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• *Review article*

Historical review of interstitial prostate brachytherapy

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In the recent years, interstitial brachytherapy implantation has become the treatment of choice for early stage prostate cancer patients. Treatment of prostate cancer with radiation is traced back to 1909. Originally this treatment modality was very crude and could not gain much popularity till 1982. Advancements in radioactive source designs, introduction of new low energy radioactive sources, and new imaging modalities made this treatment modality a treatment of choice for early stage prostate cancer patients. Popularity of this modality is due to the fact that five-and ten-year disease control rates of brachytherapy are equal to those of the surgical, whereas, the toxicity and side-effects are perceived to be lower.

This manuscript presents historical review of interstitial brachytherapy, innovations in radioactive source designs, dosimetry and dose calculations. **Iran. J. Radiat. Res., 2008; 5 (4): 153-168**

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INTRODUCTION

In the recent years, interstitial brachytherapy implantation has become the treatment of choice for early stage prostate cancer patients [1, 2, 3]. Popularity of this modality is most likely due to the fact that five-and ten-year disease control rates of brachytherapy are equal to those of the surgical and external radiation therapy, whereas, the toxicity and side-effects are perceived to be lower [4,5]. It has been estimated that up to 50% of patients with early stage prostate cancer are now treated with ultrasound-guided transperineal interstitial brachytherapy [3-7] with I-125 or Pd-103 radioactive seeds. The principal advantage of this technique is that the seeds can deliver a substantially higher radiation dose to the prostate and less radiation dose to the surrounding tissue compared with external beam irradiation [8, 9]. Iodine-125, Pladium-103, and most recently introduced Cs-131 are the most suitable radiation sources for this treatment modality. These sources emit low energy photons and the dose falls quickly with the distance and therefore, seeds deliver low dose to the adjacent rectum and bladder [10-14].

Historical Background of Prostate Brachytherapy

First use of radiation for the treatment of prostate cancer was reported by Pasteau and Degrais in 1909. They reported that first radiation use for the treatment of prostate cancer was carried out at the Biological Laboratory of Radium in Paris [14] by insertion of a radium capsule into the prostatic urethra through a catheter.

Later, in 1915 a new technique for the treatment of prostate cancer was introduced by Barringer from Memorial Sloan-Kettering Cancer Center (MSKCC) [15-16]. This interstitial implantation technique involved insertion of radium needles into the prostate gland. They inserted 4 to 6 inches long (radium) needles through the perineum into the prostate. A finger in the rectum of the

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patient was used to guide the needles. This treatment technique was named as Brachytherapy in 1930 by Forssell in Sweden [17]. Earlier this technique was limited to only Radium-226. Quimby from New York introduced dose rate tables for calculation of dose for an implant [18, 21]. Later, Paterson and Parker from of Manchester introduced radiation dose tables [22].

Although, brachytherapy at that time was very crude and limited to insertion of radium/radon seeds into the prostate gland, but prostate cancer did show good response to this treatment technique. However, brachytherapy did not gain popularity due to complications associated with high energy emissions from radium, like irritation to the bowel. In addition, structural rigidity of radium needles resulted in excessive personnel radiation doses to the physicians and their support staff [20, 22] that worked as de-motivating factor to accept this treatment modality. Due to these reasons, during mid-20th century clinical brachytherapy practices were mainly limited to brachytherapy procedures, other interstitial brachytherapy remained in decline till early 1950s.

Flocks *et al.* from Iowa State University introduced a new source, Au-198 (radioactive gold), for the treatment of prostate cancer in 1951 [23-24]. He injected Au-198 in the form of colloidal solution directly into the prostate gland. Although this technique showed a low mortality and morbidity, but it was not widely utilized by radiation oncologists and they remained inclined to treat prostate cancer with the emerging megavoltage external beam radiation therapy [25].

During 1960s and 1970s several technological advancements like, after loading of radioactive sources, nuclear reactor produced radio-nuclides as the substitutes for radium, and the introduction of computers in medicine served as re-emergence of brachytherapy. In the early 1960, Donald C Lawrence introduced I-125 source encapsulated in titanium for interstitial brachytherapy [26]. The isotope was contained in miniature, sealed titanium cylinders tailored to fit into and be administered by needles. Dr. Whitmore and colleagues at Memorial Sloan Kettering Cancer Center (MSKCC) started permanent I-125 seeds implantation through an open incision [24-27]. The prescribed dose of radiation was based on a nomogram derived from external beam and early brachytherapy planning concepts. It was predicted that implantation of low energy I-125 sources will result in drastic improvement in out come of interstitial prostate brachytherapy. However, unpredicted results were seen due too blind insertion of I-125 sources within the target volume [28-32]. Despite the limitations of these seed implantation techniques, some important informations were obtained such as local cancer control was better for the patients with low grade prostate cancer and uniform distribution of radioactive sources within the implant volume. In addition, local control rate was found to be around 60% for the patients who received prescription doses greater than 140Gy (Gray), whereas it was found to be 20 % for the patients who received less than 140Gy [30-33]. These results dictated that that accurate seed placement and proper selection of patient were important factors in outcomes of this treatment modality [34].

Dr Holm introduced transrectal ultrasound to visualize the prostate gland in 1983 [35]. With this technique I-125 radioactive seeds loaded in needles were inserted through the perineum directly into the prostate gland. This technique increased the accuracy of needles and seed placement and resulted in relatively uniform dose distribution of seeds throughout the prostate volume. Trasrectal ultrasound served as foundation for new interstitial prostate brachytherapy that also allowed computerized treatment planning of the implant rather using nomograms and look up-tables. This technique ensures the proper number, strength, and positioning of radioactive sources for the uniform and prescribed distribution within the target volume. Significance of this technique was shown by a research study at the Seattle Prostate Institute by comparison of this technique with the older one [34-36]. It was shown that the patients treated with interstitial prostate brachytherapy between 1988 and 1990 achieved higher 10-year disease free survival as compared to the

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identical patients treated in the same institute by the same physicians group during 1986 and 1987 [38]. These studies dictated that higher-quality implants results in better out come. Since the mid 1980s, the transrectal ultrasound-guided, template-guided I-125 implantation procedure has become the treatment of choice for the patients with early stage prostate cancer [39, 40].

