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BRAZILIAN DEMAND FOR IODINE-125 SEEDS IN CANCER TREATMENT AFTER A DECADE OF MEDICAL PROCEDURES

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ABSTRACT

Iodine-125 and palladium-103 are radionuclides employed to made medical devices used in cancer treatment known as brachytherapy seeds. These radioactive sealed sources are applied in brain and ophthalmic cancer as a temporary implant to irradiate the tumor, and in permanent implants to prostatic cancer. Brazilian Nuclear Energy Commission (CNEN) has the monopoly in Brazil of iodine-125 brachytherapy seeds distribution which is executed for Nuclear and Energy Research Institute (IPEN-CNEN/SP). Along a decade of use in Brazil more than 240 thousand seeds were implanted in patients or used to treat cancer tumors. In this article the Brazilian demand for iodine-125 brachytherapy seeds is analyzed. The demand behavior along a decade of using loose, strand, ophthalmic and brain brachytherapy seeds are shown. The annual quantity of seeds demanded by Brazil has dropped since 2012. The loose seeds which represented until 30% from total brachytherapy seeds used in Brazil decreased to less than 3%. The brain brachytherapy seeds had low demand along the decade and presented zero demand in several years. Concurrent treatment techniques are listed and main trends are discussed. The influence of Brazilian economic crisis and the demand behavior of the main hospitals and clinics that use iodine-125 brachytherapy seeds are shown.

1. INTRODUCTION

Brachytherapy seeds are medical devices used in cancer treatment. Iodine-125 and Palladium-103 are the main radionuclides used in brachytherapy seeds manufacture. These radionuclides have an appropriate combination between half-life and photons' energy to permanent implants into human body: 35.5 keV (6.68%)gamma ray, 27.4 keV (73.4%), 27.2 keV (39.4%), 31.0 keV (25.6%) and 3.7 keV (14.8%) X-rays; 59.4 days (iodine-125) and 20.2 keV (41.8%), 20.0 keV (22.09%), 22.7 keV (13.25%) and 2.7 keV (8.73%) X-rays; 16.99 days (palladium-103). The energy range from both of them allows maximum radiation dose distribution into target tissue, preserving healthy tissue around the tumor [1, 2].

Nuclear and Energy Research Institute (IPEN-CNEN/SP) is the unique distributor of brachytherapy seeds in Brazil. Nowadays, only iodine-125 seeds are demanded for hospitals and clinics in Brazil. There are four models of brachytherapy seeds available in Brazil:

1) Loose seeds: iodine-125 adsorbed onto a metal rod and encapsulated in a welded titanium capsule (0.8 mm diameter, 5 mm length), activity between 7.363 MBq (0.199 mCi) and 37.592 MBq (1.016 mCi);
2) Strand seeds: 10 loose seeds, spaced at a fixed distance within an absorbable braided polymer carrier;

3) Ophthalmic seeds: the same loose seed shape with activity of 208.68 MBq(5.640 mCi);
4) Brain seeds: the same loose seed shape with activity of 984.5 MBq (26.6 mCi) [3, 4, 5].

2. METHODOLOGY

The data comes from the Radiopharmacy Center Management System, a database from IPEN-CNEN/SP, where is recorded the brachytherapy seeds distributed to clinics and hospitals in Brazil.

3. RESULTS AND DISCUSSION

Fig. 1 shows the variation along the time to strand and loose type brachytherapy seeds commercialized in Brazil. There are 27 hospitals and clinics in Brazil which use strand or loose brachytherapy seeds, from which 20 use strand seeds, 11 use or used loose seed and 4 use or used both in a period of time.

The loose seeds which represented until 30% from total brachytherapy seeds used in Brazil decreased to less than 3%. This preference maybe explained by some studies reported incidence of seed migration to the chest, abdomen and pelvis after prostate brachytherapy. Comparisons between loose seeds versus strand seeds showed which loose seeds presented greater probability to migration than strand seeds [6, 7, 8].

