BIOGRAPHICAL SKETCH

NAME: Steven Chmura

eRA COMMONS USER NAME: SCHMURA

POSITION TITLE: Professor, Department of Radiation and Cellular Oncology and Medical Oncology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date MM/YYYY	FIELD OF STUDY
University of Illinois, Urbana Champaign, IL	BS	06/1992	Biology and Psychology
University of Chicago, Chicago, IL	PhD	06/1997	Pathology
University of Chicago, Chicago, IL	MD	06/1999	Medicine

A. Personal Statement

For the past decade, I have been actively involved in both the clinical implementation of stereotactic radiosurgery (SRS) and stereotactic body radiotherapy (SBRT) and related translational and clinical research, as well as the integration of SRS and SBRT into other systemic therapies. My clinical interests include breast cancer, limited metastatic disease, immunotherapy, and technologic improvements in the delivery of radiotherapy. I am an active member of the NCI cooperative group, NRG Oncology, serving on the committee for Breast Cancer and act as the liaison to the Radiation Oncology and Developmental therapeutics committees. These efforts have led to the first international trials through NRG Oncology examining the safety of treating breast cancer patients with 3-4 metastases as well as a Phase II/III trial examining potential improvements to progression-free survival and overall survival. My work in radio-immunology has also translated into seven investigator-sponsored trials along with an NCI-sponsored trial (Alliance) examining the role of SBRT combined with pembrolizumab in advanced Merkel cell carcinoma; such integration of ablative radiotherapy and immunotherapy and early stage trials is currently my research focus.

a. Salama JK, Chmura SJ, Mehta N, Yenice KM, Stadler WM, Vokes EE, Haraf DJ, Hellman S, Weichselbaum RR. An initial report of a radiation dose-escalation trial in patients with one to five sites of metastatic disease. Clin Cancer Res. 2008 Aug 15;14(16):5255-9.
b. NRG-BR002: A Phase IIR/III Trial of Standard of Care Therapy with or without Stereotactic Body Radiotherapy (SBRT) and/or Surgical Ablation for Newly Oligometastatic Breast Cancer (National PI).
c. Luke, J.J., et al. Safety and Clinical Activity of Pembrolizumab and Multisite Stereotactic Body Radiotherapy in Patients with Advanced Solid Tumors. J Clin Oncol, 2018; 36(16):1611-1618. PMC5978468
d. Chmura S, Winter KA, Robinson C, Pisansky TM, Borges V, Al-Hallaq H, Matuszak M, Park SS, Yi S, Hasan Y, Bazan J, Wong P, Yoon HA, Horton J, Gan G, Milano MT, Sigurdson ER, Moughan J, Salama JK, White J. Evaluation of Safety of Stereotactic Body Radiotherapy for the Treatment of Patients with Multiple Metastases: Findings From the NRG-BR001 Phase 1 Trial. JAMA Oncol. 2021; 7(6):845-852. PMC8063134.
e. Pointer KB, Katipally RR, Bestvina CM, Juloori A, Partouche J, Patel JD, Pitroda SP, Vokes EE, Weichselbaum RR, Chmura SJ. Evaluation of Initial Metastatic Tumor Location and Radiation Response to Determine Outcomes in Patients Who Received Combination Stereotactic Body Radiotherapy and Immunotherapy for NSCLC. Int J Radiat Oncol Biol Phys. 2021 Nov 1;111(3S):e449.

B. Positions and Honors

Academic

2021- Professor, Department of Medicine, Section of Hematology Oncology (secondary)
2020- Professor, Department of Radiation and Cellular Oncology, University of Chicago

2012-2020 Associate Professor, Department of Radiation and Cellular Oncology, University of Chicago
2007-2012 Assistant Professor, Department of Radiation and Cellular Oncology, University of Chicago
2004-2007 Instructor, Department Radiation and Cellular Oncology, University of Chicago
2004-pres Licensed Physician and Surgeon, State of Illinois

Administrative

2020- Scientific Director of the Clinical Trials Office (CCTO) University of Chicago Comprehensive Cancer Center
2017- NCI Breast Immuno-Oncology (BIO) Task Force.
2015 -2017 American Association of Physics and Medicine (AAPM) Task group No. 263
2014 - Vice Chairperson of the Scientific Advisory and Monitoring Board (SAM) for UCCC
2014- NRG Oncology PI for UCMC
2012- NRG Oncology: Breast Cancer Committee and Liaison to Radiation Oncology and Developmental Therapeutics
2012- American Board of Radiology Breast Cancer Oral Exam Writer and Examiner, Radiation Oncology Licensing Examination
2012- Breast Cancer Written Exam Writer, Radiation Oncology Licensing Examination
2012- Breast Cancer Recertification Written Exam Writer, Radiation Oncology Re-Certification Examination
2010-2018 Residency (ACGME) Program Director, Department of Radiation and Cellular Oncology, University of Chicago
2007- Director of Clinical and Translational Research, Department of Radiation and Cellular Oncology, University of Chicago

Honors (selected)

2017 Samuel Hellman Resident Teaching Award
2016 VSPO Invited Speaker McGill University, Montreal, CA
2014 Association of Residents in Radiation Oncology: Residence Teaching Award
2012 Association of Residents in Radiation Oncology: Residence Teaching Award

Other Experience and Professional Activities

Editorial Board: Journal of Clinical Oncology
Ad hoc reviewer: International Journal of Radiation Oncology, Clinical Cancer Research, Cancer, Advances in Radiation, PLOS1

