2009 International Nuclear Atlantic Conference - INAC 2009
Rio de Janeiro,RJ, Brazil, September27 to October 2, 2009
ASSOCIAÇÃO BRASILEIRA DE ENERGIA NUCLEAR - ABEN
ISBN: 978-85-99141-03-8

GAMMA SPECTROMETRY AND CHEMICAL CHARACTERIZATION OF BIOACTIVE GLASS SEEDS WITH HOLMIUM-166 FOR ONCOLOGICAL IMPLANTS

Eduardo S. Valente[1,2] and Tarcísio P. R. Campos[1]

[1] Programa de Pos-graduação em Ciências e Técnicas Nucleares
Universidade Federal de Minas Gerais
Av. Antônio Carlos, 6627 – Campus UFMG
31.270-090 Belo Horizonte, MG
campos@nuclear.ufmg.br

[2] Comissão Nacional de Energia Nuclear – CNEN
Centro de Desenvolvimento da Tecnologia Nuclear - CDTN
Av. Antônio Carlos, 6627 – Campus UFMG
30123-970 Belo Horizonte, MG
valente@cdtn.br

ABSTRACT

Bioactive glass seeds synthesized by the sol-gel technique with Si:Ho:Ca composition with natural holmium incorporated were irradiated in the TRIGA type nuclear reactor IPR-R1@100kW, in the central thimble where the thermal neutron flux is 2.8×10^{12} $n/cm^2.s$ and the epithermal neutron flux is 2.6×10^{11} $n/cm^2.s$. After an 8 hour irradiation time, with an induced activity close to 110MBq/seed, a set of seeds was submitted to Gamma Spectrometry Analysis in a counting system with an HPGe detector, ORTEC electronic instrumentation and a Camberra Multichannel Analyser, to determine all radionuclides present on the sample as well as its individual activities. Special attention was paid on the discrimination of Si, ^{40}Ca, ^{44}Ca, *C* and *Ho* as the other expected elements like ^{48}Ca, ^{2}H and ^{18}O were present in traces or have very short half-lives. The second sample was submitted to Plasma spectrometry to determine the ^{166}Ho concentration in weight. The third sample was submitted to an X-ray spectrometry in a JEOL-JXA-8900RL equipment to determine its qualitative chemical composition, in order to evaluate impurities and nominal composition. It was determined that most of the activity, after decaying of short half-life elements, was due to ^{166}Ho present on the sample, with a well-characterized β and gamma spectra. The homogeneity of the seeds was tested on the X-ray spectrometry, and verified that there is no discrepancy in composition from distinct seeds or in a same seed. The results are relevant on the investigation of the viability of producing ^{166}Ho radioactive seeds for oncological implants.

1. INTRODUCTION

The cancer is a disease that affects great part of the world population indiscriminately. The longevity extends the exposition of the people to carcinogenic agents contributing for the increase of the incidence of the disease in the modern world [1]. Therefore, besides to the search for a longer life, the society must improve the techniques of treating this disease. One of the efficient ways of tumor control is the application of implants of radioactive seeds into the tumor in order to produce a high local and controlled absorbed dose, capable of eliminating cancerous cells preserving the surrounding healthy tissue.

ISBN: 978-85-99141-03-8

The radioactive seeds for brachytherapy currently used are made of titanium capillary tube with 0.8 millimeters of diameter filled with a ceramic glass cylinder in which radioactive iodine (I-125) is adsorbed. The radionuclide I-125 has a half-life of 59.4 days [2] and decays by electronic capture, emitting 35.5 keV gamma-rays among other X-ray characteristic emissions [3]. The number of metallic capsules implanted is close to one or two hundred units. The 100 capsule dimension of 4,5mm x 0,8mm and large number, together with their indefinitely permanence in the organ, may produce unfavorable clinical situations. Therefore, those facts justifies the development of new materials to hold radioactive elements into the tumors, mainly gathering β radiation emitters that generate high doses with a limited range, definitely preserving the healthy tissue adjacent to the tumor. The suggestion of biodegradable and biocompatible radioactive ceramic seeds for brachytherapy has early been suggested by the NRI/PCTN research group at the end of 1998, RECOP project submitted to FAPEMIG [4] [5]. Two research lines have been developed: i) ceramic based on sol-gel processing, and ii) hydroxyapatite marked to beta-emitter radionuclides [6] [7].

