
BIOGRAPHICAL SKETCH

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NAME: **Natasha D. Sheybani**

eRA COMMONS USER NAME (credential, e.g., agency login): **NDS3SANIH**

POSITION TITLE: **Assistant Professor**

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion Date	FIELD OF STUDY
Virginia Commonwealth University, Richmond, VA	BS (Honors)	2015	Biomedical Engineering
University of Virginia, Charlottesville, VA	PhD	2020	Biomedical Engineering
Stanford University, Stanford, CA	Postdoc	2021	Oncology, Radiology, Biomedical Data Science

A. Personal Statement

As a biomedical engineer and Research Director of the UVA Focused Ultrasound (FUS) Cancer Immunotherapy Center, my expertise is in tuning MR- and ultrasound-imaging guided focused ultrasound (FUS) to support cancer immunotherapy paradigms. I lead a multidisciplinary, collaborative, translational research program centered on advancing applications of FUS technology and multimodality imaging for immuno-modulation and drug delivery in complex solid tumors settings such as metastatic breast cancer and brain cancers. I have also spearheaded exploration of themes in extracellular vesicle (EV) biology and nuclear medicine (i.e. immunoPET imaging) to inform FUS immuno-oncology paradigms. This research has resulted in several high impact publications (e.g., *The Journal for ImmunoTherapy of Cancer*, *Theranostics*, *Journal of Controlled Release*, *Trends in Pharmacological Sciences*), scientific meeting abstracts, presentations, invited seminars and conference talks, and prestigious awards including the NCI Predoctoral-to-Postdoctoral Fellow Transition Award (F99/K00) and NIH Director's Early Independence Award (DP5). My work deploying FUS toward immunotherapy in breast cancer has been translated into a clinical trial now ongoing at UVA (NCT04796220), and I am Co-Investigator on a recently FDA-approved clinical trial deploying sonodynamic therapy with neuronavigation-guided FUS in recurrent glioblastoma patients (NCT06039709). Current projects in my laboratory deploy image-guided thermal and mechanical FUS regimens in combination with immune checkpoint blockade antibodies, engineered T cells, or adjuvant chemotherapies in murine cancer models. Our long-term goal is to advance FUS into the era of non-invasive precision immuno-oncology by engineering strategies for risk stratification, surveillance, and rational adaptation of combinatorial FUS paradigms. As such, we are also (1) advancing roles for liquid biopsy (of EVs, for example) and molecular imaging as non-invasive, repeatable adjuncts to FUS paradigms and (2) in advanced neurosurgical applications of FUS, exploring early use cases for AI-driven outcome prediction from routine medical imaging.

Ongoing and recently completed projects that I would like to highlight include:

Translational Adult Glioma Award Sheybani (PI) 7/1/23 – 6/30/26
Ben & Catherine Ivy Foundation
Rational Combination of CAR-T Cells and MR Image-Guided Focused Ultrasound for Glioblastoma Therapy

DP5 OD031846-01 Sheybani (PI) 9/1/21 – 8/31/26
NIH/OD
Immunoengineering Next-Generation Cancer Therapies with Focused Ultrasound

F99/K00 K00CA234954 Sheybani (PI) 9/1/20 – 8/31/24
NIH/NCI

A Radiogenomics Framework for Non-Invasive Clinical Risk Prediction & Personalized Diffuse Large B Cell Lymphoma Therapy

Selected Recent Relevant Publications:

1. **Sheybani ND[§]**, Breza VR, Paul S, McCauley KS, Berr SS, Miller GW, Neumann KD, Price RJ. ImmunoPET-Informed Sequence for Focused Ultrasound-Targeted mCD47 Blockade Controls Glioma. *Journal of Controlled Release*. 2021. DOI: 10.1016/j.jconrel.2021.01.023. PMID: PMC7946780. (**§Corresponding Author**)
2. **Sheybani ND[§]**, Batts AJ, Mathew AS, Thim EA, Price RJ. Focused Ultrasound Hyperthermia Modulates Release and Immunostimulatory Capacity of Glioma-Derived Extracellular Vesicles. *Theranostics*. 2020. DOI:10.7150/thno.46534. PMID: PMC7330848. (**§Corresponding Author**)
3. **Sheybani ND***, Witter AR*, Thim EA, Yagita H, Bullock TNJ, Price RJ. Combination of Thermally Ablative Focused Ultrasound with Gemcitabine Controls Breast Cancer via Adaptive Immunity. *Journal for ImmunoTherapy of Cancer*. 2020. DOI: 10.1136/jitc-2020-001008. PMID: PMC7443308. (*Authors contributed equally)
4. **Sheybani ND[§]**, Witter AR, Garrison WJ, Miller GW, Bullock TNJ[§], Price, RJ[§]. Profiling of the Immune Landscape in Murine Glioblastoma following Blood Brain/Tumor Barrier Disruption with MR Image-guided Focused Ultrasound. *Journal of Neuro-Oncology*. 2021. DOI: 10.1007/s11060-021-03887-4. PMID: 34734364. (**§Corresponding Author**)

