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LEAKAGE TEST EVALUATION USED FOR QUALIFICATION OF IODINE-125 SEEDS SEALING

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ABSTRACT

The prostate cancer is a problem of public health in Brazil, and the second cause of cancer deaths in men, exceeded only by lung cancer. Among the possible treatments available for prostate cancer is brachytherapy, in which small seeds containing Iodine-125 radioisotope are implanted in the prostate. The seed consists of a sealed titanium tube measuring 0.8 mm external diameter and 4.5 mm in length, containing a central silver wire with adsorbed Iodine-125. The tube sealing is made with titanium at the ends, using electric arc welding or laser process. This sealing must be leakage-resistant and free of cracks, therefore avoiding the Iodine-125 to deposit in the silver wire to escape and spread into the human body. To ensure this problem does not occur, rigorous leakage tests, in accordance with the standard Radiation protection - Sealed Radioactive Sources - leakage Test Methods - ISO 9978, should be applied. The aim of this study is to determine, implement and evaluate the leakage test to be used in the Iodine-125 seeds production, in order to qualify the sealing procedure. The standard ISO 9978 presents a list of tests to be carried out according to the type of source. The preferential methods for brachytherapy sources are soaking and helium. To assess the seeds leakage, the method of immersion test at room temperature was applied. The seeds are considered leakage-free if the detected activity does not exceed the 185 Bq (5 nCi). An Iodine standard was prepared and its value determined in a sodium iodide detector. A liquid scintillation counter was calibrated with the standard for seeds leakage tests. Forty-eight seeds were welded for these tests.

1. INTRODUCTION

The use of permanent implants of Iodine-125 seeds as a treatment of prostate cancer has increased with the introduction of new products and technological advances. The seed implants provide a less aggressive type of therapy than surgical procedures. A certain amount of seed is implanted in the patient using a fine needle through the skin to the prostate. A large dose of radiation is released only in the prostate where the tumor is, not affecting healthy organs nearby. The technique of brachytherapy requires an application that varies between 80 and 120 seeds [1].

As the occurrence of collateral effects is lower, 85% of patients up to 70 years old, remain sexually active after implantation. Also urinary incontinence rarely affects them [2].

The advantages of implants with radioactive seeds are the preservation of healthy tissues and organs near the prostate, the low rate of impotence and incontinence compared to conventional treatments, such as radical prostatectomy and external beam radiation [3,4].

For most patients, seeds implantation is a low impact procedure and not a surgery. The patient can return to normal activity within one to three days, with little or no pain.

The seeds are implanted during a non-surgical procedure. Small seeds are injected directly into the prostate, between the rectum and scrotum, using a fine needle through the skin [5,6]. A large dose of radiation is released only in the tumor, as Iodine-125 radiation has a low average energy (29 keV) that is slightly penetrating, thus preserving the surrounding tissue [7,8].

The seed consists of a sealed tube of titanium (biocompatible material to human tissue) measuring 0.8 mm external diameter and 4.5 mm in length, containing a silver wire with Iodine-125 adsorbed. The sealing of the titanium tube is made, at both ends, by welding process using electric arc or laser [9].

This sealing should be watertight, free from cracks, avoiding the Iodine-125 deposited in a silver wire to escape and spread through the human body.

To ensure this does not occur, rigorous leakage tests should be applied according to the standard procedures ISO 9978 – *Radiation protection - Sealed Radioactive Sources – Leakage Test Methods* [10].

Several procedures are described in the above standard and choice must be made using the table *Selection of leakage test methods related to manufacturing technology* [10].

2. METHODOLOGY

2.1. Materials

For the leakage tests of the seeds according to the standard ISO 9978 – *Radiation protection - Sealed Radioactive Sources – Leakage Test Methods*, 48 seeds were sealed using tubes of commercially pure titanium, grade 2 (CP Titanium GR2), manufactured by the company Accellent Endoscopy, outside diameter ranging from 0.790 to 0.808 mm and wall thickness ranging from 0.043 to 0.058 mm and initial length from 6.90 to 6.97 mm. Inside the tubes silver wires with Iodine-131 were used. It was used Iodine-131, that is produced at IPEN and has the same chemical behavior of Iodine-125. The radioisotope Iodine-131 has a half life of 8 days and energy of its main gamma rays are: 80.2 KeV (2.62%), 284.3 KeV (6.06%), 364.5 KeV (81.2%) e 636.4 KeV (7.27%) [11].

