# Comparison between the Use of Loose and Stranded Seeds in Prostate Brachytherapy in Brazil

Fernando S. Peleias Jr., Carlos A. Zeituni, Elisa C. M. Rostelato, Carla D. Souza, Fabio R. Mattos, Marcos A. G. Benega

Nuclear and Energy Research Institute (IPEN/CNEN-SP), São Paulo, Brazil Email: fspeleias@ipen.br, czeituni@ipen.br, elisaros@ipen.br, carladdsouza@yahoo.com.br, fabiormattos@hotmail.com, marcosagbenega@gmail.com

Received August 5, 2012; revised September 11, 2012; accepted September 18, 2012

# ABSTRACT

Cancer is a leading cause of death worldwide. In 2030, 26.4 million new cases will be diagnosed, with 17 million deaths accounted worldwide. Prostate cancer is the sixth most common type in the world, and the second most commom in men. For Brazil, the number of new cases of prostate cancer in 2010 is estimated to 52,350. Treatment of prostate cancer may be by surgery, radiation or even vigilant observation. A method of radiotherapy which has been extensively used is brachytherapy, where Iodine-125 seeds are placed inside or next to the area requiring treatment. Iodine seeds can be introduced loose seeds or stranded in bioabsorbable polymers in order to increase the dosimetric coverage of the prostate and reducing the chance of seed migration. Data were gathered concerning the commercialization of loose seeds and stranded seeds, between 2005 and 2011, in Brazil. It was noted that the number of stranded seeds commercialized in Brazil (around 80%) has always been much greater than the number of loose seeds, reaching 90% last year. The main reason is the reduction of the seed migration events into other parts of the body, since there is a potential hazard even considering that no harmful effect has been observe. The data regarding dosimetry are still controversial, since the seeds that migrate is normally no more than 1%.

Keywords: Cancer; Prostate; Brachytherapy; Iodine-125 Seeds; Loose Seeds; Stranded Seeds

## **1. Introduction**

According to World Health Organization (WHO), it is a leading cause of death worldwide. Only in 2007, 12 million new cases of cancer were diagnosed and a total of 7.9 million deaths were accounted, about 13% of worldwide deaths [1,2]. The continued ageing and population growth will affect significantly the impact of cancer in the world. This impact will fall most heavily on countries of medium and low development [1]. Recent studies carried out by the International Agency for Research on Cancer (IARC) estimates that in 2030 will be 26.4 million new cases diagnosed, with 17 million deaths accounted worldwide [3]. The most incidents, excluding non-melanima skin cancer are prostate and lung cancer in males and breast and cervical cancer in females [1].

Prostate cancer is the sixth most common type in the world, representing about 10% of all cases of cancer [1,2]. Its incidence rate is about six times higher in developed countries compared to developing countries [1]. Prostate cancer is the second most common cancer in men, with an estimated 1.5 million diagnoses in recent years. It is also considered cancer of the elderly, since

about three-quarters of the cases occur among patients 65 years old or over [1,4-6]. For Brazil, the number of new cases of prostate cancer in 2010 is estimated to 52,350. This corresponds to an estimated risk of 54 new cases per 100,000 men [1].

Treatment of prostate cancer may be by surgery, radiation or even vigilant observation [4]. A method of radiotherapy which has been extensively used in the early and intermediate stages of the illness is brachytherapy, where radioactive seeds are placed inside or next to the area requiring treatment, which reduces the probability of unnecessary damage to surrounding healthy tissues [7-9]. The seeds have quite small dimensions and all are composed of a titanium capsule with 0.8 mm of outer diameter, 0.05 mm of wall thickness and 4.5 mm long [10-12]. The typical activity of seeds of iodine-125 is 0.5 mCi (18.50 MBq) [13].

Iodine-125 seed permanent implantation features a number of advantages over traditional methods because it is related with low rates of sexual impotence and urinary incontinence, and patients can return to normal activity, including work, within one to three days with little or no pain [14].



The introduction of seeds can be done according with various techniques. It can be used loose seeds, which are inserted with a special applicator, it can be used separated seeds, pre-loaded in needles with spacers, and finally, seeds can be placed stranded in bioabsorbable polymers using most commonly, the biopolymer polyglactin 910, with coverage of polyglactin 370 (Vicryl<sup>®</sup>) [15]. The biopolymer has two main roles: increase the dosimetric coverage of the prostate, reducing the chance of urinary incontinence, and migration from places where the seeds are supposed to stay. The latter is the main advantage, since the introduction of loose seeds within the patient's body might cause problems if the seed falls into the bloodstream and migrate to other organs and healthy tissues, damaging it and bringing problems [16-18].

The **Figure 1** shows two models of loose seeds and one model of stranded seeds.

Although stranded seeds show a couple of advantages, its use is not exclusive and generates controversy among physicians [19-24]. This paper aims to compare the use of loose and stranded seeds in the Brazilian scenario.

