Chapter 4

METHODS AND MATERIALS

This research work is mainly on HDRB of cancer of the uterine cervix of patients who were treated at Regional Cancer Centre, Thiruvananthapuram, Kerala. This chapter gives a brief description of machines such as HDRB machine, treatment planning system and simulator used throughout the procedure for the safe planning and execution of treatment. The methodology adopted for the design and development of balloon and its use in clinical situation is also explained.

Microselectron-HDR

The high dose rate machine under use in Regional Cancer Centre is Microselectron-HDR of Nucletron B.V., Netherlands. This machine has been working satisfactorily, since its installation in 1998, treating an average of five patients per day. All modes of brachytherapy are possible using this machine and the hospital has been treating an average of 35 patients (sittings) per week. All patients considered in this study were treated using this machine. The unit mainly consists of three parts namely a treatment unit (Fig 4.2), a treatment control station (Fig 4.4) and a planning system (Plato-BPS V13.7) (Fig 4.5). The radioactive source used is Ir-192 (maximum activity of 370GBq), a single cylindrical pellet having 0.6mm diameter and 3.5mm length for the active source which is encapsulated (platinum-iridium alloy) in a capsule of 1.1mm outside diameter and 5mm length (Fig 4.1). This capsule is laser welded to a stainless steel drive cable of same outer diameter. The other end of the drive cable is attached to a
precise microprocessor controlled stepper motor which can drive the source in and out from the source container through applicators with less than 1mm positional accuracy to a maximum distance of 1500mm. The source safe contains two channels, one for the source and the other for the check cable; united in a single channel inside the optopair block. A dwell position is a position at which the source is driven to stop or dwell. The duration spent by the source at a given dwell position in a catheter is termed as the dwell time. The maximum dwell time that can be set in a given dwell position is 999 Sec in steps of 0.1Sec. The distance between the centers of two adjacent dwell positions is termed as the step size. This machine has got a selection of two step sizes of 2.5mm and 5mm by which it is possible to treat a length of 12cm and 24cm respectively using 48 dwell positions. The minimum radius of curvature that the source can traverse without exerting much torque is 1.5cm. The stepping source technology uses the source to move and dwell either in the forward or backward direction. This machine uses the backward stepping and dwelling method from the distal dwell position 1 to the proximal dwell position 48.

Fig4.1. Internal construction and dimensions of Ir-192 Microselectron-HDR source
The distance between the centre of each individual source from the indexer face (D) can be connected to the step size (S) and dwell position number (P) by using the relation

\[ D = L - (P - 1) S \]

Where, L is the value of reference distance in mm.

As a safety precaution, immediately before the ‘out drive’ of the source cable, a check cable or dummy cable driven by another motor travels through the applicator a distance 5mm further than the source cable can move. The only difference between the check cable and the source cable is that the tip of the check cable is slightly larger in diameter than the source cable and does not contain radioactive material. The function of the check cable is to check whether there is an obstruction in the path by dynamically measuring the degree of friction between the cables and the applicator. Then accordingly the source/check cable will be retracted back to the safe. This check cable runs through all the channels used for a particular treatment as an initial step and provision is given to repeat the same many times if something is felt unusual in the check cable ‘out drive’ The transfer tube/adapter optopair, comprising an infrared light source and a detector sensitive to light, gives information about whether a transfer tube/adapter is connected to the selected channel. Similarly, the locking ring optopair detects if the transfer tubes/adaptors are locked in the indexer channels.
Fig 4.2. Microselectron-HDR

Fig 4.3. Treatment Simulator

Fig 4.4 Treatment Control Station

Fig 4.5. PLATO Brachytherapy Treatment Planning System
The machine has got an emergency stop motor, which is coupled to the shaft of the source stepper motor via an electrically powered clutch. When the source is not in the safe and the emergency stop circuit is activated it removes electrical power from the source and checks cable stepper motors, while turning on the emergency stop motor that is powered by a DC power supply with battery backup to operate independently of the mains supply. The latter then retracts the source with a force five times greater than the pull of the stepper motor until the wire-in switch is activated.

The planning data from the brachytherapy planning system can be transferred to the treatment control station (TCS) either via network or through a floppy disc. The planning data transferred via this media consists of the planned dwell positions, corresponding dwell times, dose to be delivered and other patient details. Manual entering and/or editing patient and treatment data can be done at the workstation during the ‘prepare mode’. The control station software not only controls the machine but provides information regarding the present activity of source, treated dwell positions, to-be-treated positions, treating position by different colors, remaining treatment duration and total treated time at a given instant of time.

The system automatically corrects for the decay of the Ir-192 source and the treatment time/dwell time is accordingly increased by a factor F,

\[ F = \frac{A_{t1}}{A_{t2}} = \exp \left(0.693\frac{(t_2 - t_1)}{T}\right) \]

where,

- \( A_{t1} \) = Initial source strength obtained by calibration of the source on the date \( t_1 \)
- \( A_{t2} \) = Source strength at the calculation date \( t_2 \)
- \( T \) = Half life of Ir-192 source (74.02 days)
- \( t_1 \) = Source calibration date
- \( t_2 \) = Date on which the dwell time to be corrected
Emergency stop button is also provided at the control station. If necessary, the control panel can initiate an emergency stop when it detects a malfunction of the treatment. The TCS will provide warning message incase of power failure, improper indexer locking or applicator connection. The control panel has the facility to interrupt treatment at any time during treatment for patient care or any other related purpose to enter inside the treatment room without loss of information of treatment. The CCTV placed in the room will help the technicians to watch the patient and to communicate with them accordingly. The radiation-warning signal placed at the room entrance will alert the radiation workers regarding the source ON/OFF condition.

The database of the TCS stores information of the treatment fractions given in the course of treatment. The full history of the actions during treatment is stored not only for the patient being treated but for all those patients whose treatment courses are completed.