B. Positions, Scientific Appointments, and Honors**Positions**

2022-	Assistant Professor (tenure-track), Department of Biomedical Engineering, University of Virginia
2021-	Research Director, UVA Focused Ultrasound Cancer Immunotherapy Center
2021-	Assistant Professor of Radiology & Medical Imaging (Courtesy), University of Virginia
2021-	Assistant Professor of Neurosurgery (Courtesy), University of Virginia
2021-2022	Assistant Professor of Research, Department of Biomedical Engineering, University of Virginia
2021-2022	Visiting Instructor, Division of Oncology, Department of Medicine, Stanford University

Selected Honors and Professional Service**Honors & Awards**

2023	International Society for Therapeutic Ultrasound “Rising Scientist in Therapeutic Ultrasound” (one of three honorees selected from international applicant pool)
2023	Appointed by UVA VPR’s Office as Research Communication Fellow
2023	Oak Ridge Associated Universities (ORAU) Ralph E. Powe Junior Faculty Enhancement Award
2023	UVA Comprehensive Cancer Center Neuro-Translational Research Team Pilot Award
2023	UVA School of Engineering & Applied Science Research Innovation Award
2023	MIT Technology Review 35 Innovators Under 35, Semi-Finalist
2022	Acoustical Society of America (ASA)-International Society for Therapeutic Ultrasound (ISTU) Early Career Investigator Travel Award
2021	NIH Director’s Early Independence Award (first-ever recipient from UVA)
2021	Forbes 30 Under 30 Class of 2022 (Science)
2021	Rising Star in Engineering in Health (awarded by Columbia University Schools of Engineering & Medicine, in partnership with Johns Hopkins University Biomedical Engineering)
2021	Council of Graduate Schools / ProQuest Distinguished Dissertation Award, Finalist
2021	Alberto Biggi Award (top abstract prize), 8th Int’l Workshop on PET in Lymphoma & Myeloma
2020	STAT Wunderkind, Finalist
2020	Society for Immunotherapy of Cancer, Young Investigator Travel Award
2018	Rising Star Award, Focused Ultrasound Foundation
2018	Young Investigator Award, 6th International Symposium on Focused Ultrasound
2018	Best Poster Presentation Award, Controlled Release Society Annual Meeting
2018	Best Oral Presentation Award, International Society for Therapeutic Ultrasound Annual Meeting
2018	Student Travel Award, International Society for Therapeutic Ultrasound Annual Meeting

2018 St. Jude National Graduate Student Symposium (Invited Presenter)
 2018 Selected to attend Cancer Biology Training Consortium 14th Annual Cancer Biology Retreat
 2018 AAAS/Science Program for Excellence in Science
 2017 Trainee Award, 1st Annual Commonwealth of Virginia Cancer Research Conference
 2013 Launch Award, VCU Annual Poster Symposium for Undergraduate Research and Creativity
 (highest undergraduate research honor; funded by the VCU National Quest for Distinction)
 2012-2015 Dean's List & University Scholar, VCU
 2012-2015 VCU Honors College, *Summa Cum Laude*
 2010 Award for Aspirations in Computing, National Center for Women and Information Technology

Fellowships & Scholarships

2018 NIH/NCI F99/K00 Predoctoral-to-Postdoctoral Transition Award (first-ever recipient from UVA)
 2017 UVA School of Engineering and Applied Science Teaching Fellowship
 2017 UVA School of Medicine Robert R. Wagner Fellowship
 2016 NSF Graduate Research Fellowship
 2012 VCU Provost Scholarship
 2012 Eugene P. Trani Scholarship (merit-based; awarded to only 4 out of ~24,000 incoming VCU
 freshmen)
 2012 The Coca-Cola Scholars Program Scholarship

