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Theoretical, Manufacturing and Clinical Application Aspects of a Prostate Brachytherapy I-125 Source in Brazil

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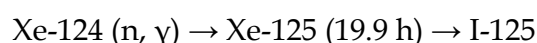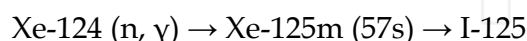*IPEN-CNEN/SP*
Brazil

1. Introduction

One of the treatments commonly applied for the treatment of prostate cancer is the brachytherapy implant with iodine-125 seeds. In this chapter, we will attempt to show how to produce seeds of iodine-125, the main requirements to have a good seed, and also we will try to discuss some issues in using this technique at the clinics.

2. Iodine-125 production

Cancer is one of the worst illnesses in the world and one of the major causes of death in Brazil [Rostelato et. al, 2008]. For this reason, the Brazilian Nuclear Energy Commission (CNEN) started a project to produce some medical radioisotopes to treat cancer. One of the main products is the iodine-125 seeds [Moura et. al, 2010]. This iodine seed can be used to treat several types of cancer: prostate, lung, occular and brain. In the first phase of this project, the iodine-125 will be acquired in international market. As Brazil will construct a new reactor to produce radioisotopes, it is necessary to define how the iodine-125 production will carry out [Cieszykowska et al., 2005; Mathew et. Al., 2002].

The main reaction of this production is the irradiation of the enriched xenon-124 in gaseous form. Natural xenon has only 0.095% of xenon-124. Xe-124 changed to iodine-125 by neutron capture following in two decays:

$$Xe\text{-}124\ (n, \gamma) \rightarrow Xe\text{-}125m\ (57s) \rightarrow I\text{-}125$$

$$Xe\text{-}124\ (n, \gamma) \rightarrow Xe\text{-}125\ (19.9\ h) \rightarrow I\text{-}125$$

The cross section for thermal neutrons (0.0253 eV) makes $\sigma = (165 \pm 20)$ b. The core product, Xe-125m, decays by isomeric transition (100%) with half-life of 57 seconds to Xe-125g which,

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in turn, decays by electron capture (99.3%) and positron emission (0.7%), with half-life of 16.9 hours, generating iodine-125. Finally, iodine-125 decays by electron capture (100%) for the Te-125. The decay of iodine-125 is accompanied by the emission of photons of 27 keV, 31 keV and 35 keV, average energy of 29 keV. Due to the low average energy of emission, such photons have low penetrating strengh. Iodine-125 has a half-life of 59.408 dias [Zeituni, 2008].

During the production of iodine-125 in a reactor, Iodine-125 produced abosorbs a neutron and it it transformed in iodine-126. Iodine-126 has a half life of 13.1 days and it has severals photons of high energy (388.6 keV, 491.2 keV, 666.3 keV, 753.8 keV, 879.9 keV and 1420.2 keV). Iodine-126 is considered a contaminant [HAN et. Al., 2007]. The research group of IPEN/CNEN-SP decided to usetwo techniques: a batch system and continuousa cryogenic system.

The batch system consists of a sealed capsule (placed in the reactor core for around 64 hours. In this type of production, some iodine-126 is produced and a certain quantity of Xe-124 is not activated. Then it is really important for economic reasons, it uses a system to retrieve the Xe-124, and it needs to wait some days to let the iodine-126 decays. Of course, during this time the iodine-125 decays, too. . Usually, it is necessary to wait around 5 to 7 half-lives to lower the the I-126 contamination level.–After this time, the quantity of iodine-125 is only 50% to 34% imediately after the reactor shutdown.

We calculated the yeald in IPEN/CNENSP reactor, IEA-R1 built in 1956. This reactor outputs around 4.5MW and the thermal flux is 8.10^{12} n/cm^2.s at the xenon/iodine capsule position. After the cycle of irradiation (64 hours) we will have 65 GBq of iodine-125. In this time we will have around 0.26% of iodine-126 produced. After 20 days, the activity of iodine-125 will be 50 GBq and 0.14% of iodine-126. After 40 days, we yield 40 GBq of I-125 with 0.06% of iodine-126.

The second technique used to produce iodine-125 is the continuous production using a cryogenic system with circulating liquid nitrogen. This technique consists in two capsules: one inside the reactor core and the second one out of the neutron flux. These two capsules will be linked with two cryogenic pumps to guarantee that all iodine-125 produced in the core will be take off the reactor core (Figure1). The cryogenic temperature, around 77 K, will turn the iodine liquid but the xenon will be pumped again to the core in gaseous form. After the irradiated cycle, we take up and seal the capsule outside of the core, and consequently yield almost onlyiodine (with a traces of xenon),) and insert another Xenon-124 enriched capsule in the reactor to continue the production. The greatest disadvantage of this technique is the using of two positions in the core of the reactor though Brazil has only one radioisotope reactor producing, andthere is a huge quantity of materials to be produced. Though the current seeds production power in Brazil is only for 3000 seeds per month, though the demand is around 3.5 Ci (around $1.3.10^{11}$ Bq) per month. This batch production may produce a small quantity, but this is more than that of batch production.