C. Contributions to Science:

1. Elucidation of the role that cell membrane alterations play in radiation-induced programed cell death
The basis of the repair of gamma ray induced DNA damage in radiotherapy and in cancer susceptibility was largely known when these experiments were performed. However, the role that the cell membrane played in altering programmed cell death was not understood. We identified that the lipid second messenger ceramide plays a critical role in programmed cell death in both b-cells and in some solid tumors following large doses of radiation. This work was subsequently validated by others and is now widely accepted as part of radiation induced death. I conceived of these ideas and personally carried out all of the experiments as part of my PhD thesis. The work was performed with Dr. Ralph Weichselbaum at the University of Chicago.

a. Chmura SJ, Nodzenski E, Kharbanda S, Pandey P, Quintans J, Kufe DW, et al. Down-regulation of ceramide production abrogates ionizing radiation-induced cytochrome c release and apoptosis. Mol Pharmacol, 2000; 57(4):792-6.
b. Chmura SJ, Dolan ME, Cha A, Mauceri HJ, Kufe DW, Weichselbaum RR. In vitro and in vivo activity of protein kinase C inhibitor chelerythrine chloride induces tumor cell toxicity and growth delay in vivo. Clin Cancer Res, 2000; 6(2):737-42.
c. Chmura SJ, Nodzenski E, Beckett MA, Kufe DW, Quintans J, Weichselbaum RR. Loss of ceramide production confers resistance to radiation-induced apoptosis. Cancer Res, 1997; 57(7):1270-5.

d. Chmura SJ, Nodzenski E, Weichselbaum RR, Quintans J. Protein kinase C inhibition induces apoptosis and ceramide production through activation of a neutral sphingomyelinase. Cancer Res, 1996; 15;56(12):2711-4. PMCID: 8665499

2. Improving breast cancer clinical outcomes through technologic advancements

Breast conservation therapy was established from randomized trials done over 30 years ago. New radiation therapy technologies and imaging modalities were developed in the late 1990's. However, few of these were implemented for breast cancer patients. My work over the last 10 years has attempted to determine which technologies can be used to improve breast cancer outcomes, including IMRT, prone radiotherapy, and image guided motion control, and stereotactic body radiotherapy. This work was performed with Dr. Hania Al-Halaq at the University of Chicago, and Dr. Joseph Salama of Duke Medical Center. I have contributed knowledge of radiation and details of critical experiments.

a. Al-Hallaq HA, Mell LK, Bradley JA, et al. Magnetic resonance imaging identifies multifocal and multicentric disease in breast cancer patients who are eligible for partial breast irradiation. Cancer, 2008; 113(9):2408-14.
b. Cao J, Roeske JC, Chmura SJ, et al. Calculation and prediction of the effect of respiratory motion on whole breast radiation therapy dose distributions. Med Dosim 2009;34(2):126-32. PMID: 19410141
c. Corbin KS, Dorn PL, Jain SK, et al. Hypofractionated radiotherapy does not increase acute toxicity in large-breasted women: results from a prospectively collected series. Am J Clin Oncol, 2014; 37:322-6.
d. Corbin KS, Ranck MC, Hasselle MD, et al. Feasibility and toxicity of hypofractionated image guided radiation therapy for large volume limited metastatic disease. Pract Radiat Oncol, 2013; 3(4):316-22.

3. Elucidating the role of Stereotactic Body Radiotherapy (SBRT) for the treatment of limited Oligometastatic Cancer

The hypothesis put forth by Hellman and Weichselbaum in 1995 – that a subset of patients exist with limited metastatic disease who could be cured by aggressive local therapy – has been a research focus of mine for the past 10 years. Through both institutional clinical trials, translational work in the laboratory to better elucidate the molecular underpinnings of this clinical presentation, and the development and (current) running of two NCI sponsored trials, we have changed how oncologists think of a small subset of metastatic patients. This work has been supported by innumerable researchers in both the basic and translational sciences as evident by the culmination of this research into two cooperative group trials.

a. Corbin KS, Ranck MC, Hasselle MD, et al. Feasibility and toxicity of hypofractionated image guided radiation therapy for large volume limited metastatic disease. Pract Radiat Oncol, 2013; 3(4):316-22.
b. Hasselle MD, Haraf DJ, Rusthoven KE, et al. Hypofractionated image-guided radiation therapy for patients with limited volume metastatic non-small cell lung cancer. J Thorac Oncol, 2012; 7(2):376-81.
c. Lussier YA, Khodarev NN, Regan K, et al. Oligo- and polymetastatic progression in lung metastasis(es) patients is associated with specific microRNAs. PLoS One, 2012; 7(12):e50141.

4. Developing the clinical and translational science to integrate SBRT and immunotherapy.

For the past decade our laboratory and many others have suggested that the efficacy of radiotherapy may be dependent, in part, on a functioning immune system. Other data has suggested radiotherapy may convert tumors into a more inflamed state and potentially improve clinical outcomes with immunotherapy. We have successfully designed the first clinical trial to test these hypothesis integrating SBRT into immunotherapy (a) and developed translation model systems to understand the underlying mechanisms that are ongoing. This work is now focused on specific hypotheses and lead to over 5 ongoing IIT and NCI sponsored trials. The first randomized trial to test the effect on PFS (commonly referred to as abscopal effect) opened in February 2018: Alliance 091605 – A randomized trial of pembrolizumab With or Without Stereotactic Body Radiation Therapy in Treating Patients with Advanced or Metastatic Merkel Cell Cancer (NCT03304639).

A. Luke, J.J., et al. Safety and Clinical Activity of Pembrolizumab and Multisite Stereotactic Body Radiotherapy in Patients with Advanced Solid Tumors. J Clin Oncol, 2018; 36(16):1611-1618. PMC5978468