BIOGRAPHICAL SKETCH

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NAME: Bertolet Reina, Alejandro

eRA COMMONS USER NAME (credential, e.g., agency login): ABERTOLET

POSITION TITLE: Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
UNIVERSIDAD DE SEVILLA, SEVILLA	BS	09/2014	PHYSICS
UNED, MADRID	MS	06/2018	MEDICAL PHYSICS
UNIVERSIDAD DE SEVILLA, SEVILLA	PHD	09/2020	BIOPHYSICS
HARVARD MEDICAL SCHOOL, BOSTON, MA	OTH	06/2022	CERTIFICATE IN MEDICAL PHYSICS
HOSPITAL UNIVERSITARIO VIRGEN MACARENA, SEVILLA	Resident	05/2018	RADIOPHYSICS
MASSACHUSETTS GENERAL HOSPITAL AND HARVARD MEDICAL SCHOOL, Boston, MA	Postdoctoral Fellow	03/2022	

A. Personal Statement

I am an Assistant Professor at the Massachusetts General Hospital (MGH) in the Division of Biophysics within the Radiation Oncology Department. My work is chiefly focused on the intersection of radiation biology, computational modeling, and radiation therapy optimization. I was granted an Early Career K99/R00 award from the NIH for a project on the dosimetry of alpha-particle radiopharmaceutical therapy. During the last year, I started a budding lab to study different aspects of radiopharmaceutical therapy and radiation biology modeling.

In addition to this primary project, I am leading two other projects at MGH that aim to (i) improve and develop new techniques in dosimetry for Y90-based transarterial radioembolization for liver cancer and (ii) explore the possibilities of alpha particle RPT for pancreatic adenocarcinoma. My research in these areas has culminated in several published articles highlighting our progress in radiobiological modeling and developing novel methods to perform dosimetry in RPT and DNA damage induction from various radiation types. Interestingly, I have been nominated as 'One to Watch' by the Society of Nuclear Medicine and Molecular Imaging for my work in radiopharmaceutical therapy, a mention reserved for the most promising researchers in the field of nuclear medicine.

Before my current position at MGH, I completed my Ph.D. thesis in two years at the University of Pennsylvania. I published multiple articles as the first author, most in prestigious journals in the Medical Physics field, about the radiobiological properties of proton therapy beams. After completing a 3-year residency program at the Hospital Virgen Macarena (Seville, Spain), I am also a certified Medical Physicist in Spain. During this time, I developed a clinical protocol for acquiring, calculating, and reporting the dosimetry of 177Lu-DOTATATE treatments for neuroendocrine tumors in peptide-receptor radionuclide therapy (PRRT). Given my experience in radiobiology, my background in physics, and my clinical training in Spain, I am eager to contribute to the proposed project and advance the field of radiopharmaceutical therapy. The development of agent-based pharmacokinetics models and their integration with our current understanding of radiation biology represents a significant opportunity to

improve patient outcomes and potentially transform the field.

As a full-standing member of the TOPAS and the TOPAS-nBio collaborations, which bring together investigators from four different institutions, I am involved in developing Monte Carlo-based computational tools to address radiation therapy and radiobiological studies. This work aligns closely with the project at hand. We are in the right spot to build bridges between dosimetric descriptions of radiation therapy and their biological and clinical effects through our world-class computational modeling team. I want to highlight the following publications as relevant to this project:

1. Bertolet A, Chamseddine I, Schuemann J, Paganetti H. The complexity of DNA damage by radiation follows a Gamma distribution: insights from the Microdosimetric Gamma Model (MGM). Frontiers in oncology. 2023 June; In press.
2. Bertolet A, Ramos-Méndez J, McNamara A, Yoo D, Ingram S, Henthorn N, Warmenhoven JW, Faddegon B, Merchant M, McMahon SJ, Paganetti H, Schuemann J. Impact of DNA Geometry and Scoring on Monte Carlo Track-Structure Simulations of Initial Radiation-Induced Damage. Radiat Res. 2022 Sep 1;198(3):207-220. PubMed Central PMCID: PMC9458623.
3. Bertolet A, Ramos-Méndez J, Paganetti H, Schuemann J. The relation between microdosimetry and induction of direct damage to DNA by alpha particles. Phys Med Biol. 2021 Jul 30;66(15) PubMed Central PMCID: PMC8483580.
4. Bertolet A, Cortés-Giraldo MA, Carabe-Fernandeza A. An Analytical Microdosimetric Model for Radioimmunotherapeutic Alpha Emitters. Radiat Res. 2020 Oct 2;194(4):403-410. PubMed PMID: 33045091.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2023 -	Assistant Professor, Massachusetts General Hospital and Harvard Medical School, Boston, MA
2022 - 2023	Instructor, Massachusetts General Hospital and Harvard Medical School, Boston, MA
2020 - 2022	Postdoctoral Fellow, Massachusetts General Hospital and Harvard Medical School, Boston, MA
2018 - 2020	Research Scholar, Hospital of the University of Pennsylvania, Philadelphia, PA
2015 - 2018	Medical Physics Resident, Hospital Universitario Virgen Macarena, Sevilla

Honors

2022 - 2023	Andrew L. Warshaw, M.D., Institute for Pancreatic Cancer Research Fellow, Massachusetts General Hospital
2022 - 2023	Loeffler Team Science Seed Funding Program Recipient, Department of Radiation Oncology, Mass General Hospital
2021 - 2022	Leadership Development Program for Researchers, Massachusetts General Hospital and Harvard Medical School
2023	Selected as Mentor for the AAPM Fellowship Program, American Association of Physicists in Medicine
2023	Early Career Investigator Travel Award, Radiation Research Society
2023	One to Watch in 2023, Society of Nuclear Medicine and Molecular Imaging
2022	Extraordinary PhD Award, Universidad de Sevilla, Spain
2022	Jack Fowler Award, Radiation Research Society
2021	Invited to the World Laureates Forum, World Laureates Association
2019	Best article of the month, University of Sevilla, Spain

C. Contribution to Science

1. My work has significantly advanced the field of microdosimetry in proton therapy, a promising area of oncology. I have developed novel methods for the calculation of dose-mean lineal energy and dose-averaged LET in proton therapy, which are key to understanding and optimizing the effectiveness of this treatment modality. My research in this area has led to more precise calculations and has provided important insights into the clinical implications of variable relative biological effectiveness in proton therapy. We have performed systematic reviews of the available experimental data on radiosensitivity to implement biophysical models in the clinical practice of particle therapy. I also have implemented the microdosimetric kinetic model in a treatment planning system, enhancing the practical applicability of this research.

    a. Suárez-García D, Cortés-Giraldo MA, Bertolet A. A systematic analysis of the particle irradiation data ensemble in the key of the microdosimetric kinetic model: Should clonogenic data be used for clinical relative biological effectiveness?. Radiother Oncol. 2023 Aug;185:109730. PubMed PMID: 37301260; NIHMSID: NIHMS1909219.
    b. Bertolet A, Cortés-Giraldo MA, Souris K, Carabe A. A kernel-based algorithm for the spectral fluence of clinical proton beams to calculate dose-averaged LET and other dosimetric quantities of interest. Med Phys. 2020 Jun;47(6):2495-2505. PubMed PMID: 32124463.
    c. Bertolet A, Baratto-Roldán A, Cortés-Giraldo MA, Carabe-Fernandez A. Segment-averaged LET concept and analytical calculation from microdosimetric quantities in proton radiation therapy. Med Phys. 2019 Sep;46(9):4204-4214. PubMed PMID: 31228264.
    d. Bertolet A, Baratto-Roldán A, Barbieri S, Baiocco G, Carabe A, Cortés-Giraldo MA. Dose-averaged LET calculation for proton track segments using microdosimetric Monte Carlo simulations. Med Phys. 2019 Sep;46(9):4184-4192. PubMed PMID: 31169910.