A liquid scintillation counter, brand Packard / Canberra, model Tri-Carb 1600 TR was used to determine the pattern of Iodine-131 and to carry out the leakage tests of the seeds.

2.2. Methods

The pattern aims to determine the region of the spectrum where is located the peak of Iodine-131 and quantified in counts per minute (cpm), the maximum activity allowed in the liquid, where the seeds had been washed after sealing. According to the standard ISO 9978, the maximum activity allowed in the sample liquid after washing is 185 Bq (≈ 5 nCi).

A sample of Iodine-131 produced in the reactor IEA-R1, was released in the chemical form of sodium iodide, with activity of 10.36 MBq (0.28 mCi) in a volume of 1 ml.

This sample was diluted in 200 ml of water purified by an ion exchange system of the brand Milli-Q, model Academic, resulting in pattern P1, with a specific activity of 51.8 KBq/ml (1.4 μCi/ml).

A sample of 1 ml was removed from the pattern P1 and added 99 ml of Milli-Q water, resulting in the pattern P2, with a specific activity of 518 Bq/ml (14 nCi/ml).

A sample of 350 μl was removed from the pattern P2 and it was obtained the pattern P3 with a medium value of (181.8 ± 4.8) Bq or (4.91 ± 0.13 nCi), measured in a dose calibrator type sodium iodide brand Capintec, model CRC 15W.

This pattern P3 was used for determining the reference value in counts per minute (cpm) in the scintillation liquid equipment.

As the value of the activity to be measured is small (less than 185 Bq (≈ 5 nCi)), two types of containers were tested, one of boron-silicate glass (Pyrex) and one of polyethylene, for counting the pattern P3, Milli-Q water BG and titanium BG samples.

The efficiency of the liquid scintillation counter for the pattern P3 was calculated, in the glass-boron silicate and polyethylene.

$$Efficiency \frac{cpm}{dpm} 100\% , \tag{1}$$

where dpm is the activity of P3 in disintegration per minute [11].

As the value obtained in cpm is relative to the pattern P3 (181.8 ± 4.8) Bq, the value in cpm for 185 Bq (≈ 5 nCi) was proportionally calculated.

The leakage test was chosen as the orientation provided in the Guide of the standard ISO 9978 that allowed the choice of tests to be performed according to the control and type of source.

As seen in TAB. 1, the sources for brachytherapy are classified as type A3 and the preferred tests are immersion (5.1) and helium (6.1) [10]. The immersion test, at room temperature (5.1), was chosen using an ultrasound to check the seeds leakage.

Table 1 - Selection of leakage test methods related to manufacturing technology [10].

Source type		Tests for production sources		Tests to establish classification of source	
		Preferred	2nd choice	Preferred	2nd choice
A	Sealed sources containing radioactive material	Immersion (5.1)	Wipe (5.3)	Immersion (5.1)	Wipe (5.3)
A1	Thin single integral window, e.g. smoke detectors				
A2	Low-activity reference sources, e.g. encapsulated in plastic				
A3	Single or double encapsulated sources (excluding ^{3}H, ^{226}Ra) for gauging, radiography and brachytherapy	Immersion (5.1) Helium (6.1)	Bubble (6.2)	Immersion (5.1) Helium (6.1)	Bubble (6.2)
A4	Single or double encapsulated ^{226}Ra and other gaseous sources	Gaseous emanation (5.2)	Immersion (5.1)	Gaseous emanation (5.2)	Immersion (5.1)
A5	Doublé encapsulated sources for teletherapy and high activity irradiation sources	Helium (6.1)	Wipe (5.3.2)	Immersion (5.1) Helium (6.1)	Bubble (6.2)
B	Simulated sealed sources			Immersion (5.1) Helium (6.1)	Bubble (6.2)
	Of Types A3, A4 and A5				
C	Dummy sealed sources			Helium (6.1)	Bubble (6.2)

Note: numbers between parentheses refer to tests of standard ISO 9978.

