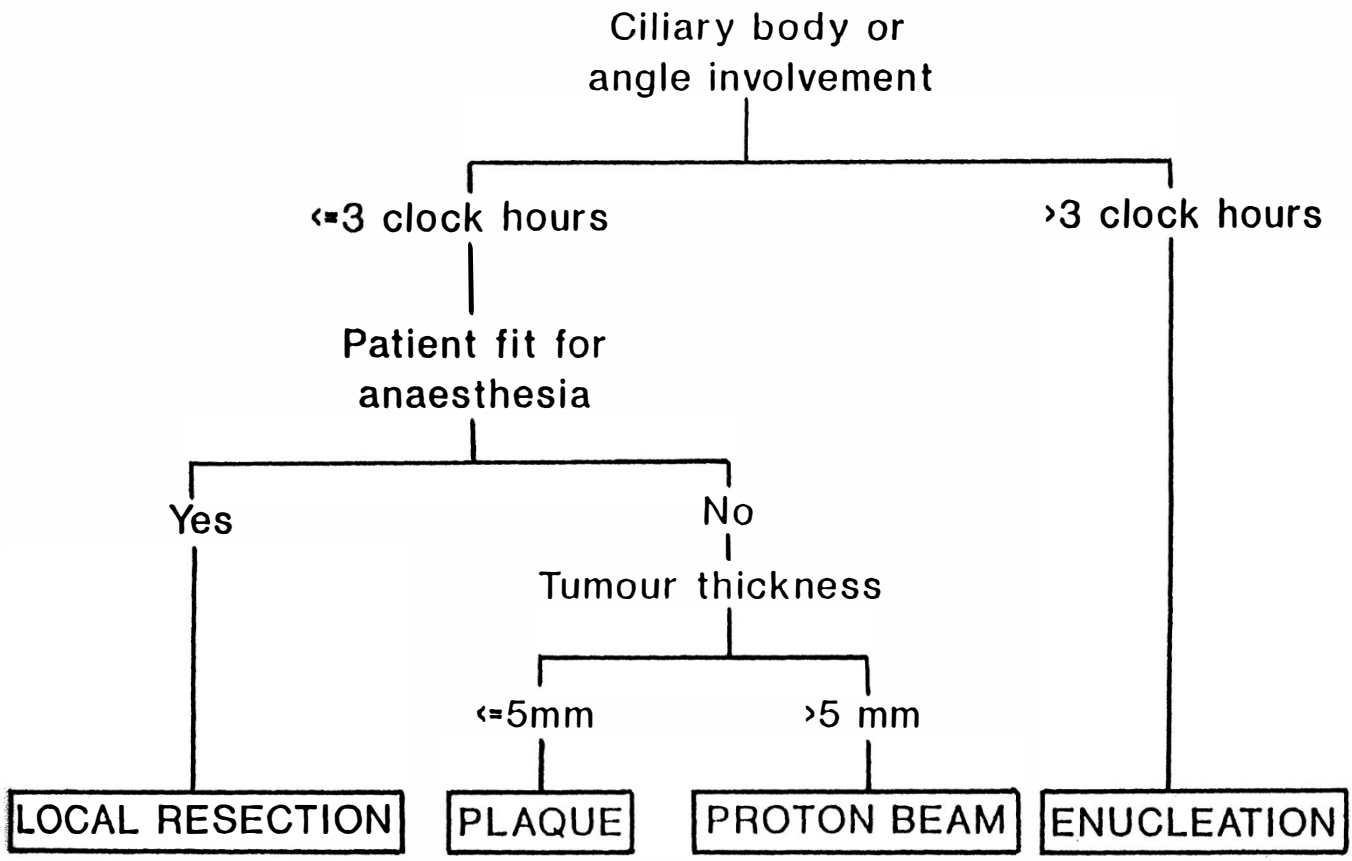

Fig. 7. *Treatment of ciliary body melanomas.*

ciliary body involvement increases the risk of enucleation[58] and external eye complications,[29] with the risk of complications such as neovascular glaucoma and cataract increasing with the size of the radiation beam irrespective of the anteroposterior location of the tumour (W. J. Meecham and associates, personal communication, ARVO 1992). With large tumours involving ciliary body and choroid it is difficult to decide between external beam radiotherapy and local resection, so that further studies are required.