**Applicators and transfer tubes supplied with HDR Machine**

Wide ranges of applicators are supplied along with the machine for treating different sites. Gynaecological applicators, bronchial applicators, esophageal applicators, nasopharyngeal applicators etc are examples. Each has got its own specific x-ray markers made of high-density material to get a clear track of the tubes/applicators inserted into the tumor sites. They aid in the reconstruction of the applicators from radiographs and fix the exact location of the implanted tubes. The distal marker always represents the dwell position number 1 and each x-ray marker is coded in different ways by adopting the combinations of small and large beads for distinguishing each catheter during catheter tracking.
Bronchial applicator has an external diameter of either 5F or 6F and when connected with the machine, the source can travel to a maximum indexer length of 1500mm. It is 995mm for the esophageal/gynaec/nasopharyngeal applicators and interstitial/implantation tubes. A guide wire is supplied with the bronchial applicator for accurately guiding the applicators in the desired position through the bronchoscope channel. Bronchial tube requires special adapters for attaching it with the machine.

The standard gynecological applicator consists of intrauterine tubes of various angulations (15, 30, 45 degrees), ovoids of different dimensions (half, small, medium and large), ovoidal tubes and dobbies of different diameters to treat the vagina. Different connectors and holders are also provided. The tubes namely ovoid1, ovoid2 and IU are connected to only specific transfer tubes which cannot be interchanged.. Each catheter has got markers which are attached to a flexible steel cable and are marked carefully. To distinguish the ovoid channels on the x-ray film, the first position x-ray marker of ovoid 2 (left ovoid) is made slightly longer compared to that of the right ovoid. The selection of the ovoids and IU is at the discretion of the clinician based on the disease and its extension.

Simulator

The simulator is an essential tool for planning and designing radiotherapy treatments. Because of the poor quality of the treatment beam and the logistic difficulty of obtaining time on the treatment machine, a simulator is an appropriate equipment to image and verify the treatment fields planned for executing external beam treatment. It mimics a teletherapy machine in the sense that it offers all type of movements that are possible with the teletherapy machine with only difference being in the type and energy of source used. A simulator consists of an x-ray source system, a gantry-couch system similar to a teletherapy machine, a unique beam
collimating system, and an image receptor and viewing assembly. A simulator can work both in fluoroscopic and radiographic modes. The diagnostic unit of the simulator operates between 50 and 125kV. Tube currents are commonly 300 or 500mA and may go as high as 1000mA in radiography mode, while in fluoroscopy mode the tube current will normally be less than 2mA.

The simulator has got immense use in brachytherapy also. For the correct localization of the source or dummy pellets, images with known magnification are needed. Most of the reconstruction algorithms used in brachytherapy planning software ask for relevant parameters such as source to isocentre, source to image distance, gantry positions etc. used during imaging. All information when fed to the software correctly, the spatial reconstruction of the catheters used for brachytherapy treatment will be accurately done. Hence, the dose distribution shown by the system will be reliable and acceptable without error. Modern brachytherapy equipments such as Integrated Brachytherapy Unit (IBU) integrates imaging, planning and treatment equipments under one roof so that treatment can be given without any physical movements and loss of time to the patient.

Our institution has one simulator Simview 3000 (Fig4.3.) manufactured by Siemens Germany installed in 1999. All orthogonal radiographs used for brachytherapy planning are being taken using this simulator. Quality assurance tests are routinely done on the system as discussed in chapter III.

Treatment Planning System (Plato BPS V13.7)

“The radiotherapy treatment planning process is defined to be the process used to determine the number, orientation, type, and characteristics of the radiation beams (or brachytherapy sources) used to deliver a large dose of radiation to a patient in order to control or cure a cancerous tumor or
other problems. Treatment planning systems are computers incorporating special software to calculate dose at various points in the medium. It is virtually simulating and aiding the treatment planning process such as defining the clinical target volume, determines beam directions and shapes, calculates the associate dose distribution, and evaluates that dose distribution. In earlier times external beam treatment planning was generally carried out through manual manipulation of standard isodose charts on to the patient body contours to obtain a distribution by judiciously selecting beam weight and wedges. Finding out an accepted dose distribution covering the tumor was a time consuming and labor intensive procedure. With the advent of computers this procedure was made simple and presently there are many planning systems with programs following different algorithms with the same aim of representing the true doses at various points in the medium. Any planning system requires a few data to be given as the input for giving an output. The reliability of the end result depends on many factors including the basic information regarding the machine, the data acquired from the machine, the beam data modeling, etc. A treatment planning system should be tested extensively before putting it in clinical use.

The goal of radiotherapy treatment of cancer of cervix is to cure or locally control the disease while minimizing complications in normal tissues. Progress of treatment planning and dosimetry in brachytherapy has not reached the level of external beam due to the lack of very accurate dosimetric systems for use with brachytherapy. Other possible reasons for the underdevelopment of brachytherapy dosimetry were the difficulty in the definition and dose specification of target volume and organs at risk, the artifacts encountered in CT images during imaging with applicators in situ, the high dose gradients existing in brachytherapy and the lack of algorithms with accurate correction factors for tissue heterogeneities, inter-source effects and complex shielded applicators. But with the advent of remote afterloaders, new radioactive sources, the increased availability of CT scan data for planning, MR images for the target delineation and the use of Monte
Carlo methods for dose calculations, the accuracy of brachytherapy dosimetry has increased. For single point sources or line sources an acceptability criterion of 5% for dose calculation in the range of clinical distances ranging from 0.5cm to 5cm with a goal of 3% is suggested. But according to TG-56, the computer assisted dose calculations should have a numerical accuracy of 2%.

