Doseplanning ocular tumors with $^{125}$I-seeds

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Abstract

Since 1986 patients with ocular malignant melanoma have been treated with Ru-106 plaques at St Erik Eye Hospital. In 1998 I-125 radioactive seed plaques was presented as an alternative to Ru-106 when treating tumors with an apical height greater than 7 mm. Until June 2005 the doseplanning of these plaques was based on a depth-dose curve made in the dose planning system Cadplan supplied by Varian Medical Systems. In the recent years the capabilities of computerized 3D dose planning system has increased greatly. The number of types of seeds on the market has also increased.

In order to implement the modern 3D dose planning system Brachy Vision 7.3.10 in planning the I-125 plaques, a review of the dose planning process have been done.

The ultra sound equipment used by the ophthalmologist to determine the apical height of the tumor has been investigated in terms of accuracy. A phantom has been developed for this task.

As new seeds entered the market a comparision have been made comparing the Amersham 6711 seed with the Bebig I25.S06 seed. A method for measuring the activity of the single seeds has also been developed.

The dose planning system Brachy Vision 7.3.10 have been compared to the old dose planning method, and an implementation of the plaques into Brachy Vision have been made.

The ultra sound equipment was accurate in the regions of interest. It was also discovered that the Bebig I25.S06 seed gave slightly higher dose compared to the Amersham 6711 with the same activity. The difference between the seeds is however small. The results indicate that the old dose planning method gave a slight underdosage.
1 Introduction

1.1 Malignant melanoma in the eye

1.1.1 Definitions

Malignant melanoma, hereby referred to as melanoma, is a type of cancer which can occur in the skin or in the eye. Intraocular melanoma can be found in all parts of the uvea, but is most commonly originating from choroidea. It is a tumor type with metastatic potential, mostly in the liver (Seregard 2006).

1.1.2 Epidemiology

About 70-80 new cases are discovered in Sweden yearly (Seregard 2006).

1.1.3 Aetiology

Melanoma is about eight times more common for white people. In a Swedish consecutive series of 2997 patients, the median age was 64 years, and 50 % of the patients were between 56 and 72 years old at the time of diagnosis (Bergman et al. 2002). There is no indication of a different incidence between the sexes. It has been proposed that intensive exposure to the sun might have an impact for developing ocular melanomas. Studies done of people born in the southern states in the USA show they have a risk that is three times greater as compared to people born in the northern states. On the other hand a Swedish study shows no increase in ocular melanoma, but an increase in skin melanoma, which indicates that UV-irradiation do not cause ocular melanoma (Bergman et al. 2002). Sunlight exposure during the childhood might, however, be an indication, since the eye is more sensitive to UV-A and UV-B during these years. At present no heridetary factors are known (Seregard 2006).
1.1.4 Symptoms

The symptoms are often rather unspecific, and do seldom give the reason to suspect melanoma. Melanomas located in the rear of the uvea often leads to gradually increasing vision field defects. If exudation from the tumor initiates a retina fall-off, the symptoms can be rapid with photopsies, myodeposies and a rapid increase in vision field defects. Melanoma situated in the frontal part of choroidea or by corpus ciliare give rise to a rather moderate increase in vision field defects. Some melanomas situated in the rear part of the uvea give no symptoms at all and are discovered at a routine examination of the eye for other conditions where the eye can be involved (Seregard 2006).

1.1.5 Investigation

The most common way to finalize the diagnosis of an ocular melanoma is by using ultrasound. Ultrasound has the advantage to be independent of optical opacity in the tissues. With the aid of a standardized A-scan, the height of the tumor can be determined with great accuracy, and with a B-scan the diameter can be measured, for information regarding the different scan-modes see section 2.1.1. Another way to investigate is by fluorescine angiography. With that method an image of the blood vessels is obtained. This technique has the advantage that it can be used to rule out differential diagnoses. Other ways to investigate are by computer tomography, magnetic resonance or nuclear medicine. However, they do not provide more information on the tumor than an experienced ophthalmologist can obtain when using ultrasound. Magnetic resonance and nuclear medicine images have also be shown to give false positive results (Seregard 2006).

1.1.6 Prognosis

Generally, the tumor related mortality of melanoma depends on the follow-up time, tumor size and a number of other tumor variables, such as location and progression. In a Swedish study, containing 2997 patients, it was stated that the tumor specific mortality was 30 % after five years and 44 % after ten years (Bergman et al. 2003). Most of the deceased
patients died within five years after diagnosis. However, there are patients that have lived with metastases 15-20 years after enucleation, and in extreme cases longer than that (Seregard 2006).