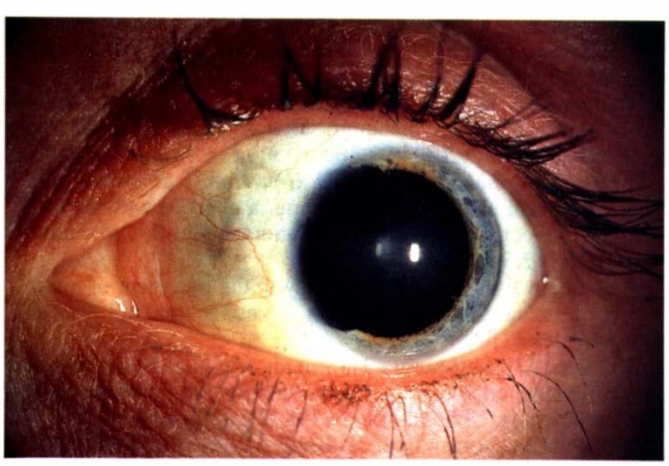

Fig. 8. *Post-operative appearance following iridocyclectomy for a nasal ciliary body melanoma in the left eye.*

OTHER FACTORS

Retinal Invasion

Retinal invasion was previously treated by retinectomy when local resection was performed, but this policy led to a high incidence of retinal detachment so that, currently, tumour within the retina is left *in situ* and treated post-operatively by photocoagulation or plaque radiotherapy. If the tumour has perforated the retina, the risk of retinal detachment is increased not only after local resection but also after radiotherapy, when the tumour has regressed, so that cryotherapy and other prophylactic measures are indicated.

Extraocular Tumour Extension

Massive extraocular extension is treated by enucleation followed by a course of external beam orthovoltage radiotherapy[59] (e.g. 4500 cGy) or by exenteration. If only a small encapsulated episcleral nodule is present, however, its treatment depends on the management of the intraocular tumour. When local resection is performed the episcleral nodule is excised *en bloc* together with a surround of full-thickness sclera, and the defect is closed with a lamellar scleral graft taken from a healthy part of the same eye. If the intraocular tumour is being treated by plaque radiotherapy or external beam radiotherapy, then the episcleral tumour nodule is included in the radiation field.

Secondary Ocular Changes

The more extensive the pre-operative exudative retinal

detachment the greater is the incidence of persistent retinal detachment after proton beam radiotherapy, increasing from approximately 35% to 60% in patients with pre-operative detachment in two quadrants and three quadrants respectively.[57] Conversely, the more extensive and exudative retinal detachment, the less chance there is of local resection being complicated by retinal damage.

Glaucoma may be caused by annular extension of the tumour around the angle, in which case conservative treatment is contraindicated; but glaucoma could also be due to melanomacrophages or pre-existing open angle glaucoma.[60]

Vitreous haemorrhage in the presence of a choroidal tumour suggests that the tumour has perforated the retina, so that preparations should be made for prophylactic measures against rhegmatogenous retinal detachment.

General Health

Systemic complications associated with the hypotensive anaesthesia have been few. In a series of 100 patients, 2 reported short-term memory loss lasting a few weeks and 2 developed temporary hemiparesis, with total recovery.[40] One patient in another series developed fatal per-operative pulmonary thrombo-embolism, which occurred before systemic hypotension had been achieved. The low incidence of morbidity occurred because hypotensive anaesthesia was not performed in the presence of severe peripheral vascular disease, ischaemic heart disease or cerebrovascular disease. In elderly patients, mild hypotensive anaesthesia is often sufficient to arrest haemorrhage, so that an age of more than 70 years is not necessarily a contraindication to local resection even when systemic hypotension is not possible. Patients who are not fit for local resection are treated by proton beam radiotherapy.

