## BIOGRAPHICAL SKETCH

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NAME: Smith, Brian J

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

POSITION TITLE: 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)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Saint Louis University | BA | 05/1993 | Mathematics |
| The University of Texas | MS | 05/1995 | Mathematical Statistics |
| The University of Iowa | PhD | 08/2001 | Biostatistics |

### A. Personal Statement

I am a Professor in the Biostatistics Department at the University of Iowa and member of the Cancer Epidemiology and Population Science (CEPS) Program in the Holden Comprehensive Cancer Center (HCCC). In addition, I have been a member of the HCCC Biostatistics Core since 2001 and Director since 2006. I provide statistical oversight and support for the Biostatistics Core, including supervision and mentoring of staff biostatisticians. During my involvement in the Core, I have collaborated with over 100 HCCC members on the statistical design, analysis, and interpretation of cancer-related research projects. These activities have led to more than 130 co-authored publications. My other Cancer Center affiliations include membership on the Leadership Committee of the CEPS Program, Advisory Committee of the Population Research Core, Protocol Review and Monitoring Committee, and Data Safety and Monitoring Committee.

As an academic biostatistician, my research focuses have been in the development and application of statistical methodology to address general classes of biomedical problems. Specific areas of contributions include statistical computing, multidisciplinary collaborative cancer research, and residential radon research. I have been involved in a broad range of research studies, including preclinical in vitro and in vivo studies, clinical trials, and observational epidemiologic studies. My recent collaborations have focused on clinical outcomes research for head and neck cancer and lymphoma as well as medical imaging; and include co-direction of the Biostatistics and Bioinformatics Core of the Iowa/Mayo P50 Lymphoma SPORE since 2006, statistical leadership on a U01 Quantitative Imaging Network grant since 2010, and statistical leadership on a P01 program project to study pharmacologic ascorbate treatment for cancer.

### B. Positions and Honors

Positions and Employment

2001-2002 Visiting Assistant Professor, Department of Biostatistics, The University of Iowa
2002-2008 Assistant Professor, Department of Biostatistics, The University of Iowa
2008-2017 Associate Professor, Department of Biostatistics, The University of Iowa
2017-present Professor, Department of Biostatistics, The University of Iowa

Other Experience and Professional Membership

1997-present Member, American Statistical Association
2001-present Member, Holden Comprehensive Cancer Center Biostatistics Core
2001-present Member, Eastern North American Region of the International Biometry Society

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|---|---|
| 2001-present | Member, Holden Comprehensive Cancer Center Protocol Review and Monitoring Committee |
| 2002-present | Member, Holden Comprehensive Cancer Center Data Safety and Monitoring Committee |
| 2004-present | Member, Holden Comprehensive Cancer Center Cancer Epidemiology Program |
| 2006 | ASA Conference on Radiation and Health, New Investigator Award for Research on Spatio-Temporal Modeling of Residential Radon, Pacific Grove, CA |
| 2006 | U.S. Environmental Protection Agency Children's Environmental Health Recognition Award for contributions by Field RW, Steck DJ, Lynch CF, and Smith BJ to The Heartland Radon Research and Education Program, University of Iowa, Iowa City, IA |
| 2016-2019 | Member, NCI, Subcommittee F, Institutional Training and Education |
| 2016-2019 | Member, Radon Expert Group, United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) |
| 2006-present | Director, Holden Comprehensive Cancer Center Biostatistics Core |
| 2016-present | Member, Veterans Affairs, Lung Cancer Surgery or Stereotactic Radiotherapy (VALOR) Cooperative Study Data Monitoring Committee |
| 2020-Present | Member, Cancer Epidemiology Expert Group, UNSCEAR |

**C. Contributions to Science**

**Statistical Computing:** Widespread use of statistical methods depends on their accessibility to practitioners. Thus, there is a need for the implementation of methods via the development of computational algorithms and software tools. Examples of my contributions in this area are the Bayesian Output Analysis (Smith 2007) and the Reparameterized and Marginalized Posterior Sampling (Smith, Yan, Cowles 2008) R software packages. Boa is a set of tools for carrying out convergence diagnostics and statistical and graphical analysis of Markov chain Monte Carlo (MCMC) sampler output. Since the majority of Bayesian analyses employ MCMC sampling, boa is generally applicable to the practice of Bayesian statistics. When first released, boa was among the most commonly used programs for Bayesian analysis and widely cited in manuscripts and books. Ramps is a package for spatial modeling that combines new methodological, algorithm, and tool development. More recent work in statistical computing includes the Mamba (2020) software that provides a framework for implementing MCMC algorithms for general Bayesian model development and MRMCaov (2020) for statistical comparison of diagnostic performance assessed in multi-reader multi-case studies.