**Inter observer variation in planning**

Most of the radiotherapy centers do not have the facility to do CT based treatment planning in brachytherapy owing to the financial constraints. This requires cross-sectional images from the CT scan and software for doing the 3D treatment planning. A CT based planning requires the clinician to contour the tumor and critical structures and physicist to do the plan, which is laborious and time consuming. Moreover busy hospitals with insufficient number of staffs were forced to do the film based planning to cater to the needs of all patients. Hence, most of the radiotherapy centers with a heavy patient load for brachytherapy are adopting orthogonal film based treatment planning. At present, this is still considered as standard of practice by the American Brachytherapy Society. In a plain radiograph, the rectum and bladder as such cannot be visualized. The bladder is visualized using Foleys bulb filled with 7cc of contrast media. For visualizing the rectum, diluted barium soaked gauze packing is used. In most of the cases, the selection of rectal points is very difficult as rectal surfaces cannot be seen clearly and leads to random selection of rectal points. Some centers use flexible wire rectal markers for calculating dose and that too will not represent the actual rectal doses. Hence, there will be differences in the selection of points especially for rectum. Moreover, the selection of the dwell positions will also depend on the dose to these critical structures. There will be a variation in rectal and bladder doses when different physicists do the planning. An inter observer variation study will throw light on this issue.
Inter observer variation was studied by seeking the help of four physicists who got sufficient experience in using the brachytherapy software for treatment planning and execution. To avoid the dependence of the algorithm of the software on the treatment planning, all were requested to plan in the same software BPS V13.7 from Nucletron. The orthogonal radiographs of thirty five patients were taken for this study. All the physicists were requested to do the whole stages of planning from reconstruction to adjusting the dwell positions so as to get an acceptable plan of their choice. They were all given the same instructions regarding the details of the film orientation, digitization of the radiograph, how to select the rectal and bladder doses etc. All the thirty-five pair of films were planned by each observer within a span of three months. The values were tabulated

**Variation in the ICRU rectal and bladder doses when dwell positions and dwell time of the plan for the first fraction is used for the remaining fractions.**

HDR brachytherapy with multiple small fractions can bring equivalent effect as that produced by the LDR treatment\(^{6,7,8}\). This concept has prompted most treatment centers to switch from low dose rate to high dose rate brachytherapy, which offers more comfort to the patient. However, this multiple fraction delivery requires careful planning and delivery as high dose rate can bring more biological harm to the normal tissues than low dose rate\(^ {9-14}\).

Therefore, individualized planning is necessary for reducing the rectal and bladder doses and the attendant late complications. Another important fact of individualized planning is that it is possible to check for variation from the ideal applicator placement using simulation. This study tries to find out the variation in the rectal and bladder doses by simulating the dwell positions and time obtained from the first plan for the successive treatments. This study considers thirty patients who were planned and
treated. The patients under consideration were simulated and planned for all the fractions (two fractions) using orthogonal films from the simulator. Even though the applicator may have reproducible geometry, it is difficult to insert the applicator in the same manner for all the fractions due to the anatomical changes taking place during the course of treatment\textsuperscript{15,16}. If the applicator geometry, the rectal and bladder points selected, and the amount of rectal and bladder packing are the same, then one could expect the same percentage of bladder and rectum doses for all fractions for a given patient. However, in a real situation a lot of variation will be seen for all these parameters. Hence, one can rarely expect the same dwell positions and dwell time for all the fractions for a given patient. An analysis of this problem will surely help to see whether the variation is significant or not.

**Development of inflatable rectal and bladder balloon using latex**

Many studies\textsuperscript{17,18} suggest that inadequate rectal and bladder packing can increase the dose to these critical organs in the brachytherapy of cervix. Adequate and uniform packing can bring down the complications to the critical organs and helps to increase the therapeutic ratio. Presently this is achieved by using gauze packing below and above the applicator to keep the rectum and bladder away from the source. This can result in rapid reduction of dose at shorter distances such as encountered in brachytherapy. This packing also helps to keep the applicator in position. Depending on the roominess of the vagina, the volume of packing will vary. This amount of packing and there by its adequacy depends primarily on the co-operation of the patient to the procedure and the person who is doing the procedure. Moreover, once this is done, further adjustments to increase or reduce the packing or adjusting the position of the ovoids to approach the ideal applicator geometry if felt during simulation, cannot be done easily. The same is the situation when we use rectal retractors. Unless the procedure is done under general anesthesia, it offers more pain to the patient during
packing. Hence, it was decided to find a new solution to reduce the above-mentioned problems without compromising on the packing effect. It was also necessary to control the amount of rectal and bladder packing independently as and when required. An inflatable balloon was considered as a reliable option. It should not introduce extra pain to the patient and it should be biocompatible, disposable and easily available at low cost.

Design Criteria of the rectal and bladder balloon.

The design criteria such as the selection of material, length, width, thickness etc are explained in the following sections.

Material of the balloon and its properties.

The selection of the material for the production of the device should satisfy criteria regarding biocompatibility. The material should not cause any allergy or toxicity to the patient. The physical form of the material should not produce any trauma to the patient. It should be free from any type of pointed edges to exclude any injury to the vagina. The material should not macerate like the gauze pack during procedure. It should be soft and should not break or burst on expansion. The introduction of the balloon should not alter the intensity distributions emitted by the source. It means that the attenuation of the radiation beam by this device in situ should be negligibly small so that the lateral throw off dose should not be affected.

Products using natural rubber are widely used in the medical field and devices such as condoms made of latex are extensively in use over years without any undesirable effects. Since it has proved its role as a safe material that can be used in contact with biological tissue, the present study used latex for making the balloon. M/s Hindustan Latex Ltd agreed to collaborate to produce the balloon for use on patients.
Latex and its products in medical fields.

The word ‘LATEX’ is of Latin origin; meaning a liquid or fluid of specifically milky appearance. In modern polymer science and technology, the word ‘LATEX’ is commonly used to denote a stable colloidal dispersion of a polymeric substance in an aqueous medium.

Natural rubber latex is found in Hevea Brasiliensis trees of family Euphorbiaceae. Natural Rubber Latex is a white or slightly yellowish opaque liquid with a specific gravity in the range of 0.96 to 0.98 and having variable viscosity. Latex and natural rubber by-products are substances found in many products present in hospital (Table4.1) and home environments. They are relatively cheap, durable, and resistant. It is from this species that the world’s supply of Natural Rubber latex (and hence of natural rubber) is obtained almost exclusively. As it flows from the tree, natural rubber latex has a rubber content of about 30%, the remainder being mainly water. The rubber content can be increased up to 60% by the process of concentration.

Natural Rubber Latex (NRL) is used widely for making products that come in contact with human body. In health care field, latex products include gloves, catheters, condoms and hundreds of different medical devices. NRL has wide applications owing to its colloidal stability, low permeation to body fluids etc. The use of Universal Precautions promoted by the Centers for Disease Control and Prevention to decrease the spread of the human immunodeficiency virus and hepatitis B and C viruses has lead to a 25-fold increase in the use of latex-containing surgical gloves.
Table 4.1. Some examples of Latex Containing Products Used in the Operating Room and Post-anesthesia Care Unit.