Initial dose rate from I-125 prostate implant is 7-10 cGy /hr it was assumed that this dose rate is close to the threshold of the prostate cancer. In 1990 a new radioactive source, Pd-103 was introduced. This source has a half life of 17 days that provides an initial dose rate of about 4 times larger than I-125. Most recently, Cs-131 has been introduced for interstitial prostate brachytherapy, this source provides much higher initial dose rate.

At present, a prostate implant involves volume study consisting of a series of cross-sectional ultrasound images of the prostate, out lining target volume, critical structures (rectum, urethra), generation of computerized ideal treatment plan, and seed placement as per preplan study [41]. This technique provides relatively uniform dose distribution within the target volume. Implant quality is evaluated by post implant CT planning, referring to out come of specific treatment [42-44]. Acceptable doses are now referenced to the prescription dose and the volume receiving the dose [43, 44]. The actual dose delivered to the prostate has remained essentially the same over the many years; however, the changes in the formulas of dose calculation for both I-125 and Pd-103 changed the prescription dose [45, 46]. Prescribed dose based on type of isotope used (eg, Pd-103 or I-125) and whether it is to be used for implantation alone (145 Gy for I-125, 125 Gy for Pd-103) or in combination with external beam radiation therapy EBRT (110 Gy for I-125, 100 Gy for Pd-103) [44].

Radioactive sources and their use in interstitial Brachytherapy

Brachytherapy is one of the oldest techniques of radiation therapy for the treatment of prostate cancer. Since its emergence various radioactive sources in different shapes and sizes have been employed for interstitial prostate brachytherapy. Very first implication for the treatment of prostate cancer was insertion of radium through catheter in prostatic urethra. In 1921, Denning *et al.* published a series of 100 cases treated through this technique [47]. Although short-term local control of the disease was surprisingly good for this crude method, the complications were significant, occurring in about 15 to 20 percent of patients.

Au-198 in the form of colloidal solution was the second radioactive source utilized for the treatment of prostate cancer in 1951 [48]. This technique involved interstitial injection of colloidal solution of radioactive gold directly into the prostate gland. Over 500 patients with non operable prostatic cancer were treated with this technique. Although the published results with this technique showed a low mortality and morbidity, the technique was not widely used. Later, Au-198 seeds were developed to provide simpler handling and easier placement. Gold 198 has a short half-life (2.7 days) and a maximum energy of 1.2 MeV. The theoretical advantage of a gold 198 implant was the delivery of radiation at a very high dose rate. It was assumed that this will help to avoid some of the radiobiologic problems associated with radium [47-51]. The higher energy of the source, however, results in less sparing of adjacent normal tissue that limits low prescription dose to the prostate in order to avoid complications to the other organs. An additional disadvantage of these two isotopes, Ra-226 and Au-198 was the risk of radiation exposure to staff performing the implantation. Because of the radiation protection problem use of gold-198 for prostate permanent implant was not widely accepted.

John Russell introduced Pd-103 source (17.0-day half-life and 22 keV mean energy), for interstitial brachytherapy in 1987 by activation of palladium-102 in a nuclear reactor to transform a portion of palladium-102 to an amount of X-ray emitting palladium-103. Pd-103 in the form of two beads was sealed into the capsule to avoid direct contact of radioactive material to

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patient's body fluid and tissue [45]. In addition, a non radioactive cylindrical as an X-ray marker made of high atomic mass was added in between the two beads. Capsule of Pd-103 source included a cylindrical body portion having a pair of open ends. The open ends were closed by a variety of end caps as shown in figure 1(b) by welding, crimping, preening or other cold flow metal treatment. Varieties of end caps were introduced. Some of them were to provide plug-like coupling to joins the pair of seeds in end-to-end in coaxial relationship. First Pd-103 seed implantation was performed in the US at Northwest Hospital and established a national brachytherapy implant course [49].

The main difference between the two isotopes is half-life. The half-life, in turn, affects the initial dose rate of the implants: I-125, with a half-life of 60 days, emits radiation at 8 to 10 cGy per hour at the time of the actual implant. Pd-103, with a half life of 17 days starts out at 20 to 24 cGy per hour. Based on animal models and radiobiological principles protocols Pd-103 is recommend for higher grade (Gleason score, greater than 6) tumors, although this concept has never been validated clinically. Recent evidence suggests that I-125 and Pd-103 have equal tumoricidal effect through the range of Gleason grades [49, 50, 51]. High initial dose rate from a shorter half life radioisotope, Pd-103 attracted the venders to introduce another radioisotope with similar features [51].

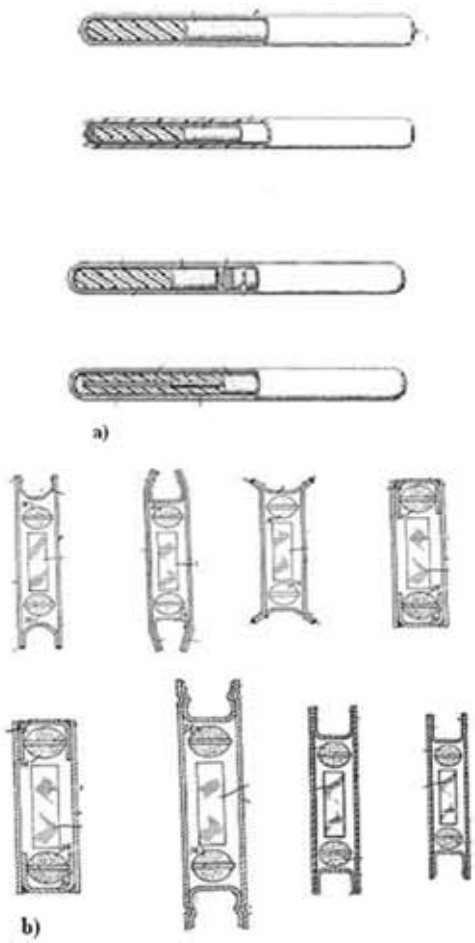

Figure 1. Schematic drawings of initial a) I-125 source design introduced by Lawrence and colleagues in 1966 and b) Pd-103 source introduced by John Russell in 1987. Please note that these drawings are not scaled.