Iodine-125 decays by electron capture (EC) and internal conversion to Tellurium-125 as shown in figure 2. Photons with 27 keV, 31 keV and 35 keV (average 29 keV) are issued.
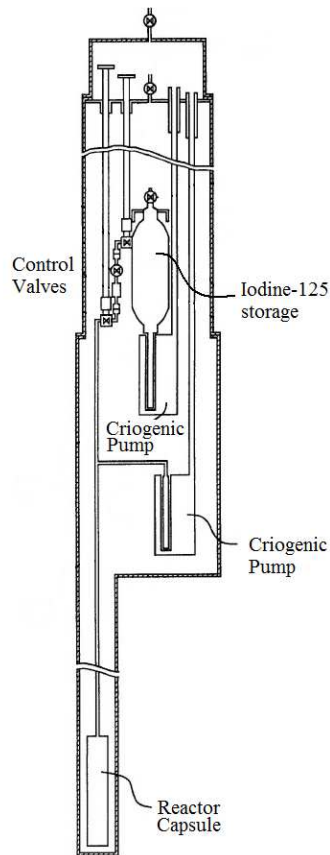
Fig. 1. Iodine-125 production system in cryogenic method [Zeituni et. Al., 2011]. (To publisher, this is too small. To authors, please indicate how to use this unit showing or describing the corresponding reactor part or position: for exapmle, "The reactor capsule part is placed into the reactor core." The figure is not enough to explain how to retrieve the capsule, where to insert next capsule, where to take up the I-125.)
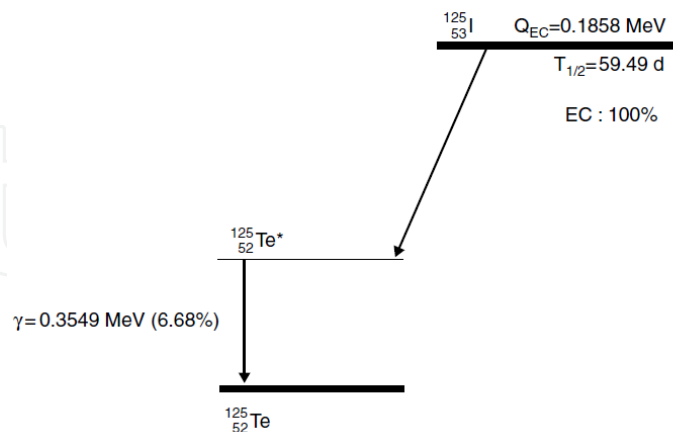

Fig. 2. Iodine-125 decay scheme [Baltas et. Al, 2006]

3. Iodine-125 seeds

Iodine-125 sources are used in the radiotherapy of brain, neck, lung, pancreas and prostate cancers, as well as intraocular tumors (choroidal melanomas and retinoblastomas). They can

be used in two different ways – permanent and temporary implants.. Iodine-125 seeds are indicated for the treatment of tumors that have some of the following characteristics: localized, slow growth rate and low to moderate sensitivity. They are also indicated for the treatment of recurrent and residual tumors following a course of external radiation therapy. The mean apparent activity of Iodine-125 seed required to be used in ophthalmic applicators is 20 mCi (740 MBq) and in other applications most often 4-5 mCi (148-185 MBq).

The treatment of prostate cancer with permanent iodine-125 seed implantation has grown dramatically in the world in recent years.

The technique is being used by hospitals and private clinics also in Brazil. Nowadays, the seeds are imported at a minimum cost of US$ 65.00 per one seed, however the high cost makes them impracticable for use in public hospitals. In a typical prostate brachytherapy 80-120 seeds are required. Generally, the seeds are composed of a titanium capsule of 0.8 mm outer diameter, 0.05 mm wall thickness and 4.5 mm in length. The internal structure varies significantly by commercial models. Some constitute of resin or ceramic embedding mixture, and others are deposited in a substrate radio-opaque substrate. Commercially available applicator devices for implantation are disigned for the general dimension.

All seeds are encapsulated in titanium because it is an inert material that does not cause rejection when in direct contact with human tissue and it is classified as biocompatible material. The seed manufacturers in the world are concentrated in the United Kingdom, Belgium and the United States of America and the seeds produced differ in the process used in manufacturing, being unique and protected by patents.

The iodine-125 seeds are classified as sealed radioactive sources as standard *International Standard Organization. Radiation Protection – Sealed Radioactive Sources – General Requirements and Classification ISO-2919.*

The seed is formed by a core that has the radioactive material attached; it is wrapped in a shell of biocompatible material sealed on both sides. A radiological marker must also be inserted. Some examples are materials used in the items below [Rostelato, 2006]:

- UroMed Corporation – Bebig GmbH (Germany) → Symmetra-125.S06: Titanium capsule sealed laser, containing a radio-opaque gold wire inside, and a ceramic layer with iodine-125.
- Best Medical International (USA) → Model 2301: The outer coat consists of double encapsulated titanium, without specifying the type of welding. The interior accommodates a marker of tungsten and iodine-125 adsorbed on an unspecified substrate.
- BARD - SourceTech Medical (USA) → BrachySource STMIodine-125: The capsule is titanium welded by laser equipment. Inside of the seed has a gold wire as a marker, a layer of aluminum and a "coating" of copper. Iodine-125 is deposited in a cylinder of aluminum with a gold core and a layer of nickel.
- Oncura GE Healthcare (USA)→ OncoSeed 6711: Radio-opaque silver core, where iodine-125 is adsorbed and the outer shell is titanium with laser sealing.
- Oncura GE Healthcare (USA)→ OncoSeed 6702: Iodine-125 is adsorbed on ion exchange resin beads. The outer shell is titanium with laser sealing.
- Mentor Corp. – North American Scientific (USA) → IoGold MED3631-A/M: Titanium capsule sealed by laser. Iodine-125 adsorbed onto four resin beads. The capsule shell

contains two inactive gold beads which serve as markers to identify and locate the source.

- Syncor (China) → PharmaSeed BT-125-I: Iodine-125 is adsorbed on palladium wire. The seed is sealed by laser.
- Med-Tec - Implant Sciences (USA) → I-Plant 3500: Iodine-125 is deposited on a ceramic coating. A silver bullet is placed inside the cylinder.
- International Brachytherapy (Belgium) → Intersource Iodine-125L. Iodine-125 is adsorbed on the inorganic matrix ring positioned in the center and beads at the ends of the source. It is used a marker of iridium and platinum.
- UroCor – Mills Biopharmaceuticals (USA) → ProstaSeed I125-SL: Iodine-125 is adsorbed by ion exchange resin in five balls.
- Imagyn Medical – International Isotope (USA) → IsoSTAR 1250I: Iodine-125 is adsorbed on the resin pellets with a diffusion barrier.
- DraxImage – Cytogen (Canada) → BrachySeed LS-1: A glass substrate doped with silver is used. A marker containing 10% platinum is used.

It is important to notice that some seeds shown under here are not produced nowadays and some of them were not commercialized.

