Evaluating Screening Performance in Practice

National Cancer Institute
Division of Cancer Control and Population Sciences
Applied Research Program

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Foreword

We have good news to report about breast cancer early detection. Research has shown that early detection, combined with effective treatment, can reduce mortality from this second leading cause of cancer deaths in women. Since the early 1990s, breast cancer mortality rates have dropped steadily, in large measure due to improvements in screening and treatment. American women have taken these findings to heart—in 1987, less than 30% of women 40 years old and older had had a mammogram, the primary mode of breast cancer screening. Ten years later, that percentage had doubled to 67% of women in the same age group, and is now at 70%. American women have increasingly come to include breast cancer screening as part of their regular health care.'

Our growing understanding of the value of breast cancer screening and the widespread use of mammography has led to a need to understand this technology as it is actually practiced in the community. How accurate is screening mammography in detecting cancer under a variety of conditions? Do differences in the practice of screening mammography and resulting diagnostic evaluation influence detection rates, stage at diagnosis, and survival? How can data from research be used to influence clinical practice? These questions and more are explored by the National Cancer Institute's (NCI) Breast Cancer Surveillance Consortium.

A centerpiece of NCI's goal of eliminating suffering and death due to cancer is the "discovery-development-delivery" approach to cancer research. Discovery is the process of generating new information about fundamental cancer processes from the genetic to the population level. Development is the process of creating and evaluating tools and interventions that are valuable in detecting, diagnosing, predicting, treating, and preventing cancer. Delivery involves promoting and facilitating the application of evidence-based cancer interventions to all people who need them. Each of these components is integrally related to the others and all three are necessary for future progress. The Breast Cancer Surveillance Consortium, a key program of NCI's Division of Cancer Control and Population Sciences, exemplifies the "delivery" component, and its research portfolio is helping to accelerate the rate at which proven interventions are put into widespread clinical and public health practice.

I am pleased to introduce this report describing the work of the Breast Cancer Surveillance Consortium. By linking surveillance data on breast screening practices with data from population-based cancer registries and by combining the expertise of seven research sites around the country, the Consortium has been able to address issues that can be adequately examined only in large samples of women, radiologists, and mammography facilities drawn from varied geographic and practice settings. The Consortium has made a major scientific contribution by creating a unique and collaborative research resource and by greatly extending our knowledge about the factors that influence the accuracy and performance of breast cancer screening technologies.

Andrew C. von Eschenbach, MD
Director, National Cancer Institute

Introduction

Detecting cancer early is critically important because, if effective treatment is provided, the burden of both illness and death can be reduced. Improvements in breast cancer treatment and early detection have resulted in a steady drop in breast cancer mortality rates since the early 1990s, but additional efforts are necessary to ensure that this trend continues.

For decades, breast cancer early detection technologies have centered on x-ray mammography, and it is the only evidence-based screening technology currently available. A number of scientific and national organizations have published guidelines supporting periodic breast screening examinations. Other organizations do not make any specific recommendations but encourage women to discuss the issue with their health care providers.

Recent studies have caused debates in the scientific community and the media about the efficacy of screening mammography and the women who are best served by regular exams. This debate has focused on a number of issues, particularly the age at which screening should begin, the optimal frequency of screening, the magnitude of the impact on mortality, and the quality of the data obtained from randomized trials. These debates have made it all the more important to assess mammography's performance in clinical practice and clarify its potential for contributing to reduced breast cancer mortality rates.

The Breast Cancer Surveillance Consortium (BCSC) was established in 1994 to enhance the understanding of breast cancer screening practices in the United States and their relation to changes in stage at diagnosis, survival, or breast cancer mortality. The BCSC is funded and coordinated by the Applied Research Program (ARP) of NCI's Division of Cancer Control and Population Sciences (DCCPS). Through integrated programs of genetic, epidemiologic, behavioral, social, applied, and surveillance cancer research, DCCPS examines the causes and distribution of cancer in populations. It also supports the development and implementation of effective interventions, and monitors and explains cancer trends in all segments of the population.