The TNM-system can be used to describe the tumor:

<table>
<thead>
<tr>
<th></th>
<th>Corpus ciliare</th>
<th>Chorioidea</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Spreading only in corpus ciliare</td>
<td>Diameter &lt; 10 mm and height &lt; 3mm</td>
</tr>
<tr>
<td>T2</td>
<td>Invasion of frontal chamber and/or iris</td>
<td>Diameter &lt; 15 mm and height &lt; 5mm</td>
</tr>
<tr>
<td>T3</td>
<td>Invasion of chorioidea</td>
<td>Diameter &gt; 15 mm or height &gt; 5mm</td>
</tr>
<tr>
<td>T4</td>
<td>Extrabulbrian spreading</td>
<td>Extrabulbrian spreading</td>
</tr>
</tbody>
</table>

1.2 Treatments

1.2.1 Conventional treatments

Enucleation is the most radical way to treat an ocular melanoma, however, other ways exist. For some small melanocytotic tumors, that have a low rate of growth and are considered to have a low risk of metastases, continuous observation is an alternative. Another way is by using transpupillary thermotherapy, where a diod laser heats up the tumor tissue to 65°C and thereby causes necrosis, mostly to a depth of 4mm (Seregard 2006).

1.2.2 Treatments with ionizing radiation

- External radiation therapy

  This type of treatment can be given with a linear accelerator or with a particle accelerator, and for the latter, preferably protons or heavier ions. The experience with conventional radiation therapy as the only form of treatment have been unsatisfactory. It was previously recommended that external radiation was to be given adjuvant before enucleation, but there are some results that indicate that the mortality does not decrease with these combined methods (Seregard 2006).
When using protons, most results have come from studies from Boston and Lausanne. The supporters of this method emphasize on the theoretical benefits with the accurate dose distribution obtained. The results have overall also been satisfactory regarding tumor control, especially when treating tumors in the back of the eye. In Sweden, some patients with melanomas not suitable for applicator treatment have been treated with protons. The preliminary results, during the last ten years, has been unsatisfactory and some of the treated eyes have been enucleated (Seregard 2006).

- Brachytherapy/plaque therapy

In an effort to preserve vision and to spare other ocular and other tissues from radiation, episcleral plaque radiation therapy has become a commonly used alternative. When the method was new, in the 1930s, radon seeds were used (Moore 1930). Later on, in the 1960s it was tried to implant seeds directly into the tumor, but it later went on to develop cobalt-60 plaque therapy (Stallard 1966). Since then a number of other radionuclides including Au-198, Ru-106/Rh-106, Ir-192, Pd-103 and I-125 have been used with varying results (Nag et al. 2003). At St Erik Eye Hospital, treatments with Ru-106/Rh-106 and I-125 are used. Ru-106/Rh-106 decays through beta-decay, and is used for tumors with a thickness of 1 to 7 mm. I-125 is used for thicker tumors. This paper will only focus on the I-125 treatments.

2 Materials and methods

2.1 Ultrasound

2.1.1 General

An experienced ophthalmologist can diagnose melanoma with the aid of ultrasound. At St Erik Eye Hospital ultrasound is routinely used to investigate patients with suspicion of melanoma. Since the information regarding the tumor dimension, which is used in
the treatment planning, is obtained through the ultra sound investigation, it is of great importance that the equipment is accurate. A phantom has been developed in order to investigate the accuracy of the ultrasound equipment.

The ultrasound equipment used is "CineScan S" from the French company Quantel Medical. This equipment allows the user to choose from two different scan-modes, A-scan and B-scan. The B-scan is conducted at 10 MHz and is designed to get an image in which the tumor location can be determined. The B-scan is focused at a distance of 24 mm from the probe, and thus must be used on the part of the eye which is opposite to the tumor to get a sharp image. Figure 1 shows a B-scan probe and and B-scan image of a malignant melanoma.

![Figure 1: B-scan probe (left) and an B-scan image of an eye with malignant melanoma(right)](image)

The theoretical precision based on the sampling frequency of 10 MHz is ±0.2 mm for the B-scan probe, and is thus too uncertain to measure the real dimensions of the tumor. Since it is focused at a fix distance, it can be difficult to cover the whole tumor in the focused region.
To determine the thickness of the tumor an A-scan is conducted. After localizing the tumor with the B-scan, the A-scan probe is placed on the opposite side of the eye compared to the side with the tumor, i.e measuring thorough the vitreous humor. The A-scan is non-focused and produce no image, instead it generates a spectrum of the signal amplitude versus distance in the tissue. Figure 2 show the A-scan probe and an image of the outdata. When conducting these measurements it is important to pan the probe around on the eye bulb until the largest tumor-thickness is found.

