UNIVERSITY OF HAWAI'I
CANCER CENTER

Population Sciences in the Pacific
Research Seminar Series

"The International Low Grade Glioma Registry: Harnessing social media for patient recruitment"

Elizabeth Claus, MD, PhD.

Professor of Biostatistics
Director of Medical Research
Yale University School of Public Health
New Haven, CT

(Thursday) February 7, 2019

3:00 pm – 4:00 pm

501 conference room

University of Hawai`i Cancer Center

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Claus, Elizabeth Brooks

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

POSITION TITLE: Professor and Director of Medical Research, Yale University School of Public Health; Attending Neurosurgeon and Director of Stereotactic Radiosurgery, Department of Neurosurgery, Brigham and Women's Hospital

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
Wellesley College	B.A.	06/81	Mathematics/French
University of Virginia	M.A.	06/83	Mathematics
Yale University	Ph.D.	06/88	Biostatistics
Yale University	M.D.	12/94	Medicine (cum laude)
Yale New Haven Hospital, New Haven, CT	Intern	07/95 – 06/96	General Surgery
Yale New Haven Hospital, New Haven, CT	Resident	07/96 – 06/02	Neurosurgery
Brigham and Women's Hospital, Boston, MA	Fellow	07/02 – 06/03	Neurosurgery (Tumor)

A. Personal Statement

Elizabeth B. Claus, MD, PhD is Professor and Director of Medical Research in the Yale University School of Public Health as well as Attending Neurosurgeon and Director of Stereotactic Radiosurgery within the Department of Neurosurgery at Brigham and Women's Hospital in Boston. She is a member of the board of advisors for the Central Brain Tumor Registry of the United States (CBTRUS) and a past board member for the Acoustic Neuroma Association (ANA). Dr. Claus' work is focused in cancer and genetic epidemiology with an emphasis on the development of risk models for breast and brain tumors. She is the overall PI of the Meningioma Consortium, the Meningioma Genome-Wide Association Study, and the Yale Acoustic Neuroma Study as well as a co-investigator of the GLIOGENE (Genes for Glioma) and International Glioma Case/Control (GICC) projects. In addition to her research activities, Dr. Claus is a board-certified neurosurgeon with fellowship training in neurosurgical oncology at Brigham and Women's Hospital; her clinical focus is on the treatment of glioma, meningioma, acoustic neuroma and brain metastases. In partnership with national patient brain tumor organizations including the American Brain Tumor Association (ABTA), the National Brain Tumor Society (NBTS) and the ANA, Dr. Claus is working to develop cost- and time-efficient web- and smartphone-based recruitment strategies to be used in the study of brain tumors. She has developed such work in collaboration with the ANA (https://www.anausa.org/component/content/article/22-menu-articles/about-ana/307-yale-university-acoustic-neuroma-study-) and recently received pilot funding from the ABTA/NBTS to commence development of a web-based registry for patients with low grade glioma in an effort to advance research efforts for this group of patients (**http://www.abta.org/about-us/news/press-releases/PFC2016_EnrollmentLGGRegistry.html?referrer=https://www.google.com/**). .

B. Positions and Honors

Positions

1978 – 1980 Research Associate, Bartholdi and Company, Wellesley, MA

09/81 – 08/83	Instructor, Department of Mathematics, University of Virginia
09/82 – 06/83	Instructor, Department of Continuing Education, University of Virginia
1982 – 1983	Consultant, School of Medicine, University of Virginia
09/85 – 12/85	Teaching Fellow, Department of Biostatistics, Yale School of Public Health
01/86 – 06/88	Instructor, Department of Biostatistics, Yale School of Public Health
07/88 – 06/90	Lecturer and Associate Research Scientist, Department of Biostatistics, Yale School of Public Health
07/90 – 06/95	Assistant Professor, Department of Biostatistics, Yale School of Public Health
07/95 – 06/07	Associate Professor, Department of Biostatistics, Yale School of Public Health
10/03 – 09/07	Permanent Member, NIH Study Section (Epidemiology of Cancer)
08/02 –	Attending Neurosurgeon, Brigham and Women's Hospital, Boston, MA
08/02-	Instructor, Harvard Medical School
10/04	Member, Brain Disease Group, Commission on Cancer, American College of Surgeons
07/07 –	Professor, Department of Biostatistics, Yale School of Public Health
07/09 –	Director of Medical Research, School of Public Health, Yale University
12/07 –	Board of Advisors, Central Brain Tumor Registry of the United States (CBTRUS)
01/11 –	Board of Medical Advisors, Acoustic Neuroma Association
01/12 – 04/12	Acting Chair, Department of Biostatistics, School of Public Health, Yale University
06/14	Director of Stereotactic Radiosurgery, Department of Neurosurgery, BWH

