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EPOXY RESINS USED TO SEAL BRACHYTHERAPY SEED

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ABSTRACT

Prostate cancer treatment with brachytherapy is recommended for patients with cancer at an early stage. In this treatment, small radioactive seeds are implanted directly in the prostate gland. These seeds are composed at least of one radionuclide carrier and an X-ray marker enclosed within a metallic tube usually sealed by laser process. This process is expensive and, furthermore, it can provoke a partial volatilization of the radionuclide and change the isotropy in dose distribution around the seed. In this paper, we present a new sealing process using epoxy resin. Three kinds of resins were utilized and characterized by scanning electron microscopy (SEM), energy dispersive X ray (EDS) and by differential scanning calorimetry (DSC) after immersion in simulated body fluid (SBF) and in sodium iodine solution (NaI). The sealing process showed excellent potential to replace the sealing laser usually employed.

1. INTRODUCTION

Treatment of prostate cancer can be performed using external (teletherapy) or internal (brachytherapy) radiotherapies [1,4]. If the cancer is classified as low risk (prostate specific antigen, PSA $\leq$ 10ng/ml, and tumor confined in the prostate region), the treatment can be performed by interstitial brachytherapy (internal radiotherapy) with low dose rate (LDR). In this case, 80 to 100 seeds are inserted directly into the prostate gland and do not need to be removed from the patient nor there is also hospitalization process. The most widely used radioisotope in these seeds is ^{125}I, ^{103}Pd and ^{131}Cs [1]. This kind of seed can also be utilized in treatment of ocular and brain tumors [4,5].

As the brachytherapy seeds are directly in contact with body fluids, the seed encapsulating material should be biocompatible. Besides this, it should also have some important characteristics as high mechanical and adhesive strength and easy handling.

Typical brachytherapy seeds are made of titanium tube and sealed with laser welding [1]. This kind of sealing can promote volatilization of the radionuclide and can also to increase the anisotropy in the dose distribution around the seeds. An alternative sealing process that can minimizes these problems it is being developed at CDTN. This process utilizes epoxy resins to seal the brachytherapy seed.

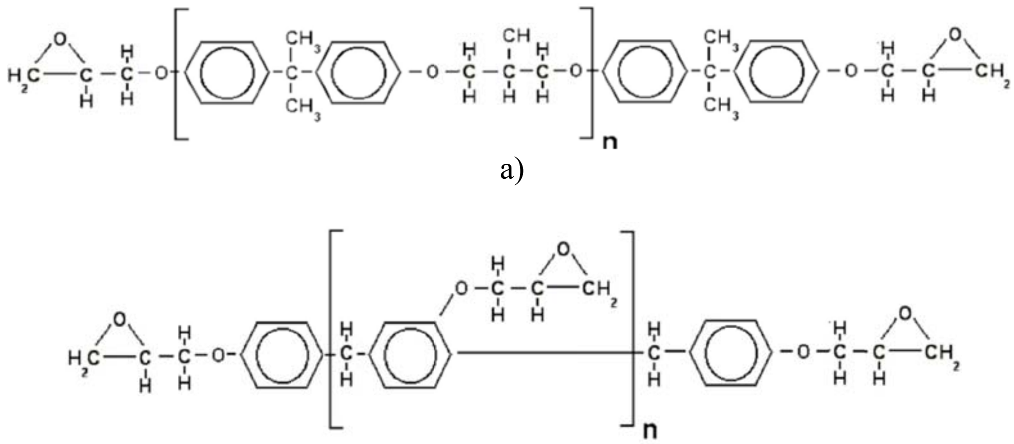
Epoxy resins are thermosetting polymers characterized by the presence of glycidyl group (also called epoxy group) with or without other functional groups that result in a three dimensional structure through reaction of the epoxy group with a suitable curing agent. The purpose of the curing agent is to promote the occurrence of crosslinking with reactive groups. They are very versatile because depending on the chemical structure of the curing agent and the curing conditions provide a wide range of processing conditions allowing to obtain products with different properties concerning to chemical and thermal resistance, mechanical strength, high adhesion, etc.

