

development of the gamma camera by Hal Anger, and the  $^{99}\text{Mo}/^{99}\text{Tc}$  generators by researchers of the Brookhaven National Laboratory, the focus was moved to research and diagnostic application of  $^{99}\text{mTc}$  radiopharmaceuticals, and these compounds have been in use until now. In that age, the chemistry of technetium, including the production of different chelators and radiolabeling processes, were developed. Cyclotron-producing radioisotopes for medical application emerged in 1955, and for a long time, it was used to produce gamma-emitting radionuclides such as  $^{67}\text{Ga}$ ,  $^{111}\text{In}$ , and  $^{201}\text{Tl}$ . After the development of PET camera around 1975, positron-emitting radioisotopes started to be produced routinely in cyclotrons, such as  $^{11}\text{C}$ ,  $^{13}\text{N}$ , and  $^{18}\text{F}$ , gaining market status for diagnostic applications after Alfred Wolf and colleagues developed the  $^{18}\text{F}$ -FDG, around 1978. In the following year, positron-emitting radiometals  $^{68}\text{Ga}$ ,  $^{64}\text{Cu}$ , and  $^{89}\text{Zr}$ , began to be produced on a large scale to label molecules with short or long circulation times in the body. The results in the specificity of the diagnostic opened the possibility of using  $^{90}\text{Y}$  and  $^{177}\text{Lu}$ , both beta-emitting radioisotopes, to label the same molecules for therapeutic purposes; thus, theranostics pair  $^{68}\text{Ga}$  or  $^{64}\text{Cu}/^{90}\text{Y}$  or  $^{177}\text{Lu}$  started to be used in nuclear medicine. From the 2010s, true theranostic pairs gain interest, such as  $^{44}\text{gSc}/^{47}\text{Sc}$ ,  $^{64}\text{Cu}/^{67}\text{Cu}$ ,  $^{83}\text{Sr}/^{89}\text{Sr}$ ,  $^{86}\text{Y}/^{90}\text{Y}$ ,  $^{124}\text{I}/^{131}\text{I}$ ,  $^{152}\text{Tb}/^{161}\text{Tb}$ , and  $^{152}\text{Tb}/^{149}\text{Tb}$ , stated to be produced and evaluated for clinical applications. All these developments in radioisotope production and imaging systems also boosted the development of molecule radiolabeling processes, mainly through automated systems, to ensure speed, reproducibility, and less exposure to professionals involved in preparing these molecules. Furthermore, several chelating agents have been developed to complex different metals in a simple, effective, and stable way, such as the DOTA, NOTA, HBED molecules, among others. **Conclusão:** Trends in radioisotopes and radiolabeling methods result from scientific and technological developments in different areas but with congruent purposes. The result is a large number of products that can be chosen by their physical, chemical, biological, or economic characteristics.

**Keywords:** Cyclotron, Nuclear reactor, Radioisotopes production, Radiolabeling methods.

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#### RADIOLIGAND THERAPY IN LYMPHOMA: PAST, PRESENT AND FUTURE

Victor C.C.R. HERINGER<sup>a</sup>,  
Ludmila S. ALMEIDA<sup>a</sup>,  
Roberto C. DELGADO BOLTON<sup>b</sup>,  
Daniel C. PANCIEIRA<sup>b</sup>, Samuel S MEDINA<sup>a</sup>,  
Elba C.S.C. ETCHEBEHERE<sup>a</sup>

<sup>a</sup> Universidade Estadual de Campinas (UNICAMP),  
Campinas, SP, Brazil

<sup>b</sup> University Hospital San Pedro, Spain

**Summary:** In the 80s, radiolabeled cells helped understand the pathology of hemato-oncology. In the 90s, pre-clinical trials evaluated radiolabeled immunotherapy with monoclonal antibodies (MoAbs) such as anti-CD20 agents labeled with