**Smith BJ**, Deonovic B (2020). Mamba: Markov chain Monte Carlo for Bayesian analysis, julia software package. *GitHub.* https://github.com/brian-j-smith/Mamba.jl

**Smith BJ**, Hillis SL (2020). Multi-reader multi-case analysis of variance software for diagnostic performance comparison of imaging modalities. In Samuelson F, Taylor-Phillips S (eds.), Proceedings of SPIE 11316, Medical Imaging 2020: Image Perception, Observer Performance, and Technology Assessment, 113160K. PMC: PMC7190386, PMID: 32351258

**Smith BJ**, Yan J, Cowles MK. (2008) Unified Geostatistical Modeling for Data Fusion and Spatial Heteroskedasticity with R Package ramps. *Journal of Statistical Software, 25*(10), 1-21.

**Smith BJ**. (2007) boa: An R Package for MCMC Output Convergence Assessment and Posterior Inference. *Journal of Statistical Software, 21*(11), 1-37.


**Predictive Modeling:** Predictive modeling is the process of developing a mathematical tool or model to accurately predict an outcome of interest. Prediction of health outcomes is a need that I have commonly encountered in my collaborative work as a biostatistician. In addressing such needs, I have developed and applied a range of modeling techniques from traditional statistical (regression) models to more flexible machine learning methods. For example, I developed a Bayesian hierarchical model and a web application for prediction of survival in pancreatic cancer patients (Smith and Mezhir 2014); used machine learning for predictive modeling of treatment response in serous ovarian cancer patients (Gonzales et al. 2016) and for classification of lung cancer nodules in screening of patients at high risk for lung cancer (Delzell et al. 2019); and developed and maintain machine learning software fitting and performance assessment of prediction models (Smith 2020). Moreover, I have taught graduate courses in Statistical Methods in Bioinformatics (2012, 2014, 2016) and Machine Learning for Biomedical Data (2018, 2020), and supervised masters research projects and PhD dissertations in machine learning.

**Smith BJ** (2020). MachineShop: Machine Learning Models and Tools, R software package. *The Comprehensive R Archive Network.* http://cran.r-project.org/package=MachineShop
Delzell DA, Sara M, Tabitha P, Michelle S, **Smith BJ** (2019). Machine learning and feature selection methods for disease classification with application to lung cancer screening image data. *frontiers in Oncology*, 9:1393. PMC: PMC6917601, PMID: 31921650
Gonzales Bosquet J, Newtson AM, Chung RK, Thiel KW, Ginader T, Goodheart MJ, Leslie KK, **Smith BJ** (2016). Prediction of chemo-response in serous ovarian cancer. *Molecular Cancer*, 15(1):66. PMC: PMC5070116, PMID: 27756408
**Smith BJ**, Mezhir JJ (2014). An interactive Bayesian model for prediction of lymph node ratio and survival in pancreatic cancer patients. *Journal of the American Medical Informatics Association*, 21(e2):e203-211. PMC: PMC4173165, PMID: 24444460

**Cancer Research:** Statistics has a role to play in most empirical studies and, as such, is an essential tool for understanding the physical world around us. I became a biostatistician out of a desire to make a broad contribution to the health and well-being of individuals. My role as Biostatistics Core Director of the Holden Comprehensive Cancer Center allows me to do that. In particular, I am heavily involved in multi-disciplinary cancer research that involves a wide range of scientific studies and aims to advance our understanding and treatment of the disease. Examples of studies include completed and ongoing clinical trials of pharmacologic ascorbate (Bodeker et al. 2019), medical imaging studies (Smith et al. 2020; Beichel et al. 2017), and cellular studies (Schoenfeld et al. 2017). Overall, I have collaborated with more than 100 cancer center members on 120+ manuscripts, 40+ clinical trials, and multiple cancer disease sites.