<table>
<thead>
<tr>
<th>Ace wraps</th>
<th>Airways</th>
<th>Ambu bag (black or blue reusable)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anesthesia circuits</td>
<td>Bandaids</td>
<td>Blood pressure cuff</td>
</tr>
<tr>
<td>Catheters, condom</td>
<td>Catheters, indwelling</td>
<td>Catheter leg bags straps</td>
</tr>
<tr>
<td>Catheter secure</td>
<td>Catheters, straight</td>
<td>Chux (washable rubber pads)</td>
</tr>
<tr>
<td>Elastic bandages, ace wrap</td>
<td>Electrode pads</td>
<td>Endotracheal tubes</td>
</tr>
<tr>
<td>Gloves, sterile and exam surgical &amp; medical</td>
<td>Gloves, latex nonsterile</td>
<td>Heplock-PRN adapter</td>
</tr>
<tr>
<td>Introducer sets</td>
<td>IV tubing, injection ports</td>
<td>Tourniquet</td>
</tr>
<tr>
<td>Jobst spandex products</td>
<td>Masks</td>
<td>Medication vials</td>
</tr>
<tr>
<td>OR caps with Elastic (bouffant)</td>
<td>Oxygen tubing</td>
<td>Stethescope tubing</td>
</tr>
<tr>
<td>Spinal/epidural kits/single epidural catheters</td>
<td>Suction tubing</td>
<td>Swan-Ganz, pulmonary artery catheter</td>
</tr>
<tr>
<td>Syringes</td>
<td>Tape—cloth adhesive, paper</td>
<td>Theraband strips and tubes</td>
</tr>
</tbody>
</table>
Selection of width of the balloon

Presently, at Regional Cancer Centre, Trivandrum, the intracavitary applications are done with "Standard Gynecological Applicator" from M/s Nucletron India Pvt Ltd (Fig4.6). The widely used applicator set consists of intrauterine tubes of angulations 15, 30, and 45 degree and ovoids of various dimensions. The ovoids are selected for a given application based on the roominess of the vagina that can accommodate it. The length of the intrauterine tube is found by sounding the uterine canal. Based on the length of the uterine canal, the IU tube is classified into three, namely, long (6cm), medium (4cm) and short (3cm). Similarly there are four types of ovoids. They are semi ovoids, small, medium and large with diameters 2cm, 2cm, 2.5cm and 3cm respectively. The width of the balloon is decided by the standard setting of the applicator with an IU and two medium ovoids. The projection of standard applicator with IU and ovoids in locked position is taken on to a paper and the distance from the left most surface of the left ovoid to the rightmost surface of the right ovoid is assumed as the maximum width of the balloon (=5.5cm). This width is sufficient to rest the ovoids on it and on expansion, the surface area of the balloon that touches the ovoids will increase and provide enough seating space for the ovoids. On expansion of the balloon the lower part should displace the whole part of the rectum in proximity to the applicator away from the ovoids. This balloon can be used along with small or semi ovoids too. The diameter of the flange is 2cm. There is no need to put the same width of 5.5cm at the joining part of the balloon because the part of the balloon in touch with the flange should not expand much so that the balloon will not displace the cervix away from the applicator. Hence, the width at the joining part is made equal to the diameter of the flange (=2cm).
Fig 4.6. Standard Gynecological applicator  
(Courtesy: M/s Nucletron)

Fig 4.7. Thickness Gauge

Fig 4.8 Differential expansion of the balloon. Thicker side expands less compared to the thin side.
Length of the balloon

The length of the vagina varies from patient to patient. The balloon under consideration is placed along with the applicator. Hence, the balloon length should not be so long that it projects out of the vagina. After a series of measurements in a group of patients, a length of 7.5cm was selected for making the balloon.

Thickness of the balloon

The thickness of the latex sheet for making the balloon is found by checking the behavior of the balloon inside the patient on expansion. The thickness of the balloon depends on the number of dipping and the viscosity of the latex solution. To keep the thickness uniform, the number of dipping is adjusted as per the viscosity of the latex. Viscosity of the latex solution can be increased by adding certain chemicals. But increasing the number of dippings can reduce the chance of the micro holes that are produced during the initial dipping. When solutions having viscosity in the range of 25-35centipoise is used, on an average eight dippings are done to make the product under consideration. At the onset of the trial, balloon having same thickness on both sides was used on the assumption that the part in contact with the applicator will expand into the space between the applicator and hold it in place. However, on use it was found that it expands differently and it was decided to reduce the expansion of the region in contact with the applicator to a minimum compared to the other side. This is achieved by increasing the thickness of that region. Hence, each side (the bladder and rectal) of the balloon has different thickness. The average thickness of the product in use for the thin part is 0.50mm and for the thicker part it is 1.7mm.

Thickness of the balloon was measured using a thickness-measuring gauge (Fig 4.7) with a least count of 0.01mm. The thickness at
various location of the thin part and thick part were measured separately and the average value was taken as the thickness (in mm)

**Preparation of the mould / former for making the latex balloon**

The mould used for making the balloon should have some desirable properties. Its surface should be so smooth that it should not contain any micro holes or projections or sharp edges on its outer surface. It should not melt during drying process which is done in a furnace. The material should withstand sufficient force for stripping the balloon from the mould. Different types of materials like glass, porcelain and stainless steel were tried for the fabrication of the mould.

Different stages of mould fabrication were carried out for choosing the right material for making the mould. In the first stage of designing, glass moulds were prepared. The surface of the glass is very smooth and the product from such a mould will have good finishing. It was difficult to get a correctly shaped glass mould because lack of resources and expertise. However, with the available resources we could make a few glass moulds. But during the stripping process force was required to strip the balloon out from the mould and in that process the glass mould was found to break. Hence, stainless steel was selected as the best choice for making mould as it is readily available, sturdy and can easily be fabricated with smooth surface by electroplating.

