

AD_____

AWARD NUMBER: W81XWH-09-1-0062

TITLE: Image Based Biomarker of Breast Cancer Risk: Analysis of Risk Disparity among Minority Populations

PRINCIPAL INVESTIGATOR: Fengshan Liu, Ph.D.

CONTRACTING ORGANIZATION: Delaware State University
Dover, DE 19901

REPORT DATE: March 2010

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: Approved for Public Release;
Distribution Unlimited

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE			<i>Form Approved</i> <i>OMB No. 0704-0188</i>		
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.					
1. REPORT DATE 1 March 2010		2. REPORT TYPE Annual		3. DATES COVERED 1 Mar 2009 – 28 Feb 2010	
4. TITLE AND SUBTITLE Image Based Biomarker of Breast Cancer Risk: Analysis of Risk Disparity among Minority Populations			5a. CONTRACT NUMBER		
			5b. GRANT NUMBER W81XWH-09-1-0062		
			5c. PROGRAM ELEMENT NUMBER		
6. AUTHOR(S) Fengshan Liu, Ph.D. E-Mail: fliu@desu.edu			5d. PROJECT NUMBER		
			5e. TASK NUMBER		
			5f. WORK UNIT NUMBER		
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Delaware State University Dover, DE 19901			8. PERFORMING ORGANIZATION REPORT NUMBER		
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) U.S. Army Medical Research and Materiel Command Fort Detrick, Maryland 21702-5012			10. SPONSOR/MONITOR'S ACRONYM(S)		
			11. SPONSOR/MONITOR'S REPORT NUMBER(S)		
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for Public Release; Distribution Unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT To enhance Delaware State University (DSU) breast cancer research resources, we (4 faculty members at DSU - mentees) have been improving our expertise in translational and clinical breast cancer research by taking a graduate cancer related course/semester/person. Together with our mentors from the University of Pennsylvania (UPENN) we have organized and attended DSU-UPENN Breast Cancer Basics seminar series at DSU. DSU and UPENN mentees and mentors meet by-weekly physically or by teleconferences. We are currently developing a database of clinical biomarkers computed from clinical breast images obtained from the ACRIN DMIST trial, and from a clinical study performed previously at UPENN.					
15. SUBJECT TERMS Breast Cancer, Risk Disparity, Minority Population, Image-Based Biomarker, Training Program					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			19b. TELEPHONE NUMBER (include area code)
U	U	U	UU	13	

Table of Contents

	<u>Page</u>
Introduction.....	1
Body.....	1
Key Research Accomplishments.....	9
Reportable Outcomes.....	9
Conclusion.....	9
References.....	9
Appendices.....	9

1. Introduction

With this funded project, we will enhance DSU breast cancer research resources. We will train a cadre of DSU faculty to the basic principles of breast cancer research in order to establish an independent breast cancer research program at DSU by performing a joint DSU–UPENN research project focused on breast cancer risk disparity in minority populations. During the first 6-months, we mainly focused on planning and training.

2. Body

With this funded project, we will enhance DSU breast cancer research resources by: improving our expertise in translational and clinical breast cancer research; developing methods for computing image-based biomarkers for breast cancer risk, as well as methods for biomarker analysis of risk disparity; developing a database of clinical biomarkers computed from images of minority women; refining the existing and developing novel data mining techniques to determine the relationship between risk and image-based biomarkers. The improvement will support further growth of a sustained breast cancer research program at DSU and help establish us as a mid-Atlantic center for analysis of breast cancer risk and risk disparity among minority women.

The specific objectives of this training program include: (1) extending the skills of a select cadre of DSU faculty, so that they may become accomplished, influential and competitive breast cancer researchers; (2) establishing an independent breast cancer research program at DSU by performing a joint DSU–UPENN research project focused on breast cancer risk disparity in minority populations; and (3) producing a corpus of high quality published work and develop a portfolio of independently funded research grants at DSU to support a sustained breast cancer research program.

