An accurate and simple method for megavoltage radiation therapy of retinoblastoma

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Summary

A simple but highly accurate irradiation method for the “conservative” treatment of retinoblastoma has been developed at the Utrecht Retinoblastoma Centre. Treatment is carried out with a 6 MV or 8 MV linear accelerator using a lateral D-shaped field of 26 x 32 mm². This D-shaped field is specially contoured to include the entire retinal surface or vitreous and 10 mm of the anterior optic nerve and to protect the sensitive anterior structures of the eye, particularly the lens, as much as possible. Accurate positioning of the sharply collimated treatment field is easily done by magnetic fixation of the eye to the beam defining collimator by use of a low vacuum contact lens. As the fixed eye is located in the isocentre of the accelerator, the radiation beam can be directed at any angle by simple rotation of the gantry or table, without alteration of the position of the eye within the treatment field. Simultaneous irradiation of bilateral retinoblastoma is just as easily possible and can be done with the same accuracy by fixation of both eyes with contact lenses and alternately applying two opposing lateral fields. Prior to treatment, the axial dimensions of each eye are determined by ultrasonic biometry to ascertain the exact volume to be irradiated.

Introduction

Retinoblastoma is a rare, highly malignant tumour which primarily affects infants and young children. The tumour growth originates from single or multiple foci in one or both retinas. The preservation of life in most and the conservation of vision in many patients is now possible by application of radiotherapy and its adjuncts, light coagulation and cryotherapy and, if all else fails, enucleation can still be performed. In the “conservative” radiation treatment of retinoblastoma the entire retinal surface or, in case of seeding, the entire vitreous must be considered as at risk. Retinoblastoma is generally treated by a single lateral portal with the intention of irradiating the entire retinal surface or vitreous and sparing the vulnerable anterior structures of the eye, particularly the lens. A disadvantage of the temporal approach is that in the attempt to spare the lens the anterior retina and vitreous might also fail to receive the full therapeutic dose. For this reason, the peripheral retina is a well-known region for recurrences and new tumours.

At the Utrecht Retinoblastoma Centre, a simple
but highly accurate irradiation method, based on the temporal approach which ensures precise delivery of a uniform radiation dose to the entire retina or vitreous with maximal sparing of the lens, has been developed. This is of special importance in cases with bilateral retinoblastoma in which both eyes are irradiated simultaneously. A description of this irradiation method, its dosimetry and the treatment procedure followed is given in this paper. Since 1971, a total of 62 eyes of 46 patients with retinoblastoma have been treated with this accurate irradiation technique. A review of the excellent treatment results will be presented in a separate report.

**Irradiation method**

Treatment is carried out with a 6 MV or 8 MV Philips SL 75 X-ray linear accelerator. The tumourous eye is generally treated with a single lateral D-shaped field of $26 \times 32 \text{ mm}^2$ (Fig. 1.). This D-shaped field is specially shaped to include the entire retina or vitreous and 10 mm of the anterior optic nerve, and to protect the sensitive anterior structures of the eye, particularly the lens, as much as possible. Only when dealing with very young and very small babies is a smaller D-shaped field of

![Fig. 1. A lateral, sharply collimated, D-shaped treatment field covering the entire retina and excluding the lens.](image)

![Fig. 2. Schematic representation of the treatment technique. Accurate alignment and positioning of the eye with respect to the radiation beam is achieved by indirect fixation of the eye to the beam-defining collimator. A low vacuum contact lens is fixed to the eye in a central position. The soft iron pin jutting out from the contact lens is magnetically coupled to the millimeter scale on the collimator holder.](image)
Precise collimation of these small fields is achieved by interposing precision machined 11 cm thick lead beam-defining blocks. An exceptionally sharp beam definition is obtained by virtue of a short (17 cm) collimator to centre eye distance and the small amount of side scatter inherent to megavoltage radiation.

