CHAPTER 7

COMPARISON OF MONTE CARLO DERIVED
DOSE RATE DISTRIBUTIONS FOR I-125 AND Ir-192
SEEDS IN A GOLD EYE PLAQUE

7.1 BACKGROUND OF THE STUDY

Plaque brachytherapy has been one of the modalities used in the treatment of localized ocular tumors such as retinoblastoma and choroidal melanoma. Retinoblastoma is a relatively uncommon tumor of retina occurring in children younger than 15 years, whereas, choroidal melanoma is the most common primary intraocular tumor in adults. This cancer may metastasize and eventually spread to other parts of the body. Over the last 30 years, treatment has evolved from simple enucleation to eye sparing radiotherapy. In the external beam irradiation, radiation may cause an increase in the risk of developing secondary cancers. It has also been noted that not all the tumors respond to external beam radiotherapy. In this context, radiation plaque therapy has been considered in the treatment of ophthalmic tumors. This is because, ophthalmic plaque radiotherapy allows higher doses to the tumors with greater sparing of non-involved tissues when compared to teletherapy. Plaque is a metallic disc containing radioactive sources. In ophthalmic plaque radiotherapy, 0.5 mm thick gold shield (as per the recommendation of COMS group) is used for keeping radioactive seeds. The metallic gold shield consisting of 77% gold, 14% silver, 8% copper and 1% palladium by weight. This is designed in such a way that more radiation to the tumor and decreasing radiation damage to the surrounding normal tissues. Generally, ophthalmic plaques are divided into two categories: (i) those that
are supplied as ophthalmic applicators (Brady et al. 1982) with relatively long-lived isotopes (Co-60 and Ru-106) and (ii) those into which sealed radioisotope sources of I-125 or Ir-192 are temporarily inserted (Astrahan et al. 1990 and Luxton et al. 1988). Treatment recommendations for retinoblastoma and choroidal melanoma are based on the size of the tumor. Beta-ray applicators such as Sr-90/Y-90 and Ru-106/Rh-106 are used for the treatment of small tumors (<3 mm in height). I-125, Ir-192, Au-198, Pd-103 can be effective in the treatment of medium sized melanomas (range from 2 mm to 3 mm up to 10 mm in apical height and have a basal diameter of less than 16 mm) (Brady et al. 1982). The larger size tumors are best treated by enucleation. Although, Co-60 plaques have been most commonly used, it has the following limitations: difficulties in shielding the remaining normal eye structures, hazards to both patient and personnel because of the associated high energy gamma radiation and side effects such as radiation induced cataracts (Luxton et al. 1988). Therefore, low energy radionuclides such as I-125, Ir-192 have been considered in the place of Co-60. Among the two isotopes, I-125 produces superior radiation safety as compared with Ir-192. As the treatment with ophthalmic plaque radiotherapy requires the doses ranging from 80-100 Gy to the tumor, an accurate dosimetry is essential in order to avoid radiation-induced side effects such as loss of vision, cataract and glaucoma. In this regard, Luxton et. al. investigated the dosimetry of ophthalmic plaques designed to hold Ir-192 or I-125 seeds experimentally and by means of a computer model (Luxton et al. 1988). Astrahan reanalyzed the Collaborative Ocular Melanoma Study (COMS) on medium tumor trial and concluded that incorporating factors to account for anisotropy, line source approximation and attenuation in the silastic seed carrier into the dose calculation, resulted in a significant and consistent reduction of calculated doses to the structures of interest, within the eye (Astrahan 2005). In this context, this chapter is aimed to study the dosimetric comparison between Ir-192 and I-125 for effective dose delivery. In this study, two different plaques, which are introduced by the COMS group were considered with two different
sizes. MCNP code was used to compute the dose rate constant and radial dose function and the computed values are compared with the published results of experimental and Monte Carlo computed values. In the dose calculation, the dose resulting from scatter into the penumbral region close to the plaque perimeter is also taken into account.

