CHAPTER 1
INTRODUCTION

1.1 DEVELOPMENT OF INTRACAVITARY RADIOTHERAPY FOR CANCER OF THE CERVIX

Immediately after the discovery of radium in 1898, Margaret Cleaves of New York, used radium for the first time for the treatment of cancer of the cervix, in 1903 [1]. Later on Stockholm method was defined, which was followed by Paris method. In 1930 Manchester method was defined. This involves physical calculations on the basis of which predetermined doses are delivered to certain points of reference in the pelvis.

In all the three methods, applicators preloaded with sources are used. To make possible the individualization, the sources are temporarily loaded, depending upon the length of the uterine canal and the space in the vagina. The main drawback with this type of loading is the radiation hazard to the personnel involved. Actually it was estimated [1], that in a busy gynaecologic oncology department, where intracavitary treatment was carried out with preloaded radium applicators, the most exposed person received a gonadal dose of 0.005–0.015 Gray (Gy) per year, handling 50,000 mgms of radium.

This indicated a need for developing after loading technique. An advantage of this technique is that the applicators can be positioned properly and can be altered after checking with radiographs to achieve the best dose distribution. Since the sources are loaded after positioning the applicators, the radiation dose received by personnel is greatly reduced but not eliminated completely.
With the advent of remote after loading technique in the present decade, even the minimal dose received by the personnel is completely eliminated. The main advantage of this system is the comprehensive radiation protection it offers right from the operation theatre through to the eventual termination of treatment. Transportation of radioactive materials is completely eliminated. One more feature with this system is the provision of individual timers. The more sophisticated the system is, the more technical support it requires to deal with the occasional faults. One more disadvantage of the remote after loading systems is that they are considerably expensive.

In this chapter, the methods developed for intracavitary treatment and some features of the 'Selectron' remote after loading system (Low Dose Rate) are described. Also the work reported in the other chapters are briefly outlined.

1.2 METHODS DEVELOPED FOR INTRACAVITARY RADIOTHERAPY

1.2.1 Principle of intracavitary treatment

The fundamental principle of intracavitary radiation is the use of an inhomogeneous, rapidly changing dose distribution. The dose distribution can be matched to the shape of the required treatment volume. The anatomy of the uterus and the upper vagina is ideal for this method of approach, because the extremely high dose volume conforms to the more central necrotic portions of the tumor whereas peripheral extensions (which are generally better oxygenated) receive a much lower dose [1].

1.2.2 The Stockholm method

The Stockholm method for intracavitary radiation for the treatment of cancer of cervix is an example of fractionated,
individualized, high intensity technique mostly employing preloaded, permanently sealed applicators. The intracavitary treatment is divided into an intrauterine and a vaginal application. The intrauterine applicators are loaded with 50-100 mg of radium (refer Figure 1.1). The amount of radium depends on the length of the applicator. Using an intrauterine applicator with 53-74 mg of radium, with Stockholm technique, the treatment time is between 27 and 30 hours for each application. The intracavitary treatment comprises of two applications with 3 weeks apart. The vaginal applicators are chosen depending on the size of the tumor, the extension of the disease and the width of the vagina.

1.2.3 The Paris method

The Paris method is characterised by a low intensity, prolonged intracavitary technique[1]. According to Paris method, the treatment technique includes an intrauterine and a vaginal application. Usually these are given together. A lower amount of radium is used, but applied for a long duration, usually as one continuous treatment. A semi-flexible silk-rubber tube is used as intrauterine applicator the length of which is fitted to the depth of the uterus. The applicator is loaded with multiple units of radium (either with 6.66 mg or 13.3 mg). In the vagina a colpostat with 2 cork cylinders is placed. The total treatment time is around 120 hours (5 days). The intrauterine radium dose varies from 1600-4600 milligram hours and vaginal dose is around 4000 milligram hours.