Forty-eight welded seeds were used to test the leakage of immersion, following the ISO 9978 standard procedure Each of the seeds was immersed, separately, in a vial containing a mixture of 8 ml distilled water and 2 ml of Extran detergent. The vials were placed on the equipment, cleaned by ultrasound for a period of 1 hour and left for another 24 hours at room temperature. After this time, the seeds were removed and, to the remaining liquid, 10 ml of scintillator solution (trade name Insta-Gel) was added; then, the activity of the radioactive solution was measured with a liquid scintillation counter.

The above procedure was repeated, except for the mixture of distilled water and detergent, which was replaced by 10 ml of distilled water only.

3. RESULTS

Table 2 - Pattern P3 measures in dose calibrator type sodium iodide.

Measures	Rating Bq	Rating nCi
1	182.0 ± 4.8	4.92 ± 0.13
2	180.1 ± 4.7	4.87 ± 0.13
3	186.9 ± 4.8	5.05 ± 0.13
4	180.2 ± 4.7	4.87 ± 0.13
5	179.7 ± 4.7	4.86 ± 0.13

In TAB. 2, the medium value activity of the pattern P3 was calculated and the following results were obtained: (181.8 ± 4.7) Bq (4.9 ± 0.13) nCi.

Table 3 - Pattern and BGs measures in the liquid scintillation counter, in boron-silicate glass and polyethylene containers (cpm).

Boron-Silicate Pattern P3	Polyethylene Pattern P3	Boron-Silicate Milli-Q Water BG	Milli-Q Water BG Polyethylene	Titanium BG Boron-Silicate	Titanium BG Polyethylene
6,158.3	6,294.0	51.8	51.8	49.2	50.0
6,227.3	6,355.3	46.2	49.6	47.6	48.2
6,203.6	6,322.9	46.2	51.8	53.2	54.8
6,180.9	6,118.7	54.8	50.0	50.2	50.4
6,148.3	6,276.1	46.4	50.6	48.2	51.4
6,187.1	6,281.6	43.2	48.8	52.0	48.8

In TAB 3, the medium value of the countings for the pattern P3, Milli-Q water BG and titanium BG were evaluated and the following results were obtained:

- Pattern P3 in boron-silicate glass - 6,184.3 cpm;
- Pattern P3 in polyethylene - 6,274.8 cpm;
- Milli-Q Water BG in boron-silicate glass - 48.1 cpm;
- Milli-Q Water BG in polyethylene - 50.4 cpm;
- Titanium BG in boron-silicate glass - 50.1 cpm;
- Titanium BG in polyethylene - 50.6 cpm.

The value obtained with the container of polyethylene was used because it presented better efficiency, 57.5% (1) with the liquid scintillation counter.

As the value obtained in cpm matches the pattern P3, it was calculated proportionally to the amount 185 Bq (≈ 5 nCi) and the following results were obtained:

- 181.8 Bq (≈ 4.9 nCi) - 6,274.8 cpm
- 185.0 Bq (≈ 5.0 nCi) - 6,385.2 cpm

Out of safety, 6,350 cpm was taken as the maximum value allowed for Iodine-131, contained in the liquid scintillator.