Honors

1981 – 1983	The Dean's List Fellowship, University of Virginia
1981 – 1983	The Gordon T. Whyburn Fellowship, University of Virginia
1981 – 1983	The Department of Mathematics Fellowship, University of Virginia
1983 – 1988	National Institutes of Health Training Fellowship, Yale University
1995	Janet M. Glasgow Memorial Achievement Citation, Amer. Med. Women's Association
2015	Top 100 Publications (Claus et al., 1991) Yale School of Public Health Centennial
2015	The Winslow Centennial Honor Roll for Excellence and Service, School of Public Health, Yale University

C. Contribution to Science

1. My research focuses on cancer and genetic epidemiology with a specific emphasis on the development of risk prediction models for breast cancer and, more recently, a focus on tumors of the central nervous system. My initial work in breast cancer began prior to the discovery of BRCA1 and BRCA2 (two genes now known to be involved in breast cancer susceptibility) with an examination of the genetic transmission of breast and ovarian cancer using data from the Cancer and Steroid Hormone (CASH) Study. Two manuscripts [a; b] provided preliminary analyses of these data and found that 1) breast cancer clusters in families, 2) this clustering is due in some families to the transmission of inherited genes, and 3) there is a relationship between age at onset and family history among breast cancer cases believed to be genetic carriers. Using the results of these papers, I constructed and fit statistical models to the age-specific familial breast cancer recurrence data in the CASH study [c]. This paper provided evidence for the existence of a rare autosomal dominant allele leading to increased susceptibility to breast cancer. The results of this work were used by the Breast Cancer Consortium (the primary working group for the discovery of BRCA1/BRCA2) as the underlying genetic model in the linkage analyses which placed the breast cancer gene, BRCA1, at chromosome 17q. Estimates of breast cancer risk to women with a family history of breast and/or ovarian cancer calculated under this model continue to be used throughout the world for genetic counseling and life insurance modeling [d] and were identified as a standard for risk prediction by the February 15, 1995 issue of the Journal of the American Medical Association "Assessment and Counseling for Women with a Family History of Breast Cancer: A Guide for Clinicians".

    a. Claus EB, Risch N, Thompson WD: Age at onset as an indicator of familial risk of breast cancer. Amer J Epidemiol 1990; 131:961-972. [PMID: 2188501].
    b. Claus EB, Risch N, Thompson WD: Using age of onset to distinguish between subforms of breast cancer. Ann Hum Genet 1990; 54:169-177. [PMID: 2382970].
    c. Claus EB, Risch N, Thompson WD: Genetic analysis of breast cancer in the cancer and steroid hormone Study. Am J Hum Genet 1991; 48:232-242. [PMCID: PMC1683001].

d. Claus EB, Risch NR, Thompson WD: Autosomal dominant inheritance of early-onset breast cancer: Implications for risk prediction. Cancer 1994; 73:643-651. [PMID: 8299086].