The centre of the tumourous eye is located exactly in the isocentre of the accelerator at 100 cm from the radiation source (i.e. FAD = 100 cm). Accurate alignment and positioning of the eye in the radiation beam is done by indirect fixation of the eye to the beam-defining collimator as schematically shown in Fig. 2. A contact lens is fixed to the eye in a central position by creating a low vacuum in the corneal chamber of the contact lens. A soft iron pin jutting out from the contact lens is magnetically coupled to a perspex millimeter scale on the collimator holder. The desired distance between the anterior extent of the cornea and the anterior edge of the treatment field can be established easily and rapidly by means of the millimeter scale. The accuracy and overall reproducibility of beam positioning with respect to the eye is within ± 0.3 mm.

Precise knowledge of the anterior axial dimensions of the eye is essential for determination of:

(a) the eye volume to be irradiated or protected;
(b) the relationship between the dose distribution in the lens and the extent and time of first appearance of a cataract that may be induced by the radiation when the lens has to be partly included in the treatment field.

In our system, the axial intraocular dimensions of the eye(s) of any individual patient are measured by ultrasonic biometry.

As the fixed eye is located in the isocentre of the accelerator, the radiation beam can be directed at any angle by simple rotation of the gantry or table, without changing the position of the eye within the treatment field. The beam is set up at a right angle if the other eye has been enucleated (field 1a or 1b in Fig. 3.). If the contralateral eye is to be spared, treatment is carried out with a 35-45° oblique lateral beam such as, for instance, to the left eye of Fig. 3 with field 2a. If the spared right eye later develops a tumour localization, the oblique lateral field 2b, which is parallel to and does not overlap with the earlier administered field 2a, is applied. Simultaneous irradiation of bilateral retinoblastoma is just as easily possible and can be done with the same accuracy by fixation of both eyes with contact lenses and alternately applying the opposing lateral fields 1a and 1b. The eye nearest to the collimator has always to be positioned in the isocentre of the treatment unit.

The actual patient set-ups for unilateral treatment with sparing of the contralateral eye and for bilateral treatment are shown in Fig. 4 and Fig. 5, respectively. An important, but not essential, aid for precise angling of the beam is a laser system designed by the author which projects a three-dimensional pattern of reference lines on the patient, as seen in Fig. 4.

A simple sliding back pointer may instead be attached to the aluminium T-bar to which the, also movable, perspex millimeter scales are fixed. A similar mounted scatterer of perspex is interposed in the beam with the aim of reducing the depth for dose build-up of the 6 MV and, particularly, of the
8 MV beam. The risk of underdosage in the temporal retina of the eye of very young children resulting from lack of dose build-up can thus be avoided. The actual scatterer-to-skin distance used for the 6 MV and the 8 MV fields are, respectively, 4 cm and 2 cm. Treatment is carried out under general anaesthesia to ensure the necessary immobilization. In the exceptional case of an older, more cooperative patient, the eye is anaesthetized with a topical anaesthetic (Novesine) before application of the contact lens. A vacuum pillow (Vac-Pac, NF1) is used for positioning and fixation of the patient’s head during treatment.

**Contact lenses**

Two types of low vacuum contact lenses are employed for fixation and positioning of the eye. Röntgen reference contact lenses of perspex [13] made by Medical Workshop, Groningen, The Netherlands, are generally used. These lenses (Fig. 6) with diameters of 20 mm and 17 mm are modified by extending the steel cannula with a soft iron rod allowing magnetic fixation. The diameter of the lens to be used for an individual patient is determined by the clearance between the eyelids. The transparancy of the lenses allows determination of

![Fig. 4. Unilateral treatment of retinoblastoma with sparing of the contralateral eye. Note the evacuated plastic pillow for immobilization of the head of the anaesthetized patient, the perspex scatterer interposed in the beam and the laser reference lines projected on the patient.](image-url)
whether there is a tight junction between the eye and the contact lens and whether the lens is positioned centrally on the eye. If there is a poor fit and, consequently, no good fixation can be achieved between the eye and one of the perspex contact lenses, a flexible contact lens is then utilized. These flexible lenses with diameters of 14 mm and 19.5 mm are made of silicone rubber (50% Sylgard 184 + 50% Sylgard 186; Dow Corning) and cast in special moulds.