During the second stage of mould fabrication, flat shaped stainless steel mould having thickness 2mm was used. Due to the sharp edges in the mould, the latex product was found to have uneven thickness at the edges. This is due to the migration of the latex particles from the sharp edges of the mould to other regions. Hence, the thickness of the mould was increased to 5mm and the edges were made rounded and smooth (Fig 9).
Two holes are made at the ends of the former for hanging it on the arm of dipping machine. The product made from such a mould is found to satisfy the required criteria.

**Sequence of operations for the development of the balloon device.**

The sequence of operations needed for the production of rubber bags (balloons) is described below.

1. **Compounding of latex.**

Centrifuged concentrated latex having a dry rubber content of 60% was used for compounding. Various compounding ingredients used were stabilizers, vulcanizing agents, accelerators, antioxidants etc. Water-soluble ingredients were added into latex as solutions in water. Water insoluble ingredients were added as dispersions or emulsions. During the addition of compounding ingredients, the mix was stirred slowly, but thoroughly.
Table 4.2:- Recipe used for dispersion

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Parts/weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulphur</td>
<td>1.5</td>
</tr>
<tr>
<td>Zinc oxide</td>
<td>0.9</td>
</tr>
<tr>
<td>Phenolic Antioxidant</td>
<td>0.5</td>
</tr>
<tr>
<td>Darwan I</td>
<td>0.046</td>
</tr>
<tr>
<td>Darwan II</td>
<td>0.046</td>
</tr>
<tr>
<td>Tamol</td>
<td>0.013</td>
</tr>
<tr>
<td>Casein (0.1%)</td>
<td>0.172</td>
</tr>
</tbody>
</table>

50% dispersion was prepared by using 1% NH$_3$. The dispersion was prepared by ball milling the above ingredients for 72hrs. Table 4.2 shows the ingredients used for preparing dispersion.

Table 4.3:- Compounding recipe

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>parts/wt</th>
</tr>
</thead>
<tbody>
<tr>
<td>NR Latex</td>
<td>166(100g rubber)</td>
</tr>
<tr>
<td>Con.NH$_3$</td>
<td>1.2</td>
</tr>
<tr>
<td>Casein (0.1%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Potassium oleate</td>
<td>0.6</td>
</tr>
<tr>
<td>Primary accelerator</td>
<td>0.5</td>
</tr>
<tr>
<td>Secondary accelerator</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Compounding was done with slow (15-20 rpm) and continuous stirring. Firstly, latex was treated with conc. NH$_3$. Then the other ingredients, as listed in Table 4.3 and the dispersion were added to latex in the same order.

After compounding, the latex was prevulcanised and then kept for maturation. When optimum cure was achieved, the latex was used for dipping.
2. Pretreatment of formers

The formers were cleaned, washed and dried before dipping.

3. Moulding of rubber bags

The straight dipping of the former or the mould into the latex solution can be done either manually or mechanically, using latex dipping machines. In manual dipping, the speed of dipping cannot be controlled and it may end up with non-uniform thickness of the latex onto the former. The latex dipping machine (Fig 4.10A) has an arm to which the former can be suspended freely. A motor can control the speed of the arm. The less the speed the more will be the amount of latex attaching to the surface of the former. The latex container, which is specifically prepared for this purpose is placed below the arm of the dipping machine and the former is slowly moved in and taken out at the same speed (Fig 4.10B). The dipped former is then detached from the arm and is dried in a furnace (Fig 4.10C). The former is then hung upside down and immersed into the latex at the same speed. Again it is allowed to dry. The same process is repeated till the targeted thickness is achieved. Similar procedure can be done by hanging more number of similar formers on the arm of the dipping machine and simultaneous immersion allows for the production of more number of products having same size. The final product is stripped off from the former (Fig 4.10D) using starch or silica powder and it is used as the rectal (R-part) or bladder (B-part) balloon.

4. Leaching

In leaching process, the product was washed in warm water having a temperature of 70-80°C for about 10-15 minutes (Fig 4.10E). During leaching, water soluble residues were removed from the product.
5. Vulcanization

Vulcanization involves heating of the product for 1 hour at a temperature of $80^\circ C$.

6. Connecting B and R part

Two such balloons (B and R-parts) are then joined together using latex adhesive such that the gap between the balloons is made equal to the diameter of the flange. Latex adhesive* is pasted (Fig 4.10F) at the joint of the B and R part of the balloon and a high pressure (Fig 4.10G) is applied for quick and strong adhesion of the part.

A hole is made at the centre of the joint for negotiating the intrauterine tube so that this joining part will seat at the upper surface of the flange, which otherwise touches the cervix.

*Latex adhesive

Centrifuged natural rubber latex concentrate can be used for the production of latex adhesive. Other compounding ingredients mixed properly with latex are listed in Table 4.4.

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>parts/wt</th>
</tr>
</thead>
<tbody>
<tr>
<td>NR latex (60%)</td>
<td>166 (100gm rubber)</td>
</tr>
<tr>
<td>Zinc oxide (50%)</td>
<td>1 *phr</td>
</tr>
<tr>
<td>Sulphur (50%)</td>
<td>2 phr</td>
</tr>
<tr>
<td>ZDC (50%)</td>
<td>1 phr</td>
</tr>
<tr>
<td>Casein (10%)</td>
<td>10 phr</td>
</tr>
</tbody>
</table>

*phr = per hundred rubber
7. Fixing the one way valves

The balloon must hold the air or solution that is pushed inside. For this purpose, the one way valves are connected to the ends of the balloon. This is done by gently inserting the valve into the rubber tube. The escape of air or fluid from the balloon when it is subjected to high pressure while expansion within patient should be prevented. The tail end of the tube surrounding the valve is covered with a shrinking sleeve of same length as that of the valve. When it is immersed in water at 100 °C for 1 to 2 minutes, it will shrink and thus tightly hold the part of latex tube without expanding (Fig 4.10 H - J).

8. Dusting

To prevent the sticking together of balloon, starch or silica powder was applied on it.