The Applied Research Program's mission is to evaluate patterns and trends in cancer-associated health behaviors, practices, genetic susceptibilities, outcomes, and

services. Research within ARP is also targeted to identifying, improving, and developing databases and methods for cancer control-related surveillance, outcomes, and applied research; maintaining, updating, and disseminating these databases and methods; and promoting and facilitating their use among investigators. The BCSC's activities are carried out as part of ARP's efforts to monitor and evaluate cancer control activities in general and in specific populations in the United States and to determine the influence of these factors on patterns and trends in cancer incidence, morbidity, survival, and mortality. Rachel Ballard-Barbash, MD, MPH, the Associate Director, Applied Research Program, is the program director for the BCSC.

This report describes the BCSC and its unique research contribution. The first section provides an overview of the BCSC's mission, history, and structure. This overview is followed by two sections that describe the BCSC's current areas of research and other accomplishments to date. Findings from published studies are described throughout. The report closes with a discussion of the challenges that lie ahead for the Consortium, both in terms of its research agenda, as well as potential opportunities for using BCSC data and findings to influence clinical practice.

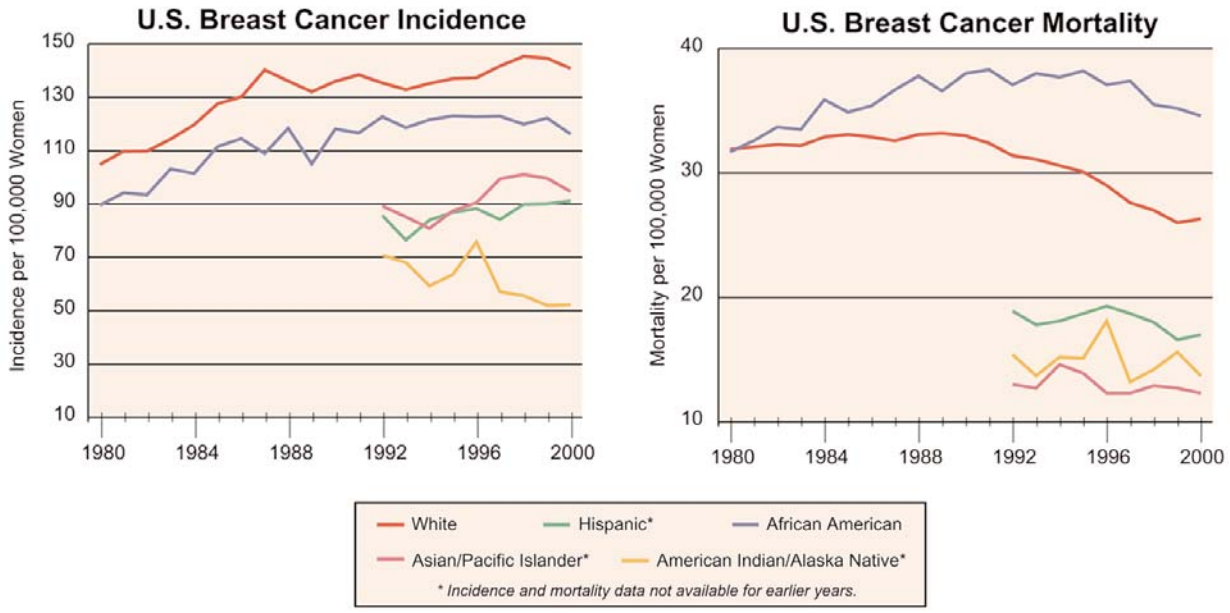
"The BCSC has proved to be an invaluable resource for all American radiologists, in its collection and dissemination of robust data on the current practice of mammography in a representative cross-section of the U.S. All participating radiologists in San Francisco directly benefit by receiving annually a comprehensive set of audit data that are used for continuing quality improvement. At UCSF, we have used audit data to facilitate the transition to providing mammography interpretive services only by radiologists who do full-time breast imaging, at a documented higher level of performance than the usual-care practice of general diagnostic radiologists. On a personal level, I have used San Francisco Mammography Registry (SFMR) data in several of my own clinical research studies and collaborated with BCSC investigators on other studies. I have used SFMR data to facilitate the successful recruitment of breast-imaging radiologists to UCSF (access to clinical material of this quality and scope almost guarantees a successful academic career), and to facilitate the successful recruitment of radiology residents to one-year fellowships in breast imaging at UCSF (these physicians will be an important part of the future of mammography in the United States).