7.2 ANATOMY OF EYE

The normal eye anatomy is depicted in Figure 7.1a. There are three layers enclosing the eye; the retina (inner), the choroids (middle) and the sclera (outer). The choroid layer is rich in vasculature. Choroidal melanoma (Figure 7.1b) is the most common tumor in choroid. The ciliary body is the anterior extension of choroids. The uveal tract consists of the iris, ciliary body and choroids. The sclera and choroids are of 1 mm thick on an average. The retina, macula, lens, optic nerve and optic disk are all critical for vision. The macula is the posterior portion of the retina crucial for visual acuity. The foveola is the floor of the central pit (fovea) of the macula. The other landmarks in the eye are the equator, the ora serrata (the anterior margin of the retina, interior to the junction of the choroids and ciliary body) and the limbus (the boundary between the cornea and sclera).

Figure 7.1 Pictorial representation of (a) normal eye and (b) a section of the eye with choroidal melanoma
(Courtesy - www.ncoptometry.org)
7.3 SOME COMMON OCULAR CANCERS

Some common ocular cancers include choroidal melanoma, choroidal haemangioma, retinoblastoma, eyelid tumor, conjunctival tumor and lymphoma/leukemia.

7.3.1 Choroidal melanoma

Choroidal melanoma is the most common primary intraocular (occurring inside the eye) tumor in adults (Figure 7.1b). It arises from the pigmented cells of the choroid of the eye and is not a tumor that started somewhere else and spread to the eye.

A choroidal melanoma is malignant, meaning that the cancer may metastasize and eventually spread to other parts of the body. Because choroidal melanoma is intraocular and not usually visible, patients with this disease often do not recognize its presence until the tumor grows to a size that impairs vision by obstruction, retinal detachment, hemorrhage, or other complications. Pain is unusual, except with large tumors. Periodic retinal examination through a dilated pupil is the best means of early detection.

Cutting out the tumor and leaving the rest of the eye is not routinely advised for this type of cancer. Opening the eye during surgery would allow the tumor cells to float around into the spaces around the eye, which could spread cancer cells to other parts of the eye. In addition, some studies have shown that up to 50% of choroidal melanomas invade the sclera. Therefore, if the tumor is removed from the eye, there is a high possibility that cancer cells will remain within the sclera. Finally, many eyes do not tolerate this procedure and severe complications may occur such as retinal detachment,
haemorrhages and recurrence of the tumor, which may result in the removal of the eye anyway.

Treatment recommendations for choroidal melanoma are usually based on the size of the tumor. Small suspicious melanomas are usually closely watched for evidence of growth, before treatment is recommended. Medium sized tumors may be treated with either radioactive plaque therapy or enucleation (removal) of the eye. The COMS supported by the National Eye Institute of the National Institutes of Health, has documented equal success rates for plaque radiation therapy or enucleation for preventing the spread of cancer. Large size tumors are usually best treated by enucleation. This is because the amount of radiation required to treat the tumor is too much for the eye to tolerate. The COMS study found no benefit to large size tumor patients having radiation therapy prior to enucleation.

7.3.2 Choroidal haemangioma

A haemangioma is a tumor comprising blood vessels and can grow within the choroids and the blood vessel layer beneath the retina. Choroidal haemangiomas are not cancers and never metastasize. However, if the haemangioma is located in the area of central vision of the eye it can leak the fluid which can causes a retinal detachment and visual function may be affected (Diener West et al 2001).

Many choroidal haemangiomas can be safely monitored without the need for further treatment. Photographs can be used to document the evidence of growth or leakage and the need for treatment. Treatment options may include laser photocoagulation to decrease the amount of fluid leakage or low doses of external beam radiation therapy.
7.3.3 Choroidal metastasis

Malignant tumors from other parts of the body can spread in and around the eye. Metastatic cancers that appear in the eye usually come from a primary cancer of the breast in women and the lungs in men. Other less common sites of origin include the prostate, kidneys, thyroid, and the gastrointestinal tract. Blood cell tumors (lymphomas and leukemia) also can spread to the eye. The care of patients with metastasis to the eye should be coordinated between the eye cancer specialist, medical oncologist and radiation oncologist. Treatment options may include chemotherapy, external beam radiation therapy or more rarely, enucleation.

7.3.4 Choroidal nevus

Like a raised freckle on the skin, a nevus can occur inside the eye and like a skin nevus, a choroidal freckle can become malignant so it should be closely monitored. A choroidal nevus should be examined by an ophthalmologist in every four to six months to check if the pigmentation or size of the nevus has changed. In most cases, the only treatment recommended is close observation and monitoring by an ocular oncologist.