Despite the high demand oscillation between the months in Fig. 1, the last months of the year present a decreased in demand, this seasonality is probably impacted by vacation taken by physicians and patients, and is according to hypothesis made in annual reports from brachytherapy seeds manufacturers [9, 10]. The annual quantity of seeds demanded by Brazil has dropped since 2012. While 36240 strand brachytherapy seeds were supplied in 2011, reaching the maximum distribution in a year, in 2016 only 15140 strand brachytherapy seeds were distributed. There are economic and concurrence reasons for this fall. Since 2011 Brazilian Gross Domestic Product (GDP) has decreased as economic crisis consequence, and there is not reimbursement for brachytherapy seeds treatment in Brazil, which is an opportunity to cheaper or refundable therapies. Some examples of treatment options for brachytherapy seeds are:

1) Radical Prostatectomy: complete surgical removal of the prostate gland, maybe executed with laparoscopy or robot;
2) External Beam radiation Therapy (EBRT): beam of radiation at the prostate gland from outside the body, Intensity Modulated Radiation Therapy (IMRT), Image Guide Radiation Therapy (IGRT),Volumetric Modulated Arc Therapy (VMAT), stereotactic radiotherapy and proton therapy are examples of EBRT;
3) Active Surveillance: to monitor the patient and determine when more active intervention is required;
4) New treatments: drugs, vaccines, focal cryotherapy, high-intensity focus ultrasound (HIFU) and other forms of radiation [9, 10, 11].

There are few studies comparing brachytherapy seeds with others types of treatment. However, the National Prostate Cancer Audit (NPCA) reports within one year in England and Wales, 10596 patients were treated with EBRT and 975 patients were treated with brachytherapy, 340 had both treatments. From whom treated with brachytherapy, approximately 66% (643 patients) were submitted to Low Dose Rate (LDR) brachytherapy, which uses implant seeds. Therefore, only 5.5% from patients were submitted to brachytherapy seeds treatment [12].