Bodeker KL, Allen BG, Smith MC, Monga V, SS, Hohl RJ, Carlisle TL, Brown HA, Hollenbeck NJ, Vollstedt S, Greenlee JD, Howard MA, Mapuska KA, Seyedin SN, Caster JM, Jones KA, Cullen JJ, Berg DJ, Wagner BA, Buettner GR, TenNapel MJ, **Smith BJ**, Spitz DR, Buatti JM (2019). First-in-human phase 1 clinical trial of pharmacological ascorbate combined with radiation and temozolomide for newly diagnosed glioblastoma. *Clinical Cancer Research*, 25(22):6590-6597. PMC: PMC6858950, PMID: 31427282
**Smith BJ**, Buatti JM, Bauer C, Ulrich EJ, Ahmadvand P, Budzevich MM, Gillies RJ, Goldgof D, Grkovski M, Hamarneh G, Kinahan PE, Muzi JP, Muzi M, Laymon CM, Mountz JM, Nehmeh S, Oborski MJ, Zhao B, Sunderland JJ, Beichel RR (2020). Multisite Technical and Clinical Performance Evaluation of Quantitative Imaging Biomarkers from 3D FDG PET Segmentations of Head and Neck Cancer Images. *Tomography*, 6(2):65-76. PMC: PMC7289247, PMID: 32548282
Beichel RR, **Smith BJ**, Bauer C, Ulrich EJ, Admadvand P, Budzevich MM, Gillies RJ, Goldgof D, Grkovski M, Mamarneh G, Huang Q, Kinahan PE, Laymon CM, Mountz JM, Muzi JP, Muzi M, Nehmeh S, Oborski MJ, Tan Y, Zhao B, Sunderland JJ, Buatti JM (2017). Multi-site quality and variability analysis of 3D FDG PET segmentations based on phantom and clinical image data. *Medical Physics*, 44(2):479-496. PMC: PMC5834232, PMID: 28205306
Schoenfeld JD, Sibenaller ZA, Mapuskar KA, Wagner BA, Cramer-Morales KL, Furqan M, Sandhu S, Carlisle TL, Smith MC, Abu Hejleh T, Berg DJ, Zhang J, Keech J, Parekh KR, Bhatia S, Monga V, Bodeker KL, Ahmann L, Vollstedt S, Brown H, Kauffman EP, Schall ME, Hohl RJ, Clamon GH, Greenlee JD, Howard MA, Shultz MK, **Smith BJ**, Riley DP, Domann FE, Cullen JJ, Buettner GR, Buatti JM, Spitz DR, Allen BG (2017). O2·− and H2O2-mediated disruption of Fe metabolism causes the differential susceptibility of NSCLC and GBM cancer cells to pharmacological ascorbate. *Cancer Cell*, 31(4):487-500. PMID: 28366679

**Complete List of Published Work:**
https://www.ncbi.nlm.nih.gov/myncbi/brian.smith.2/bibliography/public/

**D. Additional Information: Research Support and/or Scholastic Performance**

P01 CA217797 Cullen (PI), Smith (Co-Investigator) 09/19/18-08/31/23
NIH
Exploiting Redox Metabolism Using Pharmacological Ascorbate for Cancer Therapy
This research program investigates the use of pharmacologic ascorbate in the treatment of cancer.

P30 CA086862 Weiner (PI), Smith (Biostatistician) 07/14/00 - 03/31/26

NIH
Cancer Center Support Grant
This Cancer Center Support Grant is to support the research activities of the Holder Comprehensive Cancer Center at the University of Iowa.

P50 CA097274 Weiner (PI), Smith (Biostatistics Core Director) 09/01/02 - 06/30/22
NIH
NCI Lymphoma Specialized Program of Research Excellence
The objectives of the SPORE are to understand the immunological mechanisms underlying anti-lymphoma monoclonal antibody therapy in an effort to treat lymphomas using a variety of modalities.

R01 EB025174-01A1 Hillis (PI), Smith (Co-Investigator) 9/1/18-5/31/22
NIH
Generalized Obuchowski-Rockette Methodology for Analysis of Radiologic Diagnostic Imaging Studies
By providing a generalized Obuchowski-Rockette methodology for analyzing data from diagnostic imaging studies, the proposed research will result in research questions being more fully and efficiently answered. Thus the proposed research is relevant to the mission of the National Institute of Biomedical Imaging and Bioengineering, namely to improve health by leading the development and accelerating the application of biomedical technologies.