9. Inspection

The finished product (Fig 4.11) was inspected for defects such as pinholes, weak area, dust particles, thickness etc.
Fig 4.10 Different stages of production of the balloon. (A) The dipping machine (B) the former dipped into the latex solution (C) Drying in a furnace (D) stripping from the former after sufficient number of dipping and drying process.
Fig 4.10. Different stages of production of the balloon....contd

(E) Leaching using water at 80°C for 15 minutes (F) Pasting adhesive at the joining part (G) Compressing for strong bonding (H) Balloon ready for connecting valves at both ends (I) Shrinking sleeves inserted (J) Immersing it in water at 100°C for shrinking and tightly holding the valves in position.
Physical testing of the latex material

There are a few physical tests done on the latex material to check the strength of the material. They are tensile strength and elongation at break. This was done before and after ageing of the latex specimen. Ageing was done by keeping the specimen in an air oven at $70^\circ$ C for 4 days. Tensile strength is the maximum tensile stress reached in stretching a flat dumbbell shaped specimen to its breaking point. By convention, the force required is expressed as the force per unit area of the original cross section. Elongation at break or ultimate elongation at the time of rupture is expressed as a percentage of the original distance marked on the test piece before stretching.

The parameters were measured on the dumbbell shaped test piece according to the American Society for Testing and Materials standard (ASTM D412). The thickness of the narrow portion of the specimen was measured using a dual gauge. The ends of the test specimen were fixed to the Universal Testing Machine (Make-Instron, Model-4400) to measure these parameters. Tensile strength of good quality NRL products before and after thermal ageing process measured in Mega Pascal (MPa) should fall in the range of 17 to 35MPa$^{22}$. Table 4.5 given shows the test results.

Table 4.5: The tensile strength and elongation at break for latex material

<table>
<thead>
<tr>
<th>Sample No</th>
<th>Tensile Strength (MPa)</th>
<th>Elongation (%)</th>
<th>Tensile Strength (MPa)</th>
<th>Elongation (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>21.74</td>
<td>773.15</td>
<td>20.57</td>
<td>729.64</td>
</tr>
<tr>
<td>2</td>
<td>22.41</td>
<td>805.69</td>
<td>20.67</td>
<td>762.97</td>
</tr>
<tr>
<td>3</td>
<td>22.97</td>
<td>784.74</td>
<td>20.37</td>
<td>739.73</td>
</tr>
</tbody>
</table>
Measurement of attenuation by latex sheets.

The attenuation caused by latex to the radiation beam under use was determined by interposing the latex sheets of various thicknesses in between the detector and the source. The set up used (Fig 4.12) was the same as used in the measurement of activity using calibration Jig. After finding the position of maximum sensitivity in channel 1, rubber sheets of known thicknesses were introduced in between the source and detector using a wooden stand and the readings (R_t) obtained for a dwell time of 60 sec were noted (Table 4.6). After removing the sheets of latex, two samples of balloon were interposed for finding the attenuation caused by B and R part of the balloon. All these readings were normalized with respect to the readings obtained for zero thickness (R_0) to find out the attenuation caused by the latex sheets. The attenuation caused by the B and R-part of the balloon was less than 1% for each part.

Table 4.6: Attenuation of NRL sheets and balloon samples.

<table>
<thead>
<tr>
<th>Thickness of latex sheets (mm)</th>
<th>Readings (pC) obtained at the position of maximum sensitivity for 60Sec</th>
<th>R_t/R_0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>0.00</td>
<td>537.0</td>
<td>537.0</td>
</tr>
<tr>
<td>0.95</td>
<td>536.5</td>
<td>536.0</td>
</tr>
<tr>
<td>1.83</td>
<td>534.5</td>
<td>534.5</td>
</tr>
<tr>
<td>2.72</td>
<td>532.5</td>
<td>532.0</td>
</tr>
<tr>
<td>3.54</td>
<td>531.0</td>
<td>531.0</td>
</tr>
<tr>
<td>4.31</td>
<td>529.0</td>
<td>529.5</td>
</tr>
<tr>
<td>5.16</td>
<td>527.0</td>
<td>527.0</td>
</tr>
<tr>
<td>Sample1-R</td>
<td>533.5</td>
<td>533.5</td>
</tr>
<tr>
<td>Sample1-B</td>
<td>533.0</td>
<td>533.0</td>
</tr>
<tr>
<td>Sample2-R</td>
<td>533.5</td>
<td>533.5</td>
</tr>
<tr>
<td>Sample2-B</td>
<td>534.0</td>
<td>534.0</td>
</tr>
</tbody>
</table>
Fig 4.11. The balloon with B-part and R-part marked.

Fig 4.12. Experimental set up for measuring attenuation of latex/ balloon.
**Bursting volume**

The bursting volume of the R&B part of the balloon was measured by pushing air/water into the balloons using a graduated syringe. It was found that they could withstand volumes above 800cc of water/air without bursting.

**Biological testing of balloon**

Any contact with articles manufactured from natural rubber may produce dermatitic conditions (eg. allergic contact eczema) in certain individuals. These (Type IV) skin allergies are caused not by the rubber itself, but by additives such as accelerators and antioxidants. Another kind of allergy (Type I) is caused by a protein native to Hevea latex and not chemicals added in manufacture. Type I allergies are sometimes referred to as ‘immediate allergies’ because the response on exposure to the allergen is fast compared with the time scale of the reactions in Type IV allergies.

Dermal Irritation and Skin Sensitization Tests were done on the balloon at Toxicology Division, Vimta Labs Ltd, Hyderabad. The study included the following tests described in reference ‘International Organization for Standardization 10993; Biological Evaluation of Medical Devices, Part 10 and OECD Guidelines for testing of chemicals /Section 4: Health Effects, Test No.404, Test No.406.’