4. Dosimetry of Iodine-125 seeds

The dosimetric characteristics of the iodine-125 seeds are performed according to American Association of Physics in Medicine (AAPM) formalism Task Group No. 43(TG-43). This protocol was developed by a committee of brachytherapy dosimetry researchers and implements specific modifications on the physical quantities assigned to the brachytherapy sources, these measurable quantities are used to obtain the dose distribution of the brachytherapy sources [Nath et. al., 1995]. TG-43 underwent an update rendering to the TG-43U1 [Rivard et. al. 2004] and a supplement were published afterwards [Rivard et. al. 2007]. TG-43U1 dose rate calculation will be briefly described here but the details are found in the references [Nath et. al., 1995; Rivard et. al. 2004].

Basically, TG-43U1 recommends that the dosimetry distribution of brachytherapy sources will be performed with experimental and computational methods. Experimental methods usually use thermoluminescent dosimetry methods [Chiu-Tsao et. al. 1990; Nath and Yue 2002; Wallace 2000]. The majority of computational methods uses Monte Carlo (MC) radiation transport codes, for example, EGSnrc, MCNP, Geant, PENELOPE and others [Burns and Raeside 1987; Mobit and Badragan 2003; Thomson and Rogers 2009].

For both experimental and computational methods, the formalism to calculate the dose rates is based in one (1D) and a two-dimensional (2D) configuration. One-dimensional is an approximation for the isotropic point-source. Two-dimensional approximation considers a homogeneous radioactive material distribution along the longitudinal axis of seed active length (region that radioactive material was distributed).

TG-43U1 two-dimensional approximation is described by polar coordinates around a transversal bisector plane of the source. The dose rate surround the source are determined with any chosen point $P(r,\theta)$ on the transversal bisector plane. There is a reference point $P(r_o,\theta_o)$ that provides the reference dose rate $D(r,\theta)$; the reference point has distance (r_0) and

angle (θ_0) equal to one centimeter and $\pi/2$ radians, respectively. This reference point was chosen according to traditional dosimetry practices [Nath et. al., 1995]. Fig. 3 illustrates the geometry used for brachytherapy source geometry.
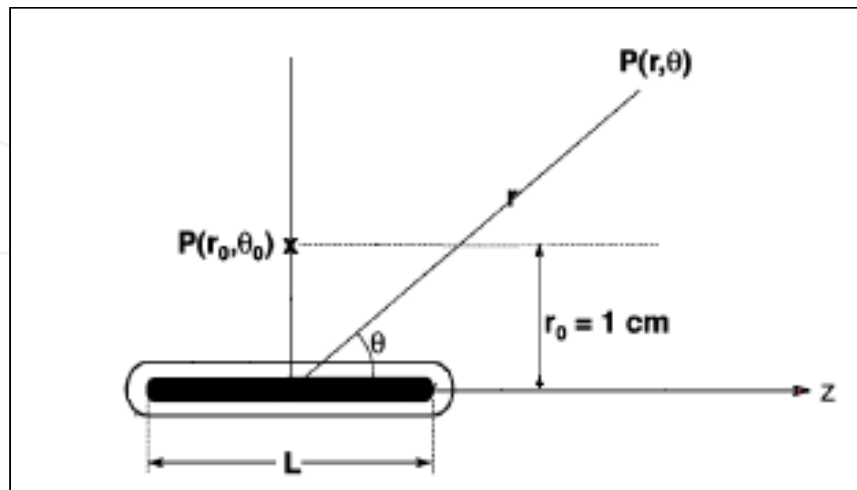

Fig. 3. Geometry used to perform the brachytherapy sources dose measurements, the L denotes the source active length (adapted from Rivard et. al., 2004**)**

According to the TG-43U1, the general two-dimensional dose rate formalism for brachytherapy sources can be expressed as:

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

where S_k is the air kerma strength ($cGy \cdot cm^2 \cdot h^{-1}$ or U), Λ is the dose constant rate (cm^{-2}), $G_L(r,\theta)$ geometry function; $g_L(r)$ Radial dose function; $F(r,\theta)$ anisotropy function. The subscript L denotes the line-source approximation (2D approximation).

Air kerma strength is determined by a single brachytherapy source model, i.e., each brachytherapy seed model has air kerma strength. This quantity is measured by a standard wide-angle free-air chamber (WAFAC) available in National Institute of Standards and Technology (NIST) laboratory [Seltzer et. al. 2003]. Dose constant rate is the ratio of the dose rate in the reference point ($D(r,\theta)$) and the air kerma strength. The geometry function is used to calculate the relative dose due to the spatial distribution of the activity within the source; this function does not consider the scattered and attenuated photons in the source. Scattered and attenuated photons effects are accounts for radial dose function along the transverse seed axis with constant angle ($\pi/2$). Anisotropy function quantify the dose distribution differences due to seed external structure, as the welds on the seeds' extremities [Ravinder et. al., 2004; Nath et. al., 1995]; scattering and absorption effects are included in this function.

Beyond the S_k and $G_L(r,\theta)$ functions, that are obtained from standards laboratories and analytical calculations, respectively, the other functions require the dose rate measurements in the point analyzed. So, the aim of the dosimetric laboratory for brachytherapy sources is to measure the experimental dose in the points-of-interest around the transversal plane seed

with the minimum uncertainties. This accuracy is important because the rate dose values in the specific point will be employed in the dosimetric calculations treatment planning. These values obtained from experimental measurements must be compared with the MC simulations, according TG43U1 recommendations.

For experimental studies, the dosimetric laboratory uses LiF:Mg,Ti (TLD-100) thermoluminescent dosimeters purchased by Thermo Scientific (Harshaw-Bricon). TLD-100 is widely used in the brachytherapy dosimetric investigations for many years [Meigooni et. al., 1988; Nath et. al., 1990; Abboud et. al., 2010]. These dosimeters can be presented in many formats and shapes; the micro-cube format with 1 mm x 1 mm x 1 mm was chosen. These dimensions avoid high gradient fields negligible due to the larger dosimeters dimensions.