Cesium-131 was initially proposed by Lawrence and Henschke (1965) but has only recently been made available for interstitial brachytherapy [49]. Cesium-131 is produced by neutron activation of Ba-130 in a nuclear reactor. Ba-130 captures a neutron, and turns to Ba-131. Ba-131 then decays with an 11.5-day half-life to cesium-131, which subsequently decays with a half-life of 9.7 days to stable xenon-130 with prominent photon peaks energies in the 29 keV to 34 keV regions. Schematic diagram of Cs-131 source introduced by IsoRay, Inc. (Richland, Washington, USA 99352) is shown in figure 2.

Dr. Korb and Dr. William Ellis, from UW Medical Center, first time implanted Cs-131 brachytherapy sources in 2006 for the treatment of prostate cancer. These sources have a shorter half-life and deliver faster radiation. Dr. Korb predicted that due to the shorter duration of treatment with Cs-131, side effects such as incontinence, urinary urgency or pain may be lessened. Although, the recent radiobiological data strongly suggests that the shorter the half-life i.e., (higher dose rate) of the radionuclide the

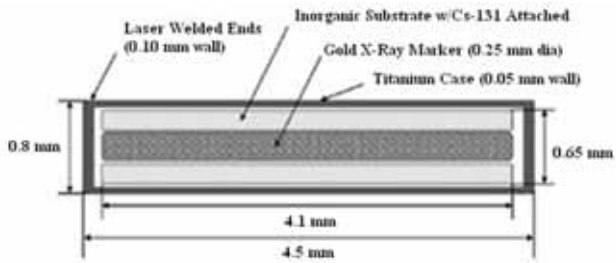

Figure 2. Schematic diagram of Cs-131 source introduced by IsoRay, Inc. (Richland, Washington, USA 99352).

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more effective it is for the treatment of prostate cancer. The American Brachytherapy society (ABS) does not recommend one isotope over the other [44].

At present various manufacturers are involved in the production of I-124 and Pd-103 brachytherapy sources [52-56]. The majority of these sources are less than 0.5cm in length and 0.8mm in diameter [45, 46]. Inner structure and design have been changed to improve the symmetric dose distribution around the source. Figure 3 shows some of commercially available seed type sources for interstitial prostate brachytherapy.

Review of Source Implantation Techniques for prostate Cancer

Interstitial implantation with radium needles inserted into the prostate gland was used in 1915 by Barringer at New York's Memorial Sloan-Kettering Cancer Center (MSKCC) [57]. Barringer inserted 4 to 6 inches long (radium) needles through the perineum into the prostate. He used his finger in the rectum to guide the needles. Later, in 1921, Denning *et al.* published treatment of prostate cancer by insertion of radioactive radium through a catheter in prostatic urethra. Denning *et al.* published out a series of 100 cases treated through this technique [47].

In 1951, Flocks *et al.* introduced a new technique for the treatment of prostate cancer [24]. They injected radioactive gold in the form of colloidal solution into the prostate gland. This treatment technique showed low mortality and morbidity, but it was not widely accepted due to radiation hazards to the radiation oncologists and staff. In addition, radiation oncologists were more inclined to treat prostate cancer with the newly emerging megavoltage external beam radiation [25].

The development of Iodine-125 sources at Memorial Sloan-Kettering Cancer Center (MSKCC) in the late 1960's attracted the oncologists to use these sources for the treatment of prostate cancer. In the same era, Dr. Whitmore and colleagues at Memorial Sloan Kettering Cancer Center (MSKCC) started permanent I-125 seeds implantation through an open incision [29]. These techniques did not allow for clear visualization of the seeds placement within the target volume and this blind insertion resulted in uneven distribution of seeds within the target volume [30].

Introduction of transrectal ultrasound by Dr. Holm in 1983 [16], strongly motivated radiation oncologist to utilize it to improve the outcomes of this treatment modality. This technique allows insertion of radioactive seeds loaded in needles through the

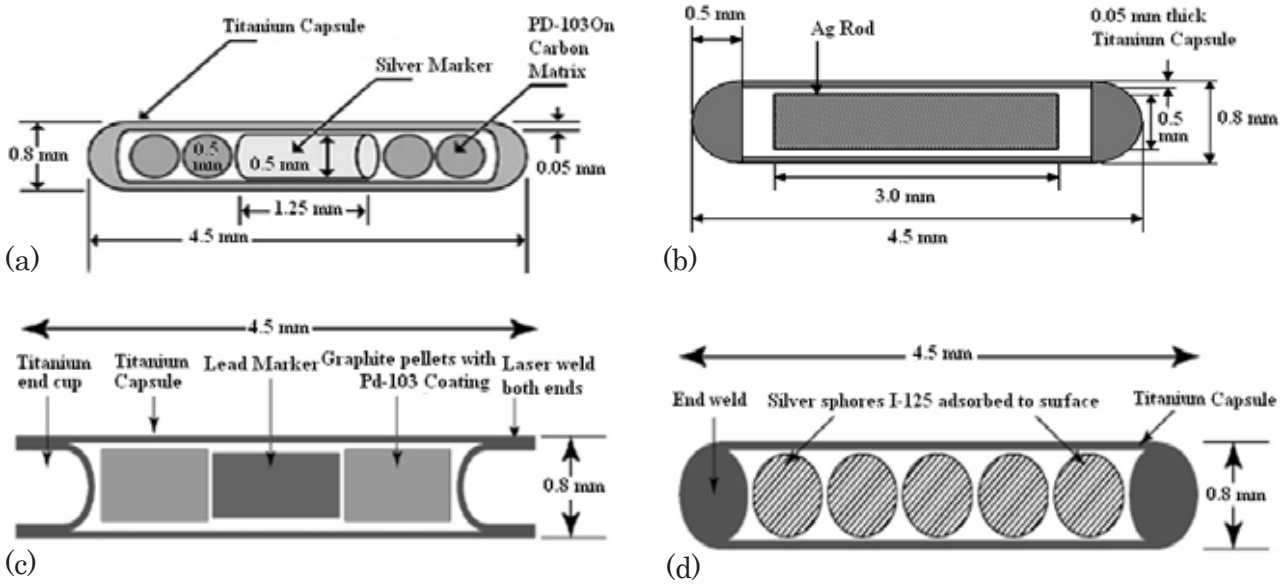

Figure 3. Schematic diagrams of some of the commercially available brachytherapy sources for interstitial prostate brachytherapy.

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perineum directly into the prostate gland, while visualizing prostate gland for the accurate placemat of radioactive sources within the prostate gland.