2.1 March 1 – April 30, 2009

We held biweekly meetings (including on-site and teleconference) with UPENN group for planning the seminars, courses for DSU group to take, and research projects.

2.2 May 1, 2009 – February 28, 2010

2.2.1 Graduate Courses Currently Taken at UPENN

Fall 2009 Semester

Fengshan Liu and Xiquan Shi took:

BE 483-401 2009C. Molecular Imaging

Course content includes: Structure of an atom, electromagnetic radiation, electron orbitals, the nucleus; radioactive decay, interactions of radiation with matter, X-ray imaging instrumentation; interactions of x-rays with tissue, computed tomography, X-ray contrast media, ultrasound image, and magnetic resonance imaging (MRI).

Dragoljub Pokrajac and Charlie Wilson took:

EP 801 Fundamentals of Epidemiologic Study Designs

This course is a series of lectures designed to teach basic principles of epidemiologic research design. Lectures include the following topics: definitions of epidemiology; measures of disease frequency; measures of effect and association; epidemiologic study designs, both experimental and non-experimental; and an overview of analysis of epidemiologic studies.

Spring 2010 Semester

Xiquan Shi is taking:

CAMB 512-001 2010A. Cancer Biology & Genetic: Cancer Biology and Genetics

The course objective is to introduce the students to important and timely concepts in Cancer Biology and Cancer Genetics. The lectures are organized into four broad thematic groups: A) Cell-Autonomous Mechanisms (e.g., tumor suppressor and oncogene function, DNA repair pathways, senescence, apoptosis); B) Non Cell-Autonomous Mechanisms (e.g., tumor microenvironment, hypoxia, angiogenesis); C) Organ Systems (e.g., pancreatic cancer, hematopoietic malignancies); and D) Therapeutic Approaches (e.g. protein kinase inhibitors, immunotherapy, radiation therapy). The organizers, along with faculty from the School of Medicine, the Wistar Institute and CHOP, with expertise

in the corresponding areas provide lectures for the course. The students are expected to present, and participate in discussions of one or more key recent papers at Journal Clubs that are held at the end of each thematic group. There will be mid-term and final exams of short essays relevant to the lectures.

Fengshan Liu and Dragoljub Pokrajac are taking:

BE545/CIS 537 Biomedical Image Analysis

This course covers the fundamentals of advanced quantitative image analysis that apply to all of the major and emerging modalities in biological/biomaterials imaging and in vivo biomedical imaging. While traditional image processing techniques will be discussed to provide context, the emphasis will be on cutting edge aspects of all areas of image analysis (including registration, segmentation, and high-dimensional statistical analysis). Significant coverage of state-of-the-art biomedical research and clinical applications will be incorporated to reinforce the theoretical basis of the analysis methods.

Charlie Wilson is taking:

GCB/CAMB 752 SEMINAR IN GENOMICS

Recent papers from the primary genomics literature will form the core material for the course. Each 3-hr session will feature a major topic or set of related topics in Genomics, with student presentations (usually two per session) centered on papers selected within the topic area(s). While the “presenting” student will give a 10- 15 min introduction to the paper and will show powerpoint slides of the data in the paper, all students in the class are expected to have read and to be prepared to discuss the papers presented.

2.2.2 Biweekly seminars at DSU, namely DSUPENN Breast Cancer Basics Seminar Series

Speakers:

Invited speakers of the biweekly seminar series include nationally renowned breast cancer researchers from UPENN Medical School, nearby hospitals and other institutions.

Before October 9, 2009: Breast Cancer Risk Factors; The Biology of Breast Cancer (I, II and III); and Cancer Imaging.

Date: July 10, 2009

Seminar title: Inverse Cell Biology Overview

Speaker: Charlie Wilson

Description: This presentation provided an introduction to the general components of animal cells and the specific types of cells found in breast tissue. The basics of cell growth dynamics and changes associated with cancer were also addressed. The role of gene products from proto-oncogenes and tumor suppressor genes in cancer were discussed.