7.3.5 Conjunctival tumors

Conjunctival tumors are malignant cancers that grow on the outer surface of the eye. The most common types of conjunctival tumors are squamous cell carcinoma, malignant melanoma and lymphoma. Squamous cell carcinomas rarely metastasize, but can invade the area around the eye into the orbit and sinuses. Malignant melanomas can start as a nevus (freckle) or can arise as newly formed pigmentation. Lymphoma of the eye can be a sign of systemic lymphoma or be confined to the conjunctiva.
Both squamous cell carcinomas and malignant conjunctival melanomas should be removed. Most small conjunctival tumors can be photographed and followed for evidence of growth prior to treatment. Small tumors can be completely removed surgically. In other instances, cryotherapy (freezing therapy) may be necessary or chemotherapy eye drops may be used to treat the entire surface of the eye.

7.3.6 Eyelid tumors

Tumors of the eyelid may be benign cysts, inflammation, or malignant skin cancers. The most common type of eyelid cancer is basal cell carcinoma. Other common eyelid cancers include squamous cell carcinoma and sebaceous gland carcinoma. Most basal cell carcinomas can be removed with surgery. If left untreated, these tumors can grow around the eye and into the orbit, sinuses and brain. A simple biopsy can determine if an eyelid tumor is malignant. Malignant tumors are completely removed and the eyelid is repaired using plastic surgery techniques. This usually results in a complete cure of the eyelid cancer. Additional cryotherapy (freezing-therapy) and radiation therapy sometimes are required after surgery.

7.3.7 Iris tumors

Tumors can grow within and behind the iris. Though many iris tumors are cysts or a nevus, malignant melanomas can occur in this area. Most pigmented iris tumors do not grow. They are photographed and monitored with a special slit lamp and high frequency ultrasound to establish a baseline for future comparisons. When an iris tumor is documented to grow, treatment is recommended. Most small iris melanomas can be surgically removed. Radiation plaque therapy or enucleation may be considered for larger iris tumors.
7.3.8 Lymphoma/Leukemia

Lymphoma tumors can appear in the eyelid tissue, tear ducts and the eye itself. In most patients with large cell non-Hodgkin's lymphoma, the disease is confined to the eye and central nervous system. In these patients, symptoms appear in the eye as early as two years before they are seen elsewhere. The disease itself as well as treatment, which may include external beam radiation, chemotherapy, or both (chemoradiation) to the central nervous system can affect the visual functioning.

7.3.9 Orbital tumors

Tumors and inflammations can occur behind the eye. These tumors often push the eye forward causing a bulging of the eye called proptosis. The most common causes of proptosis are thyroid eye disease and lymphoid tumors. Other tumors include haemangiomas (blood vessel tumors), lacrymal (tear) gland tumors, and growths that extend from the sinuses into the orbit. Though CT scans, MRI and ultrasound imaging help in the probable diagnosis, most orbital tumors are diagnosed by a biopsy.

When possible, orbital tumors are totally removed. If not, a piece of tumor may be removed and sent for evaluation. If a tumor cannot be removed during surgery, it can be treated with external beam radiation therapy. Orbital lymphomas are usually biopsied. After a complete work-up by an oncologist, treatment with radiation therapy is usually indicated. Chemotherapy may be needed if the lymphoma is found to involve other areas of the body. This is performed in conjunction with a hematologist/oncologist. Certain rare orbital tumors may require removal of the eye and orbital contents. In certain cases, orbital radiotherapy may be used to treat any residual tumor.
7.4 TUMOR SIZE

The following are the various tumor size classifications according to boundary lines:

1. **Small**: Range from 1 mm to 3 mm in apical height and have a basal diameter of at least 5 mm (COMS report No. 5 1997).

2. **Medium**: Range from 2 mm to 3 mm up to 10 mm in apical height and have a basal diameter of less than 16 mm (Diener-West et al 2001).

3. **Large**: Greater than 10 mm in apical height or have a basal diameter of at least 16 mm (COMS report No. 9 1998).

