BIOGRAPHICAL SKETCH

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NAME: **Zaver M. Bhujwalla**

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

POSITION TITLE: **Professor of Radiology; Director, Division of Cancer Imaging Research, Department of Radiology; Vice-Chair of Research, Department of Radiology**

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
Univ. of Bombay, India (St. Xavier's College)	B.Sc.	1980	Physics, Mathematics
Univ. of Bombay, India (St. Xavier's College)	M.Sc.	1982	Biophysics
Univ. of London, UK (Middlesex Hospital Med School)	M.Sc.	1985	Radiation Biology
Univ. of London, UK (Royal Postgrad. Med School)	Ph.D.	1988	Radiation Biology

A. Personal Statement

Dr. Bhujwalla's work is dedicated to the applications of molecular and functional imaging to understand and target cancer and the tumor microenvironment. She is a Fellow of the International Society of Magnetic Resonance in Medicine, the American Institute of Biomedical Engineers, and the World Molecular Imaging Society. Dr. Bhujwalla is currently associated with the editorial boards of *Molecular Imaging*, *NMR in Biomedicine*, *Cancer Biology and Therapy*, and *Tomography*. She serves as the Specialty Chief Editor-*Cancer Imaging and Diagnosis, Frontiers in Oncology*. Dr. Bhujwalla has over 195 publications in this field. At the Johns Hopkins University School of Medicine Dr. Bhujwalla serves as Director of the Division of Cancer Imaging Research, Vice-Chair of Research, and Director of the MRB Molecular Imaging Center and Cancer Functional Imaging Core in the Dept. of Radiology. She also co-directs the Cancer Molecular and Functional Imaging Program of the Sidney Kimmel Comprehensive Cancer Center (SKCCC). Dr. Bhujwalla serves as Chair of the Career Development Advisory Committee of the Dept. of Radiology.

B. Positions and Honors

Positions and Employment

1982-83	Diploma in Radiological Physics, Bhabha Atomic Research Center, Division of Radiation Protection, Mumbai, India
1983-84	Hospital Physicist, Dept. of Radiation Oncology, Tata Memorial Center, Mumbai, India
1989-91	Postdoctoral Research Fellow, NMR Research Division, Dept. of Radiology, Johns Hopkins Univ. School of Medicine, Baltimore, MD
1991-92	Instructor, NMR Research Division, Dept. of Radiology, Johns Hopkins Univ. School of Medicine, Baltimore, MD
1992-98	Assistant Professor, Division of MR Research, Dept. of Radiology, Johns Hopkins Univ. School of Medicine, Baltimore, MD
1998-02	Associate Professor of Radiology, Johns Hopkins Univ School of Medicine, Baltimore, MD
2000-02	Associate Professor of Oncology, Johns Hopkins Univ School of Medicine, Baltimore, MD
2002-	Professor of Radiology, Johns Hopkins University School of Medicine, Baltimore, MD
2002-	Professor of Oncology, Johns Hopkins University School of Medicine, Baltimore, MD

2012-	Inaugural Director, Division of Cancer Imaging Research, Department of Radiology
2016-	Vice-Chair of Research, Department of Radiology
2017-	Professor of Radiation Oncology and Molecular Radiation Sciences

Honors

2006	The Negendank Lecture "To Image and Imagine: Molecular and Functional Imaging of Cancer" Cancer Study Group of the ISMRM
2007	Fellow of the American Institute for Medical and Biological Engineering
2007	Fellow of the International Society of Magnetic Resonance in Medicine
2009	Outstanding Teacher Award, International Society of Magnetic Resonance in Medicine, Honolulu
2012-2013	President of the World Molecular Imaging Society
2012	Distinguished Investigator, Academy of Radiology Research.
2013	Fellow of the World Molecular Imaging Society
2014	The Alan C. Burton Lecture, 'Molecular and Functional Imaging of the Tumor Microenvironment', University of Western Ontario and Schulich Medical Center, London, Ontario, Canada
2015	Distinguished Lecturer, 'A Molecular Imaging Journey through the Tumor Microenvironment', Department of Radiology Grand Rounds, Emory University School of Medicine, Atlanta, Georgia
2017	Plenary Lecture, ISMRM 2017, 'Theranostic MRI in Oncology', Honolulu
2017	Gold Medal Award and Lecture, World Molecular Imaging Society, Philadelphia
2017	NCI Outstanding Investigator Award (R35)