Outreach Support

2015-2017 National Center for Women & Information Technology AspireIT K-12 Outreach Program Grant
 (Total funding awarded to date: \$6,300)

Professional Service & Leadership

2023- American Cancer Society Institutional Research Grant Review Committee
 2023- UVA Biomedical Engineering Research Success Committee
 2022-2023 Elected to Academy for Radiology & Biomedical Imaging Research Council of Early Career
 Investigators in Imaging (CECI²) – *regularly invited to engage in patient and science advocacy*
 2022- Appointed to Organizing Committee for Inaugural “Emerging Leaders in Biomedical
 Engineering” Symposium (sponsored by UVA Provost’s office)
 2021- Steering Committee, UVA Center for Focused Ultrasound Immuno-Oncology
 2021-2023 UVA Biomedical Engineering Graduate Admissions Committee
 2021- International Society for Therapeutic Ultrasound Student Membership & Awards Committee
 2021- Research Advisory Committee, Focused Ultrasound Foundation
 2021- Programming Committee, Focused Ultrasound Foundation Workshops (1. Cancer
 Immunotherapy, 2. Glioblastoma)
 2021 Guest Co-Editor for *Pharmaceutics* Special Issue (Ultrasound-Mediated Delivery of
 Nanopharmaceuticals)
 2020 Programming Committee, 7th International Symposium on Focused Ultrasound
 2020- Steering Committee, NIH Center for Interventional Oncology “Women Leaders in Academic
 Research” Seminar Series
 2020 Co-Founder, Women in Focused Ultrasound Interest Group
 2021 Session Chair (Immunotherapy/Other), 20th Annual ISTU Meeting
 2019 Session Chair (Immunotherapy), 19th Annual ISTU Meeting
 2018-2020 Ambassador, Controlled Release Society Young Scientists Committee
 2018 Programming Committee, Focused Ultrasound for Glioblastoma Workshop, FUS Foundation
 2018 Programming Committee, 6th International Symposium on Focused Ultrasound
 2018-2020 Reviewer, UVA School of Medicine Summer Research Internship Program
 2017- *Ad-Hoc* Reviewer (Journals: Scientific Reports, PLOS One, Ultrasound in Medicine & Biology,
 Theranostics, Journal of Controlled Release, PNAS, IEEE TUFFC, Frontiers in Oncology,
 Clinical & Translational Medicine)
 2017 Programming Committee, 1st Annual Commonwealth of VA Cancer Research Conference
 2016-2020 Student Editorial Board, IEEE Journal of Translational Engineering in Health and Medicine
 2016-2020 Reviewer, NSF GRFP Application Reviews at UVA (organized by Office of Graduate and
 Postdoctoral Affairs)

Grant Review

DoD CDMRP Breast Cancer Research Program (BCRP), Pathobiology Panel 6 (Dec 2022)
NIH/NCI Therapeutic Immune Regulation (TIR) study section (Nov 2022)
NIH/NIBIB Mentored Career Development Awards (Ks) and R13 SEP (July 2022)
NIH/NCI Cancer Immunopathology & Immunotherapy (CII) Overflow SEP (June 2022)

C. Contributions to Science

1. Therapeutic Ultrasound for Immunotherapy of Solid Peripheral Malignancies. During my graduate studies and now into my independent research career, I have led research centered on the implementation of FUS-mediated immunotherapy paradigms for metastatic breast cancer and melanoma. The goal of these studies has been to (i) systematically dissect mechanisms of innate and adaptive immune response elicited by various modes of FUS and (ii) use this information to design and test immunotherapeutic approaches predicted to synergize with FUS. For metastatic breast cancer therapy, we engineered a promising strategy for elevating the immune modulatory capacity of FUS partial thermal ablation through combination with gemcitabine, a myelo-reductive chemotherapy. A new clinical trial (NCT04796220; PI: Patrick Dillon, MD) directly resulting from this work is presently ongoing at UVA. This work has additionally facilitated rich opportunities to independently engage in collaborations within the clinical setting; non-profit sector (FUS Foundation Merkin Scholars); and industry (Theraclion, Adial Pharmaceuticals).