4. **Diffuse**: Horizontal, flat growth pattern, with the thickness of the tumor measuring approximately 20% or less than the greatest basal dimension; this uncommon variant of uveal melanoma seems to have a poorer prognosis (Shields et al 1996).

In clinical practice, the tumor base may be estimated in average optic disc diameters (1 dd = 1.5 mm). The average elevation may be estimated in diopters (3 diopters = 1 mm). Other techniques, such as ultrasonography, can be used in addition to provide more accurate measurements.
7.5 STANDARD TREATMENT OPTIONS

The following are the some of the treatment modalities for eye lesion based on the disease stage.

7.5.1 Plaque radiotherapy

This treatment is used for small or medium sized uveal melanomas, amelanotic tumors, or tumors that touch the optic disc for greater than 3 clock-hours of optic disk circumference (Shields et al 1998).

7.5.2 External-beam, charged-particle radiotherapy

External beam radiotherapy, provides precisely focused radiation with a homogeneous dose distribution pattern and little lateral spread requires sophisticated equipment available only at the selected centers, patient cooperation during treatment (voluntarily fixating the eye on a particular point so the tumor is positioned properly in the radiation beam) is very much important (Munzenrider 2001, Shields et al 1998).

7.5.3 Gamma knife radiosurgery

It is a newer method of radiotherapy and preliminary experience suggests that this treatment may be a feasible option for small sized to medium-sized melanomas (Woodburn et al 2000).
7.5.4 Laser photocoagulation

It can be used in very selected cases of small posterior choroidal melanoma and indirect ophthalmoscope laser therapy may be combined with plaque radiotherapy (Shields et al 1998).

7.5.5 Transpupillary thermotherapy

It causes substantial tumor necrosis in choroidal melanomas up to 3.5 mm in thickness and currently used in selected cases with deeply pigmented small choroidal melanomas in the posterior pole with minimal or no contact with the optic nerve. It can be used as a primary treatment or as an adjunctive method to plaque radiotherapy (Bartlema et al 2003).

7.5.6 Local tumor resection

Used mainly for selected ciliary body or anterior choroidal tumors with smaller basal dimension and greater thickness (Char et al 2001).

7.5.7 Enucleation

Severe intraocular pressure elevation is a factor favoring enucleation, may also be considered in small and medium sized melanomas that are invading the tissues of the optic nerve. An eye-sparing procedure rather than enucleation should be considered if there is hope for useful vision.
7.6 COMPLICATIONS OF RADIOACTIVE PLAQUE THERAPY

As the present thesis is focused on radioactive plaque therapy, possible complications of the same are discussed in this section.

Acute complications of radioactive plaque therapy are limited to an occasional case of mild local infection. The use of local anesthesia for plaque placement and its removal has been well tolerated and enthusiastically accepted by patients, since it does not require hospitalization. Clinically significant complications of radioactive plaque therapy are limited to late effects of radiotherapy. The overall incidence of these complications is reported to be up to 40% (Packer 1984). The most commonly observed complication is perimacular exudate, which tends to resolve slowly (Stallard 1966). Retinal and vitreous bleeding and vascular changes leading to retinopathy are also common (Stallard 1966). In a study published by Packer et al (1984) the overall incidence of late complications was 34%. Retinopathy, vitreous hemorrhage, cataract, and glaucoma were the most frequent complications. Shields et al (1982) reported 40% of the complications in a study of 100 patients treated with Co-60 plaque. In 23% of the patients in this study, late complications resulted in a substantial decrease in visual acuity. Serious complications requiring enucleation occur in approximately 10% of treated patients (Stallard 1966).

7.7 PLAQUE DESIGN AND CONSTRUCTION

The plaques used in the COMS group have diameters ranging from 12 to 20 mm, and lip height from 2.5 to 3.3 mm. Plaques are cast in a gold alloy as sections of a spherical shell, 25 mm in diameter, 1.5 mm thick, by the lost wax technique. Each casting includes a pattern of grooves embedded in
the concave surface of the gold shell, which are used as receptacles for radioactive seeds of Ir-192 or I-125. For most plaques, the source holders are arranged in a radial rather than in a circular or rectangular array, because more sources can be distributed over the plaque surface. This reduces the individual seed strength required for a given total activity, since excess radioactive seeds could potentially lead to treatment complications. Gold was chosen for its biological inertness and shielding advantages. Some of the commercially available plaques are shown in Figure 7.2.