Original prostate implant techniques, which are still used in many centers, involve placement of individual, or "loose," seeds into the prostate gland [13]. Spacing between the sources is accomplished in preloaded needles by absorbable spacers or, with the Mick applicator (Mick® Radio-Nuclear Instruments, Inc., Mount Vernon, NY) by mechanically depositing the seed at the required distance from the other seeds [12, 59]. Different source designs are currently employed for the treatment of prostate cancer. Some of the commercially available source designs for the treatment of prostate cancer are shown in figure 3.

Despite the enormous success and improvements in interstitial brachytherapy and source design, certain problems are still associated with loose seed implants, such as seed migration [61] and seed embolization [62, 63]. Moreover, clumping [64, 65] of loose seeds during the implant results in under-dosed or over-dosed regions in the prostate volume (figure 4) [66].

In order to minimize the problems associated with conventional seed type brachytherapy sources (0.45 cm in length and 0.8 mm in diameter), pseudo-linear or stranded source models, such as Rapid Strand™ (Oncura, 401 Plymouth Road, Suite 130, Plymouth Meeting, PA), Readi-Strand™, and Vari-Strand™ (Advanced Care Medical, inc. 115 Hurley Road Oxford, CT 06478) have been introduced (figure 5). These pseudo-linear source models are constructed by connecting a series of seeds in a linear fashion using a dissolvable tissue equivalent material [68, 69].

Recent studies demonstrated that 18% to 55% of patients treated with loose seeds via the Mick applicator experienced seed migration to the lungs whereas studies of preloaded loose seeds have reported 10% to 22% [59, 67].

The mechanism for this migration is likely seed embolization in the venous plexus surrounding the gland or inadvertent deposition in the peri prostatic region.

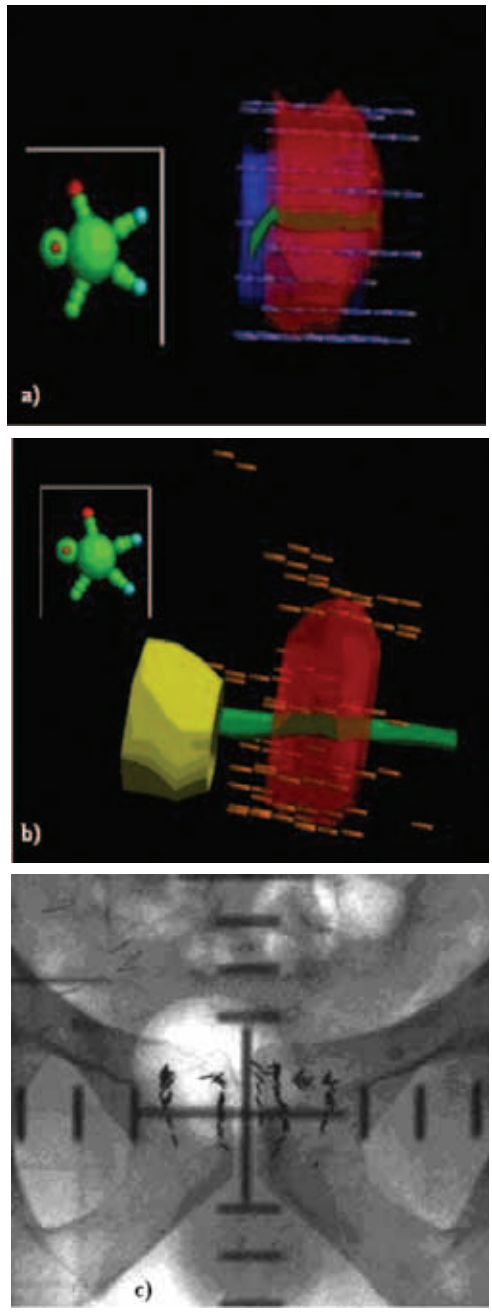

Figure 4. Distribution of seed types sources in: a) Pre-planned volume study, b): post plan CT, and c) post implant X-ray indicating bunching of sources.

Seattle group reported seeds migration to lungs in 0.7% of patients treated with stranded seeds, whereas such migration was noted in 11% of the patients implanted with loose seeds [34]. In an updated study based on 1000 patients treated at the Seattle Prostate Institute demonstrated that 24% of patients implanted with loose seeds experienced seed migration to the lung versus 2% of patients

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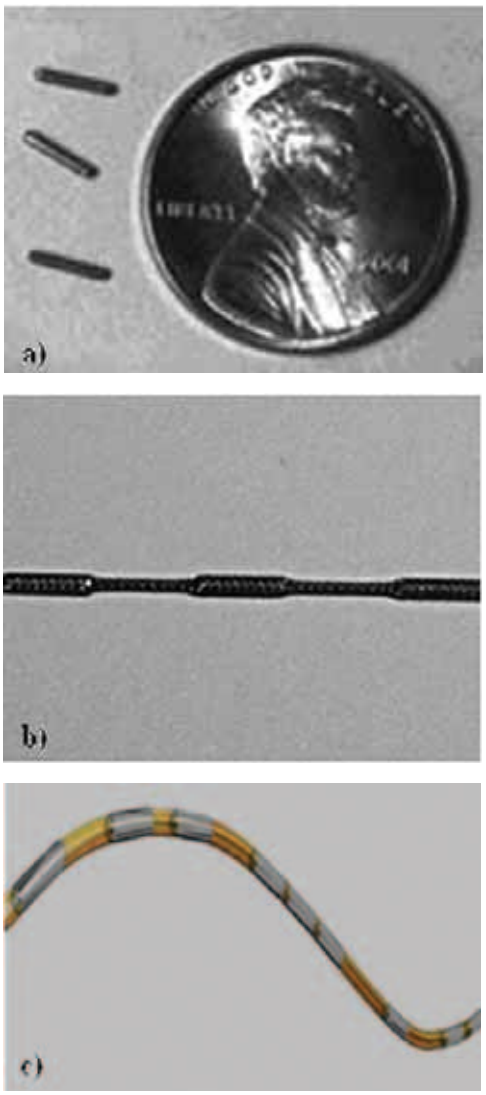

Figure 5. (a) Shows comparison of a commercially available seed type source and one penny, (b) and (c) show two different types of stranded sources.

treated with seeds stranded in Vicryl suture [34, 35, 68, 69].

