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The Brazilian panorama for the calibration of Y-90 microspheres

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Abstract: The combination therapy approaches are gaining popularity, particularly the radiopharmaceutical therapy with external radiotherapy, immunotherapy or both. Radioembolization using Yttrium-90 Microspheres, SIR-Spheres and TheraSphere, has been used clinically in the treatment of locally advanced and unresectable Hepatic Carcinomas. According to the literature, the standardization of microspheres is not yet well established. In view of the practice of ^{90}Y in therapies in Brazil, it is essential to develop solid standards for its measurement, in order to verify the absorbed radiation dose and its administration to the patient. This paper proposes a study of the existing standardization infrastructure for ^{90}Y microspheres through a literature review and analysis of the measuring instruments available at the National Laboratory for Ionizing Radiation Metrology, a general analysis was made of the spectrometry and calibration methods available in Brazil, specifically at LNMRI, evaluating those suitable for use in the standardization of Yttrium microspheres. The results showed that in the period between 2000 and 2024 ^{90}Y was widely cited in treatment by radioembolization with microspheres, qualitative and quantitative evaluation of the activity quantity in PET/CT scans and its metrological characterization involving proficiency tests, study of impurities, standardization by primary and secondary methods

Keywords: Y-90 microspheres, Radioembolization, Standardization.

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O panorama brasileiro para a calibração de microesferas de Y-90

Resumo: As abordagens com a terapia combinada estão ganhando popularidade, principalmente a terapia radiofarmacêutica com radioterapia externa, imunoterapia ou ambas. A radioembolização usando microesferas de ítrio-90, SIR-Spheres e TheraSphere tem sido usada clinicamente no tratamento de carcinomas hepáticos localmente avançados e irressecáveis. De acordo com a literatura, a padronização das microesferas ainda não está bem estabelecida. Tendo em vista a prática do ^{90}Y em terapias no Brasil, é fundamental o desenvolvimento de padrões sólidos para sua medição, a fim de verificar a dose de radiação absorvida e sua administração ao paciente. Este trabalho propõe um estudo da infraestrutura de padronização existente para as microesferas de ^{90}Y por meio de uma revisão da literatura e análise dos instrumentos de medição disponíveis no Laboratório Nacional de Metrologia das Radiações Ionizantes, foi feita uma análise geral dos métodos de espectrometria e calibração disponíveis no Brasil, especificamente no LNMRI, avaliando os adequados para uso na padronização das microesferas de ítrio. Os resultados mostraram que, no período de 2000 a 2024, o ^{90}Y foi amplamente citado no tratamento por radioembolização com microesferas, avaliação qualitativa e quantitativa da quantidade de atividade em exames de PET/CT e sua caracterização metrológica envolvendo testes de proficiência, estudo de impurezas, padronização por métodos primários e secundários

Palavras-chave: Microesferas de ^{90}Y, Radioembolização, Padronização.

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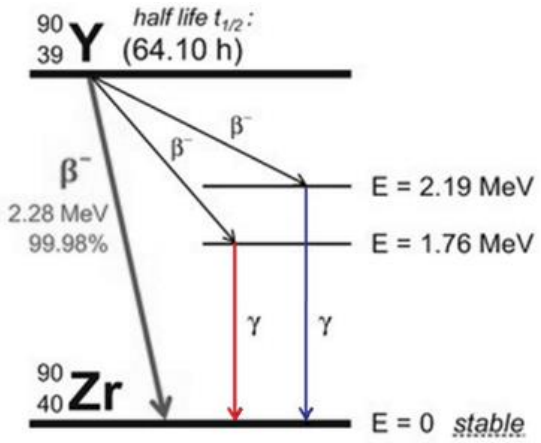
1. INTRODUCTION

The therapeutic application of radiopharmaceuticals guided by dosimetry is gaining momentum. In addition, combination therapy approaches are gaining popularity, particularly the combination of radiopharmaceutical therapy with external radiotherapy, immunotherapy or both. [1]

Radioembolization using Yttrium-90 (^{90}Y) Microspheres, SIR-Spheres and TheraSphere, has been used clinically in the treatment of locally advanced and unresectable Hepatic Carcinomas (HCC). [2]

However, according to the literature, the standardization of microspheres is not yet well established. In view of the practice of ^{90}Y in therapies in Brazil, it is essential to develop solid standards for its measurement, in order to verify the absorbed radiation dose and its administration to the patient. This paper proposes a study of the existing standardization infrastructure for ^{90}Y microspheres through a literature review and analysis of the measuring instruments available at the National Laboratory for Ionizing Radiation Metrology (LNMRI). Figure 1 shows the decay scheme of ^{90}Y and it shows the emission of photons of 511 keV, which makes it possible to form post-radioembolization images.

Figure 1: The decay scheme of ^{90}Y (adapted) [3]



The ^{90}Y offers an optimal solution for effectively treating sizable tumors and performing radiosynovectomy on joints. This pure β-emitter is characterized by its high-energy β-particles (E_{β^-} = 2.28 MeV) with a 100% emission probability and a $T_{1/2}$ of 64.1 h. It is the clear choice for those seeking to confidently overcome these medical obstacles. [2]

O ^{90}Y disintegrates by β emission mainly (99.983 %) to the stable ^{90}Zr ground state level. A weak beta branch occurs to the 1760 keV excited level which decays by an E0 gamma transition. This 0+-0+ transition undergoes with the emission of two particles materialized by the emission of two gamma, or an electron-positron pair, or internal conversion. The low positron emission of ^{90}Y (approximately 0.0032% of decays) results from the weak beta branch to the 1.76 MeV excited state of ^{90}Zr, which subsequently decays via internal pair production. This minimal positron emission is nonetheless detectable and allows for imaging via the 511 keV annihilation photons, albeit with low count rates, making it essential for accurate gamma spectrometry calibration. [3]