#### 2. Methods

Data were gathered concerning the commercialization of



Figure 1. Comparison between different models of iodine-125 seeds each mark represents 1 mm.

loose seeds and stranded seeds, between 2005 and 2011, by the Nuclear and Energy Research Institute (IPEN), which is responsible for the distribution of all seeds used in Brazil.

### 3. Results and Discussion

The data collected are shown in the Figure 2.

It is observed that the number of stranded seeds commercialized in Brazil (around 80%) has always been much greater than the number of loose seeds. This number has risen even more and reached more than 90% of the Brazilian market last year. Physicians tend to prefer stranded seeds precisely by the reduction of the possibility of seed migration. Such event, in theory, could affect the dosimetry of the region and also cause unnecessary damage to healthy tissues or organs. In a workshop about New Trends in Brachytherapy held in Nuclear and Energy Research Institute (IPEN/CNEN-SP) Dr. Brian J. Davis, presented a paper containing the **Figure 3** below [25], which shows the impact of loose/stranded/mixed implants in the migration of the seeds.

It is noted that, when using loose seeds, 46% of patients had had seed migration, and the chance of each seed to migrate was 0.75%. Using mixed (loose and stranded seeds), the number of patients that had shown seed migration had decreased to 10.3%, and the chance of each seed to migrate was 0.12%. Finally, using exclusively stranded seeds, only 1.4% of patients had shown seed migration and the chance of each seed to migrate was 0.02%. Most seeds that migrate end up stuck into the pulmonary vasculature, but it has been reported cases of migration to the right ventricle and coronary artery [26-28]. No data concerning the details of the population studied, like age, body mass index, prostate size, and biochemical recurrence was available.



Figure 2. Loose and stranded seeds commercialized in Brazil from 2005 until 2011.



#### Seed Migration: Loose, Mixed, Stranded Implants

Figure 3. Comparison between seed migration in loose, mixed and stranded implants [25].

As the number of seeds that migrate is normally no more than 1%, the efficacy of treatment will hardly be impaired [27]. However, although no harmful effect due to seed migration has been observed, the reduction of this occurrence is highly desirable for Brazilian physicians [26-28].

### 4. Conclusion

It can be concluded that the use of stranded seeds in Brazil is far superior to the use of loose seeds (more than 4 times). The main reason is the reduction of the seed migration events into other parts of the body, since there is a potential hazard, even considering that no harmful effect has been observe. The data regarding dosimetry are still controversial.

#### REFERENCES

- Brasil. Ministério da Saúde, "Estimativa 2010: Incidência de Câncer no Brasil/Instituto Nacional de Câncer," 2009. http://www1.inca.gov.br/estimativa/2010/estimativa2009 1201.pdf
- [2] World Health Organization (WHO), "Cancer," 2010. http://www.who.int/cancer/en
- [3] International Agency for Research on Cancer (IARC), "World Cancer Report 2008", 2008. http://www.iarc.fr/en/publications/pdfs-online/wcr/2008/ wcr\_2008.pdf
- Brasil. Ministério da Saúde, "Câncer de Próstata." http://www2.inca.gov.br/wps/wcm/connect/tiposdecancer /site/home/prostata
- [5] L. J. E. S. Vieira, et al., "Prevenção do Câncer de Próstata na Ótica do Usuário Portador de Hipertensão e Diabetes," *Ciência & Saúde Coletiva*, Vol. 13, No. 1, 2008. http://www.scielosp.org/scielo.php?script=sci\_arttext&pi d=S1413-81232008000100019