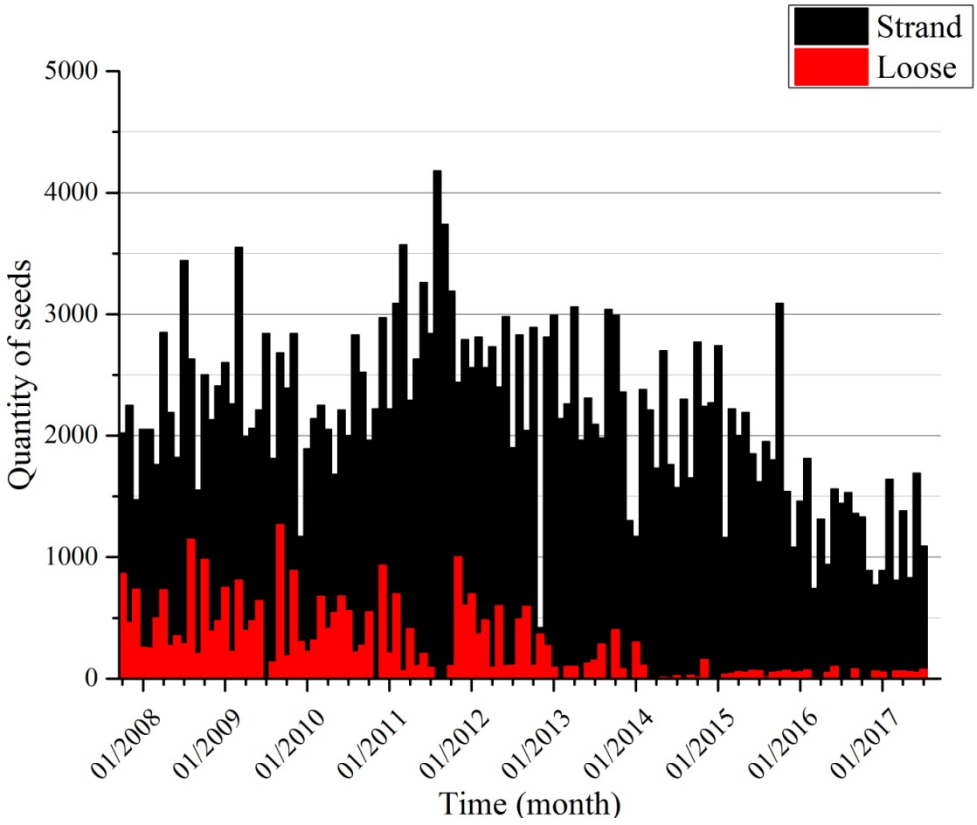

Figure 1: Strand and loose type brachytherapy seeds distributed in Brazil.

Fig. 2 shows the variation along the time to ophthalmic and brain brachytherapy seeds in Brazil. There are three hospitals in Brazil which use ophthalmic brachytherapy seeds, and there are two clinics in Brazil only which use brain brachytherapy seeds, all of them are located at São Paulo city.

The greatest demands for ophthalmic brachytherapy seeds happened in 2015 (384 seeds), 2014 (360 seeds) and 2016 (336 seeds) and, therefore, this segment of brachytherapy seed does not follow the same way than strand brachytherapy seeds, with a more stable trend. Differently from strand seeds which demand follows the number of patients, the ophthalmic seeds have the demand according the number of hospitals and clinics which provide cancer ophthalmic treatment using an eye plaque which support until 24 seeds.

The brain brachytherapy seeds had low demand along the decade, as portrayed in Fig. 2, and presented zero demand in 2009, 2013, 2015 and 2016. Brain brachytherapy with iodine-125 seeds is a complex medical procedure. The medical team inserts a 984.5 MBq (26.6 mCi) radioactive source into the patient's brain, which results in radiation exposure of medical team too.Techniques as IMRT and stereotactic radiotherapy have increased more the participation in treatment of brain tumors than brachytherapy seeds.