2. I have also focused on defining risk factors for early-stage breast cancer, i.e. breast carcinoma in-situ (BCIS). I began by conducting a large case-control study of BCIS within the state of Connecticut. This Department of Defense (DOD) funded grant was the first population-based attempt to define genetic and epidemiologic risk factors for BCIS while controlling for cancer screening practices across all categories of age and histology. [a, b, c] These data allowed for the investigation of the joint distribution of clinical, genetic and epidemiologic characteristics of BCIS as well as the development of risk models for BCIS. Cases were tested for mutations in BRCA1/2: the results indicated for the first time that ductal carcinoma in-situ (DCIS) is a part of the breast-ovarian cancer syndromes defined by BRCA1/2, with mutation rates similar to those found for invasive breast cancer. These findings suggest that breast cancer patients with an appropriate personal or family history of breast and/or ovarian cancer should be screened and followed according to high risk protocols, regardless of whether they are diagnosed with in-situ or invasive breast cancer [d].

   a. Claus EB, Schildkraut J, Iversen ES, Jr., Berry D, Parmigiani G. Effect of BRCA1 and BRCA2 on the association between breast cancer risk and family history. J Natl Cancer Inst 1998; 90:1824-1829. [PMID: 9839523].
   b. Claus EB, Stowe M, Carter D. Breast Carcinoma In Situ: Risk factors and screening practices. J Natl Cancer Inst. 2001; 93:1811-1817 [PMID: 11734598].
   c. Claus EB, Stowe M, Carter D. Oral contraceptives and the risk of ductal breast carcinoma in-situ. Breast Cancer Res Treat 2003; 81:129-136 [PMID: 14572155].
   d. Claus EB, Petruzella S, Matloff E, Carter D. Prevalence of BRCA1 and BRCA2 mutations in women diagnosed with ductal carcinoma in-situ. JAMA 2005; 293:964-969. [PMID: 15728167].

3. Over the years I have extended my work into the field of neurosurgery, working as a clinician-scientist. I was awarded an NIH grant to undertake the largest population-based case/control study for meningioma (n=3200). **Hormonal Etiology**: Among female subjects, cases were more likely than controls to report hormonally related conditions: uterine fibroids (OR=1.2, 95% CI: 1.0,1.5), endometriosis (OR=1.5, 95% CI:1.5,2.1), and breast cancer (OR=1.4, 95% CI:0.8,2.3), 2). Meningioma risk was positively associated with increased BMI (for males and females) and current use of oral contraceptives in pre-menopausal women and negatively associated with breast-feeding and current cigarette smoking (for females) [a]. **Immune Etiology**: We found significant results for a physician-diagnosed history of allergy (OR: 0.6, 95%CI: 0.5, 0.7), chicken pox (OR: 0.6, 95%CI: 0.5, 0.8) and asthma (OR: 0.7, 95%CI: 0.6, 0.9). A follow-up manuscript [b] utilized a novel assay and indicated that men with meningioma commonly react with a serologic anti-meningioma response, potentially suggestive of a distinctive etiology of the disease in men. This result may be exploitable for early detection or therapeutic modalities and is also exciting in terms of the commonly reported but little explained difference in meningioma rates for males and females. All of the above findings lend credence to the thought that the etiology of meningioma may differ for men and for women and may more specifically explain the long-hypothesized but little understood sex differences. **Ionizing Radiation Etiology**: The publication of our significant findings relative to an association between both therapeutic and diagnostic (dental x-rays) radiation attracted worldwide attention, (http://www.nbcnews.com/video/nightly-news/47010764#47010764). Our study noted that cases were twice (OR= 2.0, 95%CI, 1.4-2.9) as likely as controls to report having ever had a bitewing dental exam. **Genetic Etiology**: Cases were more likely than controls to report a first degree family history of meningioma (odds ratio (OR) =4.4, 95% confidence interval (CI):1.6,11.5) with a stronger association in younger cases. To study genes associated with meningioma risk, we were awarded additional NIH funding to undertake a genome-wide association study (GWAS) of meningioma and have identified a novel locus on chromosome 11[c] As a means of more powerfully identifying DNA repair genes associated with meningioma risk we have also focused our efforts on persons with radiation-associated meningioma (RAM). From BWH we have identified 50 persons with high-dose therapeutic radiation delivered to the head as a child, performed WGS/WES on matched normal-tumor samples for 20 of these persons and discovered mutations in at least one actionable gene [d].

   a. Claus EB, Calvocoressi L, Bondy M, Wrensch M, Wiemels J, Schildkraut J. Exogenous Hormone Use, Reproductive Factors and the Risk of Intra-Cranial Meningioma in Females. J Neurosurg Mar 2013 118(3):649-56. [PMCID: PMC3756881].

