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Leakage test methodology development in iodine-125 seeds production

João Augusto Moura [1], Carla Daruich de Souza*,[1], Maria Elisa Chuery Martins Rostelato [1], Eduardo Santana de Moura [1], Francisco Edmundo Sprenger [1], Hélio Rissey Nagatomi [1], Carlos Alberto Zeituni [1], Anselmo Feher [1], José Eduardo Manzoli [1]

National Nuclear Energy Commission (CNEN), Energy and Nuclear Research Institute (IPEN), Radiation Technology Center-CTR, Professor Lineu Prestes Avenue, 2242 05508-000 São Paulo, SP, Brazil

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ABSTRACT

Brachytherapy using iodine-125 seeds has been used in prostate cancer treatment. In the quality control routine during seed production, leakage tests are taken to detect any leakage of radioactive material from inside the titanium shield, avoiding patient contamination. Leakage tests are carried out according to the International Standard Organization – Radiation protection – sealed radioactive sources – ISO 9978. This standard recommends different methods of essay applied to radioactive seeds. The aims of this work were the study of the different leakage test methods applied to radioactive seeds recommended by the ISO 9978 and the choice of the appropriate method to be used in the seeds production. The authors evaluated five different immersion methods to detect leakage, following the standard guidance, and in some case exceeding its requirement. One hundred iodine-125 seeds were intentionally cuted, causing the release of its content. Each immersion method was applied to twenty seeds. After the immersion period, the resulting liquid activity was measured. The activity values measured in the immersion liquid indicated best results with distilled water as immersion liquid and with the application of ultrasound to the bath. The temperature of the bath ranged from 20 °C to 70 °C and the immersion time ranged from 30 min to 24 h. In this experiment, the use of scintillator liquid as immersion liquid was not effective to detect the leakage. The results allow the authors to choose the best methods to be applied in the production routine, to detect leakage in the seeds. The choice of the method will also depend on the production rhythm for schedule. In a moderate production rate, the test at 20 °C and 24 h immersion may be used. In a fast production rhythm, the shortest test 50 °C or 70 °C should be used.

1. Introduction

Today cancer is the second cause of death by disease in several countries, including Brazil (World Health Organization (WHO) apud Ministério da Saúde, 1999). Excluding skin cancer, prostate cancer is the most incident in male population (Brasil. Ministério da Saúde. Instituto Nacional do Câncer, 2009). The prostate tumor may be treated by different methods, including brachytherapy. By this technique, small iodine-125 seeds are implanted in the prostate, giving a high radioactive dose to the target and preserving the healthy neighbor tissues (Okuno et al., 1982).

Iodine-125 seeds are used in the treatment of prostate cancer in Brazil, in private hospitals and clinics, and each implantation needs, at least, 80 seeds. The current national demand is about 8000 seeds per month (Rostelato, 2005). Today, a laboratory to produce the iodine seeds is in the implantation phase at the Energy and Nuclear Research Institute (IPEN), which belongs to the Nuclear Energy National Commission (CNEN). Iodine-125 has a half-life of 59.4 days and it emits gamma radiation with medium energy of 29 keV (Rostelato et al., 2008). The seeds to be produced at IPEN have a titanium shield with 4.5 mm length, 0.8 mm diameter and 0.05 mm thick wall, with a silver rod containing iodine-125 fixated on the surface. This silver core is placed inside the titanium shield. The titanium choice was made because of its biocompatibility. The

Abbreviations: CNEN, Comissão Nacional de Energia Nuclear (Brazil's National Nuclear Energy Commission); IPEN, Instituto de Pesquisas Energéticas e Nucleares (Energy and Nuclear Research Institute); CTR, Centro de Tecnologia Nuclear (Radiation Technology Center); ISO, International Standard Organization.