In addition to reduction in seed migration and embolization, multiple studies have demonstrated improved dosimetry with seeds stranded in Vicryl suture versus loose seeds. Lee and colleagues compared 20 loose seed implants with their first 20 connected seed implants (RAPID Strand) and found significantly improved postoperative dosimetry on dose-volume histogram (DVH) analysis [70]. Fagundes also showed significant improvement in DVH dosimetry when he switched from using loose seeds and the Mick applicator to after loading the Mick

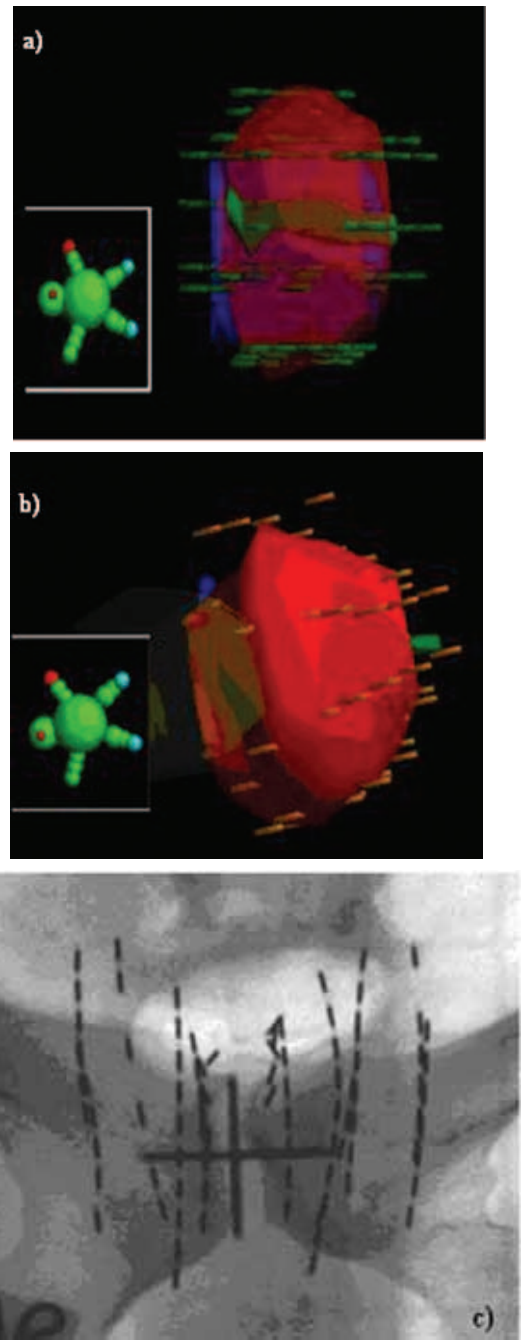

Figure 6. 3D view of Pre implant Volume study and post implant CT. Indicating a well planned uniform distribution of sources in volume study (a) and post implant study (b), while using an implant with stranded sources (c).

applicator needles with seeds stranded in Vicryl suture [71]. Similarly in a comparative study, Awan *et al.*, found large variation in seed placement in post plan studies as compared to preplan for the patients implanted with loose seeds [72]. In addition, they reported that approximately 50% of the

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patients implanted with loose seeds required additional seeds at the time of implantation, in order to achieve the pre-planned coverage. Furthermore, Lin and colleagues compared loose seed implants with stranded seed implants and found significantly improved postoperative dosimetry on dose-volume histogram (DVH) analysis [73].

Encouraging clinical results of the stranded seeds attracted the vendors to develop true linear sources. RadioMed™ Corporation (One Industrial Way, Tyngsboro, MA) introduced a linear Pd-103 source called RadioCoil™^{103}Pd [74] (figure 7). These sources have been introduced for interstitial brachytherapy implants [74, 75].

The design of this source model like a coiled ribbon in the form of a dense is helix. These sources are fabricated from a ribbon of high purity rhodium, which is bombarded with protons (^{103}Rh (p, n) ^{103}Pd) in a cyclotron to produce radioactive palladium-103. The coiled structure of the source enhances the ultrasonic visibility of the source and provides a better grip within the implanted tissue which reduces the chance of seed migration and embolization.

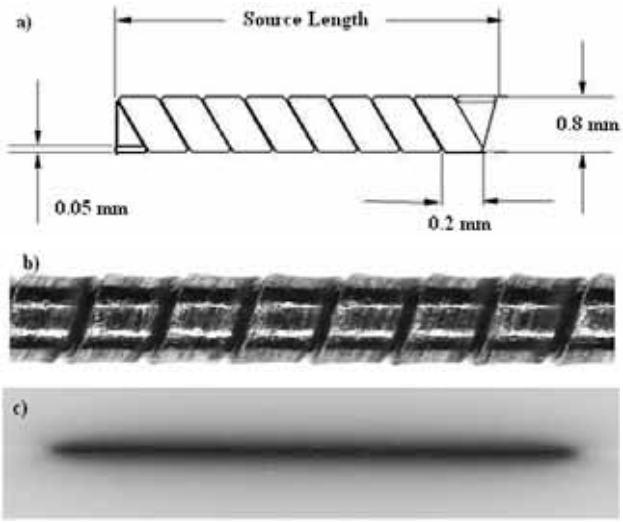

Figure 7. Schematic diagram of RadioCoil™^{103}Pd brachytherapy source. RadioCoil™^{103}Pd source, c) auto radiograph of RadioCoil™^{103}Pd source.

Historical review of brachytherapy dosimetry

Dosimetry refers to estimation of absorbed dose by means of experimental or fundamental theoretical techniques about a single brachytherapy source of a particular design and type. Early experimental quantification of radiation field associated with radioactive sources traces back to techniques introduced by Becquerel in 1900. In this technique, gold-leaf electroscope was used to quantify radiation field. Although quantities like absorbed dose had been defined in 1914 [76], but no theory existed that could relate out put of detector to radiation absorbed dose.

In 1921 Sievert integral formula was introduced by Rolf Sievert. This formula has widely been utilized for dose calculation around sealed brachytherapy sources. The Sievert integral computes dose distributions around filtered line sources and assumes that the emitted energy flounce is exponentially attenuated by the filter thickness traversed by the primary photons.

In 1922, Quimby developed a numerical technique for partitioning needles into a linear array of point sources. With the help of this technique he generated away-and-along exposure rate tables [19-22] and in 1930s, Paterson and Parker published tables for calculation of dose distribution. The aim of the Patterson-Parker dosimetry system was to plan and deliver a uniform dose (±10% from the prescribed or stated dose) throughout the target volume.