CONCLUSIONS

It is possible to conserve the eye in most patients when a uveal melanoma is less than about 17 mm in diameter and does not involve more than a third of the ciliary body or optic disc. Preservation of good vision can be expected in such patients if the tumour does not extend to within 3 mm of the optic disc or fovea. It is therefore no longer acceptable for enucleation to be performed merely on the basis of any intuitive feelings of the surgeon, especially as such mutilating surgery does not seem to improve the chance of survival as compared with conservative treatment. The term 'informed consent' implies that the patient is aware of the advantages and disadvantages of all forms of treatment. It is hoped that this overview will make it easier for the various therapeutic options and objectives to be considered when the patient with an intraocular melanoma is counselled.

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Key words: Diagnosis, Melanoma, Methods, Mortality, Uveal neoplasms, Visual acuity.

REFERENCES

1. Zimmerman LE, McLean IW. An evaluation of enucleation in the management of uveal melanomas. Am J Ophthalmol 1979;87:741–60.
2. Manschot WA, van Strik R. Uveal melanoma: therapeutic consequences of doubling times and irradiation results; a review. Int Ophthalmol 1992;16:91–9.
3. Augsburger JJ, Lauritzen K, Gamel JW, *et al.* Matched group study of preenucleation radiotherapy versus enucleation alone for primary malignant melanoma of the choroid and ciliary body. Am J Clin Oncol 1990;13:382–7.
4. Char DH, Phillips TL, Andejeski Y, *et al.* Failure of preenucleation radiation to decrease uveal melanoma mortality. Am J Ophthalmol 1988;106:21–6.
5. Matthaus W, Sporl E, Lommatzsch P, *et al.* Cryoenucleation in malignant melanoma of the choroid. Klin Monatsbl Augenheilkd 1984;185:215–8.
6. Kreissig I, Rohrbach M, Lincoff H. Irradiation of choroidal melanomas before enucleation? Retina 1989;9:101–4.
7. Kreissig I. Gas no-touch enucleation. Klin Monatsbl Augenheilkd 1988;193:489–92.
8. Smith B, Selby P, Southgate J, *et al.* Detection of melanoma cells in peripheral blood by means of reverse transcriptase and polymerase chain reaction. Lancet 1991;338:1227–9.
9. Gass JD. Comparison of prognosis after enucleation vs cobalt 60 irradiation of melanomas. Arch Ophthalmol 1985;103:916–23.
10. Augsburger JJ, Gamel JW, Shields JA. Cobalt plaque radiotherapy versus enucleation for posterior uveal melanoma: comparison of survival by prognostic index groups. Trans Am Ophthalmol Soc 1990;87:348–59.
11. Adams KS, Abramson DH, Ellsworth RM, *et al.* Cobalt plaque versus enucleation for uveal melanoma: comparison of survival rates. Br J Ophthalmol 1988;72:494–7.
12. Kiehl H, Kirsch I, Lommatzsch P. Survival after treatment for malignant choroidal melanoma: comparison between conservative therapy (Ru106/Rh106 applicator) and enucleation with and without postoperative irradiation to the orbit; 1960 to 1979. Klin Monatsbl Augenheilkd 1984;184: 2–14.
13. Seddon JM, Gragoudas ES, Egan KM, *et al.* Relative survival rates after alternative therapies for uveal melanoma. Ophthalmology 1990;97:769–77.
14. Schachat AP. Collaborative ocular melanoma study. In: Ryan SJ, editor. Retina. St Louis: Mosby, 1989:733–6.
15. Augsburger JJ, Lauritzen K, Gamel JW, *et al.* Matched group study of surgical resection versus cobalt-60 plaque radiotherapy for primary choroidal or ciliary body melanoma. Ophthalmic Surg 1990;21:682–8.
16. Foulds WS, Damato BE, Burton RL. Local resection versus enucleation in the management of choroidal melanoma. Eye 1987;1:676–9.
17. Packer S, Stoller S, Lesser ML, *et al.* Long-term results of iodine-125 irradiation of uveal melanoma. Ophthalmology 1992;99:767–74.
18. Gragoudas ES, Egan KM, Seddon JM, *et al.* Intraocular recurrence of uveal melanoma after proton beam irradiation. Ophthalmology 1992;99:760–6.
19. Robertson DM, Campbell RJ, Weaver DT. Residual intrascleral and intraretinal melanoma: a concern with lamellar sclerouvectomy for uveal melanoma. Am J Ophthalmol 1991;112:590–3.
20. MacFaul PA. Local radiotherapy in the treatment of malignant melanoma of the choroid. Trans Ophthalmol Soc UK 1977;97:421–7.
21. Cruess AF, Augsburger JJ, Shields JA, *et al.* Visual results following cobalt plaque radiotherapy for posterior uveal melanomas. Ophthalmology 1984;91:131–6.
22. Shields JA, Augsburger JJ, Brady LW, *et al.* Cobalt plaque therapy of posterior uveal melanomas. Ophthalmology 1982;89:1201–7.
23. Finger PT, Moshfeghi DM, Ho TK. Palladium-103 ophthal-