![A-scan probe](image1)

**Figure 2:** A-scan probe(left) and an example of outdata(right)

Since the ultrasound probe must be in direct contact with the eye the ophthalmologist adminsters local anesthetic solution in the patients eye. Ultrasound transmission gel is applicated on the skin around the eye. The transmission gel is used to eliminate any air between the probe and the investigated area. Because the speed of sound in air is lower than in tissue, any air would cause great artifacts in the image(Webb 1992). The examination starts with the B-scan to localize the tumor. When the tumor is located the A-scan probe is used to measure the thickness of the tumor.
2.1.2 The ultrasound phantom

It is important that the dimensions of an ocular tumor is measured with great accuracy when the measurements are used for dose planning. Therefore, to be able to ascertain the exactness of the ultrasound equipment a phantom was made. The criteria set up for the phantom was to be able to simulate different tumor thicknesses and to simulate different distances between the probe and the tumor.

Sound waves propagate with different velocities in different materials. For eye-tissue, the speed of sound is 1550 m/s, the ultrasound equipment is calibrated to assume that this is the speed of sound of the media examined. The phantom is made of PMMA. In PMMA the speed of sound is 2720 m/s. Since PMMA has a greater speed of sound than tissue, a factor describing the ratio between the speed of sound in tissue and the speed of sound in PMMA had to be calculated (Webb 1992). This factor had to be multiplied with the measurements to obtain the real distance measured. The factor is given by:

\[ f = \frac{v_{\text{PMMA}}}{v_{\text{eyetissue}}} = \frac{2720 \text{m/s}}{1550 \text{m/s}} = 1.755 \]

The measurements were carried out in water due to the fact that the speed of sound in water (1403 m/s) is close to the speed of sound in tissue (1550 m/s), and thereby simulate an environment close to the clinical situation. Therefore, the entire phantom is built in a cylindrical bowl which can be filled with water (figure 3 and 4).

The main part of the phantom is a circular disc. The thickness of the disc is 10 mm, and it has a diameter of 150 mm. Around the circumference of the disc, cavities with a diameter of 20 mm was drilled. These cavities are ranging from 1 mm to 9 mm in depths. These cavities simulate different tumor thicknesses.

A stick is mounted in the middle of the cylindrical bowl. On this rod, the disc is mounted 40 mm above the bottom, making it able to revolve.

On the rod above the disc a micrometer screw is mounted. On this micrometer screw the ultrasound probe is attached. The screw makes it able to adjust the distance between
the disc and the probe with great precision. By adjusting this, different distances to the tumor can be simulated.

The disc is fixated by a handle that can be tightened and untightened depending on if the user want to do a measurement or rotate the disc to simulate a different tumor size.

On the side of the bowl a device for locking the disc in place was mounted.

![Figure 3: Principal sketch of the ultra sound phantom](image)

### 2.1.3 Measurements

Phantom measurements were made at S:t Erik Eye Hospital. The simulated tumor thicknesses ranged from 2 mm to 10 mm and were measured at the distances 1 to 17 mm. Figure 5 shows a sketch of the measurement setup. The measurements were repeated five times per cavity to improve statistics.
2.2 Seeds

2.2.1 General

According to the AAPM (Rivard et al. 2004) a radioactive seed is:

*A cylindrical brachytherapy source with active length, $L$, less than or equal to 5 mm*

Brachytherapy seeds often consists of a titanium capsule in which the radioactive material is encapsulated. The two most common radionuclides are I-125 and Pd-103 (Finger et al. 1993). Besides treatment of ocular tumors, seeds are often used as permanent implants for treating tumors in the prostate.
2.2.2 Different types of seeds

Two different seeds has been examined in this thesis, regarding their dose distribution. The Amersham 6711 and the Bebig I25.S16. The radioactive nuclide for these seeds is I-125. The choice of seeds was due to the fact that the clinic has used the Amersham 6711 for several years and was now changing to Bebig I25.S16.

The Amersham 6711 consists of a titanium capsule in which a silver rod is placed. The $^{125}$I is adsorbed to the surface of the rod through an electrolytical process (Manolkar et al. 2003). The silver rod also acts as a x-ray indicator. The active length, i.e. the actual length of the radioactive material, is 3.0 mm (figure 6).

The Bebig I25.S16 also consists of a titanium capsule. The $^{125}$I is mixed inside a porous ceramic. In the center there is a gold marker to be able to visualize the seeds when using x-rays. The active length is 3.5 mm (figure 6).