National Committees

1996, 97, 98	Reviewer for the Radiological Sciences Study Section of the USAMRMC Breast Cancer Program
1998	Reviewer for the California Breast Cancer Research Program
1998	Reviewer for the Susan Komen Breast Cancer Foundation
1998, 99, 00	Ad Hoc Reviewer for the NIH Diagnostic Radiology Study Section
2000	Reviewer for the USAMRMC Prostate Cancer Program
2001	Reviewer for NCI RFA: 01-014 (P50) to est. *In vivo* Cellular and Molecular Imaging Cancer Centers
2006	Reviewer for NCI RFA CA-06-014, Tumor Microenvironment Network
2003-07	Reviewer for the NIH Medical Imaging Study Section
2010	Reviewer for the NIH P30 COBRE III Transitional Center
2011-	Ad Hoc Reviewer for the NIH
2015	Reviewer for the NIH R35 'Outstanding Investigator Award'

Editorial Advisory Boards

Current	*Cancer Biology and Therapy, Molecular Imaging, NMR in Biomedicine, Tomography, Frontiers in Oncology - Specialty Chief Editor- Cancer Imaging and Diagnosis*

Professional Societies

American Association of Cancer Research
American Institute for Medical and Biological Engineering - Fellow.
International Society of Magnetic Resonance in Medicine - Fellow
Radiological Society of North America – Member of the Molecular Imaging Subcommittee
World Molecular Imaging Society – Fellow

C. Contribution to Science

I. *Choline metabolism in cancer:* There are very few common pathways in cancer. In 1997 a colleague, Dr. Joseph Backer, provided me with breast cancer cells transfected with a metastasis suppressor gene and I identified differences in choline metabolism between wild type and transfected breast cancer cells. These initial observations have led me to studies, performed with my team, as well as more recently in collaboration with Dr. Glunde, of over a decade of investigating choline metabolism in cancer. With my team, we have demonstrated that aberrant choline metabolism is a common pathway and hallmark of cancer. We have identified overexpression of choline kinase as a major cause of this aberrant metabolism. These studies have

contributed to the development of ^{1}H MRS and ^{11}C and ^{18}F radiolabeled choline PET for the detection and management of cancers. I serve as the Principal Investigator in these studies.

1. Aboagye, E. and Bhujwalla, Z. M. Malignant Transformation Alters Membrane Phospholipid Metabolism of Human Mammary Epithelial Cells. Cancer Research, 59: 80-84, 1999. PRIOR TO 2008
2. Ackerstaff, E., Pflug, B. R., Nelson, J. B., and Bhujwalla, Z. M. Detection of Increased Choline Compounds with 1H NMR Spectroscopy following Malignant Transformation of Human Prostatic Epithelial Cells. Cancer Research, 61: 3599-3603, 2001. PRIOR TO 2008.
3. Glunde K, Jie C, Bhujwalla ZM. Molecular causes of the aberrant choline phospholipid metabolism in breast cancer. Cancer Res. 64: 4270-6, 2004. PRIOR TO 2008
4. Penet MF, Shah T, Bharti S, Krishnamachary B, Artemov D, Mironchik Y, Wildes F, Maitra A, Bhujwalla ZM. Metabolic imaging of pancreatic ductal adenocarcinoma detects altered choline metabolism. Clin Cancer Res. 21: 386-95, 2015. PMCID:PMC4297549