Date: July 13, 2009

Seminar title: Breast Cancer: Cells/Tissues/Types

Speaker: Charlie Wilson

Description: The anatomy of the breast to include glandular and stromal components, lymph nodes, and anatomical relationship to other structures of the torso was presented. The basics of several types of imaging techniques were discussed and some mammograms of normal and cancerous breast were shown. The terminology for different types of breast cancer (lobular vs ductal; in situ vs invasive) was described as well as the criteria used by pathologist to assign a tumor grade.

Date: July 15, 2009

Seminar title: Breast Cancer: Epidemiology

Speaker: Charlie Wilson

Description: This lecture looked at the risk factors associated with breast cancer, its incidence and mortality, and the role of BCRA1/2 in breast cancer development.

Seminar on 8/12/09

Seminar title: Inverse free boundary problem for a reaction-diffusion model of cancer growth

Speaker: Yongzhi Xu, Department of Mathematics, University of Louisville

Description: The growth of cancer cell may be modeled by a reaction-diffusion equation with free boundary. In an earlier paper, we developed a free boundary model to describe the homogeneous growth inside a cylinder, a model mimicking the growth of ductal carcinoma in situ (DCIS). Assuming that we know the coefficients of the model, we analyzed the growth tendency of DCIS. The analysis and computation of the problem show interesting results that are similar to the patterns found in DCIS. In this talk we present some inverse problems related to the free boundary model of DCIS. Assuming that we know the solution of the free boundary problem in a section of the cylinder, along with the known initial, boundary and free boundary conditions, we consider the inverse problem of finding the coefficients and the solution in the cylinder. The motivation of this problem is to develop mathematical methods to diagnose growth tendency of DCIS from biopsy data.

Date: Aug 18, 2009

Seminar title: Screening for Breast Cancer

Speaker: Shunli Zhang, MD, Kent General Hospital, Dover, DE

Description: Breast cancer is the most common and second deadliest cancer in women. The breast cancer mortality has been decreased significantly in recent years due to the screening tests. Mammography, ultrasound, and magnetic resonance imaging are the three most commonly used screening tests. Their principles, common imaging features, and guidelines are discussed.

After October 9, 2009: After running the seminars for 5 months, we named the seminar series as “DSUPENN Breast Cancer Basics Seminar Series”. A kick-off opening ceremony was held on October 9, 2009. The kick-off was well attended by 38 faculty members and students from DSU and UPENN. The DSU acting president Dr. Claibourne Smith attended the kick-off. All other seminars are well attended by an average of 22 faculty and students each seminar.

Here is the opening ceremony program:

**DSUPENN Breast Cancer Basics Seminar Series
Opening Ceremony**

**Applied Mathematics Research Center, DSU
Department of Radiology, UPENN**

Date: October 9, 2009 (Friday)

Location: BOA 309

Time:

3.00pm Introducing the speaker, Dr. Predrag Bakic, UPENN

Seminar talk by Dr. John Lynch from UPENN Medical School.

4.00pm Introduction to the seminar series

Fengshan Liu, Applied Mathematics Research Center, DSU

Andrew Maidment, Department of Radiology, UPENN

4.15pm Welcome speech

Claibourne Smith, Acting President, DSU

4.30pm Reception

This seminar series is funded by US Army Medical Research as part of a Delaware State University (DSU) and University of Pennsylvania (UPENN) joint research project “Image Based Biomarker of Breast Cancer Risk: Analysis of Risk Disparity Among Minority Populations” (award number: W81XWH-09-1-0062). Invited speakers of the biweekly seminar series include nationally renowned breast cancer researchers from UPENN Medical School, nearby hospitals and other institutions.

With this funded project, we will enhance DSU breast cancer research resources by: improving our expertise in translational and clinical breast cancer research; developing methods for computing image-based biomarkers for breast cancer risk, as well as methods for biomarker analysis of risk disparity; developing a database of clinical biomarkers computed from images of minority women; refining the existing and developing novel data mining techniques to determine the relationship between risk and image-based biomarkers. The improvement will support further growth of a sustained breast cancer research program at DSU and help establish us as a mid-Atlantic center for analysis of breast cancer risk and risk disparity among minority women.