2.2.3 Dosimetry - Formalism

The dosimetry formalism that has been used is the one stated by the AAPM (Rivard et al. 2004). They have developed a formalism describing how the dose distribution appears around the seed.

To calculate the dose rate in a certain point the following equation is used:
\[ \dot{D}(r, \theta) = S_K \cdot \Lambda \cdot \frac{G_L(r, \theta)}{G_L(r_0, \theta_0)} \cdot g_L(r) \cdot F(r, \theta) \]

where

- \( S_K \) is the air kerma strength in units of 1 \( U \) which is a short form for 1 \( \mu \text{Gy m}^2 \text{h}^{-1} \). Air-kerma strength is the air-kerma rate in vacuo (i.e., corrected for attenuation and scattering) for photons with the cut-off energy \( \delta \) (In this protocol \( \delta = 5 \text{ keV} \)) at distance \( d \) multiplied with \( d^2 \). Thus:

\[ S_K = \dot{K}_\delta(d)d^2 \]

- \( \Lambda \) is the dose rate constant in water, the ratio between the dose rate in the reference point, \( P(r_0, \theta_0) \), and \( S_K \). \( \Lambda \) is in units of \( c \text{Gy h}^{-1} \text{U}^{-1} \) which reduces to \( \text{cm}^{-2} \).

\[ \Lambda = \frac{\dot{D}(r_0, \theta_0)}{S_K} \]
Figure 7: The coordinate system recommended by AAPM

The dose rate constant depends both of the radionuclide and the model of the source. It can be determined either with Monte Carlo simulations and/or experimentally.

- $G_L$ is the geometry factor for a line source. It is defined as:

$$G_L(r, \theta) = \begin{cases} \frac{\beta}{L \cdot r \sin \theta} & \theta \neq 0 \\ \left( r^2 - L^2 \right)^{-1} & \theta = 0 \end{cases}$$

For a point source it is defined as $G_P = r^{-2}$.

- $g_L(r)$ is the radial dose function which accounts for dose fall-off on the transverse-plane due to photon scattering and attenuation

$$g_L(r) = \frac{\dot{D}(r, \theta_0) \cdot G_L(r_0, \theta_0)}{\dot{D}(r_0, \theta_0) \cdot G_L(r, \theta_0)}$$

- $F(r, \theta)$ is the two-dimensional anisotropy function. It describes the variation in dose
as a function of polar angle relative to the transversal-plane.

\[ F(r, \theta) = \frac{\dot{D}(r, \theta)}{D(r, \theta_0)} \frac{G_L(r, \theta)}{G_L(r, \theta_0)} \]

The dose-rate constant, the radial dose function and the anisotropy function are tabulated by the AAPM, the latest update is: *Update of AAPM Task group No. 43 Report, a revised protocol for brachytherapy dose calculations* (Rivard et al. 2004). The data presented therein is based on both TLD-measurements and Monte-Carlo calculations and are considered consensus data.

To be able to use a seed in the treatment planning system, the dose-rate constant, the radial dose function and the anisotropy function must be entered. The physical dimensions as well as the active length also have to be entered.

### 2.2.4 Measurements on single seeds

When seeds are delivered, a certificate containing information about activity and air kerma strength of the seeds is enclosed. Before clinical use, as part of the quality assurance, the seeds activity are measured to verify the certificate value. For the measurements an ionization chamber and an electrometer was used. The ion chamber was a well-type chamber manufactured by Standard Imaging, model HDR-1000 Plus. The electrometer was manufactured by Standard Imaging, model CDX-4000.

The chamber consists of an aluminium wall ion chamber filled with air. The collection potential applied to the chamber is 300 V. On top of the chamber is a removable PMMA jig. In the center of the jig is a catheter acting as source holder. This catheter is made of teflon, to make the seeds slide with little friction, when going down into the chamber (Khan 2003). The source holder is devised to reproduce the source geometry in relation to the surrounding chamber walls. The source holder will place the seed in the part of the chamber where the maximum sensitivity of the chamber is located (Standard Imaging Instruction Manual).

The electrometer can measure currents as low as 0.1 pA. The electrometer is connected
to the ion chamber using a coaxial/triaxial interface. The electrometer also supplies the chamber with high-voltage.