**Beam characteristics**

**Surface dose and build-up region**

When high energy photons incidence upon an air-tissue interface, the phenomenon of build-up of the absorbed dose is observed. This effect is caused by the forward scatter of secondary electrons in the first few millimeters of tissue, giving rise to a lack of electronic equilibrium and an initial increase in energy deposition with depth. As a result, superficial lesions may be underdosed. As the temporal retina in the eye of very young children may be located at only a few millimeters below the skin, this area may be underdosed when treated with a lateral megavoltage X-ray beam. The problem is illustrated in Fig. 7 for the situation where the temporal retina is at a depth of 0.5 g cm⁻². If the eye is treated with an 8 MV 26 x 32 mm² field (Focus-Skin-Distance = (FSD) = 98.5 cm), the percentage dose (curve 1) to the temporal retina is less than 75% of the maximum dose (at depth 2 g cm⁻²). The dose to the skin is about 11%.

Loss of build-up (i.e. restoration of electronic equilibrium) without total loss of skin sparing can be achieved by interposing scattering material in the beam close to the skin. In the irradiation technique described, a scatterer consisting of a slab of perspex of 8 mm thickness and of sufficient dimensions to intercept all of the incident beam is used. The distance of the scatterer to the skin can be adjusted. When the scatterer is interposed in the beam, there is a progressive loss of build-up with decreasing scatterer-to-skin distance. This is illustrated in Fig. 7 for the 8 MV field. It can be seen that the dose at the skin and at 0.5 g cm⁻² depth increases to 30% and 87%, respectively, with the scatterer at 4 cm (curve 2) and to 50% and 95% with the scatterer at the actually used distance of 2 cm from the skin (curve 3). In addition, the peak of the build-up curve is moving toward the surface.

The build-up characteristic of the 6 MV field (curve 4) is less critical. The scatterer is used here as a dosimetric refinement. The percentage dose at the skin and at 0.5 g cm⁻² depth increases from 15% and 89%, respectively, of the maximum dose (at depth 1.5 g cm⁻²) without scatterer (curve 4) to 37% and 96% with the scatterer at the actually used distance of 4 cm from the skin (curve 5).

The build-up regions of the 6 MV and 8 MV treatment fields were investigated in a polystyrene phantom with a parallel plate ionization chamber having an effective sensitive diameter of 6.5 mm and a plate separation of 2 mm. Sheets of polystyrene
of a density of $1.05 \text{ g cm}^{-3}$ and average thicknesses of $0.105 \text{ g cm}^{-2}$ and $0.20 \text{ g cm}^{-2}$ and, for measuring the dose near the surface, polyester films of density $1.4 \text{ g cm}^{-3}$ and a thickness of $0.035 \text{ g cm}^{-2}$ served as build-up material. Since the polystyrene window of the ionization chamber was equivalent to $0.05 \text{ g cm}^{-2}$, extrapolation of the measurement data was necessary for the determination of the surface dose. The build-up characteristics presented in Fig. 7 are based on the average current readings of the ionization chamber with positive and negative applied voltages. The build-up curves for the 6 MV and 8 MV fields have been normalized to 100% at depths of $1.5 \text{ g cm}^{-2}$ and $2.0 \text{ g cm}^{-2}$, respectively.

**Beam profile**

Dose profiles of the 6 MV and 8 MV treatment fields have been determined at 98 cm FSD at depths of 2 cm, 6 cm and 8 cm by means of:

(a) thermoluminiscent dosimeters (Harshaw, TLD-100 micro-rods) in a precision-machined phantom of perspex;
Fig. 7. Central axis build-up characteristics of the 6 MV and 8 MV X-ray beams (FSD = 98.5 cm; 26 × 32 mm² field) in the absence and presence of an 8 mm thick perspex scatterer at varying distances to the surface.