I very much look forward to working with the BCSC to develop interactive Internet-based tools that all American radiologists can use for the same kind of continuing quality improvement that is now available primarily to BCSC participants."

Edward A. Sickles, MD
Professor in Residence
Department of Radiology
University of California at San Francisco (UCSF) School of Medicine

The Breast Cancer Surveillance Consortium: An Overview

Breast cancer is the second leading non-skin cancer among women and the second leading cause of cancer deaths in women. Although the breast cancer mortality rate has dropped since the early 1990s, approximately 40,000 women died from the disease in 2002 and an estimated 211,000 cases have been diagnosed in 2003. Within these overall numbers, some important disparities persist among various population groups. For example, although the breast cancer incidence rate is lower for African Americans than for whites, their mortality rate is higher. Women of other racial and ethnic groups have incidence and mortality rates that are lower than those of whites and African Americans.



Source: NCI Progress Review Groups, "Charting the Course: Priorities for Breast Cancer Research—The Report of the Breast Cancer Progress Review Group." http://prg.nci.nih/gov/snapshots/Breast-Snapshot.pdf

Large randomized clinical trials conducted over the last four decades have shown that by detecting breast cancer at an early stage, mammography, combined with effective treatment, can reduce breast cancer mortality, especially among women 50 years old and older. To ensure standardized delivery of quality mammography services and encourage use of this screening technology, the Congress passed the Mammography Quality Standards Act (MQSA) of 1992. This Act required that mammography facilities meet certain quality standards and be certified by an approved accreditation body. The Act also authorized the Secretary of Health and Human Services to establish a surveillance system that could provide reliable and comprehensive data on the performance of breast cancer screening.

In response to this legislative mandate, the NCI established the Breast Cancer Surveillance Consortium. Two premises guided the NCI in designing this consortium of research sites. The first was the longstanding recognition that results from controlled clinical trials can differ from the results of screening that is practiced in community settings. To optimally evaluate breast cancer screening, it needed to be studied within the context of routine clinical practice. The second was that, to obtain truly useful information, screening patterns and associated performance parameters needed to be linked to cancer outcomes—stage at diagnosis, morbidity, and mortality. With these two premises in mind, NCI designed the BCSC to:

- Enhance the understanding of breast cancer screening practices in the U.S. through an assessment of the accuracy, cost, and quality of screening programs and the relation of these practices to changes in breast cancer stage at diagnosis, survival, or mortality
- Foster collaborative research among surveillance consortium participants to examine issues such as regional and health care system differences in providing screening services and subsequent diagnostic evaluation
- Provide a foundation for clinical and basic science research, especially basic research on biologic mechanisms that can improve understanding of the natural history of breast cancer.

The BCSC concept was initially tested through pilot studies carried out at three locations. In 1994, NCI funded three Consortium research sites

through a cooperative agreement mechanism and then further expanded the number of sites in 1995. This expansion allowed the Consortium more latitude to explore issues related to geography, urban-rural differences, and racial and ethnic diversity. In 1995, NCI also funded a Statistical Coordinating Center (SCC) to serve as the repository of data from all sites.

This has allowed the Consortium to analyze data pooled across all sites. In addition, the SCC was designed to establish and evaluate data collection and quality control procedures and to help individual sites analyze data from their own sites. In 2000, the cooperative agreements for the Consortium sites were renewed for an additional five years.