To obtain precise dose information of the seed we set TLD-100 micro-cubes around of a single iodine-125 seed in a phantom material that represents liquid water. For the iodine-125 seed emitting low energy photons (average energy 28.37 keV) [Usher-Moga et. al., 2008], the Solid Water™ phantom material showed better agreements with liquid water compared with other phantoms materials such as Polymethilmethacrilate (PMMA) and others plastics phantoms [Meigooni et. al., 1988].

Figure 4 shows a Solid Water™ slab of 30 cm x 30 cm x 2 cm in size used in the dosimetric measurements. The slabs were drilled to accommodate the dosimeters in the radial positions in 100 mm of interval, yielding 36 holes per circumference. The hole radial distances along the center of the slab vary from 0.5 cm to 10 cm (Figure 4). The geometry in this seed positioning was to determine the functions of the TG-43 protocol. During the measurement, additional slabs placed above and below the slab containing the seed and dosimeters, these slabs provide backscatter conditions
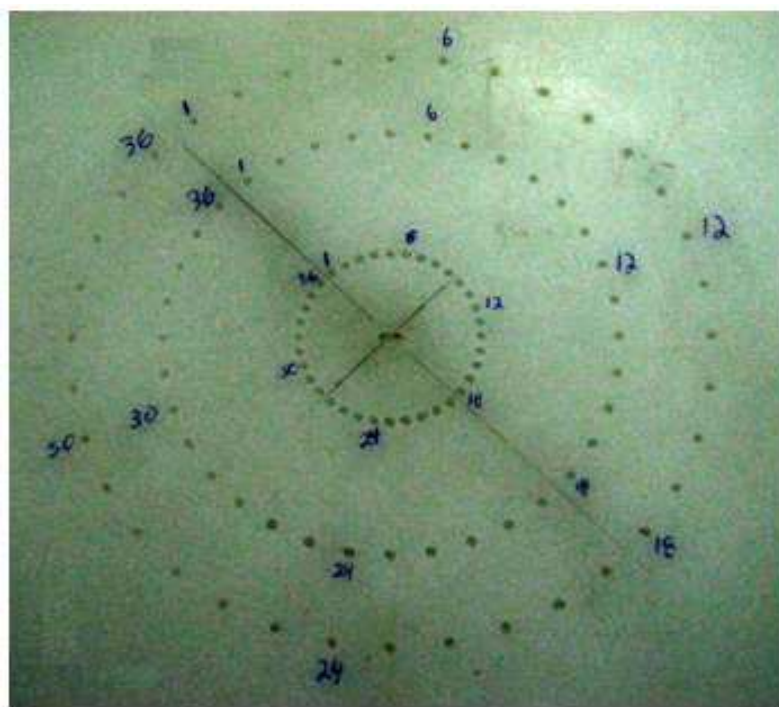

Fig. 4. Solid Water™ slab designed for experimental dosimetric measurements [Zeituni 2008].

Before the dosimetric measurements, the TLD-100 dosimeters were previously selected from a dosimeters' batch. The selected dosimeters represent the minimal uncertainties compared with the overall batch. Difference of the dosimeters masses and edges on the dosimetry structure were some parameters analyzed at the selection [Furreta and Weng, 1998].

All thermoluminescent dosimeters yield different responses of the absorbed dose rate quantity. For dosimeter responses in absorbed dose units, a calibration factor makes useful. This calibration factor is obtained from calibrated beams with a traceable reference dosimetry system, as ionization chambers with special requirements. [Meigooni et. al., 2001; Meigooni et. al., 2006; Abboud et. al., 2010].

The range of the dose delivered in the dosimeters was closed to the absorbed dose levels that will be used in experimental dosimetry routine with brachytherapy sources, it ranges from 10 to 100 cGy. Each dosimeter used in the dosimetry has an individual calibration factor, i.e., one value for the calibration factor to the whole batch was not adopted due to reduce uncertainties propagations on the dose rate calculations. These calibration factors obtained from the x-rays photons were calculated by the averaged measurements originated from the dose levels (10 – 100 cGy).

In summary, the dosimeters that will be measure in a TLD reader will yield thermoluminescent responses in arbitrary units. The intensity of these responses will be proportional to the absorbed dose in the dosimeter. To convert TLD's responses in absorbed dose rates quantities the following formula is applied:

$$\frac{\dot{D}(r,\theta)}{S_k} = \frac{R}{T \cdot S_k \cdot \varepsilon \cdot E(r) \cdot d(T) \cdot F_{lin}}$$

where $\dot{D}(r,\theta)$ is dose rate ($cGy \cdot h^{-1}$) at any point with coordinates (r,θ), S_k: initial iodine-125 seed air kerma strength ($cGy \cdot cm^2 \cdot h^{-1}$) at the start of the measurements; R: the net dosimeter response (nC) of each measured point with backgrounds subtractions,T: irradiation duration (h), ε: calibration factor (nC.cGy-1) for each TLD-100, $E(r)$: a dimensionless correction factor of the TLD-100 between the calibration beam and the iodine-125 photons and the assumed the value was 1.4 for this expression [Abboud et. al., 2010; Reniers et. al., 2002], $d(T)$: a correction factor that explains the source decay during the TLD-100 irradiations and F_{lin} represents a correction for non-linearity in TLD response and was assumed to be unity due to linear response in the doses (10 to 100 cGy) measured with iodine brachytherapy seeds [Meigooni et. al., 2006].

For the TLD-100 measurements a Harshaw 3500 TLD reader is used. The reader operates one dosimeter per load and with continuous flux of pure nitrogen (99,9995% of purity). Nitrogen fluxes are necessary to avoid the signals not delivered from the thermoluminescence dosimeter, as oxygen air induces signals. Heating rate of 10 oC.s-1 and maximum temperature of 260oC are the parameters of TLD-100 measurements used [Thermo Electron Corporation, 2002]. The measurements are performed 20 hours after the exposure; this delay is to avoid unstable glow peak which decays.