- a. **Sheybani ND***, Witter AR*, Thim EA, Yagita H, Bullock TNJ, Price RJ. Combination of Thermally Ablative Focused Ultrasound with Gemcitabine Controls Breast Cancer via Adaptive Immunity. *Journal for ImmunoTherapy of Cancer*. 2020. DOI: 10.1136/jitc-2020-001008. PMCID: PMC744330. (*Authors contributed equally)
- b. Thim EA, Fox T, Deering T, Vass LR, **Sheybani ND**, Kester M, Price RJ. Solid Tumor Treatment via Augmentation of Bioactive C6 Ceramide Levels with Thermally Ablative Focused Ultrasound. *Drug Delivery and Translational Research*. 2023. DOI: 10.1007/s13346-023-01377-w. PMCID: PMC10055354.
- c. **Sheybani ND**, Witter AR, Thim EA, Bullock TNJ, Price RJ. Focused Ultrasound Thermal Ablation in Combination with Gemcitabine Elicits an Adaptive Immune Response Against Metastatic Breast Cancer that Controls Tumor Growth and Improves Survival. (Abstract) *Biomedical Engineering Society Annual Meeting*; 2019; Philadelphia, PA.
- d. **Sheybani ND** and Price RJ. Perspectives on Recent Progress in Focused Ultrasound Immunotherapy. *Theranostics*. 2019. doi:10.7150/thno.37131. PMCID: PMC6831458.

2. MR Image-guided Focused Ultrasound for Brain Tumor Immunotherapy. I have also led or collaborated on studies examining the impact of FUS-mediated blood brain/tumor barrier disruption (BBB/BTB-D) on immune response to primary or metastatic brain tumors. Most notably in the context of glioblastoma, I have led some of the earliest studies in our field geared toward understanding how FUS BBB/BTB-D modulates the tumor-immune landscape – with specific attention to the influence of such parameters as peak negative pressure and anesthesia. As a graduate student, I also spearheaded a collaboration with faculty in UVA Radiology & Medical Imaging to investigate the impact of FUS on mCD47 delivery to gliomas using immuno-PET imaging. This collaboration has since been fortified into a robust and rapidly expanding research enterprise at the nexus of FUS and nuclear medicine research at UVA. I am currently leading a FUS Foundation-funded consortium study that has convened multiple institutions across North America to systematically evaluate the immunomodulatory impact of various thermal or mechanical FUS regimes in murine glioma. I am serving as the lead author on this manuscript, which is currently in preparation.

- a. **Sheybani ND[§]**, Breza VR, Paul S, McCauley KS, Berr SS, Miller GW, Neumann KD, Price RJ. ImmunoPET-Informed Sequence for Focused Ultrasound-Targeted mCD47 Blockade Controls Glioma. *Journal of Controlled Release*. 2021. DOI: 10.1016/j.jconrel.2021.01.023. PMCID: PMC7946780. ([§]Corresponding Author)
- b. **Sheybani ND[§]**, Witter AR, Garrison WJ, Miller GW, Bullock TNJ[§], Price, RJ[§]. Profiling of the Immune Landscape in Murine Glioblastoma following Blood Brain/Tumor Barrier Disruption with MR Image-guided Focused Ultrasound. *Journal of Neuro-Oncology*. 2021. DOI: 10.1007/s11060-021-03887-4. PMID: 34734364. ([§]Corresponding Author)
- c. Curley CT, Stevens AD, Mathew AS, Stasiak K, Garrison WJ, Miller GW, **Sheybani ND[§]**, Engelhard VH, Bullock TNJ[§], Price RJ[§]. Immunomodulation of Intracranial Melanoma in Response to Blood-Tumor

Barrier Opening with Focused Ultrasound. *Theranostics*. 2020. DOI: 10.7150/thno.47983. PMCID: PMC7392000. (§Corresponding Authors)

- d. Curley CT*, **Sheybani ND***, Bullock TN, and Price RJ. Focused Ultrasound Immunotherapy for Central Nervous System Pathologies: Challenges and Opportunities. *Theranostics*. 2017. doi:10.7150/thno.21225. PMCID: PMC5667336. (*Authors contributed equally)

3. Evaluation of Focused Ultrasound in Naïve Brain Tissue. In addition to understanding the impact of FUS BBB disruption in malignant brain tissues, we have studied the response of naïve brain tissue to this regime, placing emphasis on the roles of anesthesia and acoustic feedback monitoring in this context. I have contributed significantly to the ideation and conceptual framework underpinning collaborative studies evaluating the transcriptomic response of naïve brain tissue following FUS BBB disruption.

