BIOGRAPHICAL SKETCH

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NAME: Caigang Zhu

eRA COMMONS USER NAME (credential, e.g., agency login): cgzhu123

POSITION TITLE: Assistant Professor (tenure-track), Department of Biomedical Engineering, University of Kentucky

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
Huazhong University of Science and Technology, China	B.S.	07/2008	Biomedical Engineering
Nanyang Technological University, Singapore	Ph.D	11/2014	Biomedical Engineering
Duke University, Durham, NC, USA	Postdoc	08/2019	Biomedical Engineering

A. Personal Statement

I have over 10 years of experience in optical spectroscopy, spectral imaging, Monte Carlo modeling based data processing algorithms, microscopy, translational research and cancer metabolism imaging. As a graduate student, I have developed Monte Carlo models, depth-sensitive optical spectroscopy and imaging devices for early epithelial cancer screening and skin tissue metabolism assessment. As a postdoctoral associate at Duke, I developed high resolution microscopes to perform vasculature and/or metabolic imaging in small animal models to inform breast cancer biology study with the mentoring from Drs. Nimmi Ramanujam and Mark Dewhirst. As an Assistant Professor of Biomedical Engineering at the University of Kentucky, I plan to develop a research program in which novel optical devices and techniques are applied to physiological sensing of the tumor metabolism and vascular microenvironment, for the purposes of identifying or evaluating therapeutic targets related to the tumor metabolism and microenvironment in pre-clinical models. Specifically, I plan to focus on the development of optical technologies including high throughput intra-vital multi-parametric microscopy and quantitative spectroscopy to advance the research in radiation resistance of human cancers. In addition, I am interested in translating these optical platforms to patient-derived tumor models for designing and predicting metabolism-targeted tumor therapy of cancer patients, as a means to provide improved therapeutics for patients whose tumors may recur following therapies. I have over **18** peer-reviewed journal papers (**12 first-authored**) published by high impact journals including Optics Letters, Optics Express, Plastic and reconstructive surgery, Scientific Reports, Journal of Biophotonics, Biomedical optics express and others. My work has been cited over 365 times so far by independent and leading researchers from prestigious institutions and organizations around the world, indicating the major significance of my work.

B. Positions and Honors

Positions and Employment

2004-2008 Undergraduate student, Huazhong University of Science and Technology, China
2008-2010 Graduate student, Huazhong University of Science and Technology, China
2010-2014 Graduate student, Nanyang Technological University, Singapore
2014-2014 Postdoctoral fellow, Dept. of Bioengineering, University of Washington, Seattle, WA
2015-2019 Postdoctoral Associate, Dept. of Biomedical Engineering, Duke University, Durham, NC
2019-now Assistant Professor, Dept. of Biomedical Engineering, University of Kentucky, Lexington, KY

Other Experience and Professional Memberships

2016-present Optical Society of America
2011-present SPIE−The International Society for Optical Engineering
2011-2012 SPIE Singapore Student Chapter Secretary
2012-2013 SPIE Singapore Student Chapter Vice president

Honors

2005-2006 Outstanding student, Huazhong University of Science and Technology, China
2010-2014 Graduate student fellowship, Singapore Ministry of Education
2018 Britton Chance symposium travel award

C. Contributions to Science

Metabolic and vascular imaging

Altered vascularity and deregulated metabolism are two important cancer hallmarks. Interest in therapeutically exploiting these functional endpoints continues to grow since metabolism and vasculature significantly impact a tumor's fate. Considering the importance of metabolism to cancer biology there are surprisingly few techniques available to provide a systems level approach to image metabolism and the associated vasculature *in vivo*. Being able to quantify tumor bioenergetics, in a live tumor microenvironment and being able to look at evolution of disease in the face of transient stress, is an important new direction and the new capabilities that this technology is poised to offer will have the potential to address these important questions in the cancer biology field. During my postdoctoral training at Duke, I have developed several microscopes that are able to quantify glucose uptake, mitochondrial membrane potential, and vascular structure and oxygenation *in vivo* in tumor models. At the University of Kentucky, I will leverage my strengths in intra-vital optical technologies to establish portable multi-parametric optical devices that are able to measure several key metabolic and vascular parameters simultaneously in small animal models for cancer biology and radiation biology research. These toolboxes allow for monitoring of the similar metabolic axes as *in vitro* cellular metabolism analyzers, but with the benefit of repeated, nondestructive imaging within an intact microenvironment and at a length-scale and resolution that complements PET and MRI imaging. By quantifying multiple key endpoints *in vivo*, our techniques provide a more holistic view of metabolism than most metabolic imaging techniques that measure a single endpoint (traditionally, glucose) or lack resolution to view spatial relationships. Ultimately, the metabolic imaging toolbox can be used to better understand metabolic reprogramming for cancer therapy.