* Corresponding author.
E-mail addresses: jmoura31@yahoo.com.br (J.A. Moura), carladdsouza@yahoo.com.br (C. Daruich de Souza), elisaros@ipen.br (M.E. Chuery Martins Rostelato), esmoura@ipen.br (E. Santana de Moura), sprenger@ipen.br (F.E. Sprenger), hrnagato@ipen.br (H.R. Nagatomi), czeituni@ipen.br (C.A. Zeituni), afeher@ipen.br (A. Feher), jmanzoli@ipen.br (J.E. Manzoli).
[1] Tel.: +55 11 3133 9000; fax: +55 11 3133 9018.

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dimensions and other characteristics of this seed are coincident with the most used model in Brazil today. Fig. 1 shows a schematic drawing of the iodine-125 seed to be produced at IPEN (Rostelato, 2005).

For seed type sources capitulations, the titanium tube is welded using laser technology. This operation seals the radioisotope inside the titanium tube isolating it from the environment. Due to this fact, the seeds are classified as sealed radioactive sources. The shield allows the photons to pass through and prevent the radioisotope leakage. This condition should be verified in the final production step (quality control) by leakage tests, made according to the International Standard Organization. Radiation protection – leakage test methods – ISO 9978 standard (International Standard Organization, Feb. 15. 1992). The standard establishes the conditions and recommends the procedures to take leakage tests in sealed radioactive sources, including brachytherapy seeds. The recommended tests for brachytherapy sources are the immersion and the helium tests. The last one cannot be applied to the seeds because of their small internal volume. The immersion test uses distilled water as immersion liquid to contain the radioactive material that are release from the interior of the seeds. The activity of the water must be measured after the immersion period and the water activity must be lower than 185 Bq (5 nCi). Higher values indicate leakage and the source is not approved.

2. Objectives

The aim of this work is to make all the tests for sealed sources presented in ISO 9978 and compare the results, with the goal of select the best alternative to be implemented in the new brachytherapy sources production laboratory at IPEN.

3. Materials and methods

To determine what type of test would be the most adequate for iodine seeds production process, five recommended immersion tests were applied: Immersion in liquid scintillator; Immersion in distilled water at room temperature (20 °C) for 24 h; Immersion in hot water (50 °C) with ultrasound; Immersion in hot water (70 °C) with ultrasound; Immersion in boiling water. The following basic procedures were used for all the tests: Cleaning of the external surface of the seeds, to remove any radioactive contamination trace; Immersion of the source in the liquid for the determined time and temperature; Liquid removal; Measure of the liquid activity.

Each type of test was performed in 20 seeds, totalizing 100 seeds acquired in the market, similar to the model to be produced. Initially, each seed had its activity measured and was placed in a numbered plastic tube (1–100). The medium activity is 37.37 MBq. In the sequence, leakage was intentionally caused in each seed, through a little cut in the end of the titanium shield. A system made by a support and a diamond coated disk to make the cuts was used. Fig. 2 shows the system for cutting the seeds (a) and a schematic drawing of the operation (b). Fig. 3 shows a cuted seed. After each cutting, a careful cleaning in the cutting disk was made to prevent cross contamination. After cutting, each seed returned to its respective tube, with a rubber plug.

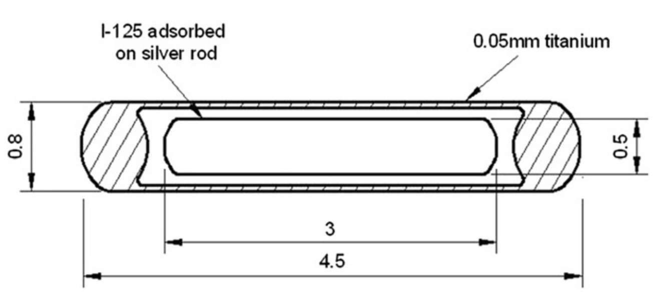

Fig. 1. Schematic drawing of the seed to be produced by IPEN (Rostelato, 2005). Dimensions in millimeter.