1.2.4 The Manchester method

To standardise the dose schedule, the Paris colpostat has been modified to a rigid system in the Manchester method. The treatment technique employs an intrauterine applicator
Figure 1.1 Intrauterine radium applicators used in the Stockholm technique (Courtesy: Kjellgren and Ragnhult, (1963) Acta Radiol.1,1)
and vaginal ovoids (of varying sizes and loadings) according to anatomical limitations. The intrauterine applicator is of soft rubber loaded with varying number of radium units according whether the uterus is short, medium or large. The vaginal applicators are of hard rubber ellipsoids with surfaces that follow the isodose curve of the radium. The ovoids are separated by either with a spacer or a washer (if the vagina is narrow). A fixed dose is delivered to point A. The point A is defined as the point, which is 2 cm above the lateral fornix and 2 cm lateral to the uterine canal. Figure 1.2 illustrates the location of points A and B. Theoretically point A lies in the paracervical area, at the crossing of uterine artery and ureter. It is not superimposed on any pelvic structure [2]. The dose at point B refers to the dose to the obturator nodes. The anatomic relationships of these two points have less significance than their use as a guide to the dose [2]. The dose rate at point A is around 0.57 Gy/hr. [3]. The intracavitary treatment is given in two sittings each of 70 hours duration, separated by 4 to 7 days, the total dose being 80 Gy to point A.

1.2.5 Afterloading technique

The main aim behind the development of afterloading technique for the intracavitary treatment of carcinoma of cervix is to reduce the radiation exposure to personnel. The three things that play the major role in radiation protection are time, distance and shielding. Hence a quick application of sources into the properly positioned applicators, from a distance, definitely reduce the radiation exposure. The advantage of this technique is that the position can be checked by X-ray films and can also be altered to achieve best dose distribution.
Figure 1.2 Diagrammatic uterus and vagina, showing position of point A and point B
1.2.6 Remote after-loading technique

The radiation exposure received in the manual after-loading is eliminated by the introduction of remote after-loading technique (or system) for the treatment of cancer of the cervix. As the system is remotely controlled, the strength of the sources could be increased, thereby increasing the dose rate and reducing the overall treatment time. This facilitates treating more number of patients. Sources could be loaded for any length (upto 8 or 9 cm) of the uterus and at any position in the applicator, to get the desired dose distribution. In this way the treatment is highly individualized.

1.3 DESIGN OF APPLICATORS

Generally speaking, the applicators should be simple and independent for placing in the uterus and the vagina. It is preferable if they are inexpensive and reusable. At the same time the applicators should be rigid and reproducible from dosimetry point of view. Plenty of designs have come out. For satisfactory use the applicator design should facilitate easy insertion and removal. The applicator should be comfortable for the patient and free from local tissue interaction. It should be suitable for bacterial sterilization.

Good designs are seen in Manchester and Houston [3] systems. Actually the former has formed the basis for many subsequent developments. Henschke [4] devised an after-loading applicator which is provided with an additional catheter or tube through which the source could be introduced, when the patient is transferred to protected environment. The Fletcher applicator, the most commonly used, is designed by G.H.Fletcher at the Department of Radiotherapy University of Texas, M.D. Anderson Hospital and Tumor
Institute. Later on this applicator is modified for after-loading system, according to Suit et al [5]. The radiation dose around the tandem and the ovoids are the same as that for the preloaded applicators.

1.4 CHOICE OF SOURCES

1.4.1 Radium-226

The main advantage of radium-226 is its long half life of 1620 years which means the treatment time need not be adjusted owing to decay. But the drawback is its high photon energy. The essential gamma-radiation from radium comes from radium-C and is equivalent to 2 MeV. This makes the radiation protection an important problem. Apart from this as radium-226 decays to lead-206, the first decay product is the radon gas which is an alpha-emitter. Hence the radium, when used for medical purposes should be hermetically sealed.