Later model of Quimby system was for calculation of uniform dose distribution and was based on a uniform distribution of source strength, accepting a non-uniform delivery of dose. Usually, the dose in the centre of the treatment volume was higher than the dose near the periphery. In 1934, a didactic system of brachytherapy the 'Manchester System' was published and have been used for many decayed as an indispensable basis of radium therapy. The 'Paris System' was proposed by Pierquin and Dutreix to predict the constant relationship between dimensions of the implanted volume and isodose lines. This remained the standard for interstitial brachytherapy for many years. This system provides some general rules for the selection

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and placement of the sources in order to achieve the desired dose distributions.

Technique for exposure measurement from radium sources was established in the 1930s by the development of practical cavity theory [26]. This technique allowed exposure measurement from small ion chambers containing condensed matter walls, with enough wall thickness that establishes transient charged-particle equilibrium.

During 1950s, computerized treatment planning and dosimetry methods in brachytherapy treatment planning made the transition from table-based systems to patient-specific 2D and 3D dose distributions. In addition, the underlying dosimetry methods successfully adapted to the replacement of radium and radon sources by artificial radionuclides. A major advance was the extension of exposure-based primary standards to the new radium-substitute sources. In the US, NIST (the National Institutes of Standards and Technology, formerly known as the National Bureau of Standards) developed reference exposure-rate primary standards based upon carbon wall spherical ionization chambers for Cs-137 and Co-60 sources in 1974 [77] and for Ir-192 brachytherapy sources in 1980 [78].

The development of modern quantitative approaches to brachytherapy dosimetry is intimately linked with clinical utilization of low-energy I-125 and Pd-103 seeds. Interest in basic experimental and computational dosimetry methods began to grow in the mid-1960s because of concerns that semi-empirical computational dose-calculation models, applied so successfully to radium equivalent radio nuclides, might not be valid for the 28 keV X-rays of I-125.

Dosimetry and calibration techniques used in the first decade of clinical I-125 practice are undocumented, although the original TG-43 report [45] hints that a very large dose-rate constant, Λ=1.7 cGy h-1 U-1 was used. The first published I-125 dosimetry studies were from Hilaris *et al.* [79, 80] and Krishnaswamy [81].

In order to resolves the above noted discrepancies, in 1986 the US National Cancer Institute funded a 3-year multi-institutional contract to perform a definitive review of low-energy seed dosimetry. The three institutions, collectively called the Interstitial Collaborative Working Group (ICWG), introduced procedures for calibrating TLD detectors and correcting for higher TLD response to low-energy photons, for quantitatively estimating absolute dose rates in water. Each of the three ICWG investigator groups independently measured transverse-axis dose distributions for the I-125 and Ir-192 then available to validate their TLD measurement methodology [82, 45]. As a result of the ICWG efforts and subsequent contributions from later investigators, TLD dosimetry was accepted as the most reliable and best validated experimental approach in brachytherapy.

Greater understandings of radiobiology combined with new technological developments have improved the science of brachytherapy. Medical physicists have developed dosimetry protocols that have also become more accurate through the years [45]. For the dosimetry of interstitial brachytherapy sources, the American Association of Physicists in Medicine (AAPM) Task Group 43 (TG 43) has developed improved dose calculation formalism [45]. The new factors and functions in these formalisms include the dose rate constant, a radial dose function, an anisotropy function, a geometry factor, an anisotropy factor and the air kerma strength. These new functions vary with the actual source construction and geometry in addition to the primary photon spectrum and medium.

Using the recommendations of TG-43, dosimetric characteristics of several new designs of I-125 and Pd-103 brachytherapy sources have been determined and published by various investigators. This protocol has introduced a universal dosimetry technique for the brachytherapy sources. This dosimetry protocol has adequately served the brachytherapy community for many years, but due to technological advancements new dose calculation formalism has been recently introduced in updated TG-43 protocol named as TG-43U1 protocol [46]. Introduction of the

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new protocol was to account for the anisotropy of many new brachytherapy sources. Original TG-43 protocol was based on photon fluence around a point source in free space. Clinical applications require that we evaluate the dose distribution inside a patient, which implies non-point source configuration as well as attenuation and scattering of the radiation within the tissue. Actual brachytherapy sources are rarely spherical in structure and exhibit anisotropy due to self attenuation of the radiation inside the source, limit the use of the point-source approximation. Therefore, in any treatment, the assumption that the radiation is isotropically produced around the source will lead to significant errors by neglecting the anisotropy of the source.

TG-43U1 protocol provides standardization of both dose calculation methodologies as well as dose rate calculation formalisms for clinical implementation of the brachytherapy source design.

TG-43U1 DOSIMETRY FORMULISMS

Recently, due to advancements in brachytherapy and introduction of new brachytherapy sources an update to the TG-43 has been introduced as TG-43U1. This protocol clarifies some of the ambiguities of the original TG-43 report and formulated few more parameters and recommendations leading to precise and unified measurement of dose calculation around the globe.

TG-43U1 addresses the parameters and measurement techniques for the determination of dosimetric parameters and calculation of dose distribution around the brachytherapy sources. TG-43U1 focuses on the development of guidelines for the determination of dosimetric parameters by both experimental and Monte Carlo methods, and to promote consistency in derivation of parameters used in TG-43 formalism. TG-43U1 recommends at least one experimental and one Monte Carlo determination of the TG-43 dosimetry parameters be published in the peer-reviewed literature before using new sources and utilization of consensus of dataset for clinical application of the source.

A. General 2D formalism

The general, two-dimensional 2D dose-rate equation is presented below is recommended by TG-43U1 for calculation of dose distribution around a brachytherapy source.

$$\dot{D}(r,\theta) = \frac{\Lambda S_K G_L(r,\theta)}{G_L(r_o,\theta_o)} g_L(r) F(r,\theta) \qquad (A)$$

where $\dot{D}(r,\theta)$, is the dose rate at (r, θ), r denotes the distance in centimeters from the center of the active source to the point of interest, r_0 denotes the reference distance which is specified to be 1 cm, and θ denotes the polar angle specifying the point-of interest, $P(r, \theta)$, relative to the source longitudinal axis. The reference angle, θ_0, defines the source transverse plane, and is specified to be 90°.