3.1. Description of the tests itinerary

The tests indicated by the ISO-9978 were made accordingly to the items that follow:

3.1.1. Test n° 1: Immersion in liquid scintillator

Tubes numbered 1 to 20, containing seeds, were filled with 10 ml of liquid scintillator, closed with a rubber tip and kept at room temperature (20 ± 5 °C) for 4 h. After that, the seeds were removed and the liquid activity was measured, using a liquid scintillator counter.

3.1.2. Test n° 2: Immersion in water at room temperature

Tubes numbered 21 to 40, containing seeds, were filled with 2 ml of distilled water, closed with a rubber tip and kept at room temperature (20 ± 5 °C) for 24 h. During the first 10 min of the immersion, ultrasound was applied to the tubes. After the immersion, the seeds were removed and the water activity was measured.

3.1.3. Test n° 3: Immersion in hot water (50°C)

Tubes numbered 41 to 60, containing seeds, were filled with 2 ml of distilled water, closed with a rubber tip and kept at 50 ± 5 °C for 4 h. During the first 30 min of the immersion, ultrasound was applied to the tubes. After the immersion, the seeds were removed and the water activity was measured.

3.1.4. Test n° 4: Immersion in hot water (70°C)

Tubes numbered 61 to 80, containing seeds, were filled with 2 ml of distilled water, closed with a rubber tip and kept for 30 min at 70 ± 5 °C. During all the immersion time it ultrasound was applied to the tubes after the immersion, the seeds were removed and the water activity was measured.

3.1.5. Test n° 5: Immersion in boiling water

The seeds from tubes numbered 81 to 100 were placed, each of them, in a becker containing 4 ml of distilled water. The becker was closed and heated until water boiling point for 10 min. After cooling, the boiling water was removed and reserved. The seeds were rinsed with distilled water and returned to the becker with the boiling water. This cycle was repeated twice, then the seeds were removed after cooling and the boiling water activity was measured.

For the activity measurement, CAPINTEC model CRC 15 W with sodium iodide detector and ionization chamber, liquid scintillator counter Packard/Canberra model Tri-Carb 1600 TR were used. For ultrasound application, AMSCO Reliance Sonic 75, 75 W, 40 kHz, with heating control was used. For immersion, distilled water and liquid scintillator Insta-gel, from Perkin Elmer were used. The cutting device used was BUEHLER–Isomet, with BUEHLER 11- 4244 disk, diameter 102 mm and width of 0.3 mm. The tests were made in sequence, in different dates. Due to the half-life of iodine-125 (59.4 days) the results were adjusted, based on the seeds activity measurement before cutting. To calculate the adjustment, the Equation (01) (Rostelato, 2005) was used:

$$A = A_0 \cdot e^{-\left(\frac{\ln 2}{T1/2}\right) \cdot \Delta t} \tag{1}$$

Where: A = current activity (Bq); A_o = initial activity (Bq); $T1/2$ = half-life of the isotope (days); Δt = time delay between the initial activity measurement and the current measurement.

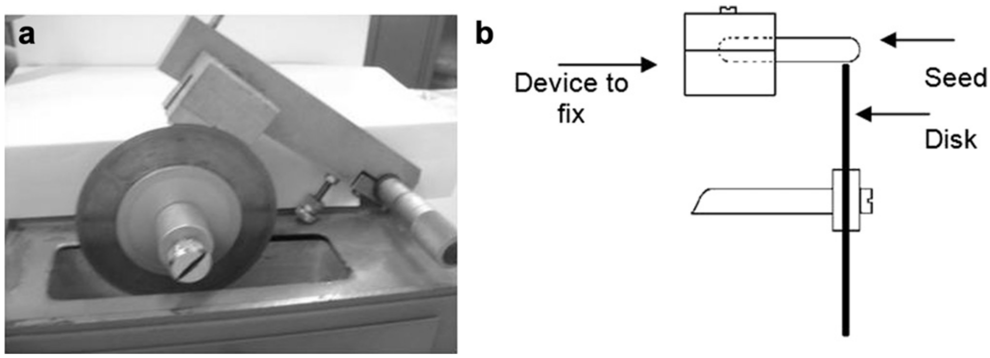

Fig. 2. Cutting system (a) and the cutting operation (b).