(b) film (Ilford N4E50 and Kodalith 2571) sandwiched between sheets of tissue equivalent Temex rubber; film density measurements were made with a scanning densitometer described previously [9]; and

(c) recently, a diamond radiation detector with a sensitive volume of 1 mm³ [3].

No gross differences were found among the dose profiles determined by use of the different dosimetry systems. The diamond detector in particular proved to be very suitable for precise and relatively rapid determination of dose distributions in narrow beams having sharp penumbras.

The transverse plots determined for both beam energies were found to be almost identical at the respective depths. The transverse plot of a 6 MV 26 × 32 mm² field along the central axis of an eye positioned in the isocentre of the accelerator (98 cm FSD; centre eye at 2 cm depth) is illustrated in Fig. 8. The beam has been positioned with the anterior edge of the field (50% dose point) tangent to the posterior pole of the lens.
posterior pole of the lens. From the data in Fig. 8, one can also appreciate the knife-edged character of the beam. The penumbra width in which the dose decreases from 85% to 15% of the central axis dose is 2 mm at a depth of 2 cm and increases to 2.5 mm at a depth of 8 cm. The latter value is of importance for patients with bilateral disease treated with opposing lateral fields.

**Calibration of beam position**

The critical distance between the cornea of the eye and the anterior edge of the treatment field is established by noting the position of the extreme end of the soft iron rod jutting out from the contact lens on the “magnetic” millimeter scale of the collimator (Fig. 2). Accurate calibration of this measurement system is essential. For ease of operation and to avoid unnecessary mistakes, all contact lenses are of equal length, as mentioned earlier. In addition, the collimators defining the different sized D-shaped fields have been designed such that the distance between the central axis and the straight side of the field is the same for all fields.

Calibration of the readings of the contact lens on the magnetic millimeter scale indicating the position of the eye in the beam is carried out by use of a simple eye phantom. The phantom consists of a block of perspex with a replica of the anterior segment of an eye and a millimeter scale representing the axial depth from the “cornea” into the “eye” on top of it. The phantom with a contact lens on it is placed in the isocentre of the accelerator in a position similar to the normal treatment position. The beam is positioned with the straight, anterior edge of the light field at different depths from the “cornea” and the corresponding readings of the contact lens on the “magnetic” millimeter scale are recorded. If both eyes of a patient are treated simultaneously, the same calibration procedure has to be performed at the more distant position of the second eye.

**Tumour dose**

The administered radiation dose is standardized at a minimum total tumour dose of 45 Gy to be delivered in 15 fractions at 3 Gy per fraction and 3 fractions per week. This corresponds to a time-dose-fractionation factor (TDF) of 85. The TDF, introduced by Orton and Ellis [10], is a simplification of the Nominal Standard Dose (NSD) concept of Ellis [4]. If a patient misses a day of treatment, an additional fraction is given in order to obtain a minimum TDF of 85. The tumour dose is normalized on a percentage depth dose of 95% for the 6 MV and 100% for the 8 MV radiation beams.

**Anaesthesia**

All young patients are treated under general anaesthesia to ensure the necessary immobilization. A slow induction anaesthesia consisting of a mixture of nitrous oxide and oxygen with 1% of halothane followed by intubation is utilized. The anaesthesia is preceded by administration of atropine. After positioning the patient, placing the contact lens on the eye and setting up the treatment field, the administration of halothane is terminated prior to irradiation. During the irradiation lasting for about 1 min, the patient spontaneously respires a mixture of nitrous oxide and oxygen. All patients are observed during radiotherapy by television monitoring. The patients are fully awake in about 10 min after termination of the treatment and can be easily managed as outpatients. No serious complications have ever occurred.