Once the seeds are implanted, they are directly in contact with the body fluid so they should be biocompatible and do not cause adverse reactions and the same is expected to the resin when it is used for sealing. Therefore, it is necessary to evaluate the epoxy resin behavior when it is immersed for some time in SBF solution. It is also important to evaluate the behavior of the epoxy resin when it is immersed in a solution of sodium iodine at pH 14, since the seed that is studied in this paper is internally composed of a matrix of Si-W impregnated with a solution of radioactive iodine which has a pH 14.

Therefore, in this paper we present a new sealing process employing three types of epoxy resins and also the characterizations of these resins after immersed in SBF and sodium iodine solutions by scanning electron microscopy, energy dispersive X ray and differential scanning calorimetry.

2. METHODOLOGY

Initially, three biocompatible epoxy resins, identified as EPOX-01, EPOX-2 and EPOX-03, were chosen for the study. The resins EPOX-01 and EPOX-02 are based on bisphenol A and the resin EPOX-03 is based on bisphenol F; their chemical structures are shown in Figure 1.



a)

b)

Figure 1: Chemical structure of epoxy resins based on a) bisphenol A and b) bisphenol F.

2.1 Obtaining and characterization of the resins

Resin samples were prepared by mechanical mixing of liquid epoxy prepolymer with its curing agent using a glass rod. After that, the homogenized mixture was placed under vacuum and then poured into plastic molds. The resins were cured under conditions provided by the manufacturer. The Table 1 shows the proportions between the part A (prepolymer) and part B (curing agent) and the cure time for each resin.

Table 1 : Data of Manufacturer resin.

Resin	EPOX-01	EPOX-02	EPOX-03
Percentage by weight Part A: Part B	20:5	20:7	20:9
Temperature/Cure time	65ºC/1 hour	80ºC/3hours	65ºC/3hours

For in vitro investigations, some samples of resins were immersed individually in SBF solution for 7, 14, 30 and 120 days and others samples of the EPOX-01 resin were immersed in the sodium iodine solution during 7, 14, and 30 days, both solutions were maintained at temperature of 36.5 °C, under agitation of 40 rpm. Some samples of the EPO-01 resin were irradiated with ^{60}Co reaching doses of 100, 150 and 300 Gy were also subjected to SBF tests during 60 days. All samples after the soaking time in each solution were rinsed with deionized water and dried at room temperature. All tests were performed in duplicates.

The SBF, the simulated body fluid, is a solution that shows a ionic composition similar to the human blood plasma and was prepared according to the preparation protocol, showing the following composition: NaCl (7,99589 g/L), $NaHCO_3$ (0,35074 g/L), KCl (0,22402 g/L), $K_2HPO_4.3H_2O$ (0,22885 g/L), $MgCl_2.6H_2O$ (0,3059 g/L), HCl (33,88 ml/L), $CaCl_2.2H_2O$ (0,3681 g/L), $NaSO_4$ (0,0715 g/L), $NH_2(CH_2OH)_3$ (6,0499 g/L). These reagents were added one by one in deionized water and the pH was adjusted to 7.35 by adding drops of HCl.

The NaI solution was prepared using 14.9893 g NaI in 100 ml of deionized water. NaOH was added to this solution until the pH reached 14.

The resins cured, irradiated and tested in SBF and iodine solutions were characterized by thermal analysis (NETZSCH, STA 449 F3 Jupiter). This analysis was performed under nitrogen gas flowing atmosphere at the heating rate of 5 °C/min in the temperature range of 25 ° to 180 °C. The surfaces of the samples that were immersed in the SBF solution were qualitatively analyzed by SEM/EDS (JEOL-JFM840A) with regard to the presence of precipitates and the surfaces of the samples soaking in sodium iodide solution in relation to the presence of iodine.

2.2 Sealing tests

Sealing tests were conducted in an assembly with a vacuum chamber containing in its interior two separate compartments. In one compartment were placed the titanium tubes containing a ceramics impregnated with non-radioactive iodine and in the other a quantity of liquid resin. At the beginning, the chamber was submitted to the vacuum pressure and after a certain time, the pressure inside the chamber was increased until to the atmospheric pressure, when the liquid resin has penetrated in the interior of titanium tubes. In the following, the titanium tubes were removed and placed to cure at 65 °C.