b. Wiemels JL, Bracci PM, Wrensch M, Schildkraut J, Bondy M, Pfefferle J, Zhou M, Sison J, Calvocoressi L, Claus EB. Assessment of autoantibodies to meningioma in a population-based study. Am J Epidemiol 2013 177:75-83. [PMCID: PMC3590036].
c. Claus EB, Cornish AJ, Broderick P, Schildkraut JM, Dobbins SE, Holroyd A, Calvocoressi L, Lu L, Hansen HM, Smirnov I, Walsh KM, Schramm J, Hoffmann P, Nöthen MM, Jöckel KH, Swerdlow A, Larsen SB, Johansen C, Simon M, Bondy M, Wrensch M, Houlston R, Wiemels JL. Genome-wide association analysis identifies a meningioma risk locus at 11p15.5. Neuro Oncol. 2018 May 12. [PMID: 29762745].
d. Claus EB, Greenhalgh S, Gaffney SG, Bilguvar K, Calvocoressi L, Lopez-Giraldez F, Lu L, Al-Mefty O, Alexander B, Arvold ND, Aizer A, Zhao ZM, Townsend JP. The somatic genetic architecture of radiation-associated meningioma. J Neurosurg (In press)

4. Glioma: In addition to caring for patients with LGG at BWH [a], I have worked closely for years with many of the world's glioma researchers including members of the Genes for Glioma (GLIOGENE) and Glioma International Case/Control (GICC) projects. GLIOGENE ascertained 435 families with two or more affected relatives with confirmed glioma; linkage analyses yielded a significant hit at 17q12-21.32 for a genetic locus for glioma ($P = 7x10^{-6}$) in ~35% of the families studied [b, c]. The group also found that *POT1* germline mutations may explain a subset of familial glioma. Our group has just completed an international mega-GWAS for glioma and found several new inherited variants associated with risk of glioma [d]. It is of note that the variants identified for glioblastoma (high grade glioma) differ from those for lower grade glioma, suggesting the etiology for the two types is different I continue to work with members of GLIOGENE/GICC as well as members of the UCSF and MAYO SPORE groups to collaborate in the field of glioma and submit this application in an effort to advance knowledge in symptom management of patients with LGG. I am a member of the newly formed low grade glioma consortium (LOGLIO) along with members of UCSF, DUKE, MAYO, YALE, BWH-the goal of this consortium is to utilize collaborative efforts to advance research for low grade glioma. I have recently been awarded funds from both the ABTA and the NBTS to commence development of "The International Low Grade Glioma Registry". Patients for the current application will be drawn in part from this registry.

a. Bainbridge M, Armstrong G, Gramatges M, Bertuch A, Jhangiani S, Doddapaneni H, Lewis L, Tombrello J, Tsavachidis S, Liu Y, Jalali A, Plon S, Lau C, Parsons W, Claus EB, … Jenkins R, et al. The Gliogene Consortium, Muzny DM, Gibbs R, Melin B, and Bondy ML. Germline mutations in shelterin complex genes are associated with familial glioma. J Natl Cancer Inst 2014 Dec 7; 107(1):384. [PMCID: PMC4296199].
b. Jalali A, Amirian ES, Bainbridge MN, Armstrong GN, Liu Y, Tsavachidis S, Jhangiani SN, Plon SE, Lau CC, Claus EB, et al. The Gliogene Consortium, Muzny DM, Gibbs RA, Melin BS, Bondy ML. Targeted Sequencing in Chromosome 17q Linkage Region Identifies Familial Glioma Candidates in the Gliogene Consortium. Nature Scientific Reports 2015 Feb 5; 5:8278. [PMCID: PMC4317686]
c. Melin B,…,Lai R+, Claus EB+, Olsen S+, Jenkins RB+, Houlston RS+, Bondy ML+. (+shared last authors) Genome-wide association study reveals specific differences in genetic susceptibility to glioblastoma and non-glioblastoma. Nat Genet 2017doi:10.1038/ng.3823 Published online 27 March 2017
d. Disney-Higg L, Cornish A, Sud A, Law PJ, Kinnersley B, Jacobs DI, Ostrom QT, Labreche K, Eckel-Passow JE, Armstrong GN, Claus EB, Il'yasova D, Schildkraut J, Barnholtz-Sloan JS, Olson SH, Bernstein JL, Lai RK, Schoemaker MJ, Simon M, Hoffmann P, Nöthen MM, Jöckel KH, Chanock S, Rajaraman P, Johansen C, Jenkins RB, Melin BS, Wrensch MR, Sanson M, Bondy ML, Houlston RS. Impact of atopy on risk of glioma: A Mendelian randomisation study. BMC Medicine 2018 16:42 Epub 2018 Feb 5