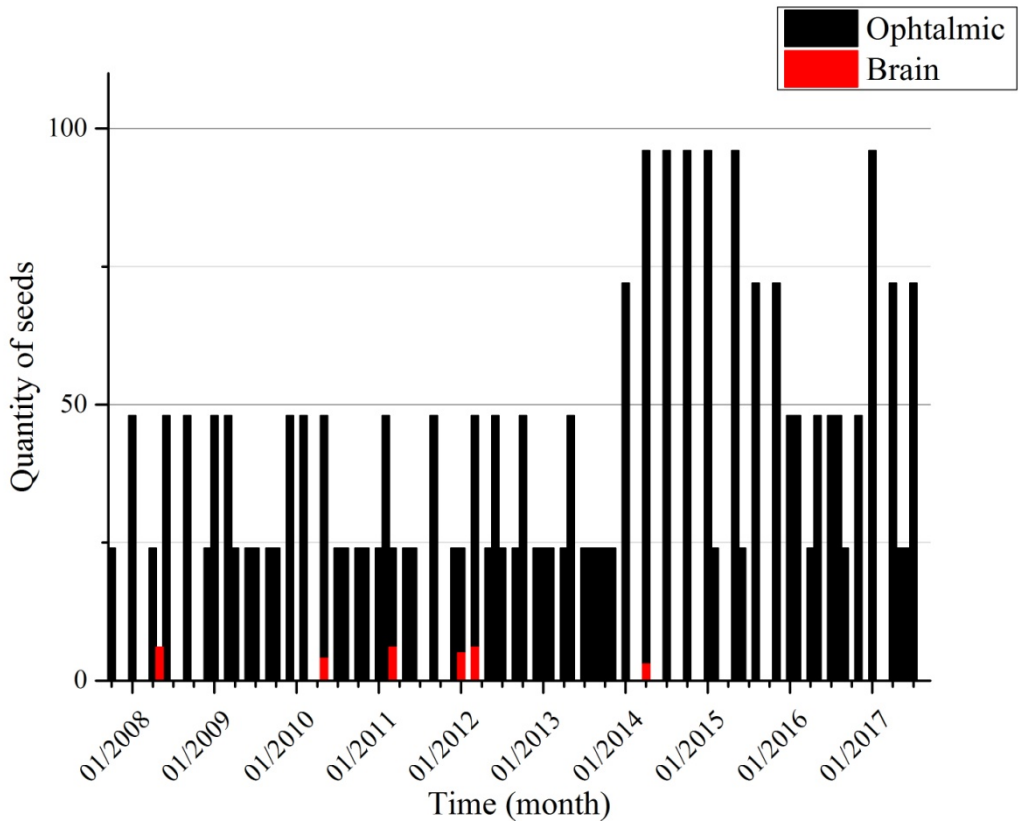

Figure 2: Ophthalmic and brain type brachytherapy seeds distributed in Brazil.

Fig. 3 shows the variation in quantity of brachytherapy seeds used by the top eight buyers hospitals and clinics in Brazil. The top eight buyers are concentrated in five cities: Campinas-SP, Juiz de Fora-MG, São Paulo-SP, Rio de Janeiro-RJ and Brasília-DF. The two clinics from Campinas-SP are noteworthy. Instituto Radium de Campinas is the top buyer of decade, more than 50000 brachytherapy seeds demanded and, Diagmed Clinic had an extraordinary growth during all the decade until become the leader in 2015 and 2016. The most of top eight buyers presented a decline between 2012 and 2016.

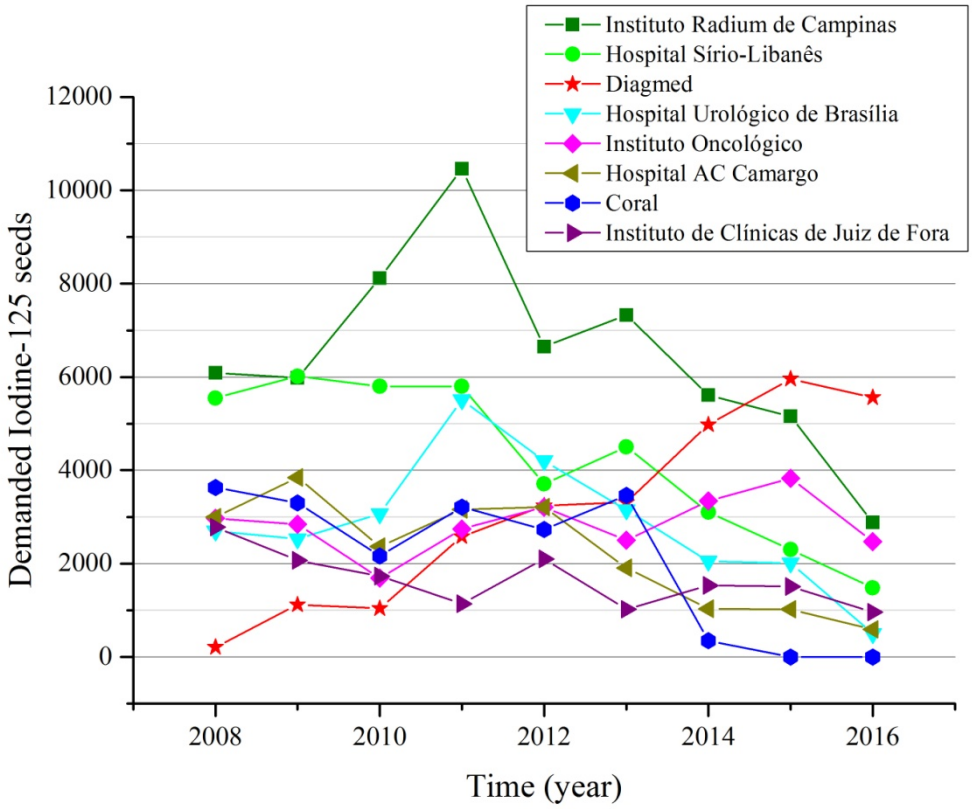

Figure 3: Brachytherapy seeds used by the top eight buyers hospitals and clinics in Brazil.