The specific objectives of this training program include: (1) extending the skills of a select cadre of DSU faculty, so that they may become accomplished, influential and competitive breast cancer researchers; (2) establishing an independent breast cancer research program at DSU by performing a joint DSU–UPENN research project focused on breast cancer risk disparity in minority populations; and (3) producing a corpus of high quality published work and develop a portfolio of independently funded research grants at DSU to support a sustained breast cancer research program.

Date: October 9, 2009 (Friday)

Location: BOA 309

Seminar Title: Cell to Cell and Cell-ECM Adhesion in Cancer

Speaker: Dr. John Lynch, UPENN Medical School

Description: Cell adhesion mechanisms are especially important for the development and function of normal epithelium in many tissues including the breast. Disruption of the normal cell-cell and cell-extracellular adhesion processes contributes to carcinogenesis by promoting cell proliferation and permitting cancer cell metastasis. We will discuss several common mechanisms by which cell adhesion processes are disrupted in carcinogenesis and how they promote cancer progression.

Following this very successful opening lecture, we held 6 bi-weekly seminars to date, with another 5 scheduled by the end of Spring 2010 semesters. All the seminars were very well attended; an average attendance was 18. Following is the list of speakers and topics presented at the seminar series.

Date: October 23, 2009

Location: ETV 131

Title: Future Trends in Breast Imaging

Speaker: Andrew D. A. Maidment, Ph.D., FAAPM, Associate Professor of Radiology, Chief, Physics Section, University of Pennsylvania

Description: Medical radiography is undergoing a revolution towards quantitative tomographic imaging. As currently practiced, quantitative imaging involves the extraction of quantifiable features from images; these features add to the clinical assessment of the severity, degree of change, or relative status of a disease or injury. The field of quantitative imaging includes the development, standardization, and optimization of anatomical, functional, and molecular imaging acquisition, data analyses, display methods, and reporting. Current research is focused on the development and validation of precise image-derived metrics (image-based biomarkers) with physiologically relevant parameters, including treatment response to interventions and clinical outcomes.

As with morphologic imaging, quantitative imaging is best performed tomographically; the removal of superimposed anatomy results in more accurate and precise quantification and localization. There are two trends in tomographic x-ray imaging. The first is the increased use of computed tomography (CT); the second, is the development and implementation of tomosynthesis or limited-angle computed tomography. Given that there has been significant attention paid to the high-doses associated with traditional CT, tomosynthesis is likely to become far more prevalent in the next decade. Finally, there is a revolution in radiographic contrast agents. Taking inspiration from nuclear medicine and optical imaging, we are seeing an increase in research into radiographic contrast agents. These developments are made possible given recent advances in nanoparticles such as designer liposomes, polymersomes and nanospheres. Both blood-pool and targeted contrast agents are under investigation.

Date: November 6, 2009

Location: ETV 131

Title: Breast Cancer Epidemiology

Speaker: Shannon Lynch, University of Pennsylvania

Description: Breast cancer epidemiology is the study of the distribution and determinants of breast cancer in human populations. In the early 1990s, breast cancer incidence and mortality rates were higher in the Northeastern United States and in California, prompting breast cancer advocates to unite and push a national breast cancer agenda. Today, incidence rates and mortality rates of breast cancer are on the decline in the U.S., mostly due to advances in the prevention, screening, and treatment of breast cancer. Risk factors or determinants of breast cancer will be reviewed, as well as the role of breast cancer treatment, stage, and disease type in affecting breast cancer survival. Future directions in breast cancer research, including a focus on health disparities and environmental determinants of disease across critical periods of the human lifespan will be discussed.

Date: Dec 18, 2009

Location: ETV 131

Title: Clinical Breast Imaging

Speaker: Sara Gavenonis, University of Pennsylvania

Description: Abstract - This lecture will serve as a general overview of current breast imaging technologies, including mammography, ultrasound, and breast MRI. The current discussion regarding screening mammography will also be reviewed. Future directions in breast imaging research will be covered briefly.