Air-karma strength

Air-karma strength, S_K, is defined, as product of air kerma rate and square of the distance. TG-43U1 recommends determination of Air-karma in void phantom with tally points filled with dry air. Equation for determining air kerma is defined as.

$$S_k = K\delta\,(d)^2 \qquad (1)$$

The distance d can be any distance that is large relative to the maximum linear dimension of the source. $K\delta\,(d)$ is determined in transverse direction of the source.

Dose-rate constant

The dose rate constant is defined as the dose rate at the reference point along the transverse bisector of the source per unit air kerma strength. The dose rate constant in water has the units of cGy h^{-1} U^{-1}. U is the unit of air kerma strength, where 1 U = 1 cGy cm^2 h^{-1}. The dose rate constant is defined as

$$\Lambda = \frac{\dot{D}(1cm,\pi/2)}{S_K} \qquad (2)$$

Where $\dot{D}(1cm,\pi/2)$ is the dose rate at 1cm from the source at a 90° angle from the longitudinal axis of the source. The dose-rate constant depends on both the radionuclide and source model, and is influenced by both the source internal design and the experimental methodology used by the

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primary standard to realize S_K.

Geometry function

The geometry function evaluates the spatial distribution of activity along the source. The geometry function, $G_L(r,\theta)$, is determined using three different forms of the geometry function equation. When the angle of interest is at 0° to the longitudinal axis of the source, the following equation is used.

$$G_L(r,0°) = \frac{1}{X^2 - (L/2)^2} \quad (3)$$

At 90° the following equation is used.

$$G_L(r,90°) = \frac{2\tan^{-1}(L/2Y)}{LY} \quad (4)$$

At all other angles the geometry function was determined using the following equation.

$$G_L(r,\theta) = \frac{\tan^{-1}[(X+(L/2))/Y] - \tan^{-1}[(X-(L/2))/Y]}{LY} \quad (5)$$

L is the active length of the source, and X and Y refer to the longitudinal and transverse components, respectively, of the distance from the center of the active length of the source to the point of interest. Physically, the geometry function neglects scattering, attenuation, and provides an effective inverse square-law correction based upon an approximate model of the spatial distribution of radioactivity within the source. In the case where the radioactivity is distributed over a right-cylindrical volume or annulus, this protocol recommends taking active length to be the length of this cylinder. For brachytherapy sources containing uniformly spaced multiple radioactive components, L is taken as the effective length, L_{eff}

$$L_{eff} = \Delta S^* N \quad (6)$$

Where N represents the number of discrete pellets contained in the source with a nominal pellet center-to-center spacing ΔS.

Radial dose function

The radial dose function is concerned with scatter and tissue attenuation effects on dose, in the transverse plane of the source bisector, as a function of radial distance away from the source. The radial dose function of the source is determined using the following equation.

$$g_L(r) = \frac{\dot{D}(r,\pi/2)G_L(1cm,\pi/2)}{\dot{D}(1cm,\pi/2)G_L(r,\pi/2)} \quad (6)$$

$\dot{D}(r,\pi/2)$ is the dose rate at some distance r from the center of the source at a 90° angle from the longitudinal axis of the source. The geometry function was evaluated as in Equation [3-5] above. The radial dose function is defined as unity at the reference point (i.e. $g_L(1cm) = 1$).

2D anisotropy function

The anisotropy function is concerned with the effects on dose due to attenuation through the source capsule and self absorption at varying angles relative to the transverse plane. The anisotropy function was determined using the following equation.

$$F(r,\theta) = \frac{\dot{D}(r,\theta)G_L(r,\pi/2)}{\dot{D}(r,\pi/2)G_L(r,\theta)} \quad (7)$$

$\dot{D}(r,\theta)$ is the dose rate at some distance r and angle θ from the center of the longitudinal axis of the source. The anisotropy function is defined as unity on the transverse plane (i.e. $F(r, \pi/2) = 1$), all other $F(r,\theta)$ numbers were referenced back to this value. The 2D anisotropy function describes the variation in dose as a function of polar angle relative to the transverse plane. While $F(r, \theta)$ on the transverse plane is defined as unity, the value of $F(r, \theta)$ off the transverse plane typically decreases as r decreases, as θ approaches 0° or 180°.

1D anisotropy function

As per TG-43U1 recommendations anisotropy factors, $\phi_{an}(r)$, is calculated from the measured dose distributions at given radii as follows

$$\phi_{an}(r) = \frac{\int \dot{D}(r,\theta)d\Omega}{4\pi\dot{D}(r,\pi/2)} \quad (8)$$

Where Ω is the solid angle around the source, The arithmetic mean of all anisotropy factors for a given medium was termed as anisotropy constant, $\bar{\phi}_{an}$ of the source. At a given radial distance, $\bar{\phi}_{an}$ is the ratio of the

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solid angle weighted dose rate, averaged over the entire 4π steradian space, to the dose rate at the same distance r on the transverse plane.

Original and updated TG-43U1 protocols are basically based on experiences with seed type sources (≤1.0cm in length) and have been extensively utilized for determination of the dosimetric characteristics of various source types and models. Dose distributions around brachytherapy sources with active lengths ≤1.0cm are nearly spherical (figure 8A). Therefore, use of a polar coordinate system in the TG-43 and TG-43U1 recommendations is a logical choice for these sources [45, 46]. However, dose distribution around elongated sources, such as RadioCoil™^{103}Pd (1.0cm to 6.0cm) is cylindrical in nature (figure 8B) and dictates that use of spherical coordinates may lead to large discrepancies.

Awan *et al.* showed that TG-43U1 dosimetric parameters in polar coordinate system are not optimum for calculation of dose distribution around elongated brachytherapy sources [72]. Therefore, a different approach may be needed to accurately calculate dose around elongated brachytherapy sources. They introduced modified TG-43U1 parameters for calculation of dose distribution around elongated sources.