Luxton et al (1988) studied the dose distribution experimentally for a clinical procedure with a plaque containing 18 seeds of Ir-192. The similar setup was considered in this study in order to compare the Monte Carlo computed results of present study with the experimental results of Luxton et al. The source distribution in the plaque is symmetrical and their arrangements are as follows: six seeds positioned radially at 60° increments centered on a 3 mm radius circle, and 12 seeds positioned radially at 30° increments centered on a 5.5 mm radius circle. All seeds were assumed to have the same activity. Side view of the Monte Carlo modelled 14 mm COMS standard plaque is shown in Figure 7.3. The concave aspect of the silastic insert has a radius of curvature of 12.3 mm designed to confirm to the eye surface curvature. The stacked picture of Monte Carlo modeled slices of 12 and 14 mm I-125 COMS standard plaque, 14 mm COMS Ir-192 plaque and 14 mm Ir-192 plaque for a clinical procedure using ImageJ software (NIH Image, Bill Heeschen, Analytical Sciences, The Dow Chemical Company) is shown in Figures 7.4 (a-d) respectively. The calculated dose rate of 1 Gy/hr at 5 mm depth along the central axis was taken as 100%.
Figure 7.2  Some of the commercially available plaques
(Courtesy of eye cancer network)

Figure 7.3  Side view of the Monte Carlo modelled geometry of 14 mm COMS standard plaque
Figure 7.4  The stacked picture of Monte Carlo modelled geometry of, (a) 12 mm I-125, (b) 14 mm I-125, (c) 14 mm Ir-192, COMS standard plaques and (d) 14 mm Ir-192 plaque for a clinical procedure
The dose distribution for two different plaques of sizes 12 mm and 14 mm with I-125 seeds was computed. From the Figures 7.5 and 7.6, it is observed that 90%, 70%, 50% and 30% isodose lines of 12 mm diameter plaque with eight I-125 seeds are at distance of 0.54, 0.64, 0.78 and 1.03 cm respectively, from the center of the source. Further, the 90% isodose line is extended longitudinally upto 0.4 cm. In the case of 14 mm diameter plaque with thirteen I-125 seeds, it is observed that the 90%, 70%, 50% and 30% isodose lines are identified at 0.54, 0.64, 0.785 and 1.05 cm distance respectively from the center of the source (Figure 7.6). The 90% isodose line is extended longitudinally upto 0.6 cm. Comparing the Figures 7.5 and 7.6, in the case of 14 mm plaque, it is observed that there is no change in the central axis doses upto 70% for both 12 and 14 mm plaques. However, the longitudinal isodose line has extended to 1.5 fold with that of 12 mm plaque for 90% isodose line.

Figure 7.5  Monte Carlo computed dose distribution of 12 mm standard COMS plaque with I-125 seeds
In order to compare the dose distribution between two different radioactive sources viz, Ir-192 and I-125, the dose distribution were computed for 14 mm plaque with Ir-192 source and the values were compared with that of 14 mm I-125 plaque. From the Figure 7.7, it is observed that 90%, 70%, 50% and 30% isodose lines of 14 mm diameter plaque with Ir-192 seeds are at 0.54, 0.625, 0.795 and 1.05 cm distance respectively from the center of the source. Also, the 90% isodose line is extended longitudinally upto 0.70 cm. Comparing Figures 7.5 and 7.7, it is observed that there is no change in the central axis doses upto 1 cm distance for both 14 mm I-125 and Ir-192 COMS plaques. However, the longitudinal isodose line has extended to 1.2 fold with that of 14 mm plaque with I-125 seeds.
Figure 7.7  Monte Carlo computed dose distribution of 14 mm standard COMS plaque with Ir-192 seeds