Several tests were conducted only with titanium tubes to establish the best conditions for sealing process. Afterwards, tests were carried out with titanium tubes inserted with impregnated ceramic with non-radioactive iodine.

The seeds after sealing tests were prepared by the usual metallographic techniques to assess the sealing process. Thus, the tubes were embedded in an adequate resin, sanded with silicon carbide paper and polished with diamond paste.

3. RESULTS AND DISCUSSION

3.1. Characterization of the resins

By means of the DSC thermograms obtained in the resins before and after immersion in SBF and NaI solutions it was evaluated the possible changes in the glass transition temperature of each resin. Thus, glass transition temperature results are shown in Tables 2 and 3 for SBF solution tests and in Table 4 for NaI solution tests. In Table 2 are presented glass transition temperature results for resins that were immersed during 0 and 120 days in SBF solutions. In Table 2 are shown the results of the glass transition temperature of the samples of the resin EPOX-01 that were immersed during 60 days in SBF solution and after γ irradiation with a radiation dose of 100, 150 and 300Gy. Table 3 shows the glass transition temperatures for the three types of resins soaking in NaI solution until 30 days.

An increase in TG value may indicate that there was a raise in the crosslinking of the polymer and the structure is more closed. Otherwise, breakage of the crosslinking can occur and the resin structure becomes more open [7]. It can be observed, as shown in Table 2, that the glass transition temperature of the resins EPOX-01 and EPOX-03 increased slightly while the one of resin EPOX-02 decreased. The sample EPOX-01 with irradiation dose of 150 Gy showed a higher TG, but this value has become equal to the non-irradiated resin for irradiation dose of 300 Gy. On the results of tests in NaI solution (Table 4), it was noted that the resin EPOX-02 showed a higher Tg than the other two resins after 14 days. It was also verified for this resin a pronounced variation in TG.

Table 2: Glass transition temperatures for samples after immersion in SBF solution.

	EPOX-01		EPOX-02		EPOX-03	
Tempo (days)	0	120	0	120	0	120
Tg (°C)	68.5	71.4	85.0	75.7	67.5	73.5

Table 3: Glass transition temperatures for samples after irradiation and SBF tests.

	EPOX-01 after 60 days			
Dose(Gy)	0	100	150	300
Tg(°C)	68.5	72.2	73.7	68.5

Table 4: Glass transition temperatures for samples after immersion in NaI solution.

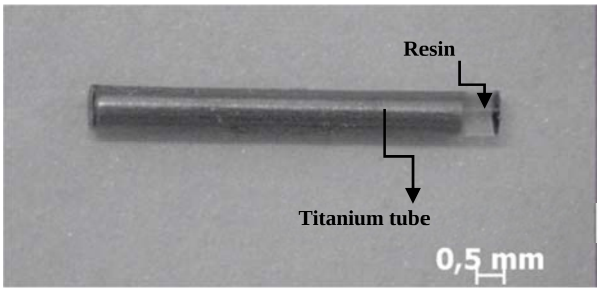
Resin EPOX-01				
Time (days)	0	7	14	30
Tg (°C)	68.5	67.0	71.6	71.4
Resin EPOX-01 150 Gy				
Tempo (dias)	0	7	14	30
Tg(ºC)	67.3	69.4	67.2	66.9
Resin EPOX-02				
Time (days)	0	7	14	30
Tg (°C)	85.0	85.9	89.2	79.7
Resin EPOX-03				
Time (days)	0	7	14	30
Tg (°C)	67.5	67.0	67.1	68.1

The analysis made by SEM/EDS in the samples immersed in SBF solution showed that there was no significant formation of precipitates on the surfaces of the resins. In the analysis carried out on samples immersed in the sodium iodide solution was not found significant presence of iodine on the resin surfaces.