The Theragenics Corporation is a good visible example to analyze the brachytherapy seeds market. The company was founded in 1981 in USA, between 1987 and 2003 palladium-103 brachytherapy seeds were the only company product. Fig. 4 shows the revenue grew until 2001, when began to decrease until 2004. In 2004 Theragenics started the iodine-125 brachytherapy seeds production, with production line purchased from BEBIG Eckert & Ziegler. In 2005 Theragenics established in surgical products business with acquisition of CP Medical (manufacturer of products for wound closure and surgical devices) and started to diversify the product portfolio. The brachytherapy seeds revenue had an increase between 2004 and 2005, however presented a long drop between 2005 and 2010, reaching a more stable revenue between 2010 and 2012. In 2012 Theragenics acquired the Core's Oncology (a distributor of brachytherapy seeds and medical products) prostate brachytherapy customer base. Recently in 2016 acquired the US and Canadian brachytherapy seed business of BEBIG Eckert & Ziegler. While the brachytherapy seeds business decreased, Theragenics expanded your surgical products business with acquisition of Galt Medical in 2006 and the NeedleTech in 2008, presenting a great increase in the revenue between 2004 and 2010, and stability between 2010 and 2012 [9, 10, 13].

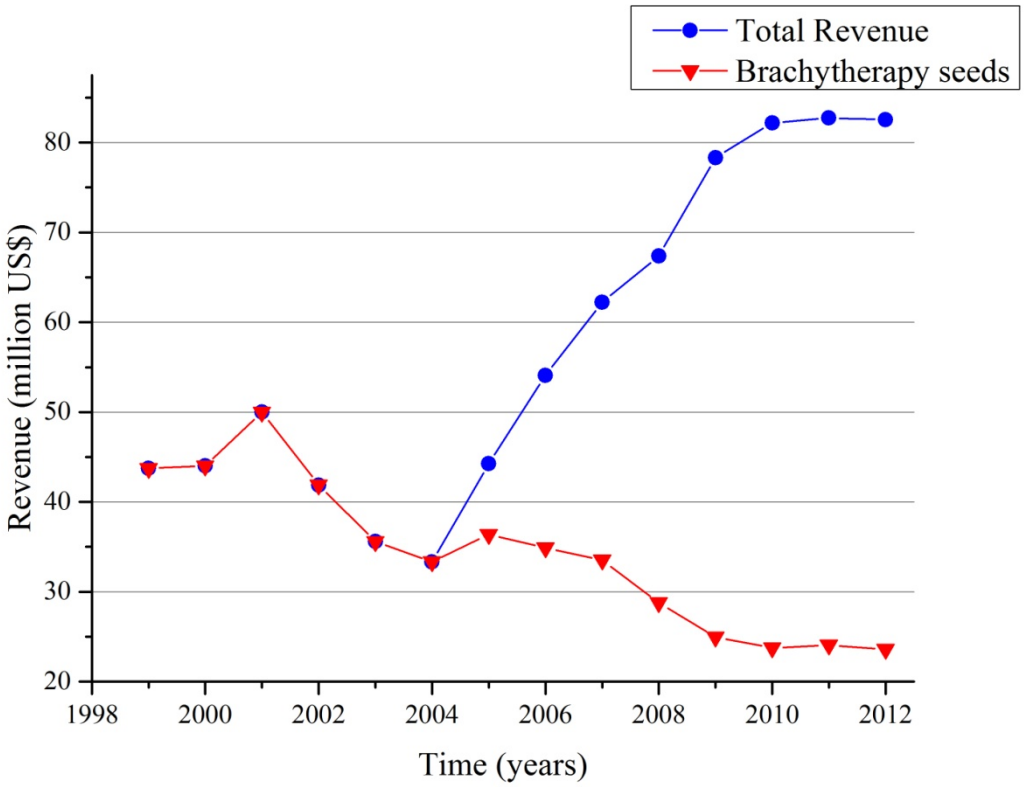

Figure 4: Theragenics revenue along the time, comparison between brachytherapy seeds revenue and total revenue.