The electrometer was reset to zero to subtract background radiation. The seed was placed in the source holder and a measurement was taken when the value had stabilized. The temperature and pressure was noted, and the measured currents were corrected to be made in an environment with the temperature T=20°C, and P=101.325 kPa. To be able to control the activity of the seeds a reference seed with well-defined activity was used. This seed was measured at a regular basis for 35 days to obtain an activity-response-curve which could be used to estimate the activity of the treatment seeds. In the near future the chamber will be cross-calibrated with a chamber calibrated by a NIST (National Institute of Standards) certified laboratory. Since the activity of the seed was well-defined and traceable to NIST, and the half-life also is well-defined, the measurements describes a curve which can be used to calibrate the chamber to measure activity of single seeds.

2.2.5 Comparing the dose distribution between the seed types

To be able to compare the dose distribution between the Amersham 6711 and the Bebig I25.S16, the data tabulated in the TG-43 update, described in section 2.2.3, was entered into the dose planning system. A dose plan of a single seed was done and the dose at a number of points along the central axis was measured in the planning system. The activity of the seed was set to 10 mCi, and the measurement time was 24 hours. The dose was normalized to the highest dose 2 mm from the center of the seeds. The reason for placing the first measurement point 2 mm away is because of the very steep dose-gradient close to the seed.

2.2.6 ¹²⁵I

I-125 decays with a half-life of 59.46 days through electron capture to Te-125, and emits the photons presented in table I(Kocher 1981)

The weighted mean energy per decay is 28.1 keV. Auger electrons is also emitted in
<table>
<thead>
<tr>
<th>Origin</th>
<th>Energy</th>
<th>Probability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gamma</td>
<td>35 keV</td>
<td>6.5 %</td>
</tr>
<tr>
<td>$K_\alpha$ X-ray</td>
<td>27 keV</td>
<td>112.5 %</td>
</tr>
<tr>
<td>$K_\beta$ X-ray</td>
<td>31 keV</td>
<td>25.4 %</td>
</tr>
</tbody>
</table>

Table 1: Photons emitted in the $^{125}$I decay.

the decay. In the seeds the I-125 is encapsulated in titanium, effectively absorbing these Auger electrons inside.

The Half-Value Layer of I-125 photons is 20 mm in tissue. The typical size for a tumor eligible for treatment with I-125 is between 7 mm to 15 mm in height between base and apex. The tumor size and the half-value layer are close to each other, making I-125 a suitable radionuclide for treating ocular tumors.

It is also worth mentioning that 25 % of the spectrum from the Amersham 6711-seed consist of characteristic X-rays from the silver rod which is encapsulated in the seed (Ling et. al)

2.2.7 Plaques

The applicators for I-125 treatments are often called plaques. The plaques are available in different sizes and designs, for example cut-outs to spare the iris or optic nerve. There is a number of suppliers of plaques. The plaques used at S:t Erik Eye Hospital are manufactured by Bebig. A typical plaque is circular and shaped like an arched lens to fit the rounded eye. The plaques have eyelets to make it possible to suture them to the scleral surface, so they do not move during treatment. Plaques for I-125 treatments are made of gold with a thickness of 1 mm. Gold is a very dense metal ($\rho = 19.32 \text{ g cm}^{-3}$), making it improbable that the photons emitted by I-125 would penetrate, consequently the radiation is only directed from the concave side of the plaque. The Half Value Layer in gold for I-125 photons is 0.014 mm. The gold also absorbs more photons through photoelectric effect than water, and since the TG-43 formalism is based on the dose distribution in water, the dose will be approx 8 % lower at a 15 mm distance away than what TG-43
suggests (Weaver 1986).

The different plaques from Bebig used at St Eriks Eye Hospital are named CCA, CCB, COB and CIB (figure 8). In table 2 the dimensions of the plaques are listed. The radius is the radius of the imaginary sphere that would be created if the plaques were part of a sphere (fig 11). The diameter is the maximum diameter of the plaque (Ruthenium-106 Augenapplikatoren für die Brachytherapie, Bebig, 1993).

<table>
<thead>
<tr>
<th>Type</th>
<th>Diameter [mm]</th>
<th>Height [mm]</th>
<th>Radius [mm]</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCA</td>
<td>15.3</td>
<td>3.3</td>
<td>12</td>
</tr>
<tr>
<td>CCB</td>
<td>20.2</td>
<td>5.4</td>
<td>12</td>
</tr>
<tr>
<td>COB</td>
<td>19.8</td>
<td>5.2</td>
<td>12</td>
</tr>
<tr>
<td>CIB</td>
<td>20.2</td>
<td>5.4</td>
<td>12</td>
</tr>
</tbody>
</table>

**Table 2:** The dimensions of the plaques used in treatment

Some tumors are close to the optic nerve or the iris. To spare these tissues as much as possible the CIB- or COB plaques (figure 8) are used in such cases. The tumor base diameter also varies and it is sometimes sufficient to choose a plaque with lesser diameter, resulting in a lower dose to surrounding tissue.