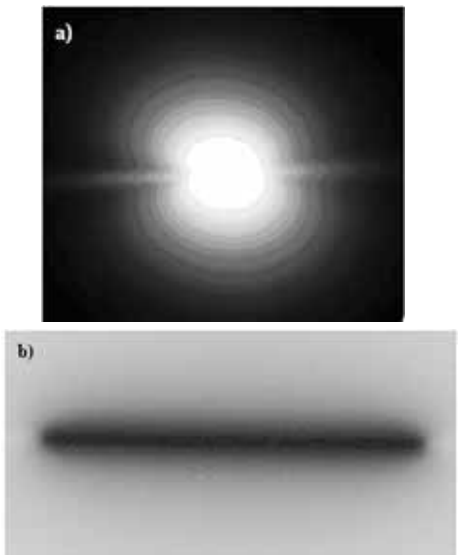

Figure 8. Auto radiographs of a conventional seed type source (A) and a 5.0cm long RadioCoil™^{103}Pd linear source (B).

TG-43U1 DOSIMETRY FORMULISMS MODIFIED IN CYLINDERICAL COORDINATES

As an alternative approach, Awan *et al.* introduced TG-43U1 parameters modified in cylindrical coordinates systems. The cylindrical coordinate based formalism allows calculation of 2D anisotropy function as close as the surface of the source, and facilitate the interpolation and extrapolation of this parameter for dose calculation purpose. In addition, they demonstrated the advantages of these formalisms relative to the polar coordinate system. The cylindrical coordinate formalisms make a significant improvement on the dosimetric evaluation of elongated sources. However, the similarity in the mathematical description with the polar coordinate based formalism should facilitate its adoption in the treatment planning systems. In addition, the application of the cylindrical coordinate based TG-43U1 formalism could be extended for the dosimetric evaluations at close vicinity of the conventional seed type sources.

$$Z = r \cos(\theta) \quad (9)$$

$$R = r \sin(\theta) \quad (10)$$

The main formalism for 2D dose calculation in the two coordinate systems is shown below:

$$\dot{D}(R,Z) = S_K \cdot \Lambda \cdot \frac{G(R,Z)}{G(R_o,Z_o)} \cdot g(R) \cdot F(R,Z) \quad (11)$$

Where, R_o=1.0cm, and Z_o=0 are the values of coordinates of reference points in the two systems. Dose rate constants in polar and cylindrical coordinate systems are defined in equation 12.

$$\Lambda_{cyl} = \frac{\dot{D}(R = 1cm, Z = 0)}{S_K} \quad (12)$$

Where P(r=1.0cm, =90 deg) is the same as P(R=1.0cm, and Z=0). Therefore, the dose rate constants in these two systems are the same. Radial dose function in cylindrical coordinate system is presented in equation 13.

$$g_L^{cyl}(R) = \frac{\dot{D}(R,Z_o)G(R_o,Z_o)}{\dot{D}(R_o,Z_o)G(R,Z_o)} \quad (13)$$

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Geometry function in cylindrical coordinate system is given as follows:

$$G_{cyl}(R,Z)=\frac{\tan^{-1}[(Z+L/2)/R]-\tan^{-1}[(Z-L/2)/R]}{R.L} \quad (14)$$

For the points falling on the longitudinal axis of the source, (R= 0 in cylindrical coordinate system) this equation will simplify to:

$$G_{cyl}(0,Z)=\frac{1}{Z^2-(L/2)^2} \quad (15)$$

2D anisotropy function of brachytherapy sources in cylindrical coordinate systems is defined in equation 16.

$$F_{cyl}(R,Z)=\frac{\dot{D}(R,Z)G(R,Z_o)}{\dot{D}(R,Z_o)G(R,Z)} \quad (16)$$

Considering the relation between the polar and cylindrical coordinate systems shown in equations 1 and 2, one can show that the geometry function, radial dose function, and dose rate constant are the same.

CONCLUSION

Within the last decade, brachytherapy treatments have been widely expanded for management of various tumor sites such as prostate, breast, and cervix. The success of this treatment modality is partially attributed to the advancement of dosimetric evaluation of brachytherapy sources and treatment procedures. The original and updated recommendations by task group 43 (TG-43) of the American Association of Physicists in Medicine (AAPM) are the foundation of present brachytherapy source dosimetry procedures. These protocols have been extensively utilized for determination of the dosimetric characteristics of various source types and models with active lengths ≤1.0cm. The original TG-43 protocol introduced in 1995 was based on recommendations of the Interstitial Collaborative Working Group (ICWG) and contained limited published dosimetric data. An update to the TG-43 protocol (TG-43U1) was introduced in 2004 as a result of technological developments and the introduction of new source models.

Dose distributions around brachytherapy sources with active lengths ≤1.0cm are nearly spherical (figure 8 A). Therefore, use of a polar coordinate system in the TG-43 and TG-43U1 recommendations is a logical choice for these sources. However, this concept has not been fully explored for elongated brachytherapy sources (i.e. Active length >1 cm). This lack of information is a hindrance for clinical application of elongated sources such as recently introduced RadioCoil™ ^{103}Pd sources by RadioMed™ Corporation (One Industrial Way, Tyngsboro, MA). Awan *et al.*, evaluated the use of TG-43U1 recommended parameters in a polar coordinate system for dosimetric characterization of a 5.0cm long RadioCoil™ ^{103}Pd source. The results indicated that the use of TG-43U1 recommendations lead to discrepancies of up to 30% as compared to the Monte Carlo simulated data. These differences were attributed to the limited data points for the 2D anisotropy function and inadequacy of the linear interpolation technique for dose distribution around an elongated source with this limited data. These discrepancies were reduced to about 10% by using smaller radial increments for F(r, θ) but could not be reduced to the TG-43U1 recommended 2% error using a reasonable number of radial increments. Figure 8B shows that the pattern of radiation distribution around an elongated brachytherapy source is not spherical. Hence, the use of polar coordinate based parameterization may not be the most effective system to implement for these sources. In this project, dosimetric characteristics of 1.0cm 3.0cm and 5.0cm long RadioCoil™ ^{103}Pd sources were determined using the cylindrical coordinate based TG-43U1 formalism.

In summary, cylindrical coordinate based TG-43U1 recommended dosimetric characteristics are more suitable and better represent the dose distribution around elongated sources. The advantages of these formalisms relative to the polar coordinate

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system have also been confirmed by Awan *et al.* [72]. They demonstrated that, the cylindrical coordinate formalisms make a significant improvement on the dosimetric evaluation of elongated sources. However, the similarity in the mathematical description with the polar coordinate based formalism should facilitate its adoption in the treatment planning systems. In addition, the application of the cylindrical coordinate based TG-43U1 formalism could be extended for the dosimetric evaluations at close vicinity of the conventional seed type sources.

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