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

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<b>13. SUPPLEMENTARY NOTES</b>					
<b>14. ABSTRACT</b> 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.					
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## Table of Contents

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

## **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:

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**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