The seeds are glued to the plaque using a silicon based glue. The name of the glue is "3140 MIL-A-46146 RTV coating" and it is manufactured by Dow Corning. The glue is applied in a thin layer on the concave side of the plaque and are left to harden for 30 minutes. After the 30 minutes the seeds are carefully placed in a predetermined pattern using tweezers. The time for the glue to harden properly is 48 hours. The number of seeds depends on the choice of applicator. The pattern for the different plaques is illustrated in figure 8. After the glue has hardened the plaque is sterilized in a high steam pressure process, autoclave, and is ready to use for treatment. When the seeds have decayed, they can be easily removed, and new seeds can be glued to the plaque.

The procedure for placing the plaque in place is performed under general anesthesia. The ophthalmologist uses transillumination (Transillumination is the shining of a bright light
Figure 8: The plaques used at S:t Erik Eye Hospital, not according to scale. The red lines shows the desired seed positions.

through a body cavity or organ for diagnostic purposes.) to locate the tumor. The tumor boundaries are marked with a special pigment. Before the plaque is sutured to the scleral surface a dummy plaque without seeds are placed on the tumor. The sutures are placed with the aid of the eyelets on the dummy. The dummy plaque is then removed and the therapy plaque is sutured in place using the premade sutures to keep the exposure to the staff in the operating theatre to a minimum. The ophthalmologist and the theater nurse are using lead aprons and lead thyroid shielding during the procedure. Figure 9 show the dummy plaque before the sutures have been made.
2.3 Treatment Planning

2.3.1 General

The aim of the treatment is to deliver the prescribed dose to the apex of the tumor (figure 10). The information needed to achieve this dose distribution is the distance between the base and the apex of the tumor because the plaque is situated against the base of the tumor.

Until June 2005, the determination of the treatment time was made by using a depth-dose curve. This depth-dose curve was obtained using calculations from the old treatment planning system Cadplan from Varian Medical Systems. By taking the decay of the iodine seeds into consideration, the treatment time could be calculated.

The treatment planning system Brachy Vision 7.3.10 was taken into clinical practice in June 2005 to dose plan ocular tumors. Brachy Vision 7.3.10 is a 3D treatment planning
Figure 10: Transversal drawing of the eye

system from Varian Medical Systems Inc. The system can be used both for high dose rate treatments as well as for seeds. Both DICOM (Digital Imaging and Communications in Medicine,) and TIFF-images (Tagged Image File Format) can be imported into the system. The DICOM format has the advantage to include patient data and the alignment within the file. When using TIFF-files it is necessary to scale and align the images manually.

To be able to do dose plans with seeds, the seed data had to be entered into Brachy Vison. The data was taken from the TG-43 update when entering for both the Amersham 6711 seed and the Bebig I25.S16 seed.

There are no plaque models available in the software, these have to be implemented manually. Since the plaques are part of an imaginary sphere, see figure 11 it was possible to calculate the diameter at different distances from the surface perpendicular to the center of the sphere.
Figure 11: The imaginary sphere with the applicator shaded

When the diameters were calculated, 12 TIFF-images were created. Each image with a centered circle, in the xy-plane, depicting the applicator at 12 different depths ranging from the bottom (height=0 mm) to the end (height=5.5 mm). The images was imported into Brachy Vision and was aligned with the proper z-coordinate. The result was an outlined model of the applicator. Since the images in Brachy Vision is opaque in relation to each other, contours was drawn in each of the images. This resulted in an easily understandable image of the applicator (figure 12).

The green cylinders in figure 12 are the seeds. In Beachy Vision, the seeds can be positioned arbitrary. When gluing, the aim is to place the seeds as depicted in figure 8. However, if, the seeds would slide, or in other way change position, it is possible for the treatment planning system to calculate the dose distribution for these new seed positions.

The information regarding the apical height of the tumor comes from S:t Eriks Eye Hospital, where the tumor has been measured with ultrasound by the ophthalmologist. A safety margin of 1.5 mm is added to the size to ascertain that the whole tumor get the prescribed dose (Bergman et al. 2005). The information of the apical height of the tumor is entered into the treatment planning system by defining a reference point below the applicator at the same distance as the tumor height (in figure 13 the reference point is
**Figure 12:** A CCB applicator in the treatment planning system, the green cylinders represents the seeds.

named "fulldos").