1. Primary Skin Irritation tests in Albino rabbits
2. Irritation to Vaginal Mucosa in Female Albino Guinea pigs
3. Skin Sensitization Test in Albino Guinea pigs

All these tests produced no adverse reactions in the animals.
Procedure for placing the device in patients

Two weeks after the completion of external beam therapy, the first fraction of brachytherapy is given. The patient is ideally fasted for 6 hours before the procedure. On the day of the procedure, the lower abdomen and mons veneris are shaved thoroughly. The lower bowel is emptied by an enema. After premedication, the patient is made to lie on an adjustable couch in the lithotomy position. The clinical examination of the lower abdomen, uterus, cervix, vagina, and uterus to determine the extent of disease is carried out by the radiation oncologist. After defining the external Os, the length of the intrauterine canal and position of the uterus are determined with the help of a uterine sound. The cervix is dilated using Hegar's dilators of various diameters. A Foley's catheter is inserted and 7cc of diluted contrast media is injected into the bulb for visualizing the position of the bladder in the radiograph. The length of the uterine tube (IU) and the size of the ovoids required, based on the roominess of the vagina are decided by the radiation oncologist. At first the IU should be placed and then the ovoids. The IU is negotiated through the hole provided between the R and B part of the balloon. It should be done in such a way that the thick side of the balloon comes in touch with the applicator, with B part on the dorsal side and R part on the ventral side of the applicator. The applicator and the tails of the balloons are held together as shown in Figure 4.13B. The IU is then introduced into the uterus. The tails of the balloon are held apart to ease placement of the ovoids, without kinking the balloon. The left ovoid is placed first followed by the right ovoid and then locked together with the IU. Approximately 20cc of saline (4cc contrast media plus 16cc of saline for radiographic visualization) is introduced into the B and R part using a syringe. The balloons are filled in stages rather than at a stretch to avoid patient discomfort. The remaining required amount of saline can be pushed in B or R part during simulation. The applicator can be immobilized using the applicator fixation device and a custom-made harness using roller gauze.
Simulation

The patient is then transferred to simulator couch. The patient is positioned with legs apart symmetrically. Make sure that the tails of the balloon are accessible for further pushing saline into B or R part. Take a fluoroscopy with gantry at $0^\circ$. Adjust the table lateral/longitudinal position so that the centre of the crosswire coincides with the flange. Now rotate the gantry to $90^\circ$ and expose. By adjusting the table up or down bring back the cross wire centre to the flange position. Now the flange is said to be at isocenter. From lateral radiograph the bladder and rectal balloons are visible. Push additional amount of saline into the balloon as tolerated by the patient. Again make an exposure to see for the proper positioning of the applicator. Now go for gantry $0^\circ$ and make sure the applicator is not shifted. Take an Anterior-Posterior radiograph and a lateral radiograph. Note down the source to film distance (SFD) in both cases for calculating the magnification. As a standard, this study used an SFD of 120cm and SAD of 80cm for getting a magnification of 1.5.

The present study took two sets of AP and LAT films, one set with B and R part filled with 20cc and other set with 30cc to study whether there is any drastic shift in applicator position during balloon inflation. The same procedure is repeated for second and third sittings.
Figure 4.13. Illustrating the placement of applicators.  
(A) Applicator and balloon with B-part above and R-part below.  
(B) Inserting the applicator. (C) Intrauterine tube in position.  
(D) Inserting the right ovoid. (E) Whole applicator in position.  
(F) Inflating the bladder and rectal balloons.
Treatment Planning using Plato BPS

The AP and Lateral radiographs are aligned on the digitizer. The applicators are reconstructed. The rectal and bladder points are marked as per ICRU-38 guidelines. An anterior posterior line is drawn on the lateral radiograph in such way that it passes through the centre of the ovoidal sources, touches the vaginal surface, along the line 5mm posterior from vaginal surfaces and a point is marked as ICRU rectal point. On AP radiograph this is marked at the centre of the ovoids. In this study nearly 5 rectal points were marked including the ICRU defined rectal points. The points are separated by 7.5mm on the film (5mm without magnification). On the lateral radiograph, the posterior part of the Foley’s balloon which is very close to the applicator is chosen as the ICRU bladder point. Two more points were marked, one at the centre and other at the other end of the Foley’s balloon. On AP radiograph, the three points were taken at the centre of the Foley’s balloon. All these rectal and bladder points were digitized by the planning system for dose calculation.

Two points which are at 2cm along the applicator from flange and 2cm lateral to the applicator were defined as point A on right and left side of the patient respectively. The dose is normalized to point A and prescribed. The dwell positions were selected so that the rectal and bladder gets the minimum possible dose. The rectal and bladder doses were noted. The dose prescribed to point A is 700cGy per sitting for three sittings with one-week gap in between.

The finalized plan is then sent to the treatment control station via network. The patient is connected to the machine using transfer tubes. After the preliminary patient specific quality assurance tests, the plan is loaded and treated. After treating the patient, the balloon is deflated and the applicator is removed from the patient.
Figure 4.14. Lateral and AP radiograph showing the rectal and bladder points taken for dose calculation.

Figure 4.15. Isodose distribution from TPS through transverse, coronal and sagittal sections
Reproducibility of Rectal and Bladder doses and effect of balloon on the reduction of dose

Whether the introduction of the balloon can really reduce the dose to critical structures, will be evaluated by comparing the dose received by the rectum and bladder using normally adopted protocol of gauze packing. The introduction of the balloon can avoid variation due to packing. This will also be evaluated. The analysis of rectal and bladder doses obtained between fractions will enable to assess the reproducibility between fraction while using the balloon. The rectal and bladder doses obtained for the first two fractions and all the three fractions will be considered separately.

Study of Geometrical variation

The differences in rectal dose between fractions of HDR treatment is partly due to the change in applicator geometry. The reduction in geometrical variation between fractions is a matter of concern. The present study also puts effort to evaluate whether the introduction of the balloon can reduce the geometrical variation of the applicator.

The evaluation of the magnitude of geometrical variation of the applicator is done in two ways: - the mutual relationship of various components of the applicator and the spatial relationship of the applicator with respect to patient’s anatomy. For this study all the AP and LAT radiographs taken with balloons inflated to 20cc and 30cc were considered. In some situations the volume of air or water that could be pushed into balloon as tolerated by the patient was different. These films were also considered if all the fractions were done with the same volume. The present study considered 20cc of water as the normal standard volume that when pushed into each balloon would stabilize the applicator without causing discomfort to the patient. Two orthogonal films were taken with this volume.
to check for the variation in applicator position within fraction when the balloon is inflated to a higher volume. Due to conditions beyond control such as simulator breakdown and bad quality of the films, a few orthogonal films could not be taken and were excluded from this study.