**Ultrasonic biometry**

**Measurement technique**

The axial dimension of the eye(s) of each patient are determined by ultrasonic biometry. The measurement system used is an industrial ultrasonograph of Krautkrämer, type USM2 with a 12 MHz/5 mm transducer. An A-scan of the anterior segment of an eye showing the echoes of the front and rear surfaces of the cornea and the anterior and posterior surfaces of the lens is shown in Fig. 9a.
Fig. 9. (a) A-scan through the pupillary axis of the anterior segment of an eye at 12 MHz. The echoes shown from left to right are the anterior and posterior corneal interfaces, the anterior lens interface and the posterior lens interface. (b) The transducer is distanced from the cornea by use of a “diabolo” shaped saline filled contact lens that is fixed to the sclera by the eyelids.

To avoid inaccuracy in the measurement due to interference from the transmission pulse, the transducer is distanced from the cornea by use of a “diabolo” shaped contact lens water bath that is fixed to the sclera by the eyelids (Fig. 9b). The distal end of the contact lens is smeared with 2% methylcellulose (Methocel), placed on the eye and filled with sterile physiological saline. Flattening or distortion of the cornea is almost completely avoided with this type of contact lens. The contact lenses used are made of perspex and have diameters of the distal end of 20 mm and 16.5 mm.

The transducer can be moved freely within the contact glass. The oscilloscope trace is photographed with a Polaroid camera when the pulse amplitudes from the echo-producing interfaces are maximal. The ultrasonic beam will then almost coincide with the optic axis. All patients are examined under the same conditions as are those for irradiation.

**Calibration**

The time base of the oscilloscope is adjusted for the three ranges used such that any 0.2 scale division (s.d.) on the horizontal scale corresponds to 0.2 mm, 0.5 mm and 1.0 mm of tissue, respectively, having a standard ultrasonic velocity of 1545 m · s⁻¹. Prior to each examination, the time base settings are verified by use of a calibration block of perspex. The propagation velocity in perspex was determined to be (2695 ± 5) m · s⁻¹. The oscilloscope is correctly adjusted in, for instance, the 0.2 mm tissue/s.d. range if the perspex calibration block (physically, 17.3 mm thick), produces echoes from end-to-end that correspond to a tissue thickness of:

\[
\frac{1545 \text{ (v standard tissue; m · s}^{-1})}{2695 \text{ (v perspex; m · s}^{-1})} \times 17.3 \text{ mm (perspex)} = 9.9 \text{ mm}
\]

The velocity of 12 MHz ultrasound in perspex was established by determining the time interval between the echoes returning from the calibration block by use of a time interval averager counter (HP 5326). The propagation velocity of (2695 ± 5) m · s⁻¹ found was in good agreement with reported velocities of 2680 m · s⁻¹ [5] and 2700 m · s⁻¹ [8].

**Computation of axial intraocular dimensions**

After determination of the distance between the various echoes on the photograph of the A-scan trace (Fig. 9a), it is necessary to correct these measurements for the appropriate tissue velocities to obtain the true tissue dimensions. In our system, we
use the propagation velocities of ultrasound of 1532 m · s⁻¹ for aqueous and vitreous and 1640.5 m · s⁻¹ for lens determined by Jansson and Kock [7].

The correction factors applied are:

for the lens:

\[
\frac{v_{\text{lens}}}{v_{\text{standard tissue}}} = \frac{1640.5 \text{ m} \cdot \text{s}^{-1}}{1545 \text{ m} \cdot \text{s}^{-1}} = 1.06
\]

and for the aqueous and vitreous:

\[
\frac{v_{\text{vitreous}}}{v_{\text{standard tissue}}} = \frac{1532 \text{ m} \cdot \text{s}^{-1}}{1545 \text{ m} \cdot \text{s}^{-1}} = 0.99
\]

The measurement accuracy in the 0.2 mm tissue/s.d. range of the distances between the anterior extent of the cornea and the posterior pole of the lens is within ± 0.1 mm of tissue thickness; for the anterior extent of the cornea and the anterior pole of the lens, it is within ± 0.1 to 0.2 mm because of interference between the echoes of the lens surface and the undilated iris.