II. *Inflammation and COX-2 in breast cancer*: The initiative for these studies arose in 1997 because of my strong interest in tumor hypoxia and pH that led me to think that these 'hostile tumor environments' may lead to invasion and metastasis through upregulation of inflammation. With my team, we have, over the past decade, applied molecular and functional imaging techniques to uncover new roles for COX-2 in breast cancer. I serve as the Principal Investigator in these studies. Recently, in collaboration with Dr. Steven An of the School of Public Health, we have uncovered the role of COX-2 in mechanotransduction.
1. Stasinopoulos I, O'Brien DR, Wildes F, Glunde K, and Bhujwalla ZM. Silencing of cyclooxygenase-2 inhibits metastasis and delays tumor onset of poorly differentiated metastatic breast cancer cells. Mol Cancer Res. 5: 435-42, 2007.
2. Stasinopoulos I, Mori N, Bhujwalla ZM. The malignant phenotype of breast cancer cells is reduced by COX-2 silencing. Neoplasia. 10: 1163-9, 2008. PMCID:PMC2570592
3. Shah T, Stasinopoulos I, Wildes F, Kakkad S, Artemov D, Bhujwalla ZM. Noninvasive imaging identifies new roles for cyclooxygenase-2 in choline and lipid metabolism of human breast cancer cells. NMR Biomed. 25: 746-54, 2012. PMCID:PMC4337877
4. Yoon AR, Stasinopoulos I, Kim JH, Yong HM, Kilic O, Wirtz D, Bhujwalla ZM, An SS. COX-2 dependent regulation of mechanotransduction in human breast cancer cells. Cancer Biol Ther. 16: 430-7, 2015. PMCID: PMC4622920

III. *Vascularization, cancer stem cells, hypoxia, pH, collagen, macromolecular transport:* I have, for more than a decade, been actively working on understanding the relationship between vascularization, hypoxia, pH, cancer stem cells, and the extracellular matrix and their roles in invasion and metastasis using molecular and functional imaging. These studies performed in collaboration with Drs. Artemov, Gillies, and with members of my team, have uncovered novel aspects of the tumor microenvironment and its role in invasion and metastasis. I serve as the Principal Investigator in these studies.
1. Danhier P, Krishnamachary B, Bharti S, Kakkad S, Mironchik Y, Bhujwalla ZM. Combining Optical Reporter Proteins with Different Half-lives to Detect Temporal Evolution of Hypoxia and Reoxygenation in Tumors. Neoplasia, 17:871-81, 2015. PMCID: PMC4688563
2. Kakkad S, Zhang J, Akhbardeh A, Jacob D, Krishnamachary B, Solaiyappan M, Jacobs MA, Raman V, Leibfritz D, Glunde K, Bhujwalla ZM. Collagen fibers mediate MRI-detected water diffusion and anisotropy in breast cancers. Neoplasia. 2016 Oct;18(10):585-593. doi: 10.1016/j.neo.2016.08.004. Epub 2016 Sep 19. PMCID: PMC5035345.
3. Penet MF, Kakkad S, Pathak AP, Krishnamachary B, Mironchik Y, Raman V, Solaiyappan M, Bhujwalla ZM. Structure and Function of a Prostate Cancer Dissemination-Permissive Extracellular Matrix. Clinical cancer research: an official journal of the American Association for Cancer Research. 2017;23(9):2245-54. doi: 10.1158/1078-0432.CCR-16-1516. PubMed PMID: 27799248; PubMed Central PMCID: PMC5411337.
4. Krishnamachary B, Stasinopoulos I, Kakkad S, Penet MF, Jacob D, Wildes F, Mironchik Y, Pathak AP, Solaiyappan M, Bhujwalla ZM. Breast cancer cell cyclooxygenase-2 expression alters extracellular matrix structure and function and numbers of cancer associated fibroblasts. Oncotarget. 2017;8(11):17981-94. doi: 10.18632/oncotarget.14912. PubMed PMID: 28152501; PubMed Central PMCID: PMC5392301.

IV. *Theranostic imaging for precision medicine:* Recently, I and my team have become actively engaged in developing theranostic imaging for precision medicine in cancer. The combination of detection and treatment provides exciting new avenues for minimizing damage to normal tissue and delivering tumor-specific treatments. These studies are being expanded to photoimmunotherapy and to theranostic imaging of the

tumor microenvironment with multiple collaborators such as Drs. Kobayashi and Pomper. I serve as the Principal Investigator in these studies.