TLD-100 dosimeters demand thermal treatments to be reused. Theoretically, the thermal treatment will quench the dose information of previously irradiations. The thermal treatment

adopted for the dosimeters is composed by two steps: a) 400ºC for one hour and b) 100ºC for two hours. The thermal variations are performed using the slow cooling rates of approximately 4ºC.min^{-1} [Oster et. al., 2010]. A special oven was designed for the laboratory to attend the slow cooling rates. This oven has coupled cooler that realizes a linear temperature reduction automatically. During the temperature reduction the dosimeters stay inside the oven avoiding drastic changes in the crystal of the dosimeter caused by the gradient temperature.

5. Introduction for hospital methodology

For adenocarcinoma of the prostate conventional treatment options that should be discussed with each patient in this category include radical prostatectomy, external beam radiation therapy, interstitial brachytherapy and watchful waiting, according to the NCI Consensus Conference in 1988 [Lee, 2003].

There are two types of prostate cancer radiation treatments: external and internal (interstitial). Brachytherapy is the interstitial one, meaning treatment is administered "within the tissue." External radiation therapy involves the projection of photon, electron, neutron, or proton beams into the prostate gland from a remote tool called the linear accelerator.

Ionizing radiation is used in the treatment of prostate cancer because exposure to this radiation damages the DNA of cells. Cells will not be damaged unless they attempt to divide. Cancerous cells divide more quickly than healthy cells. Therefore, healthy cells are able to repair damage before undergoing mitosis, while cancerous cells are not. Unfortunately, if the absorbed dose is strong enough, healthy cells will be damaged to the point where they cannot repair themselves before division. Interstitial brachytherapy is able to deliver higher doses of radiation to an area concentrated within the prostate gland [Van Dyk, 1999].

The use of brachytherapy as the sole modality of treatment for early-stage prostate cancer has gained popularity over the past decade due to the advent of the transrectal ultrasound-guided technique (TRUS) and the favorable reports of imaged-based brachytherapy with isotope Iodine-125 (I-125). At the same time, dose escalation 3-dimensional conformal radiation therapy (3D CRT) has revealed promising results, especially for patients with early stage disease [Halperin et. al., 2008].

5.1 Brachytherapy process at the Albert Einstein hospital

Initially the patient is referred to radiotherapy or search for a consultation with a radiation oncologist which defines the treatment plan in conjunction with the urologist involved in the process. The evaluation of radiotherapy will consist of complete history, complete physical examination including digital rectal examination, analysis of all imaging (transrectal ultrasound, computed tomography, magnetic resonance imaging, and / or chest radiography) and laboratory (complete blood count with coagulation, all measures of serum PSA). Additional investigations may be required to meet specific needs of each patient (diabetes, epilepsy, heart disease, renal disease, lung disease, etc). Therapeutic options, including observation, hormone therapy, radical prostatectomy, external beam radiotherapy or implantation of Iodine-125 seeds as well as acute and late side effects, expected or possible, are explained to the patient mainly by the urologist.

5.2 Indication for brachytherapy

The transperineal prostate implants guided by ultrasound is the most indicated and has a great potential to cure the patients diagnosed with prostate cancer with the following conditions:

For treatment alone:

- Stage I or II (the T2aN0M0 T1C);
- Gleason ≤ 6; (no individual values > 3; e.g. 2 +4 +2 or 4 will not be accepted);
- ≤ initial PSA 10 ng/ml;
- Prostate volume ≤ 45 grams;
- Absence of prior transurethral resection (TUR) and
- Absence or small number of microcalcifications.
- Intended dose: 90% of the target volume covered by the CT isodose 160Gy - (144Gy according to recommendations of the TG 43) [Nath et. al., 1995]

Pre Planning and Ultrasound - The examination will be conducted with the equipment Leopard 2001 - B & K, using the ultrasonic transducer type 8558, coupled with the "Stepping Unit" UA1084. The "template" is B & K and the whole system is fixed to the stand Brachystand.

The exam aims to:

- Obtaining images of the entire prostate, with 5mm spacing between slices;
- Transfer these images via cable or VCR to the planning system TherpacPlus (MMS);
- Determination of the volume (in cubic centimeters) of the prostate, using the HWL (Height x Width x Length) x Factor, being the factor of 0.523 for the prostate;
- Identifying in advance the technical feasibility of the implant (anterior urethral defects, pubic arch interference or micro macrocalcifications).
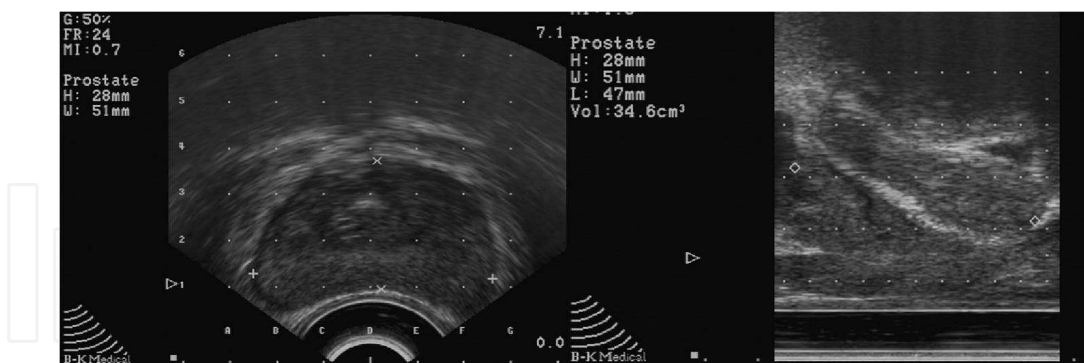

Fig. 5. Prostate volume determination.

Identified clinically relevant changes in the query or ultrasound are discussed with other doctors responsible for feasibility of the procedure (heart disease, diabetes, clotting disorders, use of medications with potential interactions with the procedure used, calcifications, urethral defects, etc.).

5.3 Drawing the boundary of the prostate

In the planning system:

- A new file is created, corresponding to the patient in question;
- A coordinate system is created from the information of the "template" images superimposed on the TRUS (transrectal ultrasound);
- Radiotherapist draws the boundaries of the prostate, seminal vesicles, rectum and ureter in each section of the TRUS;
- Prostate volume is determined by the volumetric reconstruction of the U.S. Distribution and quantity of seeds mCi.