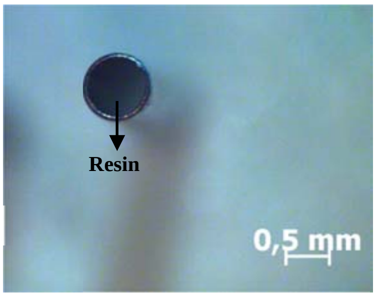
Accordingly to the cure time and TG results, the EPOX-01 and EPOX-03 resins were chosen for sealing tests.

3.1. Sealing Tests

Some preliminary tests with empty titanium tubes were carried out to establish the optimal conditions of pressure and time vacuum for each type of liquid resin. The established test conditions were vacuum pressure of ~10^{-7} MPa and vacuum time about 10 min before to place titanium tube in contact with the liquid resin. Figure 2 shows images of titanium tubes sealed with resin excess for better visualization of the resin aspect (Fig.2a) and with an adequate quantity of resin (Fig.2b).



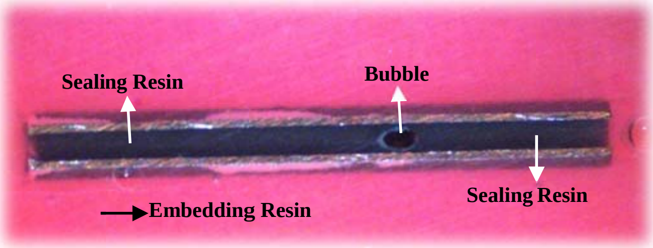
a)



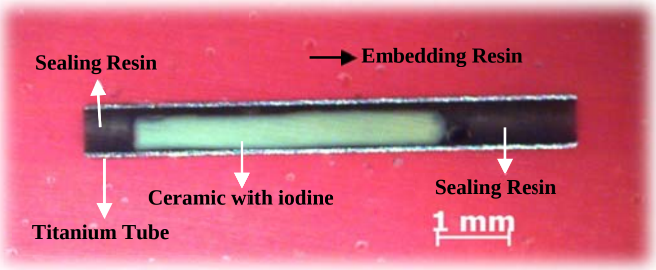
b)

Figure 2: Titanium tubes filled with resin: a) Aspect of the resin; b) Sealed tube.

In Figure 3 are shown typical metallographic images of a titanium tube and two seeds resin sealed. The seed consists of a titanium tube containing a ceramic impregnated with iodine. In this figure, the pink color is the embedding resin and the transparent color is the sealing resin. In Figure 3a, it is seen that the vacuum conditions to seal the tube were not sufficient to prevent the formation of bubbles. It can be seen in Figure 3b that the ceramic was not centered inside the tube and had the presence of one bubble. After adjusting the vacuum conditions, it was possible to obtain seeds with the centralized ceramics and without the occurrence of bubbles as shown for one typical seed in Figure 3c.



a)



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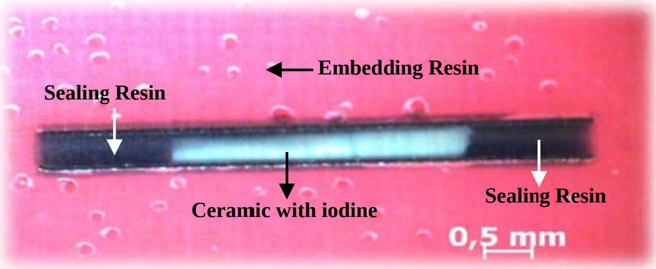

c)

Figure 3: Metallographic Images after sealing tests: a) Empty tube; b) Decentralized seed and; c) Centralized seed.

No significant differences were observed with respect to the use of the chosen resins in sealing tests.

4. CONCLUSIONS

It was evaluated three types of biocompatible epoxy resins in the new sealing process. The non-significant presence of precipitates on the surface of the resins and the absence of iodine, even after 30 days of the resins in contact with NaI solution, favors the use of epoxy resin in sealing the brachytherapy seed. The changes in Tg were favorable in most samples. Thus, the obtained results have shown that the sealing process using epoxy resins as sealants is feasible and may in future replace the sealing process with laser welding. This will contribute to greater nationalization of the manufacturing process of brachytherapy seeds.

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