To be able to compare this dose planning method with the old dose planning method a depth dose curve along the central axis of an CCB-applicator was obtained for each of the two seeds. A depth dose curve using the old dose planning method was also obtained, and the two curves were compared. The activity of the seeds was set to 10 mCi and the time was set to 24 hours. The doses were normalized to the highest dose from the Bebig seed.
Figure 13: Brachy Vision windows, with the reference point "fulldose" visible.

3 Results

3.1 Ultrasound

According to the manual of the ultrasound equipment, the uncertainty when measuring with the A-scan probe is ±0.2 millimeters. There is also an uncertainty when reading the measurements on the screen of the equipment, this uncertainty is estimated to ±0.1 millimeters. This gives a total uncertainty of $\sqrt{0.1^2 + 0.2^2} \approx 0.22\text{mm}$

When measuring, the disc of the phantom was revolved until the desired simulated tumor thickness was directly beneath the probe. The probe was adjusted to touch the disc, and was elevated in to the distances 1, 3, 5, 7, 10, 13, 15 and 17 millimeters above the simulated tumor. This was repeated five times with each of the different simulated tumor thicknesses of 2, 3, 4, 5, 6, 7, 8 and 9 millimeters. All measurements was conducted in water, due to the fact that water and tissue almost have the same speed of sound.
However, as stated in section 2.1.2, PMMA has a greater speed of sound than tissue, and therefore the measured value had to be multiplied with a constant given by the ratio between the speed of sound in tissue, and the speed of sound in PMMA:

$$f = \frac{v_{PMMA}}{v_{tissue}} = \frac{2720 m/s}{1550 m/s} = 1.755$$

Table 3 shows the mean from the measurements, corrected for the speed of sound in PMMA. In the tissue column, the simulated tumor thickness is presented, i.e the thickness of the PMMA. In the upper most row is the actual distance between the probe and the PMMA tabulated. The values are the mean of the measurements made. For example, the measured value for a tumor thickness of 4 millimeters with a distance of 10 millimeter from the tumor is 4.30 millimeters.

<table>
<thead>
<tr>
<th>Tumor real thickness[mm]</th>
<th>1.00</th>
<th>3.00</th>
<th>5.00</th>
<th>7.00</th>
<th>10.00</th>
<th>13.00</th>
<th>15.00</th>
<th>17.00</th>
</tr>
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<tbody>
<tr>
<td>2.00</td>
<td>2.48</td>
<td>2.37</td>
<td>2.29</td>
<td>2.27</td>
<td>2.27</td>
<td>2.18</td>
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<td>3.00</td>
<td>3.47</td>
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<td>3.43</td>
<td>3.50</td>
<td>3.49</td>
<td>3.47</td>
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<td>4.25</td>
<td>4.31</td>
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<td>4.30</td>
<td>4.27</td>
<td>4.28</td>
<td>4.20</td>
</tr>
<tr>
<td>5.00</td>
<td>5.05</td>
<td>5.01</td>
<td>4.99</td>
<td>4.99</td>
<td>5.02</td>
<td>5.05</td>
<td>5.05</td>
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<tr>
<td>6.00</td>
<td>5.91</td>
<td>5.91</td>
<td>5.90</td>
<td>5.90</td>
<td>5.87</td>
<td>5.90</td>
<td>5.86</td>
<td>5.84</td>
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<tr>
<td>7.00</td>
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<td>9.00</td>
<td>8.79</td>
<td>8.87</td>
<td>9.10</td>
<td>9.10</td>
<td>8.92</td>
<td>9.00</td>
<td>8.93</td>
<td>8.89</td>
</tr>
</tbody>
</table>

**Table 3:** Measured tumor thickness corrected for the ultra sound accuracy measurement

Table 4 shows the percentual errors of the measurements. In the first column, the thicknesses of the PMMA are shown, in the middle column, the mean measured distances, corrected for speed of sound, are shown, and in the right column, the percentual errors are shown.
In figure 14 the percentual errors are plotted against the actual thickness. It is possible to see that the thicker the tumor is, the lesser the error.