The following parameters were used for evaluating the orthogonal films\textsuperscript{23,17}. Figures 16A-D show the parameters measured on AP and Lateral radiographs.

1. Alpha angle (\(\alpha\)-angle): It is the angle between the intrauterine tube and the vaginal axis at the Os marker in the LAT radiograph. The straight portion of the intrauterine tube is taken as the vaginal axis.

2. Pelvic angle: it is the angle between a line drawn along the anterior body of L5 and the anterior body of S1 (Lateral film)

3. IU tube angle: It is the angle between the intrauterine tube and a line drawn joining the highest points on the right and left acetabulae in the AP radiograph.

4. Beta angle (\(\beta\)-angle): It is the angle between the axis of vagina and the intrauterine tube measured at the Os marker from the AP radiographs. The angle was considered as positive if it was towards left and negative if it was to the right of the vaginal axis.

5. Bladder-Ovoid axis Angle (BOA): It is the angle between the line joining the ICRU bladder point to ovoid source, and the straight axis of the applicator (LAT). This angle is measured from the lower straight part of the applicator to the bladder ovoid line.
Fig 4.16A. Lateral radiograph showing Pelvic angle, Alpha angle, Bladder-Ovoid axis angle, the vertical distance from Os to Right Ovoid (b) and to Ovoid (d).

Fig 4.16B. AP radiograph showing IU-Tube angle and beta angle
6. Right ovoid to the Os (ROV): It is taken as the distance between the middle of the right ovoid and the cervix marker, corrected for clockwise/anticlock-wise rotation and is given by $\text{ROV} = (a^2 + b^2)^{1/2}$ where, ‘a’ is the horizontal separation between the middle of the right ovoid and the Os marker measured from the AP radiograph, and ‘b’ is the vertical separation between the right ovoid and the Os marker measured from the LAT radiograph.

7. Left ovoid to the Os (LOV): It is taken as the distance between the middle of the left ovoid and the cervix marker corrected for clockwise/anticlock-wise rotation and is given by $\text{LOV} = (c^2 + d^2)^{1/2}$ where, ‘c’ is the horizontal separation between the middle of the left ovoid and the Os marker measured from the AP radiograph, and ‘d’ is the vertical separation between the left ovoid and the Os marker measured from the LAT radiograph. The position of the flange of the applicator is taken to represent the position of the Os.

8. Inter ovoid distance (IOV): It is the distance between the centers of right and left ovoids from AP radiograph.

9. Vertical displacement (VDL): It is the distance between the midpoint of centre of ovoids and the Os marker measured from LAT radiograph.

10. Os-Ovoid distance (OSD): The AP position of the Os to the mid point of the line joining the centre of the ovoids was measured from the LAT radiograph. All cases where the Os was anterior to the ovoids were recorded as positive and those posterior to the ovoids were taken as negative.
Fig 4.16C. Lateral radiograph showing sacral promontory to IU (SP-IU) distance, S1S2 junction to bladder (S1S2-B) distance, Bladder-Rectum (B-R) distance, Bladder-Ovoid (B-O) distance, Os to Ovoid distance (OSD) and vertical displacement (VDL). AP radiograph on the right shows Inter-ovoid (IOV) distance, the horizontal separation between right ovoid (a) and left ovoid (c) from the Os marker.
11. The distance between sacral promontory to the tip of IU (SP-IU) is measured from the lateral film.
12. The distance (S1S2-B) from S1S2 junction to ICRU bladder point (Bmax) was also measured from the lateral film.
13. Bladder to the midpoint of Ovoids distance (BOD) was measured from the lateral radiograph.
14. Separation between ICRU bladder to ICRU rectum point (BR) was also measured from lateral radiograph.

Spatial relationship of the applicator in terms of the fixed pelvic bony landmarks

X, Y and Z coordinates are required to define the position of a point in space. For this a coordinate system has to be defined. In the AP radiograph, a line was drawn joining the S1-S2 junction and the pubic symphysis (Y-axis). Another line was drawn joining the highest points on the right and left acetabulae (X-axis). The intersection point of these two lines was taken as the origin in the AP radiograph. The origin in the LAT radiograph was obtained as intersection point of two lines, a) the line joining the junction of S1-S2 vertebrae with pubic symphysis and b) a line drawn perpendicular to the table top when extended through the midpoint of highest points of acetabulae (Z-axis). Thus, the X co-ordinates measured from origin towards left of the patient is taken as positive and right as negative.
Fig 4.16D. Lateral and AP radiographs showing the X, Y and Z co-ordinates of IU, Right Ovoid, Left Ovoid, and Os
The Y-co-ordinates were recorded as positive or negative displacements cranially or caudally respectively from the origin in AP radiograph. From the LAT radiograph, the Z-co-ordinate displacements from origin towards anterior or posterior were taken as positive or negative respectively. The X, Y and Z co-ordinates of the following applicator points were recorded:

1. The X, Y and Z co-ordinates of the tip of the uterine tandem were taken as IUX, IUY and IUZ respectively.
2. The X, Y and Z co-ordinates of the centre of right ovoid were taken as ROX, ROY and ROZ respectively.
3. The X, Y and Z co-ordinates of the centre of left ovoid were taken as LOX, LOY and LOZ respectively.
4. The X, Y and Z co-ordinates of the cervix marker were taken as OSX, OSY and OSZ respectively.

All parameters were noted from the orthogonal films obtained by inflating the balloon with 20cc and 30cc of water within fraction in the patients studied. This data was used for analysing the geometrical variation within fractions. The geometrical variation between fractions was studied by using the films obtained with 30cc (or the maximum tolerated volume) for consecutive (two or three) fractions.

**Interobserver variation study using films obtained from patients treated with balloon.**

The same procedure followed for the interobserver variation study for patients whose rectal packing was done using wet gauze piece, was adopted to study the interobserver variation in planning when balloon is used. In this study, 30 pairs of orthogonal films obtained from 30 patients who were treated with balloon were given to four planners with the same instructions. The data from each physicist was tabulated and analysed.
References


17 Thayalan K, Physical and dosimetric studies of High Dose Rate Brachytherapy system with clinical correlation, in carcinoma of the uterine cervix., Thesis submitted to MGR Medical University, 2002