mic plaque radiotherapy. Arch Ophthalmol 1991;109: 1610–3.
24. Lommatzsch PK. Results after beta-irradiation (106Ru/106Rh) of choroidal melanomas: twenty years' experience. Am J Clin Oncol 1987;10:146–51.
25. Earle J, Kline RW, Robertson DM. Selection of iodine-125 for the Collaborative Ocular Melanoma Study. Arch Ophthalmol 1987;105:763–4.
26. Liggett PE, Ma C, Astrahan M, *et al.* Combined localized current field hyperthermia and irradiation for intraocular tumors. Ophthalmology 1991;98:1830–5.
27. Mieler WF, Jaffe GJ, Steeves RA. Ferromagnetic hyperthermia and iodine-125 brachytherapy in the treatment of choroidal melanoma in a rabbit model. Arch Ophthalmol 1989;107:1524–8.
28. Finger PT. Microwave plaque thermoradiography for choroidal melanoma. Br J Ophthalmol 1992;76:358–64.
29. Char DH, Castro JR, Quivey JM, *et al.* Uveal melanoma radiation: ^{125}I brachytherapy versus helium ion irradiation. Ophthalmology 1989;96:1708–15.
30. Gragoudas ES, Seddon JM, Egan K, *et al.* Long-term results of proton beam irradiated uveal melanomas. Ophthalmology 1987;94:349–53.
31. Linstadt D, Castro J, Char D, *et al.* Long-term results of helium ion irradiation of uveal melanoma. Int J Radiat Oncol Biol Phys 1990;19:613–8.
32. Vail DT. Iridocyclectomy: a review. Am J Ophthalmol 1971;71:161–8.
33. Forrest AW, Keyser RB, Spencer WH. Iridocyclectomy for melanomas of the ciliary body: a follow-up study of pathology and surgical morbidity. Ophthalmology 1978;85: 1237–49.
34. Stallard HB. Partial choroidectomy. Br J Ophthalmol 1966;50:660–2.
35. Foulds WS. The local excision of choroidal melanomata. Trans Ophthalmol Soc UK 1973;93:343–6.
36. Foulds WS, Damato BE. Surgical resection of choroidal melanomas. In: Ryan SJ, Ogden TE, Schachat AP, editors. Retina. St Louis: Mosby, 1989:713–20.
37. Damato BE, Foulds WS. Ciliary body tumours and their management. Trans Ophthalmol Soc UK 1986;105:257–64.
38. Shields JA, Shields CL, Shah P, *et al.* Partial lamellar sclerouvectomy for ciliary body and choroidal tumors. Ophthalmology 1991;98:971–83.
39. Billson FA. Microsurgery of choroidal melanoma: surgical techniques of local excision. Aust J Ophthalmol 1983;11:21–7.
40. Todd JG, Colvin JR. Ophthalmic surgery. In: MacRae WR, Wildsmith JAW, editors. Induced hypotension. London: Elsevier, 1991:257–69.
41. Peyman GA, Gremillion CM. Eye wall resection in the management of uveal neoplasms. Jpn J Ophthalmol 1989;33:458–71.
42. Peyman GA, Charles H. Internal eye wall resection in the management of uveal melanoma. Can J Ophthalmol 1988;23:218–23.
43. Meyer Schwickerarth G, Vogel M. Treatment of malignant melanomas of the choroid by photocoagulation. Trans Ophthalmol Soc UK 1977;97:416–20.