R25 HL131467 Zamba (PI), Smith (Co-Investigator) 3/1/19-2/28/22
NIH
Iowa Summer Institute for Research Education in Biostatistics
This is a proposal to the National Institutes of Health (NIH), National Heart, Lung and Blood Institute (NHLBI), from the University of Iowa, in response to RFA-HL-16-017 for a Summer Institute for Research Education in Biostatistics. The ultimate vision of our proposed research education program is to increase the number of undergraduates who enter graduate programs in Biostatistics and to maintain a solid underrepresented minority pipeline into biostatistics graduate programs. The proposal is for the University of Iowa (UI) Department of Biostatistics to recruit a diverse group of 18 trainees each year, from 2016 to 2018, with focus on minority, underrepresented and disadvantaged students who wouldn't have otherwise been exposed to the field of biostatistics.

**Completed**

G-17-1500 PI: Allen (PI), Smith (Co-Investigator) 1/1/18-12/31/20
Gateway for Cancer Research
Pharmacological Ascorbate Combined with Radiation and Temozolomide in GBM
Phase 2 clinical trial assessing the efficacy of pharmacological ascorbate as an adjuvant therapy in glioblastoma multiforme (GBM).

U01 CA140206 Buatti (PI), Smith (Biostatistician) 04/01/10 - 08/31/20
NIH
Quantitative Imaging to Assess Response in Cancer Therapy Trials
This U01 mechanism is designed to promote research on quantitative imaging of tumor response in clinical trials settings with the overall goal of facilitating clinical decision making. All are committed to fully contribute toward our efforts to the envisioned Quantitative Imaging Network (QIN) and will use familiar common platforms of caBIG, NCIA (National Cancer Imaging Archive) and caBIG Imaging Workspace.

R21 CA209874-01 Wu (PI), Smith (Co-Investigator) 9/6/16-7/31/18
NIH
Developing Enabling PET-CT Image Analysis Tools for Predicting Response in Radiation Cancer Therapy
This research proposes to develop fast and objective PET-CT analysis methods to facilitate the utilization of the dual modality imaging for both large-scale clinical trial research and daily clinical care. The novel feature of the proposed methods is the first time to introduce co-segmentation for PET-CT tumor delineation, which recognizes the contour difference of tumors in PET from those in CT. New PET-CT specific priors will be explored and incorporated into the segmentation framework, further improving the accuracy of segmentation. The novel response prediction method is built on the accurate tumor definition from our PET-CT co-

segmentation approach, with an innovative design of a convolutional neural network for automatically leaned hierarchical features directly from the PET-CT scans, leading to highly accurate prediction of response. The developed methods will be tested in comparison with state-of-the-art methods utilized today. The performance of the methods will be statistically assessed in data samples of sufficient sizes.

R01 CA099908 Leslie (PI), Smith (Biostatistician) 07/1/13 - 04/30/18
NIH
Targeted Therapy for Endometrial Cander
The major emphasis of this study is on the rational development of novel therapeutic strategies for molecularly enhanced chemotherapy in endometrial cancer that will have a significant potential for early translation to the clinic. The findings from this comprehensive research plan will be rapidly deployed in future clinical trials.

R01 CA184101 Meng/Lesilie (PI), Smith (Co-Investigator) 09/18/14 - 08/31/19
NIH
MTDH Regulates Fanconi Anemia Repair Pathway to Mediate Drug Resistance
The major emphasis of this grant is on translational studies that will provide novel insight into the mechanisms by which regulation of RNA translation produces alterations in DNA repair pathways, thereby leading to drug resistance.

W81XWH-16-1-0180 Giangrande (PI), Smith (Co-Investigator) 9/15/16-9/14/19
DOD
PR150627P1: Targeting Extracellular Histones with Novel RNA Bio-Drugs for the Treatment of Acute Lung Injury
This project will study in vitro characterization and optimization of RNA aptamers that selectively bind to human histone and will evaluate efficacy and safety of histone-specific RNA aptamers in vivo.