3. CONCLUSIONS

The Brazilian demand for brachytherapy loose seeds had a great decrease along the last decade, and is losing the concurrence for strand seeds. The Brazilian demand for brachytherapy strand seeds had shown an increase until 2012, however started a decline and reached the worst demand level of decade in 2016.

The Brazilian demand for brachytherapy brain seeds have shown intermittent in the last decade and may disappear substituted by others medical procedures. The Brazilian demand for brachytherapy ophthalmic seeds have shown an increase in the last decade, with a small decrease between 2015 and 2016.

The brachytherapy seeds have been losing marketshare along the last decade for other types of therapies.

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REFERENCES

1. C. A. Zeituni; C. D. Souza; E. S. Moura; R. K. Sakuraba; M. E. C. M. Rostelato; A. Feher; J. A. Moura; S. Somessari; O. L. Costa, *Theoretical, Manufacturing and Clinical Application Aspects of a Prostate Brachytherapy I-125 Source in Brazil,* In: Dr. Kazuchi Kishi (Ed.), *Brachytherapy*, InTech (2012), https://www.intechopen.com/books/brachytherapy.
2. Isotope Browser, IAEA Nuclear Data Section, Android OS, v. 3.9.26, International Atomic Energy Agency (2017), https://play.google.com/store/apps/details?id=iaea.nds.nuclides&hl=pt-BR (2017)
3. Instituto de Pesquisas Energéticas e Nucleares IPEN-CNEN/SP, Produtos e serviços, https://www.ipen.br/portal_por/portal/produtos.php?secao_id=35&Area_atuacao=Sa%C3%BAde&Mercado=Braquiterapia (2017).
4. Instituto de Pesquisas Energéticas e Nucleares IPEN-CNEN/SP, Produtos e serviços comercializados pelo IPEN, https://www.ipen.br/portal_por/conteudo/institucional/arquivos/ipen-produtos_servicos_comercializados.doc (2017).
5. Best Medical International, Radioactive Seeds, http://www.bestmedical.com/product_seeds_ip.html (2017).
6. C. A. S. Franca; S. L. Vieira; A. C. P. Carvalho; A. J. S. Bernabe; A. B. R. Penna, Radioactive seed migration after prostate brachytherapy with iodine-125 using loose seeds versus stranded seeds", *Int. Braz. J. Urol.*, **Vol. 35**, n. 5, pp. 573-580, (2009).
7. D. R. Reed; K. E. Wallner; G. S. Merrick; S. Arthurs; A. Mueller; W. Cavanagh; W. B. Butler; E. Ford; S. G. Sutlief, "A prospective randomized comparison of stranded vs. loose 125I seeds for prostate brachytherapy", *Brachytherapy*, **Vol. 6**, n. 2, pp.129-134, (2007).
8. B. Al-Qaisieh; B. Carey; D. Ash; D. Bottomley, "The use of linked seeds eliminates lung embolization following permanent seed implantation for prostate cancer*", Int. J. Radiat. Oncol. Biol. Phys.*, **Vol. 59**, n. 2, pp. 397-399, (2004).
9. Theragenics Corporation, *2007 Annual Report on Form 10-K* (2008).
10. Theragenics Corporation, *2012 Annual Report on Form 10-K* (2013).
11. P. Vigneri; A. S. Herati; L. Potters, "The second decade of prostate brachytherapy: evidence and cost based outcomes", *Urologic Oncology: Seminars and Original Investigations*, **Vol. 28**, pp. 86-90, (2010).
12. National Prostate Cancer Audit, *Third Year Annual Report – Results of the NPCA Prospective Audit and Patient Survey*, The Royal College of Surgeons of England, London, https://www.npca.org.uk/annual-report-2016/ (2016).
13. Theragenics Corporation, *2003 Annual Report* (2004).