Iodine-131 (Bexxar<sup>®</sup>) or Yttrium-90 (Zevalin<sup>®</sup>). Due to the safe and durable responses of radiolabeled-MoAbs, the FDA approved these agents in the 2000s. Despite radioimmunotherapy's long journey, its application has recently decreased. This review will discuss the historical timeline of radioimmunotherapy, debate on advantages and difficulties, and explore trials. Furthermore, we will examine future directions of radioimmunotherapy in hemato-oncology, considering emerging molecules that may become the next theragnostic trend. **Conclusão:** Since the 1980s, radiolabeled cells have been instrumental in understanding the pathological dynamics of hemato-oncological diseases. The evolution of this approach traversed the hybridoma technique in the 1990s, leading to numerous pre-clinical trials involving Monoclonal Antibodies (MoAbs). Subsequent clinical trials, predominantly in the 2000s, extensively explored MoAbs, focusing on anti-CD20 agents labeled with either  $^{131}\text{I}$  (Bexxar) or  $^{90}\text{Y}$  (Zevalin). The FDA approved these therapies in 2002 and 2003, marking significant milestones recognizing their safety and enduring therapeutic responses. Despite this journey, there has been a consistent decline in prescriptions. Various factors contribute to this trend, encompassing availability issues, reimbursement challenges, regulatory complexities, the need for trained personnel, and intricate logistics. Recent pre-clinical and clinical trials have shifted the spotlight onto novel antibodies, peptides, and further applications of known tracers. This renewed exploration may incentivize new suppliers to redirect their attention, potentially heralding the next wave of theragnostic trends in the near future.

**Keywords:** Immunotherapy, Lymphoma, Radioligand, Theranostics, Therapy.

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#### PROFILE OF MENINGIOMAS IN DOTATOC-68GA, FDG-18F AND PSMA-68GA PET/CT STUDIES: REALITY OF A PRIVATE SERVICE OF NUCLEAR MEDICINE AND LITERATURE REVIEW

Jorge Augusto Gomes CAVALCANTE,  
Marcelo Moreira da SILVA,  
Romel Jefferson HILGEMBERG JUNIOR,  
Carla Lima Santos VIVIANI

*Imagens Médicas de Brasília, Brasília, DF, Brazil*

**Summary:** Meningiomas represent the most common group of central nervous system primary tumors, and are often incidental findings on neuroimaging exams. The World Health Organization classifies meningiomas into three grades (grades I-III), varying in risk of recurrence and mortality. Approximately 100% of meningiomas present expression of the somatostatin receptor type 2 (SSTR2), which, in recent years, has been highlighted by the literature as a possible theragnostic tool, confirming the relevance of PET/CT with SSTR ligands in this context. Based on a narrative literature review, the objective was to analyze the main characteristics of meningiomas found in DOTATOC-68Ga PET/CT, FDG-18F PET/CT and PSMA-68Ga PET/CT exams performed in a private

nuclear medicine service. Subsequently, the data obtained was compared with evidence from the studies consulted. A search tool connected to the RIS database was used, utilizing the search word meningioma in PET/CT exam reports, from February 2019 to January 2024. As a result, exams from 68 patients were found, including 19 PET/CT DOTATOC-68Ga, 45 PET/CT FDG-18F and 4 PET/CT PSMA-68Ga. The absolute number per age group was 8 (40-49 years), 12 (50-59 years), 15 (60-69 years), 19 (70-79 years) and 14 (80 years or more), among which 47 were women and 21 men. Among all studies, 12 (17.6%) were indicated for meningioma specific evaluation, varying between initial diagnosis, radiosurgery programming, post-resection evaluation and unclear focal neurological signs, which represented 57.9% (11) of the DOTATOC-68Ga PET/CT sample and 2.2% (1) of FDG-18F PET/CT. All PSMA-68Ga PET/CT studies had another indication. Within all lesions evaluated, 61 were unifocal and 7 were multifocal. The largest diameter of the lesions analyzed ranged from 5 to 66 mm (average 23 mm). Based on the 68 patients analyzed in the sample, highlighting the existence of multifocal lesions, the topographies observed were: parasagittal 23, hemispherical convexity 30, sphenoid and middle cranial fossa 12, cere-

bellar convexity 1, frontobasal 4, posterior fossa 2 and foramen magnum 1. All lesions evaluated by DOTATOC-68Ga PET/CT showed tracer uptake (SUV between 2.5 and 17.8, mean SUV 8.9), compared to 3 lesions evaluated by FDG PET/CT-18F (SUV between 4.9 and 7.2, mean SUV 6.1). No lesion showed significant uptake of PSMA-68Ga. **Conclusão:** In the context of increasing advances in molecular imaging with SSTR ligands for meningiomas, PET/CT studies have showed relevance, above all, in the initial evaluation (pre-surgical/pre-radiotherapeutic), in the scenario of suspected tumor recurrence, as well as for candidates to radionuclide therapy. The present work sought to analyze information that could corroborate the characteristics of such tumors in hybrid images, comparing the data found with current literature. In addition, highlight the potential use of FDG-18F uptake in the non-invasive assessment of the aggressiveness of meningiomas.

**Keywords:** DOTATOC-68Ga, FDG-18F, Meningiomas, PET/CT, PSMA-68Ga.

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