The element Holmium-166 incorporated in bioactive glasses produced by the sol-gel [8] technique provides a suitable solution for producing new materials for seed implants applied to brachytherapy. Those materials have reduced seed dimension, incorporated β particle emission of high energy and γ radiation of 80 keV, and short-half life. After its radioactive decayment, its possible solubility in corporeal fluid shall be acceptable [9]. These suitable properties suggest that the seeds shall be investigated deeply. In near future, those seeds may provide an efficient radiation therapy for many types of tumors. The seeds performance on animal implants, its biocompatibility and degradability, will also provide information for a system which can incorporate holmium-166, and also other radionuclides which are subject of study in the NRI/PCTN research group.

2. MATERIALS AND METHODS

A set of seeds synthesized by the sol-gel technique will be produced with silicon, holmium and calcium chemical elements presented as SiO_2, $Ho(NO_3)_3$ and CaO, respectively. These seeds will be characterized both physicaly and chemicaly by different analytical techniques and later a sample will be irradiated in a research reactor for determination of the induced activity and the presence of contaminant radionuclides.

The dimensional characterization and electronic microscopy images will be taken from the set of seeds. The chemical characterization of the seeds will be made using the x-ray spectrometry analysis in JEOL-JXA-8900RL spectrometer.

In the preparation of the bioactive glass seeds by sol-gel technique [4], natural holmium will be added in order to achieve concentration of 20% in weight. As the sol-gel technique involves physical transformations in the material it is important to verify the final concentration of the holmium element in the seeds. Based on this purpose, Plasma Spectrometry technique shall be used.

The induced activation will be performed on a set of seeds and gamma spectrometry will be taken. The following method will applied. A set of three micro seeds was irradiated in the research TRIGA type reactor, IPR-R1 in an irradiation position in which thermal neutron flux is $2.8x10^{12}\ {}^{n}/_{cm^2.s}$ and the epithermal neutron flux is $2.6x10^{11}\ {}^{n}/_{cm^2.s}$ [10]. It is important to consider the epithermal neutron flux in the calculation of the induced activity because the neutron absorption cross section for ^{166}Ho in this range of energy is 670 barn whereas for thermal neutrons is 58 barn. The induced activity will be, therefore, obtained to a large extent through the epithermal neutron flux. The induced seed activity submitted to the IPR-R1 reactor neutron flux is given by the expression [11]:

$$A_0 = \frac{m \cdot \Theta}{A} \cdot N_A \cdot \left[\left(\sigma_\gamma \cdot \Phi_{th} \right) + \left(I_\gamma \cdot \Phi_{epi} \right) \right] \cdot (1 - e^{(-\lambda \cdot t)}) \cdot e^{(-\lambda \cdot t_d)} [Bq] \quad (1)$$

where m is the mass of the element to be irradiated in grams, the factor Θ is isotopic abundance of target nucleus, A is the atomic mass of the element, N_A is the Avogadro's number, Φ_{th} is the thermal neutron flux, Φ_{epi} is epithermal neutron flux, σ_γ is the neutron capture cross section of the target nucleus in cm², I_γ is the resonance integral for the epithermal neutron flux of the target nucleus in cm ², λ is the decay constant of the produced radionuclide, t is the time of irradiation in seconds and t_d is the time to decay after irradiation in seconds.

3. RESULTS

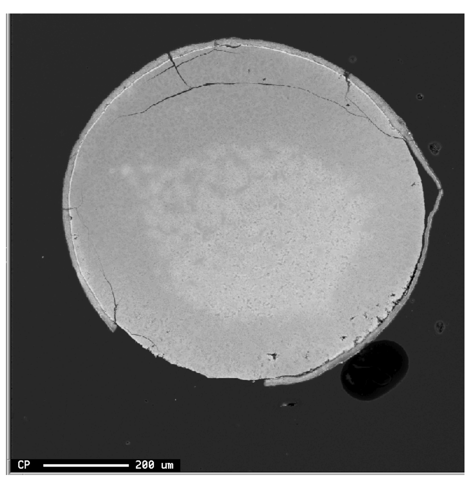
3.1. Dimensional characterization and electronic microscopy.

Based on a set of 20 seeds, the following average dimensions were obtained:

Weight - 1.81±0.09 mg
Diameter - 0.75±0.06 mm
Length - 1.62±0.08 mm

The diameter of the seeds allows to set an application tool with a lower diameter than the I-125 ones, minimizing the effect of needling the tumor that may produce a spilling of tumoral cells in the blood vessels and the consequent production of metastasis.

Images by electronic microscopy in longitudinal cuts in two seeds had been made using the X-ray spectrometer JEOL-JXA-8900RL, in which the physical homogeneity of the seed can be observed.



ISBN: 978-85-99141-03-8

Figure 1. Image by electronic microscopy in cross section of the seed sample.

Figure 2. Image by electronic microscopy in longitudinal cut of the seed sample.