Table 4 - Leakage test of the 48 seeds (1st cleaning)

Seed	Liquid remainder (cpm)	Seed	Liquid remainder (cpm)
1	213.2	26	785.4
2	1,284.8	27	1,136.6
3	521.8	28	1,174.0
4	654.8	29	815.0
5	709.6	30	1,435.0
6	685.4	31	872.2
7	984.6	32	4,399.8
8	1,037.6	33	6,530.0
9	806.4	34	2,039.8
10	518.0	35	2,524.8
11	455.2	36	737.4
12	655.8	37	1,837.6
13	498.0	38	726.8
14	699.2	39	1,315.4
15	1,221.4	40	1,346.6
16	990.6	41	2,234.6
17	1,272.2	42	1,776.2
18	1,527.0	43	1,419.2
19	2,373.8	44	10,258.4
20	5,790.8	45	3,145.4
21	2,359.0	46	1,332.2
22	671.0	47	2,304.6
23	1,291.0	48	1,722.4
24	3,026.8	Milli-Q Water BG	47.6
25	2,465.8	Titanium BG	50.2

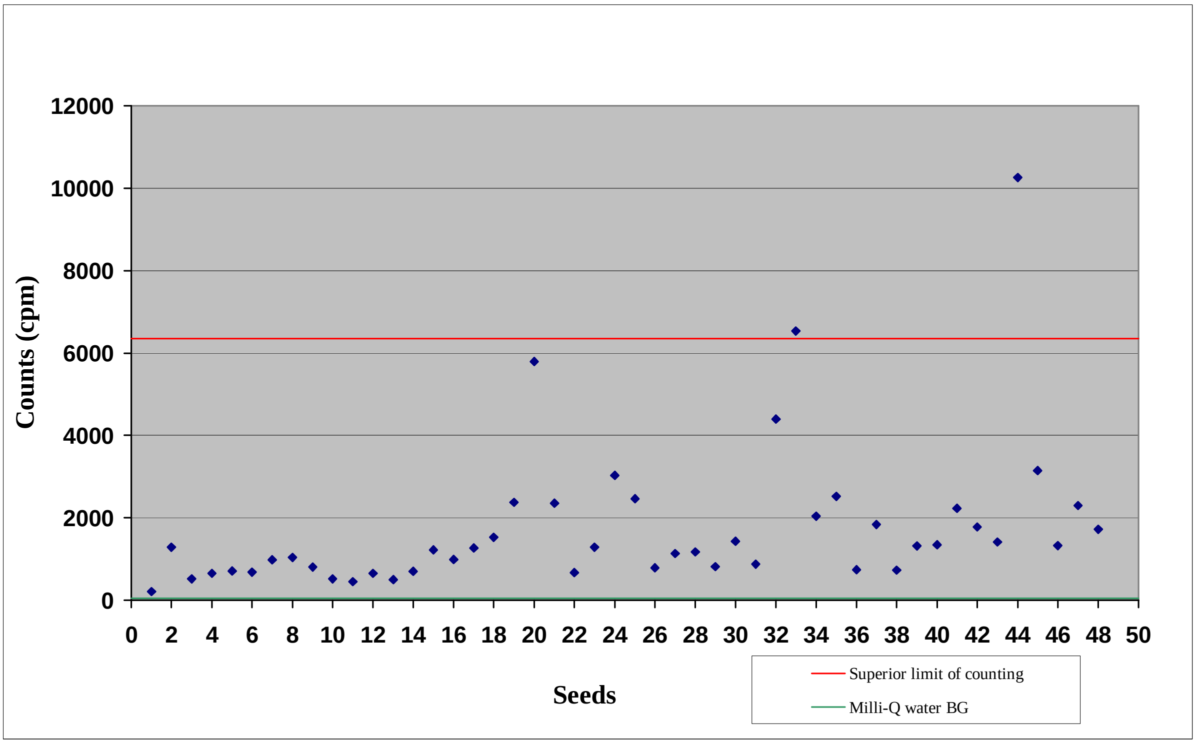

Figure 1 - Activity in water after leakage test (1st cleaning).

After the first cleaning, as showed in TAB. 4 and in FIG. 1, a large variation in the values of the radioactivity counts of the remaining liquid occurred, since they were below the limit of 6,350 cpm, except for the seeds numbers 33 and 44. The range indicates the need for a greater number of cleaning procedures.

In TAB. 5, below, the values obtained in leakage tests, after the 2nd cleaning, may be seen.

Table 5 - Leakage test of the 48 seeds (2nd cleaning).