<table>
<thead>
<tr>
<th>Real thickness</th>
<th>Measured thickness</th>
<th>Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.00 mm</td>
<td>2.26 mm</td>
<td>12.9 %</td>
</tr>
<tr>
<td>3.00 mm</td>
<td>3.48 mm</td>
<td>15.9 %</td>
</tr>
<tr>
<td>4.00 mm</td>
<td>4.27 mm</td>
<td>6.73 %</td>
</tr>
<tr>
<td>5.00 mm</td>
<td>5.02 mm</td>
<td>0.46 %</td>
</tr>
<tr>
<td>6.00 mm</td>
<td>5.89 mm</td>
<td>-1.91 %</td>
</tr>
<tr>
<td>7.00 mm</td>
<td>6.91 mm</td>
<td>-1.22 %</td>
</tr>
<tr>
<td>8.00 mm</td>
<td>7.97 mm</td>
<td>-0.42 %</td>
</tr>
<tr>
<td>9.00 mm</td>
<td>8.93 mm</td>
<td>-0.77 %</td>
</tr>
</tbody>
</table>

**Table 4:** Average percentual error at the different measured distances

### 3.2 Seeds

To obtain the "calibration constant", measurements was carried out over 35 days. In table 5 the measurements are presented. In the first column is the number of days from the source certificate. In the second column is the activity according to the certificate, corrected for decay. In the third column is the measured value, and in the fourth column is the measured value corrected for temperature and pressure changes. In the fifth and last column is the "calibration constant".

The average value of the constant is 0.158 mCi/pA.

Figure 15 visualizes the dose distribution around the Bebig and Amersham seeds. One doseplan for each seed was made, the dwell time of 60 hours, and the activity of 15 mCi was entered, and a visual image of the dose distribution around the seeds were obtained.

Figure 16 shows the depth dose curve from a single seed from both Bebig and Amersham. The values have been normalized to the highest dose at 2 mm of the Bebig seed.
Figure 14: The percentual errors of the ultrasound measurement

3.3 Treatment planning (verification)

To compare the method for dose planning in Brachy Vision with the old method, a depth dose curve using both the Bebig and the Amersham seeds was obtained in Brachy Vision and plotted into a diagram. A depth dose curve from the old method was plotted in the same diagram; this depth-dose curve was obtained using data from the CAD-plan treatment planning system. The activity of the seeds was set to 10 mCi and the time was set to 24 hours. The doses were normalized to the highest dose from the Bebig seed. (figure 17).
<table>
<thead>
<tr>
<th></th>
<th></th>
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</thead>
<tbody>
<tr>
<td>-5</td>
<td>16.99</td>
<td>106.2</td>
<td>106.54</td>
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<tr>
<td>-4</td>
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<tr>
<td>1</td>
<td>15.84</td>
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<td>7</td>
<td>14.77</td>
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<td>10</td>
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<tr>
<td>20</td>
<td>12.81</td>
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<td>74.21</td>
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<td>0.1577</td>
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<td>35</td>
<td>10.66</td>
<td>68.82</td>
<td>70.04</td>
<td>0.1522</td>
</tr>
</tbody>
</table>

**Table 5:** Measuring data from the determination of the calibration constant

**Figure 15:** The dose distribution around the two different seeds with activity 15 mCi and time 60 hours
Figure 16: The depth dose curves from the Bebig and Amersham seeds
Depth Dose Curve Along Central Axis of the Applicator

Figure 17: Dose profile from the central axis of an CCB-applicator
4 Conclusion

The ultrasound measurements show an increasing error with smaller tumor thicknesses. However a typical thickness of a tumor eligible for I-125 seed treatment is larger than 7 millimeters, and the results for tumors more than 7 millimeters in thickness shows a good correspondence. To further investigate the ultrasound, it would be interesting to compare the different ophthalmologists methods when measuring on a real patient.

When comparing the seeds, they are almost equivalent in terms of dose-distribution, whether looking at one single seed, or a full plaque-configuration of seeds. The Bebig I25.S16 gives a slightly higher dosage compared to the Amersham 6711, when using the same dwell times and activities. This difference have no clinical implication, since the increasing treatment time using Amersham instead of Bebig would be negligible. Instead other factors should be taken into consideration, for example how big the difference between the strongest and weakest seed are in terms of activity or how reliable the shipment time is.

There is a difference between the old dose planning method and the Brachy Vision dose planning method. The old method gave a slight underdosage. This underdosage is of the order 1-2 %. But since we always uses a safety margin of 1.5 millimeters, no patients have been undertreated.

5 Acknowledgements

I would like to thank all the kind people working at the Radiotherapy department at Karolinska University Hospital in Solna. Special thanks go out to all my physicist colleagues. I want to particularly thank my supervisor Marie Lundell for great guidance and support. I also want to thank Pierre Barsoum and Simone Eriksson for reading the manuscript and giving me constructive feedback. Special thanks also goes to Åsa Carlsson-Tedgren for introducing me to the world of brachytherapy dosimetry and the kind staff of the oncology department at S:t Erik Eye Hospital.
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