3.2. Chemical characterisation of the seeds.

The chemical characterization of the seeds was made using the X-ray spectrometry analysis in JEOL-JXA-8900RL spectrometer. The presence of the chemical elements Homium, Calcium, Silicon and Oxygen was evident, uniformly distributed throughout the seed as shown in the spectra collected in a randomly chosen point of the sample. The other spectra were not presented due to their large similarity to each other. The amplitude of the corresponding peaks of each element points out, comparatively, the concentration of the element in the analyzed point. Oxygen, holmium, calcium and silicon keep peaks with constant intensity throughout the seed, suggesting a high level of homogeneity.

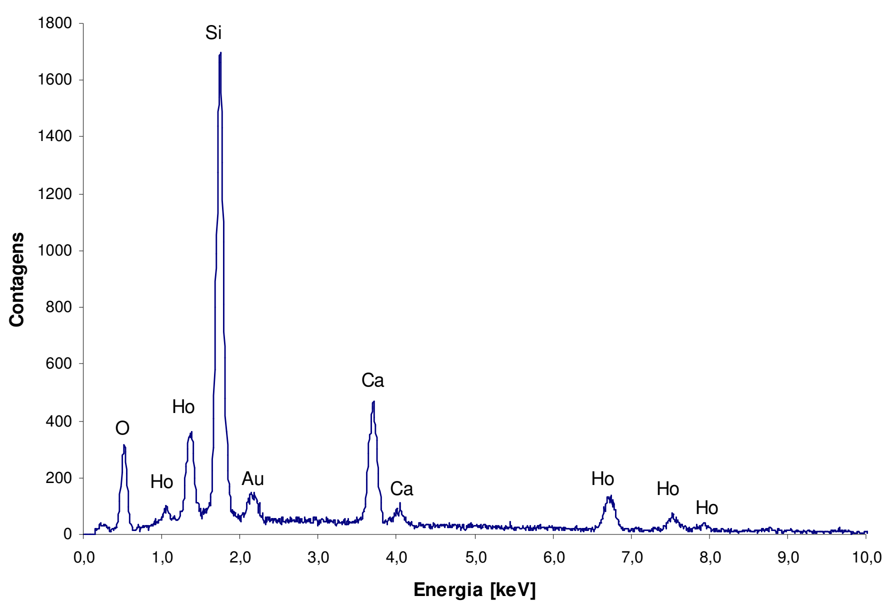


Figure 3. X-ray emission spectrum collected in a randomly chosen point of the seed sample.

Figure 3 shows the X-ray emission spectra. The element gold is present due to the conducting film laid over the sample to make it thermal conductor.

3.2. Determination of holmium concentration in the seeds.

The result of the analysis from plasma spectrometry technique is shown in Table 1.

Table 1

Analysis technique	Holmium concentration in weight (%)
Plasma spectrometry ICP/AES – SPECTROFLAME Analytical Instruments	23±3

3.3 Induced activation and gamma spectrometry

The activity related to ^{166}Ho to each 1.81m*g* seed, calculated by the expression *(1)* compared with the measured value, are shown in Table 2.

Table 2

	^{153}Sm activity (mCi) / (MBq)
Calculated	2.52 / 68
Measured	3.57 / 96

Table 3

Nuclide	Half-life	Activity after 2 hours MBq/seed
Si-31	157.3 min	0.004997
Ca-41	103000 a	0.0
Ca-45	162.61 d	0.000014
Ca-47	4.536 d	0.000001
Ca-49	8.718 min	0.001388

2009 International Nuclear Atlantic Conference - INAC 2009
Rio de Janeiro,RJ, Brazil, September27 to October 2, 2009
ASSOCIAÇÃO BRASILEIRA DE ENERGIA NUCLEAR - ABEN
***ISBN:* 978-85-99141-03-8**

The gamma spectrometry analysis demonstrates that the highest present activity in the seeds is due to ^{166}Ho. The gamma radiation spectrum of this sample of seeds is shown in Figure 6 where peaks of higher activity correspond to the energies of gamma radiation emitted by ^{166}Ho. Other expected radionuclides, such as ^{31}Si, ^{41}Ca, ^{49}Ca, have short half-life or their precursors have low neutron capture cross section. Table 3 shows induced activity of these nuclides calculated through expression *(1).*