Seed	Liquid remainder (cpm)	Seed	Liquid remainder (cpm)
1	70.0	26	59.4
2	69.2	27	66.0
3	65.0	28	59.6
4	63.4	29	66.6
5	60.0	30	73.8
6	68.6	31	76.0
7	68.2	32	59.4
8	69.2	33	4,687.8
9	58.6	34	67.4
10	66.6	35	67.8
11	63.4	36	68.2
12	66.4	37	70.6
13	63.6	38	70.6
14	73.4	39	66.4
15	69.4	40	95.4
16	71.0	41	67.0
17	89.8	42	64.2
18	67.2	43	64.0
19	71.0	44	695.0
20	146.8	45	138.8
21	69.2	46	65.6
22	62.6	47	69.0
23	61.4	48	106.2
24	58.2	Milli-Q Water BG	62.0
25	63.8	Titanium BG	47.8

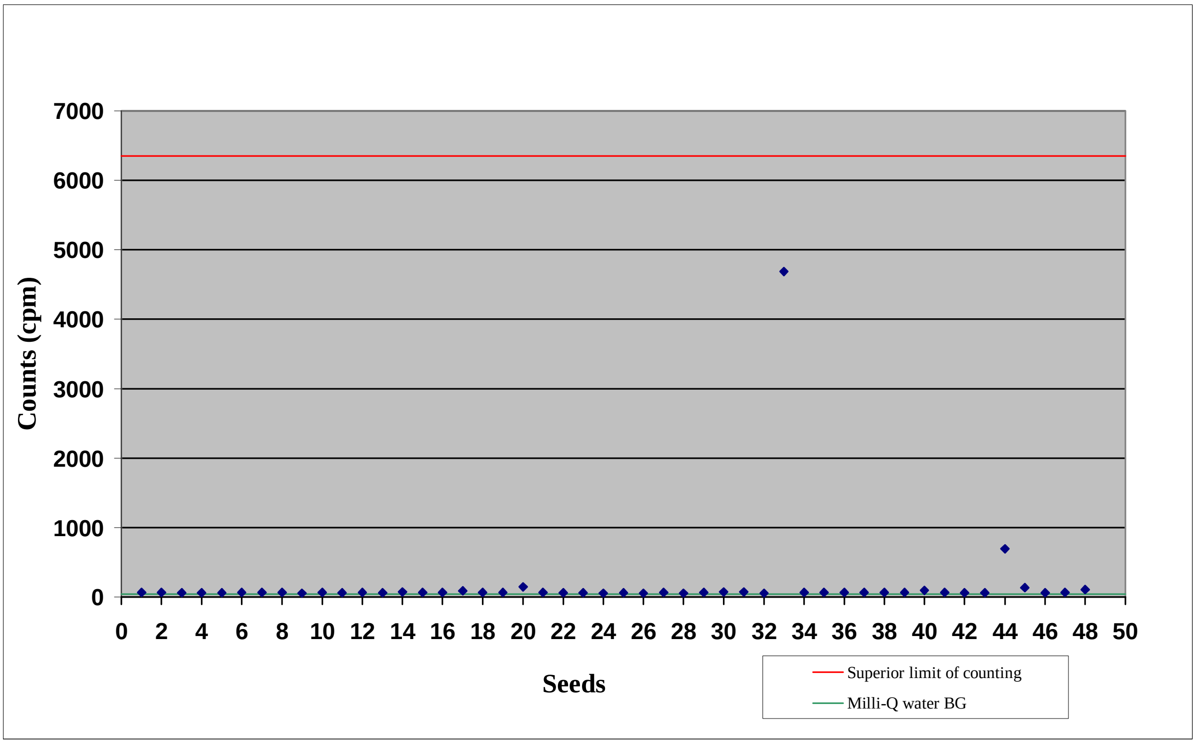

Figure 2 - Activity in water after leakage test (2nd cleaning).

After the second cleaning, it can be observed in FIG. 2 that the values of the counts of the liquid remaining seeds were much lower than 6,350 cpm, including the values of seeds 33 and 44. Some values were close to the Milli-Q water BG.