Date: January 21, 2010

Location: ETV 131

Title: Synopsis of Breast Pathology

Speaker: Shunli Zhang, MD, Kent General Hospital, Dover, Delaware

Description: Breast cancer is the 2nd most common malignant neoplasms in women and more than 44,000 deaths occur each year in US. Although the classification of breast neoplasms is very complicated, this lecture will cover 12 most common breast lesions, their pathological changes and the clinical significance. The pathologists' role in treating breast cancer will also be discussed.

Date: January 29, 2010

Location: ETV 131

Title: Surgical Approaches in Breast Cancer Treatment

Speaker: Julia Tchou, M.D., Ph.D., University of Pennsylvania

Description: It is an overview talking about various surgical techniques from diagnosis to treatment. I will include discussion of breast conserving surgery vs. mastectomy and sentinel node biopsy in the talk.

Date: Feb 19, 2010

Location: ETV 131

Title: The Pathology of Breast Cancer

Speaker: Carolyn Mies, MD, Associate Professor, Department of Pathology and Laboratory Medicine, University of Pennsylvania

Description: The presentation is designed to introduce the basic vocabulary & histology of human breast cancer & to describe the pathologist's role in estimating prognosis & guiding treatment.

The following two seminars have been held but are outside the reporting period of this report:

Date: March 5, 2010

Location: ETV 131

Title: Genetic Counseling and Testing for BRCA1 and BRCA2 Mutations in African American Women

Speaker: Chanita Hughes Halbert, PhD, Department of Psychiatry and Center for Community-Based Research and Health Disparities University of Pennsylvania

Description: This presentation will describe research that is being conducted to improve decision making about genetic testing for inherited breast cancer risk among African American women at increased risk for hereditary disease. Research on psychological and behavioral outcomes following genetic counseling will also be discussed.

Date: March 26, 2010

Location: ETV 131

Title: Genetic Treatment of Breast Cancer- The Medical Oncologist's Approach

Speaker: Keerthi Gogineni, MD, Department of Medicine, Division of Hematology/Oncology, University of Pennsylvania

Description: This presentation will describe fundamentals of breast cancer, with a focus on the medical treatment of the disease.

The following are scheduled seminars to be held by the end of Spring 2010 semester:

Date: April 9, 2010

Title: Radiation Treatment of Breast Cancer

Speaker: Tim Zhu, Ph.D., Department of Radiation Oncology, University of Pennsylvania

Date: April 26, 2010

Title: Computer-Aided Detection and Diagnosis of Breast Cancer

Speaker: Robert Nishikawa, Ph.D., Department of Radiology, University of Chicago

Date: May 7, 2010

Title: Breast Cancer Risk Image Based Biomarkers

Speaker: Despina Kontos, Ph.D., Department of Radiology, University of Pennsylvania

2.2.3 Conferences attended

Fengshan Liu attended the 2009 Annual Health Research Conference Oct. 13-14, Dover, DE on health disparity.

2.2.4. Readings and discussions

Fengshan Liu, Xiquan Shi, Charlie Wilson and Dragoljub Pokrajac read journal papers and books on breast cancer related to the courses we took and the seminars we

participated. Informal discussions with UPENN on breast cancer are done by informal meetings and telephone. We have discussed with the seminar speakers and the professors at UPENN from whom we took the courses about Breast Cancer Risk Disparity. Working with the mentors at UPEEN, we are planning to organize a 2-day Breast Cancer Disparity Symposium at UPENN.

3. Key Research Accomplishments

N/A

4. Reportable Outcomes

We are learning the basic breast cancer knowledge through seminars, reading papers and books, taking courses at UPENN and informal discussions with UPENN. We reached a Data Sharing Agreement with ACRIN. We are transferring ACRIN and other breast cancer imaging data to DSU.

5. Conclusion

To reach the proposed goals, we planned and organized all training activities as we proposed in the proposal in the first year.

6. References

N/A

7. Appendices

N/A