Using system resources Variseed obtain:

- The distribution of seeds, according to the TG 43 protocol and prescribed dose [Rivard et. al., 2004];
- The number of seeds;
- Activity (mCi or units of air kerma) of each seed;
- The number of needles and distribution of seeds per needle.

5.4 Preparation of material for the implant

The team involved in the procedure of radiation therapy (medical, physical, and nursing assistants) handles the preparation of the material to be used in the procedure [Yu et. al., 1999].

The charge physicist needs to control and verify the seeds that reach for each patient. It is recommended that the physicist verify at least 10% of the batch using a well chamber and the measure has a limit of 5% difference between the measured activity and the certificate

The physicist is responsible for taking the seeds in magazines mounted to the center of the second material (Surgical Center Medical Center-CCCM).

Fig. 6. Dosimetric verification of seeds for implant. Seed container (left). Measurement of each seeds using a well chamber (right).

5.5 Standards for sterilization of seeds

- The seeds are sterilized in an autoclave system the temperature of 121 °C and a pressure of 15 psi for 15 to 30 minutes, or the temperature of 133 °C and pressure of 30 psi for about 3 minutes ("flash").
- After sterilization, using Geiger monitor to check radioactivity inside of the autoclave. Place the test material (seed) in the sterilizer.

- After sterilization, the inside level was checked agian.
- Though the possibility of loss of seeds during sterilization is practically small because of strict arrangement of seeds in the container magazines.[Is this correct?], if it occurs, using the Geiger to direct the search and the use of tweezers to put the seeds in ahead container that bear any responsible for sterilization.
- The physicist takes the seeds to the location of the procedure, where the material will be stored in proper place, behind the screen of lead radiation symbol and more isolated as possible.

5.6 Surgical Room procedures

On the day of the procedure the patient is transferred to the operating room of the radiotherapy center through the nursing assistant of radiation therapy [Prestidge, 2008].

5.7 Positioning the patient on the table

The positioning of the patient on the operating table, and supine and lithotomy position with legs flexed according to the survey pre-planning.

5.8 Anesthesia, monitoring and premedication

The anesthesia may be Epidural, spinal or general. They vary according to the anesthesiologist responsible for assessment and multidisciplinary team member. Aabsolute immobility is essential. The timeis 2-3 hours for one procedure. We set up patient monitorings, and administrate prophylactic intravenous or perineal antibiotic treatment according to official regulation standateds established by Department of Anesthesia, and Office of Infection Control (SCIH), respectively. Saline via the urethral catheter is used to complete the volume, if necessary [Nath et. al., 2009].

5.9 Images of the prostate via ultrasound

- Choose the largest cross section of the prostate, transrectal ultrasound, as the target volume.
- Transrectal ultrasound images has a 5 mm separation of each other, and each image is overlap with the image developed by the planning system. It is used to call this planing image as a template image.
- Adjust the image of the ultrasound so that the "line 1" from the "template" is about 5 mm above the mucosa of the anterior rectal wall, and "column D" centered on the urethra.
- Transfer images to the planning system identifying the prostate, urethra and rectum.
- Revaluate of prostate volume and calculating the number of seeds and needles.

5.10 Insertion of needles and seeds

- Insertion of the needles is by the urologist, according to the shape and size of the prostate and activity of the seeds under the guidance of radiotherapist.
- Identify of each needle in the template and each length to be loaded; Use annotation data file card (We use "Diagram for Seed Implant Prostate with I-125 ultrasound-guided").
- Insert of two needles, via transperineum, approximately 1 to 1.2 cm in the direction of the urethra after 4 and 8 hours as stabilizers.

- Put the needle on the edge first and place them top to bottom.
- Check the positioning of each needle with sagittal images of the ultrasound.
- The needles placed in the periphery are spaced between 0.5 to 1.0 cm and 0.5 cm inside the periphery of the prostate. The typical number of needles in the periphery is 9 to12 needles.
- The needles placed in the "Line 1" (the lowest) are separated by 1.0 cm and about 0.5 cm from the anterior rectal wall mucosa.
- The needles in the central region of the prostate are placed at least 1.0 cm apart from the urethra. The typical number of needles in the central region is 3 to 5.
- The standard distribution of the loads is 75% -80% of the total activity in the periphery and 20% -25% in the center.
- Fill the forms of calculation and distribution of seeds.

5.11 Placement of seeds

- Guided by fluoroscopy and ultrasound at the time the surgery;
- Using the Mick applicator for the loading of individual seeds in each needle according to the pre-planning and the eventual corrections in the time of implantation.
- Check the seed deposition with the help of sagittal ultrasound image to the last needle;
- The physicist and radiotherapist individually confer the number, distribution and spacing of each seed needle immediately prior to their placement, as well as checking the needle by fluoroscopy.
- At the end of seed deposition, potentially cold areas identified by fluoroscopy and ultrasound should be filled with seeds individually.