The separate representation of the echoes from the front and rear surfaces of the approximately 0.5 mm thick cornea in the A-scan of Fig. 9a, illustrates the longitudinal resolution of the measurement system.

Discussion

The main aim of external irradiation in retinoblastoma is to sterilize the entire retina and vitreous from tumour cells with minimal risk to the patient’s vision.

The direct anterior field technique as advocated by Bedford [2] irradiates the entire eye and can thus be applied to anterior tumours over the ora and vitreous seedlings. Treatment is technically easy and, as beam positioning is not critical, requires no anaesthesia.

The two main disadvantages of this treatment method are:

1. all irradiated eyes will invariably develop a radiation cataract after about 18 months;
2. a relatively large brain volume is included in the beam.

With a temporal beam technique, the radiation dose to the sensitive anterior structures of the eye may be considerably reduced and the irradiated brain volume is minimal, particularly when employing straight lateral fields. Although cataracts may be induced when the inclusion of a portion of the lens in the treatment field cannot be avoided, they are less serious than when the entire lens is included in the beam.

Accurate and reproducible irradiation of an eye with a lateral field with the aim of treating the entire retina, including its anterior extent, or the entire vitreous with a uniform dose and of excluding the lens as much as possible, makes high demands upon the treatment technique employed. This may be better appreciated if one considers the small dimensions of the human eye at a young age. The axial length of the eye of a child at the age of 6–12 months is about 18–19 mm and the axial distance between the front surface of the cornea and the posterior pole of the lens about 7 mm (Fig. 2), leaving a vitreous length of only 11–12 mm. Use of a conventional field generated by a 4–10 MV X-ray linear accelerator cannot meet the above demands, as the penumbra width (90–20%) at a depth of 2 cm is at least 6 mm. Therefore, additional collimation is required to obtain a sharp-edged beam.

Consequently, positioning of the treatment field becomes more critical. The generally applied methods of beam positioning by placing the anterior border of the beam at the lateral orbital rim [11, 12], at the outer angle of the eyelid [6] or at any other extraocular anatomical site, are by no means of sufficient accuracy. The technique described by Bagshaw and Kaplan [1] employing röntgen reference contact lenses for localization of the eye may, theoretically, increase precision. Skin marks are used for daily positioning of the beam. However, submillimeter precision cannot be achieved with marks on a movable skin, as we experienced in the treatment of patients with intraocular metastases.
using this technique for eye localization and beam positioning. Besides, the localization technique is complicated and time consuming. Accurate and reproducible beam positioning can be achieved only with a technique such as described here, in which the eye is fixed and the set-up of the treatment field is based entirely on the actual position of the eye and its anterior intraocular dimensions.

A disadvantage of the lateral beam technique is the necessity of anaesthesia to ensure immobilization of the young patient during treatment. It has been attempted several times to immobilize a patient by means of a large Picker-Flexicast vacuum pillow and to administer only a local anaesthetic to the eye before placing the contact lens. Unfortunately, it proved to be impossible to sufficiently immobilize the patient. The applied halothane anaesthesia, however, has proved to be safe and very suitable for a short-lasting treatment of these outpatients. Rotation of the eye of the anaesthetized patient, which may result in partial underdosage of the anterior retina, is automatically prevented by the fixation of the eye with a low vacuum contact lens.

The treatment method described is an easy and highly accurate means of irradiating the entire retina or vitreous with maximal protection of healthy radiosensitive anterior structures of the eye. The irradiation technique can be used on any megavoltage X-ray unit in the energy range of 4 to 10 MV. The optimum energy is about 5-6 MV. At higher energies, the depth for maximum dose build-up has to be artificially reduced. The build-up characteristics and dose profiles of the beam must be measured separately for any particular application of this technique.

**References**