Proton beam therapy for the treatment of uveal melanoma
Australian Safety and Efficacy Register of New Interventional Procedures - Surgical (ASERNIP-S)

Record Status
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Citation

Authors' conclusions
Proton beam therapy has been utilised to treat uveal melanomas since the late 1980s. The procedure involves the placement of tantalum clips onto the sclera around the tumour base, followed by the construction of a precise 3D model of the patient’s eye, including the lens, optic nerve and fovea utilising specialised treatment planning software (EYEPLAN). The tumour margins are drawn onto this model by the ophthalmologist and verified by the radiation oncologist. This information is then relayed to the proton beam accelerator (synchrotron) where the protons will be delivered into the targeted tumour. The procedure involves the use of high-tech equipment, requiring input from several medical and scientific specialists. At the time of writing, over 39,000 patients around the world have received proton therapy either alone or in conjunction with conventional radiotherapy (Levin et al. 2005), of which at least 8000 were treated for uveal melanomas (Blomquist et al. 2005).

Existing comparators for proton beam therapy includes other forms of external beam radiotherapy (photons, helium ions etc.), brachytherapy, laser photocoagulation, transpupillary thermotherapy, sclerouvectomy and endoresection. The key disadvantage of other radiotherapy treatments (photon beam therapy and brachytherapy) is the irradiation of healthy tissue located in close proximity to the target tumour. Research has revealed that protons have inherent dose-distribution characteristics that may confer substantial advantage over photon radiotherapy and brachytherapy (as illustrated in Figure 1).

The majority of studies included were low quality (level IV intervention evidence). The key measures of the effectiveness of proton beam therapy for the treatment of uveal melanoma were local tumour control, survival and retention of the treated eye. Meanwhile, the key complications assessed following proton beam therapy were the incidence of rubeosis, neovascular glaucoma, cataracts and vision loss. Radiotherapeutic treatment of uveal melanomas is often associated with various complications, and proton beam therapy is no exception. Two of the most severe complications after proton beam therapy are rubeosis and neovascular glaucoma, due to the high risk of enucleation associated with these conditions. There is substantial variation between studies with regards to the incidence of rubeosis (~8%) and neovascular glaucoma (9% to 29%).

However, research has shown that both these conditions contribute significantly to secondary enucleation after proton beam therapy. The development of cataract is another common complication (ranging from 6% to 62%) following proton beam therapy, and contributes significantly to vision loss in the treated eye. In addition, the incidence of visual deterioration after treatment with proton beam therapy is considerable and appears to be more severe compared to brachytherapy. However one study noted that despite experiencing substantial decrease of visual acuity, most patients retain useful vision (Seddon et al. 1987). Overall, the utilisation of proton beam therapy for the treatment of uveal melanomas appears to be associated with substantial complications. Several researchers have noted that most of these complications are highly dependent on tumour characteristics (size, location) as well as pre-treatment patient characteristics (e.g. pre-treatment visual acuity, glaucoma etc.). The lack of comparative studies severely limits the conclusions that can be drawn from the available evidence.

Local tumour control rates achieved with proton beam therapy was approximately 95%, indicating that this treatment is capable of preventing recurrence in most patients. Studies have shown that the possibility of recurrence is highly correlated to tumour size, in particular the height of the tumour. Nevertheless, the available literature is generally supportive that good local tumour control can be achieved with proton beam therapy. The incidence of metastasis appears to be comparable to other treatment modalities, with 5-year metastasis-free survival ranging from 73% to 80%. Overall patient survival after proton beam therapy ranged from 78% to 85% at 5-years post-treatment, which...
appears to be equivalent to patients treated with brachytherapy. At the time of writing, there were no cost-effectiveness studies on the utilisation of proton beam therapy for the treatment of uveal melanomas. One study, by Goiten and Jermann (2003) reported that that proton beam therapy will continue to be more expensive compared to conventional X-ray/photon therapy despite future assumptions of cost reductions (Goitein and Jermann 2003).

There are substantial amount of studies on the utilisation of proton beam therapy for the treatment of uveal melanomas. However, these studies often varied in treatment doses, did not use a concurrent control, tumour characteristics (location and size) were markedly different, and treatment margins were not standardised. Despite the heterogeneity between the included studies, proton beam therapy appears to be capable of achieving high rates of local tumour control. Nevertheless, many issues remain with regards to the use of this technology. Studies need to be conducted to determine the optimal dose for various types of uveal melanomas (taking into account tumour size, distance from sensitive structures, involvement of the ciliary body etc.) and to refine the technique with the aim of reducing complication rates. In addition, long-term comparative studies with existing techniques of treating uveal melanomas are required to provide more definitive results as to whether proton beam therapy is indeed more effective in the treatment of uveal melanomas.

Project page URL

Indexing Status
Subject indexing assigned by CRD

MeSH
Humans; Melanoma; Protons; Radiotherapy, High-Energy; Uveal Neoplasms

Language Published
English

Country of organisation
Australia

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AccessionNumber
32010001682

Date abstract record published
22/12/2010