3.2. Uncertainty

The measurement purpose is to provide information about a quantity of interest, called measurand. For example, the measurand might be the volume of a vessel, the light intensity, or the radioactive activity (BIPM et al., 1993).

No measurement is exact. When a quantity is measured, the outcome depends on the measuring system, the measurement procedure, the skill of the operator, the environment, among other effects. Uncertainty of measurement is a parameter, associated with the result of a measurement, that characterizes the dispersion of the values that could reasonably be attributed to the measurand (BIPM et al., 1993).

When a measurement has more than one identifiable source of measurement uncertainty, then the combined uncertainty must be calculated. Calculating the combined standard uncertainty is a two-step process. The first step is to determine the uncertainties measured directly and the second step is combine the uncertainties using summation in quadrature (Equation (02)) (BIPM et al., 1993).

$$\text{Combined Uncertainty} = \sqrt{E1^2 + E2^2} \qquad (2)$$

where: E_1 = equipment error; E_2 = randomic error (random errors are errors in measurement that lead to measurable values being inconsistent when repeated measures of a constant attribute or quantity are taken) (BIPM et al., 1993).

4. Results

Results of the leakage tests carried out in 100 seeds with 5 different methods are shown in Table 1.

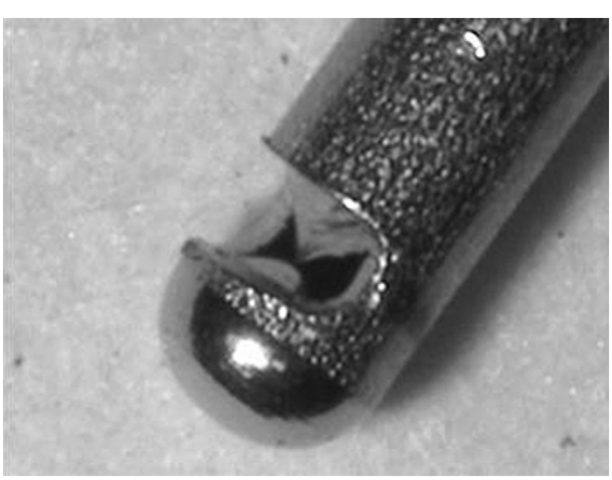

Fig. 3. Seed after cutting.

The values obtained with seeds n° 47 (58.9 Bq) and n° 60 (4.7 Bq) showed absence of leakage. Seed n° 47 was just scratched and seed n° 60 was not even scratched. During cutting, a deviation in the fixation device of the cutting system occurred, causing mispositioning of the seeds. The results confirm the condition of these two seeds. Fig. 4 show the images of seeds n° 47 (a) and n° 60 (b).

The values used to compare the methods are presented in Table 2. The limit for leakage detection is 185 Bq. The minimum value should be as far as possible otherwise a false negative can occurs. The data presented in Fig. 6 shows that the best result is with water with 20 °C. The scintillator and the boiling water tests have the worst results. The medium value was also used to compare the methods. The best result was with water 20, 50 and 70 °C. Again the scintillator and the boiling water tests end up with the worst results.Fig. 5.

5. Discussion

The test with scintillator liquid did not detect the leakage efficiently, and it will be discarded for this application. The test with boiling water presented many problems to be applied, including

Table 1
Results of the tests carried out in 100 seeds. Activity measured in the immersion liquid.