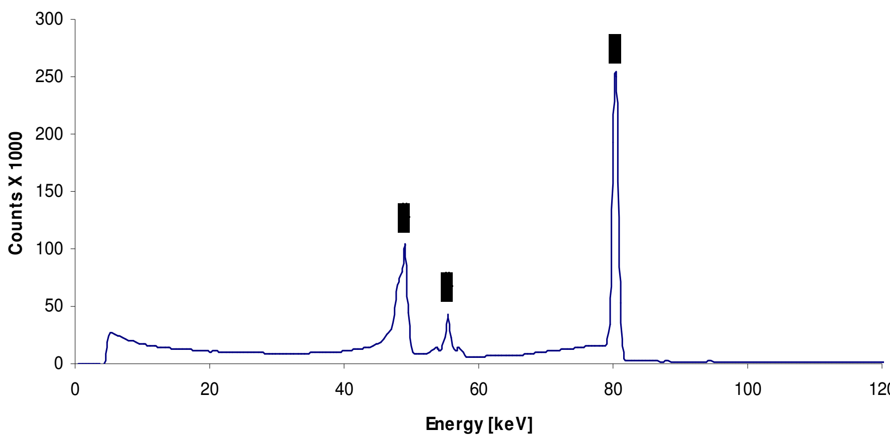


Figure 6. Gamma spectrometry of the seed sample.

4. CONCLUSIONS

The use of ^{166}Ho in brachytherapy is very interesting due to the characteristics of this radionuclide that are: β particle emission with maximum energy of 1854keV, 80keV gamma radiation emission and half-life of 26.8 hours. These characteristics provide high dose rate in the tumor and reduce the treatment time. Further studies *in vivo* should demonstrate the efficiency of the therapy as well as permit adjustments of the activity that will provide the application of therapeutical dose.

ACKNOWLEDGMENTS

The authors are thankful to the Universidade Federal de Minas Gerais and to the Centro de Desenvolvimento da Tecnologia Nuclear for allowing the accomplishment of this work in the scope of their professional and academic activities. They are also thankful to the colleagues, Andréa Vidal Ferreira, Ângela Maria Amaral, Geraldo Frederico Kastner, Robson Cota de Oliveira and to the team of operators of IPR-R1 reactor for the elaboration of the analysis, the expressed opinions and the offered suggestions during the elaboration of this work. The authors are also thankful to the colleague Luciana Batista Nogueira for helping preparation of the seeds used in the experiments. The authors are thankful to CNPq – National Counsel of Technological and Scientific Development to the financial support to the NRI-research group.

REFERENCES

1. "O que causa o câncer", http://www.inca.gov.br/conteudo_view.asp?id=81 (2007).
2. "Desenvolvimento e produção de fontes radioativas para braquiterapia", http://www.ipen.br/sitio/index.php?idc=239 (2007).
3. H. Cember, *Introduction to Health Physics*, Mc Grow Hill, Oxford, United States (1989).
4. B. M. Mendes; T. P. R. Campos, "Investigation of the Specific Energy Deposition from Radionuclide-Hydroxyapatite Macroaggregate in Brain Interstitial Implants", *Key Engineering Materials*, V**ol. 254-256**, pp.83-86 (2004).
5. W. S. Roberto; M. M. Pereira, T. P. R Campos, "Dosimetric Analysis And Characterization Of Radioactive Seeds Produced By The Sol-Gel Method", *Key Engineering Materials*, **Vol. 240-242**, pp.579-582 (2002).
6. B. M .Mendes; T. P. R. Campos; C. H. T. Silva, "Radiological Response of Macroaggregates Implants in an In-Vitro Experimental Model", *Key Engineering Materials*, **Vol. 254-256**, pp.87-90 (2004).
7. G. X. O. Silva; T. P. R. Campos; S. L. Siqueira; M. B. Maciel, "The Surgical Viability and Radiological Monitoring of Brain Implants of Bioactive Micro-seeds in Animal Model", *Brasilian Archives of Biology and Technology an International Journal,* **Vol. 48**, pp.109-113 (2005).
8. L. L. Hench, J. K. West, "The Sol-Gel Process". *American Chem. Soc*. **Vol. 90(n. 1)**, pp.33-72 (1999).
9. W. S. Roberto; M. M. Pereira, T. P. R Campos, "Caracterização de Vidros Bioativos para Tratamento de Câncer de Próstata", *2º Congresso Latino Americano de Orgãos Artificiais e Biomateriais*, Belo Horizonte, Brasil (2001).
10. Zangirolami, D. M., Fluxo neutrônico a 100kW nos terminais de irradiação do reator TRIGA IPR-R1. Master degree Monografy, Curso de Ciências e Técnicas Nucleares, Universidade Federal de Minas Gerais. Belo Horizonte, 2009, 101p.
11. PARRY, S. J.. Handbook of Neutron Activation Analisys. Surrey, United Kingdon, Viridian Publishing, 2003. 243 p.