7.10  COMPARISON OF DOSE DISTRIBUTION BETWEEN STANDARD AND CLINICALLY USED 14 mm COMS PLAQUE WITH Ir-192

In order to compare our Monte Carlo computed results with the published experimental data of Luxton et al, a similar configuration of plaque was considered and the dose distribution was compared. From the Figure 7.8, it is observed that the 90%, 70%, 50% and 30% isodose lines of 14 mm COMS plaque for clinical Ir-192 seed distributions are at 0.55, 0.675, 0.84 and 1.135 cm distance respectively from the center of the source. Also, the 90% isodose line is extended longitudinally up to 1.0 cm. Comparing Figures 7.7 and 7.8, in the case of 14 mm plaque with clinically used Ir-192 source distribution, it is observed that the central axis dose exhibits higher value for all the ranges than that of 14 mm standard Ir-192. However, the longitudinal isodose line has extended to 1.4 fold with that of 12 mm plaque.
Figure 7.8 Monte Carlo computed dose distribution of 14 mm COMS plaque with clinically used Ir-192 seeds distribution

7.11 COMPARISON OF CENTRAL AXIS DEPTH DOSE

A measurable but meagre difference was observed between our computed values and Luxton et al experimental result, which is shown in Figure 7.9. Even though, the deviations at closer distances are more, it is not taken into consideration, because this region is located within the plaque. From the Figure 7.9, it is also observed that the reported values of Luxton et al shows only a minimal variation of the order of 3.2, 3.9 and 2.9% at distances 1, 1.5 and 2.5cm respectively with respect to our Monte Carlo computed values.
Figure 7.9  Comparison of central axis dose between Monte Carlo computed and experimentally measured values of Ir-192 plaque for clinical source distribution

Central axis depth dose for different plaque and source configuration at distances ranging from 0.5 to 2.5 cm from the centre of the source is shown in Figures 7.10 a and b. Similarly, comparison was also made between two different commercially available COMS plaques of diameters 12 and 14 mm with I-125 and Ir-192 seeds (Figure 7.10a). Figure 7.10b with an importance to larger distance of greater than 1 cm. From the Figure 7.10a, it is observed that there is no significant variation in percentage of central axis depth dose for all the plaque dimensions as well as source type and their distribution. However, from the Figure 7.10b, it is observed that there is a considerable variation with respect to nature of source, its distribution and plaque dimension. For example, 12 mm plaque with I-125 gives 9.4, 9.9 and 12.3% lesser dose than that of 14 mm plaque at central axis distances 1, 1.5 and 2 cm respectively.
Figure 7.10a Central axis depth dose for different plaques, sources and source configuration, at distances ranging from 0.5 to 2.5 cm from the centre of the source.

Figure 7.10b Central axis depth dose for different plaques, sources and source configuration, at distances ranging from 1.0 to 2.5 cm.
The percentage of central axis depth dose was also compared between I-125 and Ir-192 in 14 mm COMS plaque, it is observed that 14 mm plaque with I-125 shows 1.1%, 9.68% and 16% lesser dose than that of Ir-192 at distances 1, 1.5 and 2.5 cm respectively. This clearly suggests that for tumors of thickness greater than 1 cm, Ir-192 is preferred for better dose delivery than that of I-125. On the other hand, for tumors of thickness lesser than 1 cm, I-125 is preferred due to its technical advantages. Further, for same dimension of plaque (14 mm) with Ir-192, the percentage of central axis depth dose was also compared, but with two different conditions of source distribution (i.e. comparison of standard COMS plaque with plaque suggested by Luxton et. al.), the Monte Carlo computed value for standard source distribution shows 13.4%, 16.42% and 17.63% higher value than that of clinical source distribution at distances 1, 1.5 and 2.5 cm respectively. This suggests that instead of using standard plaque, plaque with different source distribution may be tried depending upon the geometry of the tumor.

7.12 CONCLUSION

In conclusion, the comparison of dose distribution between two different eye plaques of dimensions such as 12 and 14 mm with two different radioisotopes was made. Although, the dose distribution in the lateral distance is not showing much of difference with respect to plaque dimension as well as isotopes at distances lesser than 1 cm. The longitudinal distribution depends on the nature of source and plaque dimension for both the sources even at smaller distances. However, at distances greater than 1 cm, Ir-192 gives higher percentage of central axis depth doses than that of I-125. Hence, Ir-192 may be preferred for the plaque therapy of larger tumors. As there is no significant difference in the dose distribution between I-125 and Ir-192 was found for tissues thicknesses upto 10 mm and by considering minimal radiation safety problem in shielding, smaller tumors of choroidal melanoma may be treated with I-125 plaque.