Seed n°	Activity KBq	Seed n°	Activity KBq	Seed n°	Activity KBq	Seed n°	Activity KBq
1	0.3102	6	0.4701	11	0.1980	16	0.5256
2	0.3565	7	0.7120	12	0.3023	17	0.7760
3	0.5465	8	0.6400	13	0.2261	18	0.6787
4	0.2945	9	0.6819	14	1.0940	19	0.6260
5	0.5861	10	0.8006	15	1.5161	20	0.1649
21	967.9	26	2852.0	31	2474.7	36	2731.9
22	1779.4	27	4225.7	32	1944.9	37	1596.0
23	3269.4	28	2976.1	33	1888.0	38	2486.3
24	934.3	29	2579.4	34	1660.6	39	1806.6
25	514.3	30	1860.9	35	1611.5	40	1373.7
41	121.2	46	4411.8	51	1417.6	56	219.0
42	127.5	47	0.0589	52	72.0	57	318.0
43	639.9	48	1683.8	53	2461.8	58	1558.5
44	360.9	49	1049.3	54	1699.3	59	581.5
45	756.2	50	1796.2	55	821.9	60	0.0047
61	581.8	66	2475.0	71	7925.7	76	227.2
62	247.1	67	1978.1	72	4053.0	77	2358.6
63	3149.6	68	1921.9	73	3442.5	78	643.3
64	739.0	69	2915.6	74	264.6	79	529.6
65	1247.3	70	5990.7	75	2672.4	80	175.8
81	68.0	86	61.0	91	47.7	96	49.8
82	110.8	87	52.2	92	74.4	97	147.8
83	63.8	88	103.3	93	139.1	98	76.8
84	76.7	89	69.3	94	72.8	99	85.8
85	95.2	90	107.7	95	64.2	100	101.4

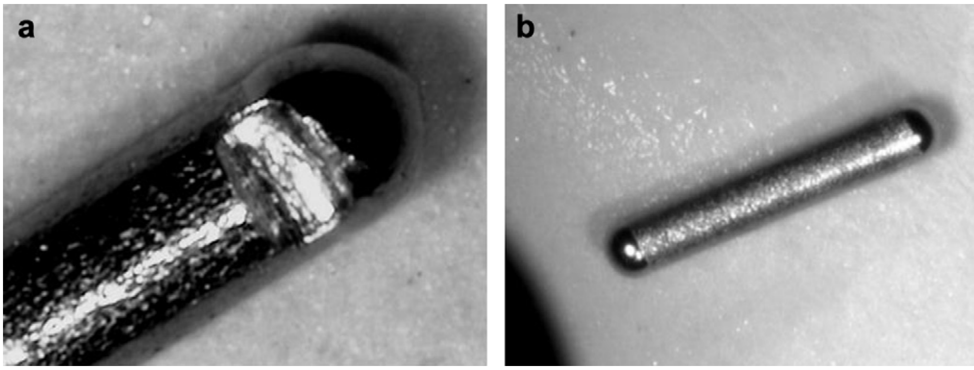

Fig. 4. Images of seeds n° 47 (a) and n° 60 (b).

Table 2
Medium and minimum values obtained in the different tests.

	Liquid scintillator	Water at 20 °C	Water at 50 °C	Water at 70 °C	Boiling water
Médium value (KBq)	0.575	2076.7	1116.4	2053.5	83.3
Minimum value (KBq)	0.164	514.3	71.9	175.8	47.6

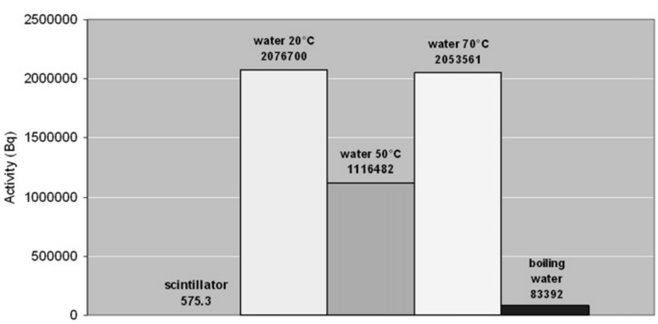

Fig. 5. Comparison between medium values obtained.

the higher temperature, evaporation, pressure inside the container and high energy needed to reach boiling water. Also, the results were not as good as the other methods. Due to these facts, this test will be discarded for this application.