1.4.2 Cobalt-60

Cobalt-60 has the advantage of being mouldable and cheap. The sources can be reactivated in the nuclear reactors. Produced by the n-\(\gamma\) reaction,

\[
\begin{align*}
27 \text{Co (n-}\gamma\text{)} & \rightarrow 27 \text{Co} \\
59 & \rightarrow 60 \text{Ni} + 0 \text{e} + \gamma
\end{align*}
\]

Cobalt-60 decays by beta and gamma-emission to form stable nickel-60

The main drawback with Cobalt-60 is its relatively short half-life (5.3 years) which makes it necessary to increase the treatment time due to decay. After few years (nearly 3 or 4 years) the treatment time increases beyond an
impracticable length of time. Cobalt-60 emits two gamma-rays of energies 1.17 MeV and 1.33 MeV. Hence from the protection point of view cobalt-60 is comparable with radium-226.

1.4.3 Caesium-137

The radiobiological effect of caesium-137 is comparable with that of radium-226 [1]. It is favourable from protection point of view, as it emits mono energetic gamma-ray of 0.664 MeV. Caesium-137 decays by beta-and gamma-ray emission to the stable isotope barium-137.

$$\text{Caesium-137: } ^{137}\text{Cs} \rightarrow ^{137}\text{Ba} + ^0\text{e} + ^\gamma$$

The half-life of caesium-137 is 30 years. Hence it is enough to apply the decay correction of 2% per year. The half-value thickness of lead for caesium-137 is 6.5 mm, whereas for radium-226 it is 16.6 mm. This facilitates design of applicators with shielding against bladder and rectum.

1.4.4 Iridium-192

Iridium-192 finds use in the rapid dose (high dose rate) remote afterloading systems, instead of cobalt-60. The isotope is produced by n-\(\gamma\) reaction

$$\text{Iridium-192: } ^{191}\text{Ir} \ (n-\gamma) ^{192}\text{Ir}$$

Iridium-192 decays by emitting beta-and gamma-rays to form the stable isotope platinum-192.

$$\text{Iridium-192: } ^{192}\text{Ir} \rightarrow ^{192}\text{Pt} + ^0\text{e} + ^\gamma$$

The problem with iridium-192 is its short half-life of 74.4 days. Iridium-192 emits a spectrum of gamma-ray energies
from 0.201 MeV to 1.062 MeV. The maximum energy which is significant is 0.613 MeV and the mean energy is 0.370 MeV. This makes the radiation protection easier. One more advantage with Iridium-192 is, sources with higher specific activity could be produced, which outweighs the fact of short half-life.

1.4.5 Californium-252

This nuclide decays both by alpha-emission and spontaneous fission with an effective half-life of 2.65 years. This time is inconveniently short as compared to cobalt-60 and caesium-137. But this is the only nuclide which could be fabricated into small sources which emit neutrons intensely, according to E.J. Hall et al. [6]. As a neutron source, the portability is only depending on the shielding requirements. The biological effectiveness of neutrons is relatively high compared to gamma-rays, which results in an inherent hazard in the practical use of Californium-252.

1.5 SOME FEATURES OF SELECTRON AFTERLOADING SYSTEM

The Selectron LDR (Low Dose Rate) was developed in 1977 in Holland. To position the sources accurately, to improve the dose distribution and to eliminate the radiation exposure to staff completely, the remote controlled afterloading technique is developed. After making a study of the existing treatment methods and systems, the Selectron afterloading system is designed in a most versatile manner.

The equipment consists of small spherical radioactive caesium-137 sources. Actually the source is caesium-137 glass bead of diameter 1.5 mm, which is encapsulated in a stainless steel sphere of external diameter 2.5 mm. The Radio-Chemical Centre at Amersham, manufactures sources of strength 10 mCi, 20 mCi, 30 mCi and 40 mCi. The equipment
Figure 1.3 Selectron afterloader
installed at Cancer Institute, Madras is provided with a source strength of 40 mCi. Figure 1.3 shows the photograph of Selectron.