doi:10.1590/S1413-81232008000100019

- [6] R. Gomes, et al., "A Prevenção do Câncer de Próstata: Uma Revisão da Literatura," Ciência & Saúde Coletiva, Vol. 13, No. 1, 2008, pp. 235-246. doi:10.1590/S1413-81232008000100027
- [7] P. A. Balter; J. F. Aguirre and W. F. Hanson, "Practical Considerations for the Calibration of Low Energy/Low Activity Seeds," *World Congress on Medical Physics and Biomedical Engineering*, Vol. 4, 23-28 July 2000, pp. 2761-2764.
- [8] L. Zuofeng, "Monte Carlo Calculations of Dosimetry Parameters of the Urocor Prostaseed I-125 Source," *Medical Physics*, Vol. 29, No. 6, 2002, pp. 1029-1034. doi:10.1118/1.1478559
- [9] T. Romero, "Radioterapia Para Câncer de Próstata Ganha Prêmio International," 2009. http://www.diariodasaude.com.br/news.php?article=radiote rapia-cancer -prostata-ganharemio-internacional&id=4410
- [10] C. A. Zeituni, "Dosimetria de Braquiterapia," Ph.D Thesis, University of São Paulo, São Paulo, 2010. http://pelicano.ipen.br/PosG30/TextoCompleto/Carlos%2 0Alberto%20Zeituni\_D.pdf
- [11] M. E. C. M. Rostelado, "Estudo e Desenvolvimento de uma Nova Metodologia para Confecção de Sementes de Iodo-125 Para Aplicação em Braquiterapia," Ph.D Thesis, University of São Paulo, São Paulo, 2005. http://pintassilgo2.ipen.br/biblioteca/teses/23214.pdf
- [12] J. F. Williamson, "On the Dosimetric Influences of Air-Kerma Strength Calibration Geometry and Internal Source Structure for Pd-103 and I-125 Brachytherapy Sources," World Congress on Medical Physics and Biomedical Engineering, Vol. 1, 23-28 July 2000, pp. 368-371.
- [13] J. J. Blasko, M. J. Datolli and K. Wallner, "Prostate Brachytherapy," Smart Medicine, 1997.
- [14] C. A. Franca, et al., "The Seven-Year Preliminary Results of Brachytherapy with Iodine-125 Seeds for Localized Prostate Cancer Treated at a Brazilian Single-Center," *International Brazilian Journal of Urolpgy*, Vol. 33, No. 6, 2007, pp. 752-762. doi:10.1590/S1677-55382007000600003
- [15] J. Varregoso, "Braquiterapia Prostática," Acta Urológica, Vol. 23, 2006, pp. 21-30. http://www.apurologia.pt/acta/3-2006/braquit-prost.pdf
- [16] J. J. Batterman, *et al.*, "Results of Permanent Prostate Brachytherapy, 13 Years of Experience at a Single Institution," *Radiotherapy and Oncology*, Vol. 71, No. 1, 2004, pp. 23-28. <u>doi:10.1016/j.radonc.2004.01.020</u>
- [17] C. M. Agrawal and J. E. Lin, "Synthetic Bioabsorbable Polymers for Implants," ASTM Special Technical Publications, Pensilvânia, 2000. <u>doi:10.1520/STP1396-EB</u>
- [18] Inion Ltd., "Sport Medicine: General FAQ," Inion Ltd., London, 2012.
- [19] D. Fuller, J. J. Koziol and A. C. Feng, "Prostate Brachytherapy Seed Migration and Dosimetry: Analysis of Stranded Sources and Other Potential Predictive Factors," *Brachytherapy*, Vol. 3, 2004, pp. 10-19. doi:10.1016/j.brachy.2004.02.003

- [20] R. Lee, et al., "Radioactive Sources Embedded in Suture Are Associated with Improved Post-Implant Dosimetry in Men Treated with Prostate Brachytherapy," *Radiotherapy* and Oncology, Vol. 65, No. 2, 2002, pp. 123-127. doi:10.1016/S0167-8140(02)00305-5
- [21] H. Fagundes, *et al.*, "Transperineal TRUS-Guided Prostate Brachytherapy Using Loose Seeds versus Rapid Strand: A Dosimetric Analysis," *Brachytherapy*, Vol. 3, 2004, pp. 136-140. <u>doi:10.1016/j.brachy.2004.05.006</u>
- [22] I. Kaplan, *et al.*, "A Comparison of the Precision of Seeds Deposited as Loose Seeds versus Suture Embedded Seeds: A Randomized Trial," *Brachytherapy*, Vol. 3, No. 1, pp. 7-9. <u>doi:10.1016/j.brachy.2003.12.003</u>
- [23] V. R. Heysek, et al., "A Dosimetric Analysis of Unstranded Seeds versus Customized Stranded Seeds in Transperineal Nterstitial Permanent Prostate Seed Brachytherapy," Brachytherapy, Vol. 5, 2005, pp. 244-250. doi:10.1016/j.brachy.2006.08.003
- [24] K. A. Hinnen, et al., "Loose Seeds versus Stranded Seeds in I-125 Prostate Brachytherapy: Differences in Clinical Outcome," Radiotherapy and Oncolology, Vol. 96, No. 1,

2010, pp. 30-33. doi:10.1016/j.radonc.2010.02.012

- [25] C. C. Goulet, *et al.*, "Comparison of Seed Migration to the Chest after Permanent Prostate Brachytherapy with Loose Seeds, Stranded Seeds, or Both," *International Journal of Radiation Oncology*, Vol. 66, No. 3, 2006, p. 391. doi:10.1016/j.ijrobp.2006.07.732
- [26] E. M. Tapen, et al., "Reduction of Radioactive Seed Embolization to the Lung Following Prostate Brachytherapy," *International Journal of Radiation Oncology*, Vol. 42, No. 5, 1998, pp. 1063-1067. doi:10.1016/S0360-3016(98)00353-8
- [27] B. J. Davis, et al., "Prostate Brachytherapy Seed Migration to a Coronary Artery Found during Angiography," *The Journal of Urology*, Vol. 168, No. 3, 2002, p. 1103. doi:10.1016/S0022-5347(05)64589-2
- [28] B. J. Davis, *et al.*, "Prostate Brachytherapy Seed Migration to the Right Ventricle Found at Autopsy Following Acute Cardiac Dysrhythmia," *The Journal of Urology*, Vol. 164, No. 5, 2000, p. 1661. doi:10.1016/S0022-5347(05)67061-9