ISO 9978 Standard recommends the application of ultrasound in the immersion test at 70 °C, not in the others. Due to the good results obtained applying ultrasound, it was included in the tests at 20 °C and 50 °C. All the procedures were added by this resource. This improvement exceeds the ISO 9978 requirements. The same ultrasound cleaning equipment will be used in both stages, initial washing and immersion stage.

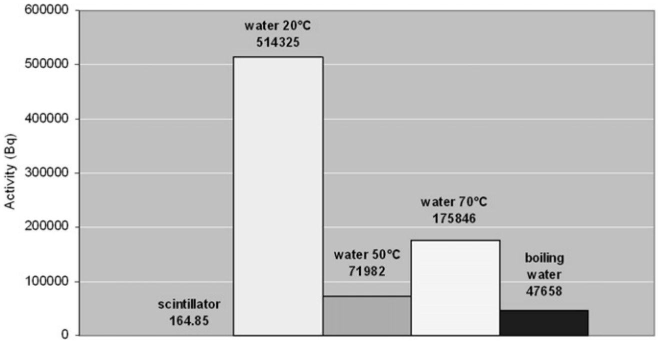

Fig. 6. Comparison between minimum values obtained.

To choose with method to implement in the production line, time is an important factor. The choice of the method will depend on the production rhythm. In a moderate production rate, the test at 20 °C and 24 h immersion may be used. In a fast production rhythm, the shortest (50 °C or 70 °C), should be used. This last method is under implementation at IPEN's laboratory.

To evaluate the uncertainty of the results, the measurement equipment error and randomic errors inherent to the process were considered, including those due to the operator. The values declared by the equipment supplier were adopted and to estimate the operator error, 2 series of 10 measurements with the same sample were made, by the same operator. The procedures were performed always using the same schedule. The results obtained were E_1 = equipment error: ±2% of measured value; E_2 = randomic error: ±0.82% of the measured value; Combined uncertainty: ±2.16% of the measured value (calculations followed Equation (02)). All of these errors are within the limits acceptable.

6. Conclusions

The best results and the indicated tests to be used in the seeds production are: Test with distilled water at room temperature (20 ± 5 °C), immersion during 24 h and application of ultrasound during the first 10 min of immersion; Test with distilled water at 50 ± 5 °C, immersion during 4 h and application of ultrasound during the first 30 min of immersion; Test with distilled water at 70 ± 5 °C, immersion during 30 min with simultaneous application of ultrasound. The choice of the method will depend on the production rhythm. According with the results, the test at 20 °C and 24 h immersion may be used in a moderate production rate. In a fast production rhythm, the shortest (50 °C or 70 °C), should be used.

References

BIPM, IEC, IFCC, ISO, IUPAC, IUPAP, OIML, 1993. Guide to the Expression of Uncertainty in Measurement, first ed., ISBN 92-67-10188-9

Brasil. Ministério da Saúde. Instituto Nacional do Câncer, 2009. Estimativa 2010: Incidência de câncer no Brasil. Rio de Janeiro (access date 30.10. 10.). <www.inca.gov.br>.

International Standard Organization, Feb. 15. 1992. Radiation Protection – Sealed Radioactive Sources – Leakage Test Methods (ISO 9978).

Okuno, E., Caldas, I.L., Chow, C., 1982. Física para ciências biológicas e biomédicas. Harper & Row do, Brasil. São Paulo.

Rostelato, M.E.C.M., 2005. Estudo e desenvolvimento de uma metodologia para confecção de sementes de iodo-125 para aplicação em braquiterapia Doctorate thesis. Instituto de Pesquisas Energéticas e Nucleares (IPEN). São Paulo. Brazil.

Rostelato, M.E.C.M., Rela, P.R., Zeituni, C.A., Feher, A., Manzoli, J.E., Moura, J.A., Moura, E.S., Silva, C.P.G., 2008. Development and production of radioactive sources used for cancer treatment in Brazil. Nukleonika 53 (Suppl. 2).

World Health Organization (WHO) apud Ministério da Saúde, 1999. Instituto Nacional de Câncer. Estimativa da incidência e mortalidade por câncer no Brasil. Rio de Janeiro.