a. **Caigang Zhu**, Martin Li, Thomas Vincent, Hannah L. Martin, Brian T. Crouch, Amy F. Martinez, Megan C. Madonna, Gregory M. Palmer, Mark W. Dewhirst, Nimmi Ramanujam, "Simultaneous optical quantification of key metabolic and vascular endpoints reveals tumor metabolic heterogeneity in murine flank tumor models ", Journal of Biophotonics, e201800372, 2018.

b. **Caigang Zhu**, Hannah L. Martin, Brian T. Crouch, Amy F. Martinez, Martin Li, Gregory M. Palmer, Mark W. Dewhirst, Nimmi Ramanujam, "Near-simultaneous quantification of glucose uptake, mitochondrial membrane potential, and vascular parameters in murine flank tumors using quantitative diffuse reflectance and fluorescence spectroscopy", Biomed. Opt. Express 9, 3399-3412 (2018)

c. **Caigang Zhu**, Amy F. Martinez, Hannah L. Martin, Martin Li, Brian T. Crouch, David Carlson, Timothy A.J. Haystead, Nimmi Ramanujam, "Near simultaneous intra-vital microscopy of glucose uptake and mitochondrial membrane potential, key endpoints that reflect major metabolic axes in cancer". Scientific Reports, 7: 13772. (2017)

d. Fangyao Hu, Robert Morhard, Helen Murphy, **Caigang Zhu**, Nimmi Ramanujam, "Dark field optical imaging reveals vascular changes in a spontaneous hamster cheek pouch model for pre-cancer/cancer detection". Biomed. Opt. Express 7, 3247-3261 (2016)

Monte Carlo modeling of light-tissue interaction

As a graduate student, I was responsible for a four-year study of the Monte Carlo modeling, which is a gold standard method relied on for optical spectral data processing. Although this is a highly recognized technique, there are few limitations for its applications in early epithelial cancer diagnosis: (1) assuming tissue samples to be simple homogenous or layered structure which could cause significant errors; (2) it is immensely time-consuming as it relies on intensive computation to ensure accuracy. I addressed the first limitation by developing a novel Monte Carlo method that is able to simulate light transport in a layered tissue model with a finite-sized tumor-like target to represent the early epithelial cancers. The proposed method could significantly improve the clinical diagnostic accuracy of diseases because of the more realistic tissue model used in the data processing. I addressed the second issue by developing a hybrid method which relies on a multilayered scaling method and perturbation method to quicken the Monte Carlo simulation for cancer researchers. The hybrid method has been demonstrated to shorten simulation time by several orders of magnitude. I also contributed to this community by writing a first-author Monte Carlo review paper to my peers, guiding their utilization of MC methods. This review paper published in Journal of Biomedical Optics has gained over 180 citations so far, which makes this article being one of the most cited engineering articles published in 2013.

a. **Caigang Zhu** and Quan Liu, “Hybrid method for fast Monte Carlo simulation of diffuse reflectance from a multi-layered tissue model with tumor-like heterogeneities”, Journal of Biomedical Optics, 17(1), 2012.

b. **Caigang Zhu** and Quan Liu, “Validity of the semi-infinite tumor model in diffuse reflectance spectroscopy for epithelial cancer diagnosis: a Monte Carlo study”, Optics Express 19, 17799-17812 (2011)

c. **Caigang Zhu** and Quan Liu, “Review of Monte Carlo modeling of light transport in tissue”, Journal of Biomedical Optics, 18 (5), (2013).

Depth sensitive optical spectroscopy and imaging

As a graduate student, I also conducted a study that included the design of a Monte Carlo method-based software and a novel non-contact depth sensitive imaging setup for cancer research. The software developed during this work is used to model non-contact diffuse reflectance and fluorescence measurements within an optical lens-based setup that provides different optical illumination and signal detection configurations. We used this software to provide simulations of diffuse reflectance measurements from an epithelial cancer model to provide depth-sensitive non-contact optical measurements. These depth sensitive measurements were achieved by controlling the depth of focal point of the imaging lens in tissues for the cancer model as well as the optical lens radius. We tested this model by simulating fluorescence signals on that same cancer model and equated it with actual experimental measurements. Our Monte Carlo method-based software provides accurate, usable results equal to real optical experiments. I also developed a novel non-contact depth sensitive imaging setup for cancer detection based on the knowledge gained from the numerical simulation studies. Our novel imaging setup contains a micro-lens array and tunable lens that enables the alteration of the imaging focal depth without moving any optical component or tissue samples. We evaluated this setup using tissue-mimicking phantoms and validated its efficacy as a clinical tool for cancer diagnosis. This technique is particularly well-suited for clinical settings as it does not require any moving of optical devices or tissue samples.