5. Collaboration at Brigham and Women's Hospital. As part of the Brain Tumor Group at BWH/DFCI I have had the opportunity to share patient care and collaborate with a number of fellow researchers. The current effort will continue to benefit from these collaborations and allow for continued follow-up of the BWH glioma patients.

a. Martin AM, Cagney DN, Catalano PJ, Warren LE, Bellon JR, Punglia RS, Claus EB, Lee EQ, Wen PY, Haas-Kogan DA, Alexander BM, Lin NU, Aizer AA. Brain Metastases in Newly Diagnosed Breast

Cancer: A Population-Based Study. JAMA Oncol. 2017 Mar 16. PMID: 28301662.

b. Dasenbrock HH, Yan SC, Smith TR, Valdes PA, Gormley WB, Claus EB, Dunn IF. Readmission After Craniotomy for Tumor: A National Surgical Quality Improvement Program Analysis. Neurosurgery. 2017 Apr 01; 80(4):551-562. PMID: 28362921.
c. Arvold ND, Shi D, Aizer AA, Norden AD, Reardon DA, Lee EQ, Nayak L, Dunn IF, Golby AJ, Johnson MJ, Claus EB, Chiocca EA, Ligon KL, Wen PY, Alexander BM. Salvage Re-Irradiation for Recurrent High-Grade Glioma and Comparison to Bevacizumab Alone. J Neurooncol. 2017 Dec;135(3):581-591. doi: 10.1007/s11060-017-2611-9. Epub 2017 Oct 3
d. Olar A, Goodman LD, Wani KM, Boehling NS, Sharma DS, Mody RR, Gumin J, Claus EB, Lang FF, Cloughesy TF, Lai A, Aldape KD, DeMonte F, Sulman EP. A gene expression signature predicts recurrence-free survival in meningioma. Oncotarget. 2018 Mar 23; 9(22):16087-16098. PMID: 29662628.

Complete List of Published Work in My Bibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/elizabeth.claus.1/bibliography/40762139/public/

D. Research Support

Ongoing Research Support

National Brain Tumor Society (Claus) 04/01/16 - 3/31/18
The International Low Grade Glioma Registry
To develop an web-based registry for the development of a genetic epidemiologic project for patients with low grade glioma
Role: PI

American Brain Tumor Association (Claus) 06/30/15 – 06/29/18
The International Low Grade Glioma Registry
To develop an web-based registry for the development of a genetic epidemiologic project for patients with low grade glioma
Role: PI

Completed Research Support

ANA (Claus) 07/01/13 – 06/30/17 (NCE)
Acoustic Neuroma Association
Genetic Epidemiology of Acoustic Neuroma
The overall goal of this project is to develop secure and cost efficient methods to collect epidemiologic and clinical data as well as biologic specimens appropriate for a genetic epidemiologic (including GWAS, candidate gene, etc) as well as a clinical outcome study via use of the world wide web by partnering with the Acoustic Neuroma Association.
Role: PI

5 R01CA151933 (Claus) 07/01/10 – 06/30/17 (NCE)
NCI
The Meningioma Consortium: Genome-Wide Association Study
To genotype the blood/saliva specimens to provide important replication for observed associations between DNA repair genes and meningioma risk as well as perform the first genome-wide association (GWAS) study of meningioma risk.
Role: PI

5 RO1 CA109468 (Claus) 04/01/06 – 03/31/14
NIH
Meningioma: Risk Factors and Quality of Life
To examine environmental and genetic risk factors for meningioma.
Role: PI