The Selectron (LDR) mainly consists of (a) a lead safe and a sorting mechanism designed to offer protection as per ICRP recommendation. The ICRP Report No.33 states that for a radiotherapy equipment, the leakage radiation shall not exceed 200 Gy/hr (23 mR/hr) at 5 cm [7] (For Selectron afterloader the leakage radiation is a little less than 1 mR/hr at 5 cm). (b) 36 radioactive caesium-137 sources and 288 stainless steel ferromagnetic spheres, (c) microprocessor controlled electronic system, (d) 6 channels each of which can be loaded with 48 pellets and (e) printer, which prints out the patient number, the channels used, the position of the sources and the time of treatment.

The sources are pneumatically transferred from the lead safe to the applicator. The system operates at a pressure of 1 bar. The time of transportation of sources from the safe to the applicators (through the polythene tubes each of 3 metres in length) is less than 2 seconds. The applicator is a modified Fletcher design. The Selectron (LDR) system lay out is shown in Figure 1.4. The control mechanism is outside the treatment room. This enables the nurse to stop or start the treatment. A door safety-interlock is provided. This triggers the stop control, if the door is opened without giving the stop command. Similarly if the air supply or power supply is cut, the sources automatically return back to the safe. The system is provided with a back-up battery (rechargeable). Hence even if the power supply is cut during treatment, the program is not erased. When the power supply resumes, the machine can be put into treatment.
Figure 1.4 Selectron LDR system layout
In short, from the operation point of view, the system is not complicated to operate. From the dosimetry point of view, the source train could be altered to make the dose distribution to suit a particular patient. From the protection point of view, it is highly safe, as the design conforms to ICRP recommendation.

1.6 STUDIES WITH SELECTRON AFTERLOADER

Already it has been mentioned that the system is provided with caesium-137 sources each with an apparent activity of 40 mCi. But all the sources may not be with 40 mCi activity, though the dose calculations are done based on this value. Measuring the individual activity of the sources is difficult but not impossible. Hence it is decided to measure the exposure rate of each source and study the variation in the exposure rate values which in turn reflect the variation in the activity of the sources.

To calculate the dose in tissue at short distances, from a point source, it is enough to apply the inverse square law. To calculate the dose at points which are farther away, the attenuation by tissues should also be taken into account. Meisberger et al. [8] derived a formula for calculating the attenuation of gamma-rays in water. Using Selectron afterloader, the attenuation in different tissue equivalent materials is studied. Tissue equivalent materials used for the study are water, paraffin wax, perspex, tissue equivalent rubber and pressd-wood. Chapter 2 deals with the procedures followed for the calibration of the sources and for the measurements of attenuation in tissue equivalent materials.

Chapter 3 deals with the role of computers in radiotherapy and software developed especially for the intracavitary therapy. The software computes the dose distribution.
around the Selectron applicators, in all the three planes. Direct measurements are also carried out by constructing a wax phantom embedding the applicators. The effect of tissue attenuation is also studied.

Chapter 4 deals with the film dosimetry of Selectron afterloading system. Harnessing the facts that the films are thin and also have high intrinsic spatial resolution, the dose distributions around the Selectron applicators in the coronal plane are obtained. The dose distributions are compared with the computed dose distributions, obtained using the software described in Chapter 3.

Mayneord's contour projector has been used to find the dose from intracavitary insertion to selected points of interest. Using the anteroposterior shift X-ray film the positions of the sources are reconstructed. The dose to the points of interest, from each of the sources is calculated. The radiation midline is drawn after finding the dose to a number of points. This will be useful in treating the parametria by external beam therapy. The reliability of this method of finding the dose is confirmed by making direct measurements in a wax phantom, using a semiconductor probe. The procedures followed for reconstruction of the sources and for the measurements are detailed in Chapter 5.

Chapter 6 deals with some clinical studies. In Cancer Institute at Madras, 2 systems of intracavitary treatment are followed, one is the manual afterloading technique using cobalt-60 sources and the other is the Selectron remote afterloading technique using caesium-137 sources. The dose rate in the latter is more than twice that in the former. The total dose delivered is also different for each. An analysis has been done to evaluate the bladder and rectal morbidity in both the systems. The
dose distribution around the patients undergoing the Selectron application is also studied.

The conclusions of the work done and the suggestions for further study are reported in Chapter 7.