a. **Caigang Zhu**, Ong Yi Hong, and Quan. Liu, “Multifocal non-contact color imaging for depth sensitive fluorescence measurements of early epithelial cancer '', Optics Letters, Vol. 39, Issue 11, pp. 3250-3253 (2014).

b. **Caigang Zhu** and Quan. Liu, "Numerical investigation of lens based setup for depth sensitive diffuse reflectance measurements in an epithelial cancer model," Optics Express 20(28), 29807-29822 (2012).

c. **Caigang Zhu***, Ong Yi Hong*, and Quan. Liu, “Phantom Validation of Monte Carlo Modeling for Non-contact Depth Sensitive Fluorescence Measurements in an Epithelial Tissue Model '', Journal of Biomedical Optics, 19 (8), 085006 (2014). (*Equal contribution),

Tissue metabolism assessment in Skin flap surgery

Skin flap plastic surgery and grafting is a reconstructive technique used to transplant the skin and is often used for burn or trauma victims, or as a result of surgeries that require skin grafts to heal properly. One major issue with the surgery itself is that 6% to 25% of the flaps need surgical re-exploration for vascular compromise. Of this percentage, an estimated 10% of the skin flaps are not capable of being saved. The greatest risk to skin flap loss occurs in the 72-hour window after the surgery, so early detection is important to ensure a higher rate of flap salvage. During my Ph.D. career, I have created a dual-model spectroscopy and spectral imaging system to provide non-invasive measurements of three specific physiological parameters for skin tissue assessments before and after flap surgery and improve the best possible patient care. These parameters include oxygen saturation, tissue hemoglobin concentration, and redox ratio. We used a rat model to test the system’s ability to assess skin tissue undergoing a flap surgery. The data demonstrated that the optical spectra obtained by the system allow for accurate prediction of the flap’s condition after flap surgery. Furthermore, the dual-modal optical spectroscopy and spectral imaging technique predicts skin status as early as 15 minutes after the surgery has been initiated. This in turn allows doctors to save most flaps before the tissue becomes unviable. The study also found that this technique distinguishes venous and arterial occlusion in skin flaps in the rat model, which could help doctors as they make decisions regarding what type of secondary surgery to perform.

a. **Caigang Zhu**, Shuo Chen, Christopher Hoe-Kong Chui, Bien-Keem Tan, and Quan Liu, "Early detection and differentiation of venous and arterial occlusion in skin flaps using visible diffuse reflectance spectroscopy and autofluorescence spectroscopy," Biomed. Opt. Express 7, 570-580 (2016)

b. **Caigang Zhu**, Shuo Chen, Christopher Hoe-Kong Chui, Bien-Keem Tan and Quan. Liu, “Early prediction of skin viability using visible diffuse reflectance spectroscopy and auto-fluorescence spectroscopy'', Plastics and reconstructive surgery, Vol.134 (2), pp. 240-247 (2014). **(#1 journal in Plastic Surgery**)

c. Shuo Chen, **Caigang Zhu**, Christopher Hoe-Kong Chui, Gyanendra Sheoran, Bien-Keem Tan, and Quan Liu, “Spectral Diffuse Reflectance and Autofluorescence Imaging can perform early prediction of Blood Vessel Occlusion in Skin Flaps”. Journal of Biophotonics, 2017. (**Cover paper**)

d. Shuo Chen , Xiaoqian Lin , **Caigang Zhu** and Quan Liu "Sequential weighted Wiener estimation for extraction of key tissue parameters in color imaging: a phantom study", Journal of Biomedical Optics 19(12), 127001 (2014).

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

Ongoing

Uky start up **(Zhu)** **8/16/2019 – 8/15/2022**

Project: Intra-vital microscopy for imaging the adaptive metabolic and vascular landscape of radiation response and recurrence in head and neck squamous cell cancers

The goal of this program is for the PI Dr. Zhu to establish a novel multi-parametric microscope to image tumor metabolism, vascular function and architecture at high resolution to address questions in the field of human cancer radio-resistance and recurrence in pre-clinical tumors. The microscope will provide the metabolic underpinnings of therapy resistance and recurrence, and facilitate advances in the understanding of tumor biology and function, assessment of recurrence risk and design of therapies that can mitigate radio-resistance and recurrence altogether.