44. Vogel MH. Xenon arc photocoagulation of small malignant melanomas of the choroid. In: Peyman GA, *et al.*, editor. Intraocular tumours. New York: Appleton/Century/Crofts, 1976:155–66.
45. Meyer Schwickerath G, Vogel MH. Malignant melanoma of the choroid treated with photocoagulation: a 10-year follow-up. Mod Probl Ophthalmol 1974;12:544–9.
46. Foulds WS, Damato BE. Low-energy long-exposure laser therapy in the management of choroidal melanoma. Graefes Arch Clin Exp Ophthalmol 1986;224:26–31.
47. Tse DT, Dutton JJ, Weingeist TA, *et al.* Hematoporphyrin photoradiation therapy for intraocular and orbital malignant melanoma. Arch Ophthalmol 1984;102:833–8.
48. Favilla I, Barry WR, Gosbell A, *et al.* Phototherapy of posterior uveal melanomas. Br J Ophthalmol 1991;75:718–21.
49. Schuitmaker JJ, van Best JA, van Delft JL, *et al.* Bacteriochlorin a, a new photosensitizer in photodynamic therapy: *in vivo* results. Invest Ophthalmol Vis Sci 1990;31:1444–50.
50. Grange JD, Gerard JP, Ragab M, *et al.* [Evaluation of 100 melanomas of the choroid and ciliary body treated by application of ruthenium (Ru106/Rh106)]. Bull Soc Ophthalmol Fr 1989;89:679–82.
51. Lommatzsch PK. Results after beta-irradiation (106Ru/106Rh) of choroidal melanomas: 20 years' experience. Br J Ophthalmol 1986;70:844–51.
52. Foerster MH, Bornfeld N, Wessing A, *et al.* [Treatment of malignant melanomas of the uvea with 106-ruthenium applicators: report on the first 100 Essen cases]. Klin Monatsbl Augenheilkd 1984;185:490–4.
53. Seddon JM, Gragoudas ES, Egan KM, *et al.* Uveal melanomas near the optic disc or fovea: visual results after proton beam irradiation. Ophthalmology 1987;94:354–61.
54. Lommatzsch PK, Lommatzsch R. Treatment of juxtapapillary melanomas. Br J Ophthalmol 1991;75:715–7.
55. Char DH, Castro JR, Kroll SM, *et al.* Five-year follow-up of helium ion therapy for uveal melanoma. Arch Ophthalmol 1990;108:209–14.
56. Lovato AA, Char DH, Castro JR, *et al.* The effect of silicone nasolacrimal intubation on epiphora after helium ion irradiation of uveal melanomas. Am J Ophthalmol 1989; 108:431–4.
57. Zografos L, Perret C, Gailloud C. Conservative treatment of uveal melanomas by accelerated proton beam. In: Bornfeld N, Gragoudas ES, Hopping W, Lommatzsch PK, Wessing A, Zografos L, editors. Tumours of the eye. Amsterdam: Kugler, 1991:497–506.
58. Egan KM, Gragoudas ES, Seddon JM, *et al.* The risk of enucleation after proton beam irradiation of uveal melanoma. Ophthalmology 1989;96:1377–82.
59. Hykin PG, McCartney AC, Plowman PN, *et al.* Post-enucleation orbital radiotherapy for the treatment of malignant melanoma of the choroid with extrascleral extension. Br J Ophthalmol 1990;74:36–9.
60. Foulds WS, Lee WR. The significance of glaucoma in the management of melanomas of the anterior segment. Trans Ophthalmol Soc UK 1983;103:59–63.