1. Li C, Penet MF, Wildes F, Takagi T, Chen Z, Winnard PT Jr, Artemov D, Bhujwalla ZM. Nanoplex delivery of siRNA and Prodrug Enzyme for Multimodality Image-Guided Molecular Pathway Targeted Cancer Therapy. ACS Nano, 4: 6707-16, 2010. PMCID:PMC2991391
2. Chen Z, Penet MF, Nimmagadda S, Li C, Banerjee SR, Winnard PT Jr, Artemov D, Glunde K, Pomper MG, Bhujwalla ZM. PSMA-Targeted Theranostic Nanoplex for Prostate Cancer Therapy. ACS Nano. 6: 7752-62, 2012. PMCID:PMC4066818
3. Chen Z, Penet MF, Krishnamachary B, Banerjee SR, Pomper MG, Bhujwalla ZM. PSMA-specific theranostic nanoplex for combination of TRAIL gene and 5-FC prodrug therapy of prostate cancer. Biomaterials. 2016;80:57-67. PMCID: PMC4706473
4. Jin J, Krishnamachary B, Mironchik Y, Kobayashi H, Bhujwalla ZM. Phototheranostics of CD44-positive cell populations in triple negative breast cancer. Scientific reports. 2016;6:27871. PMCID: 4908597.

V. *Cancer-induced cachexia:* Cancer-induced cachexia results in 20% of all cancer related deaths and is a major cause of morbidity. Molecular and functional imaging provide unique abilities to investigate this syndrome with a 'holistic' approach. I am actively investigating this syndrome, together with team members, using molecular and functional imaging to identify early biomarkers and novel metabolic targets that may have an impact in arresting this syndrome. I serve as the Principal Investigator in these studies.

1. Penet MF, Gadiya MM, Krishnamachary B, Nimmagadda S, Pomper MG, Artemov D, Bhujwalla ZM. Metabolic signatures imaged in cancer-induced cachexia. Cancer Res. 71: 6948-56, 2011. PMCID:PMC3217079
2. Penet MF, Winnard PT Jr, Jacobs MA, Bhujwalla ZM. Understanding cancer-induced cachexia: imaging the flame and its fuel. Curr Opin Support Palliat Care. 5: 327-33, 2011. PMCID:PMC4155489
3. Penet MF, Bhujwalla ZM. Cancer cachexia, recent advances, and future directions. Cancer J. 21:117-22, 2015. PMCID: PMC491015
4. Winnard PT Jr, Bharti S, Penet MF, Marik R, Mironchik Y, Wildes F, Maitra A, Bhujwalla ZM. Detection of Pancreatic Cancer-induced Cachexia using a Fluorescent Myoblast Reporter System and Analysis of Metabolite Abundance. Cancer Res. 2016; 6(6):1441-50. PMCID: PMC4794402

A full list of my published work can be found at: http://www.ncbi.nlm.nih.gov/pubmed/?term=bhujwalla+z

D. Research Support

Ongoing Research Support as Principal Investigator or Project Leader

R35CA209960 (Bhujwalla) 09/04/17- 08/31/24
NIH-NCI
Molecular Imaging and Theranostics of Cancer
Three broad interactive focus areas will be pursued: (1) investigating the tumor microenvironment (TME) to include understanding and imaging the extracellular matrix and mechanotransduction; (2) investigating the tumor – body interactions (the tumor macroenvironment, TMacE), to advance understanding of the cachexia syndrome; (3) development of cancer cell membrane biomimetic theranostic agents to induce an anti-tumor immune response.

P41EB024495 (Pomper) 09/15/17- 06/30/22
NIH-NIBIB
TR&D1 Co-Leader
Resource for Molecular Imaging Agents in Precision Medicine
To develop and disseminate an array of translational molecular imaging agents for precision medicine. Our purpose is to serve as a resource for small molecule and macromolecular multi-modality imaging agents.