5.12 Cystoscopy

Realization of cystoscopy is performed by an urologist at the end of the introduction of seeds into the prostate.
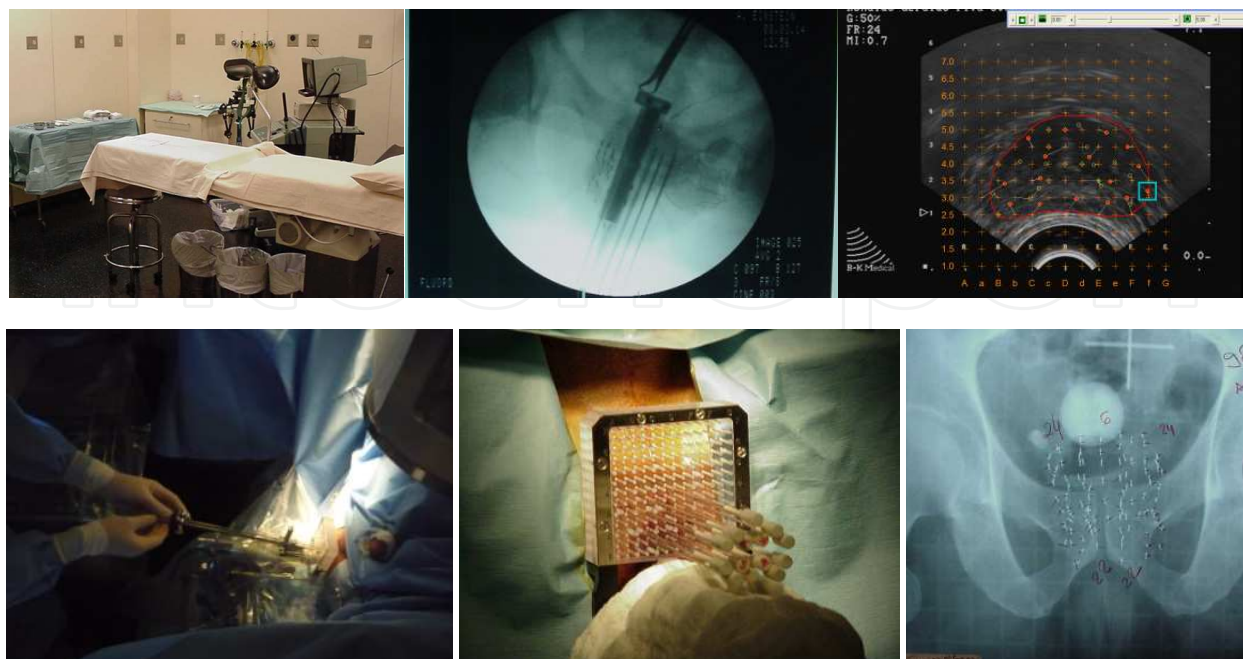

Fig. 7. Insertion of needles and seeds.

5.13 Radiometric survey of the room and the patient

-   Counting the number of remaining seeds and deployed to confirm the number of seeds initially loaded in magazines.
-   Monitor the environment, professionals and the patient with the monitor Geiger Muller, using the window opened because of the low energy iodine-125.
-   The whole procedure for individual and environmental radiological protection is described in "Radiation Protection" section in a published documents by Brazilian Nuclear Energy Commission.

5.14 X-ray control

After the procedure the patient is referred Ximatron CX simulator for the performance of anterior-posterior radiographs and lateral-lateral control and for dosimetric calculations.

5.15 Dose analysis

A quantitative dose analysis must be carried out for each patient post implantation. This statement is based on the premise that it is as important to know and document the dose delivered by a permanent seed implant as by an external beam treatment. The importance of a post implant analysis cannot be overemphasized for the purposes of multi-: institutional comparison, improving techniques, evaluating outcome, and identifying patients who might benefit from supplemental therapy or be at risk for long-term morbidity [Yu et al., 1999].

5.16 Brachytherapy dosimetry

Calculations are performed in accordance with NIST 1999 calibration standards, the point source formalism described in by AAPM Task Group 43, and AAPM Subcommittee Reports [Nath et al., 1995; Rivard et al., 2004; Rivard et al., 2007].

5.17 Prescribed dose

The recommended prescription doses for Iodine-125 are 145 Gy and 110 Gy for monotherapy and boost implants, respectively. The prescription of minimum peripheral dose (mPD) is intended to cover the CTV, and is the reference dose for the treatment.

