Epimacular brachytherapy

Dr Douglas Clarkson reports on the treatment of wet AMD patients with epimacular brachytherapy, a promising and cost effective technique that is under trial at present

The emergence of the standard treatment for wet age-related macular degeneration (AMD) as intraocular injections of the anti-VEGF drug Lucentis (ranibizumab) presents a significant increase in current and anticipated drug expenditure. In the UK the Macular EpiRetinal Brachytherapy versus Lucentis Only Treatment (MERLOT) national multi-centre study is currently recruiting patients as part of an evaluation of the use of epimacular brachytherapy as a means to reduce the number of Lucentis injections required as a treatment for wet AMD. The MERLOT study has been adopted in the UK into the National Institute for Health Research CRN Portfolio. This study is using the VIDION epimacular brachytherapy system developed by Neovista of Freemont, California.

Current cost estimations based on typical requirement patterns involving Lucentis treatment indicate an initial two-year cost in the UK of around £16,000. With a single component of epimacular brachytherapy within this period, it is anticipated that a cost reduction of around £6,000 within the second year could be achieved. In addition, the reduction in number of Lucentis injections is associated with a reduction in the risk of complications such as endophthalmitis and retinal detachment.

With current predictions suggesting that patient workload relating to wet AMD is set to grow by around 30 per cent per year, there is obvious interest in more cost effective yet clinically effective treatment programmes for this eye condition. Currently the treatment is available within Europe, with anticipation of availability of treatment in the USA during 2011.

Epimacular brachytherapy

Epimacular brachytherapy is a procedure performed via a standard pars plana vitrectomy, which delivers a targeted dose of beta-radiation to the leaking blood vessels that cause wet AMD (*Optician* 22.05.09). Surgery is undertaken as a day case in theatre under local anaesthetic, and takes about 30-40 minutes. The beta radiation is effectively delivered by point source of high energy electrons which have a typical path length in tissue of between 2mm and 4mm. The aim of epimacular brachytherapy is to introduce highly localised tissue damage within the immediate affected retinal site. This contrasts with the technique of external beam radiotherapy treatment where significantly wider beams are externally generated but without any significant degree of target selectivity. The clinical effectiveness of epimacular brachytherapy has been identified within a set of randomised controlled studies.[1,2,3,4,5] Understanding of the response to the eye to ionising radiation has largely come from delivery of conventional radiation therapy using externally generated radiation beams.[6]

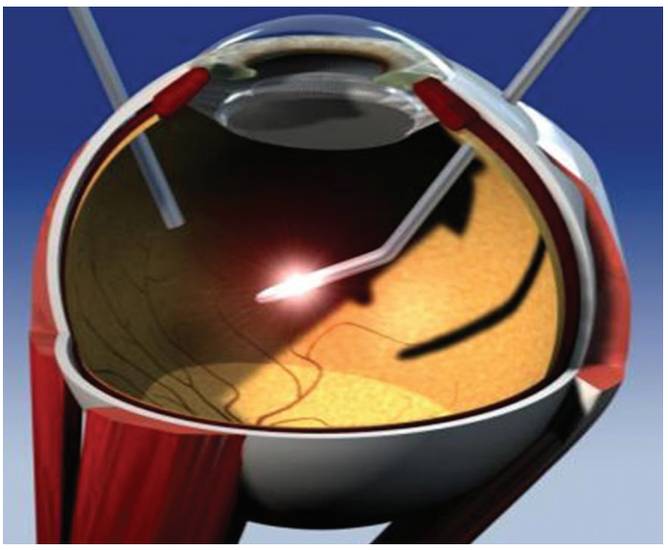

Figure 1 Illustration of the VIDION brachytherapy probe in position over AMD lesion. (Image: NeoVista)

Figure 1 indicates diagrammatically the beta source within the applicator probe over the area of treatment during the vitrectomy procedure. The radiation source utilised is Strontium 90, a high-energy beta ray emitter with a half life of 28.5 years. The source is located within the end section of a specialist wire extrusion unit derived from a 20 gauge needle. The source is guided into the treatment site by means of a specialist application device. At stages of device deployment, the status of the source positioning is indicated in the applicator handpiece. Once in position over the wet AMD site, the source is held in position for a designated time period – usually between two to three minutes to achieve the designated dose. At the end of the vitrectomy treatment, an injection of Lucentis is also administered.