P30CA06973 (Nelson) 05/07/97 - 04/30/22
NCI Cancer Center Support Grant
Cancer Functional and Molecular Imaging Program - Co-Director
Cancer Functional Imaging Core - Resource Director
The Sidney Kimmel Comprehensive Cancer Center conducts basic, clinical and translational research to reduce cancer morbidity and mortality. As Resource Director, my goal is to provide an imaging resource for the Sidney Kimmel Comprehensive Cancer Center.

R01CA82337 (Bhujwalla) 07/01/99 - 03/31/18- 2nd NCE
NIH-NCI

Hostile Environments Promote Invasion and Metastasis
We intend to uncover new targets that interact with COX-2, and identify the effect of COX-2 expression on extracellular matrix structure and function. We also intend to develop probes to noninvasively image COX-2 expression and activity.

R01CA136576 (Bhujwalla) 07/01/09 - 05/31/18 (relinquished for R35)
NIH-NCI
Imaging Hypoxia and Cancer Stem Cells
The goal of this project is to understand the role of the tumor microenvironment in harboring or creating stem-like cancer cells.

R01CA073850 (Bhujwalla) 04/01/97 - 11/30/17 – 2nd NCE
NIH-NCI
Functional Imaging of the Metastatic Phenotype
To apply molecular and functional imaging to understand prostate cancer invasion and metastasis. These studies are being performed with a specially designed MR compatible cell perfusion system that can be used to understand the interaction between prostate cancer cells and stromal cells under carefully controled physiological conditions of oxygenation and pH. *In vivo* studies are being performed with human prostate cancer xenografts.

R21 CA198243 (Bhujwalla) 07/01/15-06/30/18- NCE
NIH-NCI
Decoy Nanoparticles to disrupt cancer cell-stromal cell networks
Here we have focused on developing decoy nanoparticles (NPs) to disrupt the interactions between cancer cells and stromal cells, in an effort to define novel biomembrane coated NP based strategies to prevent or attenuate breast cancer metastasis.

R01 CA193365 (Bhujwalla/Horton MPI) 12/01/15-11/30/20 (modified for R35)
Molecular Imaging of Cachexia in Pancreatic Cancer
NIH-NCI
Cachexia-induced weight loss of 5% over 3 to 6 months is associated with poor treatment outcome, fatigue and poor quality of life, and a weight loss of 30% is frequently lethal. We use metabolic imaging in combination with molecular characterization to understand cancer-induced cachexia and the cachexia cascade in pancreatic cancer xenograft models and human subjects.

Commonwealth Foundation (Bhujwalla) 04/01/16-3/31/18
The purpose of these studies is to develop phototheranostic imaging strategies for targeting cancer cells and the tumor microenvironment.

Emerson Collective Cancer Research Fund (Bhujwalla) 02/01/17- 01/31/19
JHU
Molecular Imaging of Biomimetic Cancer Immunosome Nanoparticles for Pancreatic Cancer Immunotherapy
The overall goal is to design and develop cancer cell membrane (CCM) coated FDA approved ploy (lactic-co-glycolic acid) PLGA nanoparticles (NPs) in different shapes partly mimicking viruses to determine the ability of these immunosomes to activate the adaptive immune response and increase tumor effector T cell infiltration in the Panc02 Syngeneic model of PDAC.

Completed Projects Within Last Three Years as Principal Investigator

P50CA103175 (Bhujwalla) 09/22/03-07/31/17
NIH-NCI
JHU ICMIC Program
This center grant funds an *in vivo* Cellular and Molecular Imaging Center at Johns Hopkins. The program consists of four research components, four developmental projects, one career development award and four resources.

R01CA138515 (Bhujwalla) 07/01/09 - 05/31/16
NIH-NCI
Image-Guided Prodrug and siRNA Targeting of Cancer
This purpose of this grant is two-fold – to develop effective treatment strategies utilizing image guided prodrug enzyme-siRNA treatment that will minimize damage to normal tissue and secondly to use these strategies to target metastatic lesions.