X-ray CT examination is performed immediately after implant and 3 to 5 weeks after. The patient is scanned in a supine position usually with bladder contrasting. Slices with thickness of 3 mm or less are acquired from 2 cm cephalad to the base of the gland to 2 cm caudad to the apex. All of the seeds used in the implant should be encompassed in the scan. ETVs (-Evaluation Treatment Volume) are determined from this scan, as the location of the urethra and the rectum. Due to the difficulty in CT visualization of the urethra, use of Foley catheterization is strongly recommended. The urethra and the rectum contours are drawn as the outer surface of the Foley catheter and the rectal wall, respectively. The CT images are used to create a post-implant treatment plan (post plan). An AP or anterior oblique pelvic radiograph is used to verify the number of sources and this will be recorded. A surview chest CT image is obtained to check any pulmonary migration of the source.
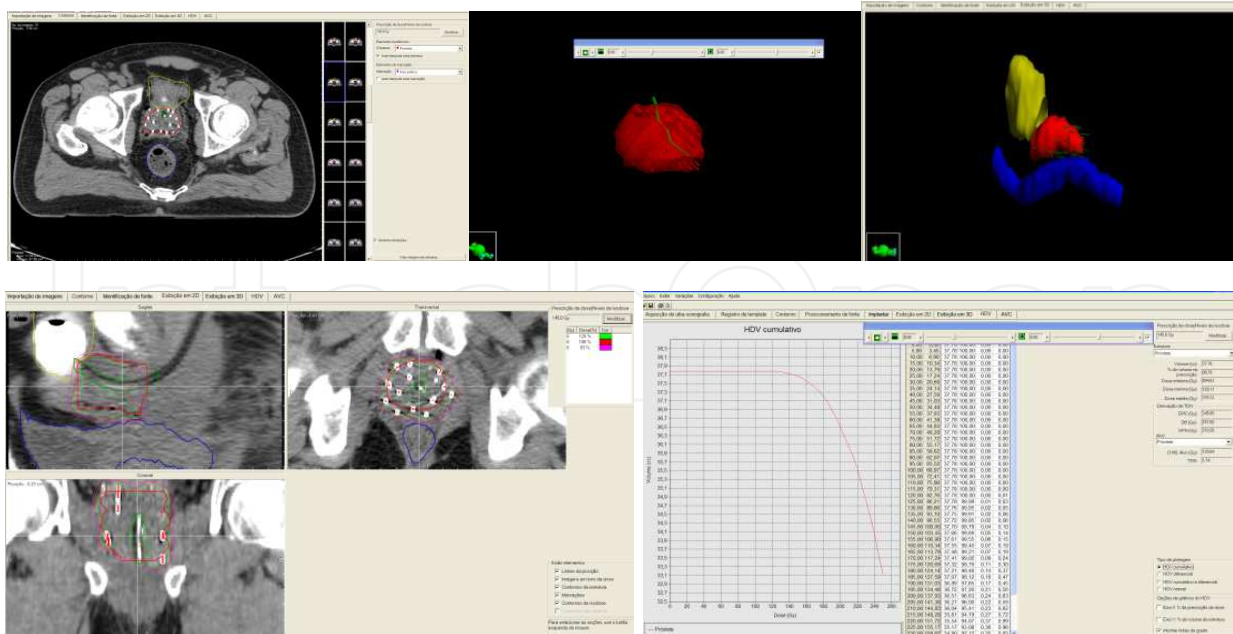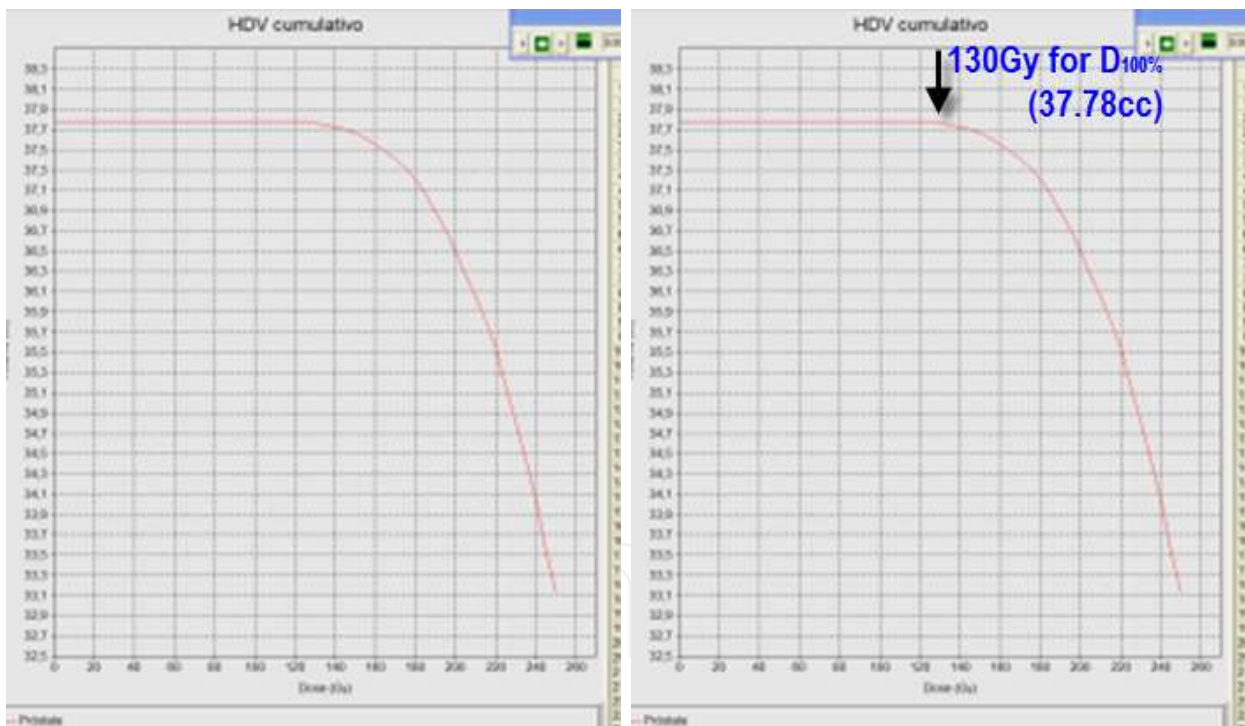
Fig. 8. CT images in the 3D planning system and prostate histogram

5.18 Dose volume analysis

The planning system facilitates structure-based analysis from axial image sets. This includes evaluation and analysis of isodose curves and generation of Dose-Volume Histograms (DVH). The calculation grid should be set no larger than (2 mm x 2 mm x the axial slice thickness). ABS and ESTRO Guidelines are available [Merrick et al., 2007]. DVH-based analysis must be completed in the post plan evaluation. The following values should be reported:

- Coverage. V100, V90, V80, D90.
- Uniformity. V150.
- Urethra. The maximum dose to the urethra and volume of urethra (in cm^3) that received more than 200% of the prescription dose [U200 (cm^3)].
- Rectum. The outer rectal wall will be contoured behind every axial slice of the prostate.

where Vn is the percentage of the ETV that received at least n% of the prescription dose. Dm is the minimum dose received by m% of the ETV. [Merrick et. al., 2007]:

The maximum dose to the rectum and the volume of the rectum (cm^3) that was received more than 100% of the prescription dose.

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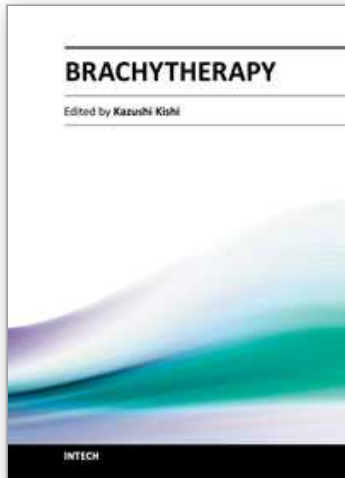
Brachytherapy

Edited by Dr. Kazushi Kishi

Importance of brachytherapy is currently increasing in cancer therapy. In brachytherapy each treatment is best fitted by physician's' hand, and appropriate arrangement and selection of radiation sources facilitates the fitting. This book is full of essences to make a breakthrough in radiation oncology by brachytherapy. I hope this book will encourage all people related. Contents 1: problem of currently popular dosimetric method; 2: Monte Carlo dose simulation of ruthenim-106/rhodium-106 eyes applicators; 3. Progress in Californium-252 neutron brachytherapy; 4. Clinical aspect of endobronchial brachytherapy in central airway tumor obstruction; 5. Review from principle and techniques of Iodine-125 production at nuclear reactor plant to their clinical practive in prostate cancer treatment; 6. Stereotactic Brachytherapy for Brain Tumors using Iodine-125 seed; 7. A brachytherapy procedure with organ-sparing hyaluronate gel injection for safe and eradicative reirradiation.

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