2. I have made several major contributions to the application of Monte Carlo simulations in radiation therapy. My team and I have advanced the understanding of initial radiation-induced damage through the impact of DNA geometry and scoring on Monte Carlo track-structure simulations. We also have developed a Monte Carlo dose calculation system for ophthalmic brachytherapy based on a realistic eye model, and we have proposed a modified geometry of 106Ru asymmetric eye plaques to improve dosimetric calculations.

    a. Bertolet A, Chamseddine I, Schuemann J, Paganetti H. The complexity of DNA damage by radiation follows a Gamma distribution: insights from the Microdosimetric Gamma Model (MGM). Frontiers in oncology. 2023 June; In press.
    b. Bertolet A, Ramos-Méndez J, McNamara A, Yoo D, Ingram S, Henthorn N, Warmenhoven JW, Faddegon B, Merchant M, McMahon SJ, Paganetti H, Schuemann J. Impact of DNA Geometry and Scoring on Monte Carlo Track-Structure Simulations of Initial Radiation-Induced Damage. Radiat Res. 2022 Sep 1;198(3):207-220. PubMed Central PMCID: PMC9458623.
    c. Miras Del Río H, Ortiz Lora A, Bertolet Reina A, Terrón León JA. A Monte Carlo dose calculation system for ophthalmic brachytherapy based on a realistic eye model. Med Phys. 2021 Aug;48(8):4542-4559. PubMed PMID: 34250607.

3. My work in alpha particle radiotherapy has contributed to the development of novel methods for dosimetry and radiobiological modeling. I've developed an analytical microdosimetric model for radiopharmaceutical alpha emitters and elucidated the relation between microdosimetry and the induction of direct damage to DNA by alpha particles. This research has the potential to lead to more effective treatments for a range of cancers.

    a. Bertolet A, Ramos-Méndez J, Paganetti H, Schuemann J. The relation between microdosimetry and induction of direct damage to DNA by alpha particles. Phys Med Biol. 2021 Jul 30;66(15) PubMed Central PMCID: PMC8483580.
    b. Bertolet A, Cortés-Giraldo MA, Carabe-Fernandeza A. An Analytical Microdosimetric Model for

Radioimmunotherapeutic Alpha Emitters. Radiat Res. 2020 Oct 2;194(4):403-410. PubMed PMID: 33045091.

4. I have also explored the potential of an alternative technique to deliver proton radiotherapy, coined as Proton Monoenergetic Arc Therapy (PMAT). The main idea is to enhance the RBE within the tumor by using monoenergetic beams whose ranges are approximately at mid-target. Explanations for these ideas, experimental studies with in-vitro clonogenic assays for diverse cell lines and the implementation of the PMAT plan creator/optimizer can be found in:

    a. Carabe A, Karagounis IV, Huynh K, Bertolet A, François N, Kim MM, Maity A, Abel E, Dale R. Radiobiological effectiveness difference of proton arc beams versus conventional proton and photon beams. Phys Med Biol. 2020 Aug 31;65(16):165002. PubMed PMID: 32413889.
    b. Bertolet A, Carabe A. Proton monoenergetic arc therapy (PMAT) to enhance LETd within the target. Phys Med Biol. 2020 Aug 19;65(16):165006. PubMed PMID: 32428896.
    c. Carabe-Fernandez A, Bertolet-Reina A, Karagounis I, Huynh K, Dale RG. Is there a role for arcing techniques in proton therapy?. Br J Radiol. 2020 Mar 1;93(1107):20190469. PubMed Central PMCID: PMC7066964.

5. While working as Medical Physicist at the Hospital Virgen Macarena in Seville, Spain, I developed a system integrated into the Oncology Information System of the Radiation Oncology department to (i) produce a paperless, automated workflow; and (ii) export structured patient-wise clinical data from the radiotherapeutic treatments.

    a. Bertolet A, Wals A, Miras H, Macías J. Organic generation of real-world real-time data for clinical evidence in radiation oncology. Int J Med Inform. 2020 Dec;144:104301. PubMed PMID: 33091831.