With the counting of the liquid still remaining high, seed nº 33 and other seeds that were close to a value above 100 cpm were separated and submitted to a further leakage test, as shown in TAB. 6.

Table 6 - LeakageTest of the 5 seeds (3rd cleaning)

Seed	Liquid remainder (cpm)
20	116.4
33	309,920.0
44	107.6
45	72.2
48	67.0
Milli-Q Water BG	52.2
Titanium BG	49.7

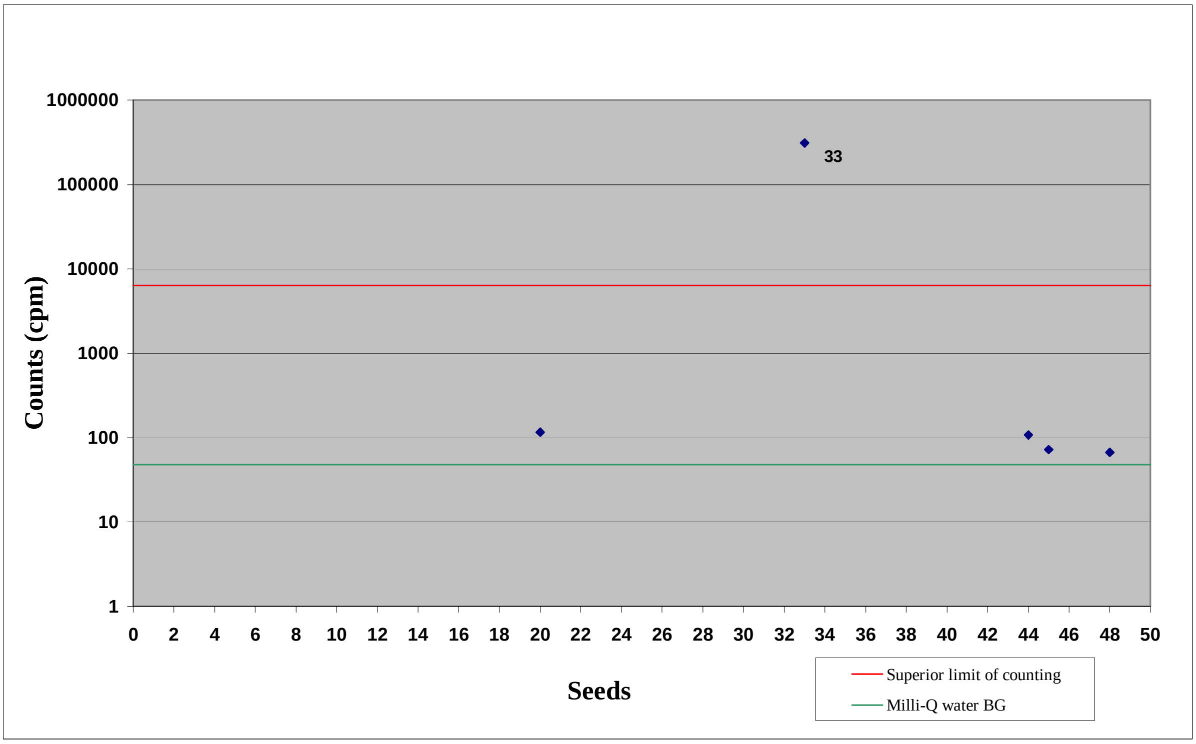

Figure 3 - Activity in water after leakage test (3^{rd} cleaning).

In FIG. 3, the counts values of the liquid remaining after the third leakage test were below the limit. However, the count value of the liquid of the seed 33 increased drastically and exceeded the limit determined by the standard ISO 9978, confirming a leak.

4. CONCLUSIONS

The procedure used to verify the leakage of the 48 seeds proved to be efficient in relation to approval criteria described in the standard for immersion tests.

It could be determined the need to apply this method, at least three times, for each batch of Iodine-125 seeds production.

The procedure used above should be part of the qualification tests of the sealing procedures to be used in the production of Iodine-125 seeds.

Other procedures of immersion test, described in ISO 9978, are recommended to determine which one presents better efficiency.

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