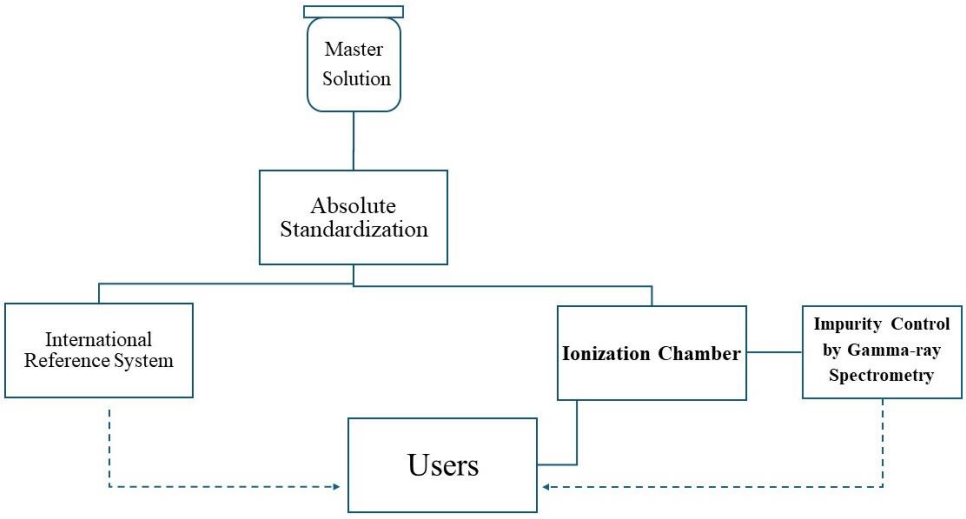
2. MATERIALS AND METHODS

A survey was conducted across databases, listing the primary studies identified using the keywords "SIR-Spheres and calibration" and "TheraSphere and calibration" separately. The selected studies were analyzed, focusing on the calibration of ^{90}Y sources, followed by a general evaluation of spectrometry and source characteristics. Additionally, an analysis of spectrometry and calibration methods at LNMRI was performed to assess their suitability for the standardization of Yttrium-90 microspheres.

3. RESULTS AND DISCUSSIONS

In Brazil, ^{90}Y for the preparation of radioactive sources is currently produced at the Institute for Energy and Nuclear Research (IPEN) nuclear research reactor and these are prepared at the LNMRI. This means that the calibration of these sources can be done directly in the LNMRI's measurement and calibration systems using the mother solutions supplied by IPEN. The calibration systems available at LNMRI are the well-type ionization chamber for activity determination, and the gamma spectrometry system with hyperpure germanium detector for identification and quantification of impurities. Figure 2 shows the dilution scheme to be used by LNMRI.

Figure 2 - ^{90}Y solution preparation and calibration scheme.



The standardization of radioactive samples begins with the preparation of a master solution following international standards, taking into account mass and radiochemical purity. Primary measurements are performed using absolute methods, such as 4πβ-γ coincidence counting, ensuring precision and metrological traceability. These results are then transferred to secondary systems, such as ionization chambers, enabling practical application by end-users. Simultaneously, impurities are monitored using gamma spectrometry (HPGe), ensuring quality. Finally, the standardization is disseminated to end-users (hospitais and laboratories), guaranteeing reliability in clinical and industrial applications.

The activity determination of ^{90}Y in manufacturer-specified measurement geometry will be performed through a secondary calibration procedure using a high-purity germanium (HPGe) gamma spectrometry system. This methodology focuses on the 511 keV photopeak from positron annihilation events, following primary standardization. The spectrometer efficiency calibration employs LNMRI-certified reference sources (^{152}Eu, ^{60}Co, ^{137}Cs, ^{57}Co, ^{54}Mn, and ^{241}Am) measured in identical vial geometry. The ^{90}Y sample is analyzed in a dedicated polyethylene holder (Figure 3), maintaining the exact geometric configuration required for traceability in clinical dosimetry applications.

Figure 3. Photograph of custom high-density-polyethylene source holder and example SIR-Spheres patient vial [1].

According to the state-of-the-art related to ^{90}Y, in the period between 2000 and 2024, ^{90}Y is widely cited in treatment by radioembolization with microspheres, qualitative and quantitative evaluation of the activity quantity in PET/CT scans and its metrological characterization involving proficiency tests, study of impurities, standardization by primary and secondary methods [4 - 24]. According to the scenario proposed here and with the data from the recently published articles, the expectation is that the well-type ionization chamber and HPGe gamma spectrometry standardization methods will provide consistent and accurate results for the calibration of ^{90}Y microspheres. Both methods are available at LNMRI

4. CONCLUSIONS

Yttrium-90 is a vital therapeutic radionuclide for liver cancer treatment, particularly in radioembolization procedures. Currently, Brazil lacks a national primary standard for ^{90}Y in nuclear medicine applications, as the National Ionizing Radiation Metrology Laboratory (LNMRI/IRD) has not yet established absolute calibration capabilities for this radionuclide, nor has its metrological traceability been verified by the International Bureau of Weights and Measures (BIPM). To bridge this gap and ensure the metrological precision required for clinical applications, LNMRI must acquire certified ^{90}Y samples from commercial microsphere sources (SIR-Spheres® or TheraSphere®). These reference materials must demonstrate traceable activity measurements, documented quality controls, and reproducible performance characteristics. The laboratory's existing measurement infrastructure confirms the technical feasibility of establishing this secondary calibration capability nationally, which would significantly enhance treatment quality assurance across Brazilian nuclear medicine centers.

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CONFLICT OF INTEREST

All authors declare that they have no conflicts of interest.

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