- a. Mathew AS, Gorick CM, Thim EA, Garrison WL, Klibanov AL, Miller GW, **Sheybani ND**[§], Price RJ[§]. Transcriptomic Response of Brain Tissue to Focused Ultrasound-Mediated Blood-Brain Barrier Disruption Depends Strongly on Anesthesia. *Bioengineering & Translational Medicine*. 2020. DOI: 10.1002/btm2.10198. PMCID: PMC8126816. (§Corresponding Authors)
- b. Gorick CM, **Sheybani ND**, Curley CT, Price RJ. Listening in on the Microbubble Crowd: Advanced Acoustic Monitoring for Improved Control of Blood-Brain Barrier Opening with Focused Ultrasound. *Theranostics*. 2018. DOI: 10.7150/thno.26025. PMCID: PMC5996352.

4. Focused Ultrasound and Extracellular Vesicles. With an eye toward expanding our armamentarium of tools for non-invasive cancer management and advancing our mechanistic understanding of how FUS can be leveraged for precision oncology paradigms, we are interested in interrogating the tumor circulome using liquid biopsy techniques. To this end, we have active interest in extracellular vesicles (EVs) owing to their emerging role as promising biomarkers to inform the surveillance and adaption of cancer treatment. Very few studies have been published at the interface of FUS and EVs to date. As a graduate student, I pursued an independent line of investigation exploring the impact of FUS hyperthermia on EV release and profile – the first study to evaluate (i) the impact of a thermal FUS regime on EVs and (ii) the immunomodulatory capacity of FUS-exposed EVs. We demonstrated that both hyperthermia and microbubble activation with FUS augment glioma-derived EV release. In the context of FUS hyperthermia, we also demonstrated shifts in proteomic profile and innate immune stimulatory capacity of FUS-exposed EVs. I subsequently led the publication of an invited review paper on the functional intersections of non-viral oncolytic therapies and EVs.

- a. Clark RA, Garman ZG, Price RJ, **Sheybani ND**[§]. Functional Intersections Between Extracellular Vesicles and Oncolytic Therapies. *Trends in Pharmacological Sciences*. 2021. DOI: 10.1016/j.tips.2021.09.001. PMCID: PMC8526420. (§Corresponding Author)
- b. **Sheybani ND**[§], Batts AJ, Mathew AS, Thim EA, Price RJ. Focused Ultrasound Hyperthermia Modulates Release and Immunostimulatory Capacity of Glioma-Derived Extracellular Vesicles. *Theranostics*. 2020. DOI:10.7150/thno.46534. PMCID: PMC7330848. (§Corresponding Author)

5. Nanoformulations for Oral and Ocular Drug Delivery. Previously as a high school and undergraduate research assistant (including two terms as an NSF REU student) in the lab of Dr. Hu Yang (VCU Biomedical Engineering), I performed research centered on fabrication and characterization of (i) semi-interpenetrating polymer networks for transbuccal insulin delivery and (ii) cyclodextrin-dendrimer nanoformulations for pediatric ocular siRNA delivery. This work yielded multiple peer-reviewed publications, abstracts, presentations and awards - a fraction of which are highlighted herein.

- a. Xu L, **Sheybani N**, Yeudall WA, Yang H. The effect of photoinitiators on intracellular AKT signaling pathway in tissue engineering application. *Biomater Sci*. 2015;3:250-5. doi: 10.1039/C4BM00245H. PMCID: PMC4335638
- b. Xu L, **Sheybani N**, Ren S, Bowlin GL, Yeudall WA, Yang H. Semi-Interpenetrating Network (sIPN) Co-Electrospun Gelatin/Insulin Fiber Formulation for Transbuccal Insulin Delivery. *Pharm Res*. 2015;32:275-85. doi: 10.1007/s11095-014-1461-9. PMID: 25030186.
- c. **Sheybani ND**, Yang H. Pediatric ocular nanomedicines: Challenges and opportunities. *Chinese Chemical Letters*. 2017. doi: http://dx.doi.org/10.1016/j.ccllet.2017.07.022. PMCID: PMC5683720.

Link to publications: <https://www.ncbi.nlm.nih.gov/myncbi/natasha.sheybani.1/bibliography/public/>