Radiation-induced effects

Beta-radiation preferably damages the proliferating endothelium, fibroblasts and inflammatory cells that cause visual damage. Strong inhibitory effects associated with such radiation-induced antiagiogenic (inhibits blood vessel growth), anti-inflammatory (inhibits inflammation) and antifibronic (inhibits scar formation). Slowly growing cells are less susceptible to lethal damage.

Dosimetry details

Table 1 outlines the doses for critically observed damage and the corresponding dose delivered by the VIDION device. This confirms that limit dose levels delivered by the VIDION device to peripheral areas of the targeted eye are well below levels delivered associated with critically observable damage.

Such a localised delivery profile cannot be achieved by means of external beam treatment. Figure 2 indicates the typical dose intensity field delivered to the retina.

In line with radiation protection procedures, occupational exposure to staff in the operating environment

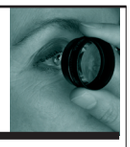

TABLE 1
Details of dose for critically observable radiation damage (after Finger *et al*[7]) compared with dose delivered by VIDION device

Tissue	Effect	Dose for critically observable damage	
(After Finger *et al*[7])	Dose delivered by VIDION device		
Cornea	Keratitis	30-50 Gy	0.00039 Gy
Conjunctiva	Conjunctivitis	55-75 Gy	0.00040 Gy
Lacrimal system	Atrophy	50-60 Gy	0.00040 Gy
Lens	Cataract	2 Gy (threshold)	0.00056 Gy
Retina	Retinopathy	35-55 gy	24 Gy
Optic nerve	Optic retinopathology	>55 Gy	2.4 Gy

require to be monitored. Such areas in theatre will also require to be radiation controlled areas and subject to local safety rules. Due to the nature of the radiation, however, and the method of deployment of radiation source, doses to staff from the procedure will typically be less than 1 per cent of the annual occupational dose for the surgeon and less than this for other theatre staff.

Clinical trials

The HORIZON trial which is an extension of the ANCHOR[8] and MARINA[9,10] trials with conventional Lucentis only, showed that even after two years of routine monthly dosing, patients were prone to significant decline in visual acuity in the third year of treatment. This has provided the 'ever after' concept of conventional Lucentis treatment.

The initial MERITAGE I feasibility study within which 50 patients were recruited suggested reduced retreatment with Lucentis when used with the VIDION device for epimacular brachytherapy. In addition, patients seemed to achieve greater visual stability than 'as required' Lucentis.

NeoVista has recently completed enrolment for the trial CNV Secondary to AMD Treated with Beta Radiation Epiretinal Therapy (CABERNET). This multi-centre, randomised, controlled clinical study has enrolled more than 450 subjects at 45 sites worldwide and is evaluating the safety and efficacy of epimacular brachytherapy performed concomitantly with Lucentis compared with Lucentis therapy alone. The CABERNET trial is a pivotal study for FDA approval.

For the MERLOT trial – currently around 20 UK hospitals are either recruiting into the study or are about to do shortly.

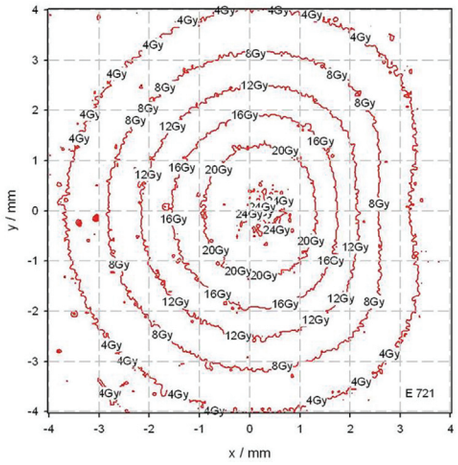

Figure 2 Indication of retinal radiation dose contours – showing a rapid fall off of radiation dose as a function of distance from centre of radiation field using the VIDION device (Image: NeoVista)

Discussion

The repetitive treatment method of Lucentis injections coupled with the significant cost of drug provision, are responsible for consideration of alternative or supplementary treatment regimes for wet AMD. Epimacular brachytherapy is a technique which is currently being assessed within specific patient groups and is showing promise as a means of reducing both the cost of overall treatments and the number of Lucentis drug administrations for specific patients. Initial observations of clinical outcomes are promising, though careful analysis of outcomes of current trials is awaited before epimacular brachytherapy becomes a routine method of treatment of wet AMD. Of particular interest will be the levels of incidence of complications associated with vitrectomy procedures and the longer-term stability of patient vision.

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Points of contact

www.neovistainc.com/index.html
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