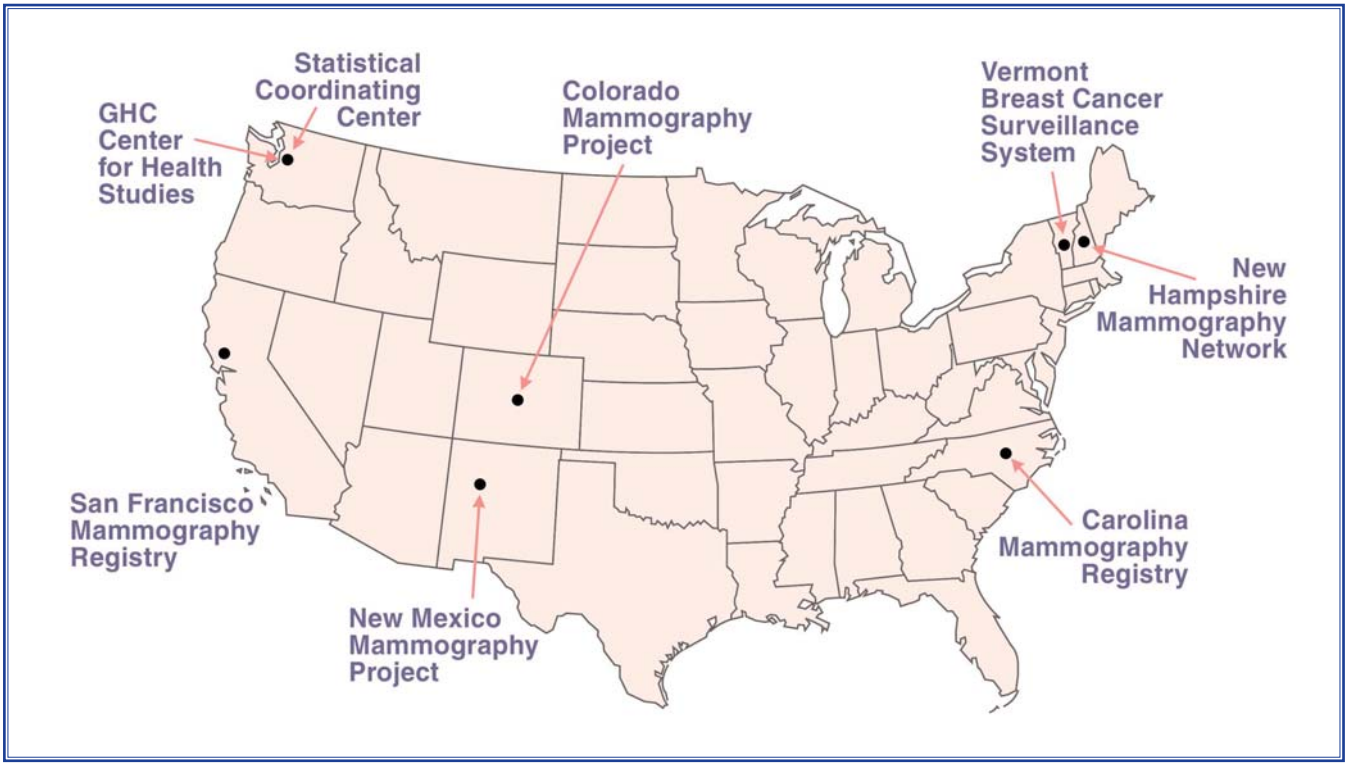
BCSC: A Snapshot of Progress

Phases	Research	Group Interactions
Pilot studies, 1990-2	Conducted at three sites	
First RFA release, Phase I, 1993 3 centers funded	Sites: ➢ Agree on goals and data elements ➢ Set up systems	
Second RFA release, Phase II, 1994 Added 3 centers and created SCC as supplement to one center	Sites: ➢ Establish data standards and Certificates of Confidentiality for women and providers ➢ Begin transition from paper to electronic systems ➢ Improve data editing ➢ Actively conduct research ➢ Begin planning for pooled analyses	➢ Establish governance and research priorities ➢ Institute publications committee and management system
Renewal Phase III, 2000-2004 Independent SCC	Sites: ➢ Add new data ➢ Make major progress in site and pooled research	➢ Refine systems ➢ SCC develops interactive research Web site for BCSC sites

The Consortium currently consists of the SCC and seven data collection and research sites. Six sites are defined by geographic region; the seventh (Group Health Cooperative) is defined by membership in a health maintenance organization:

- Carolina Mammography Registry
- Colorado Mammography Project
- Group Health Cooperative, Center for Health Studies
- New Hampshire Mammography Network
- New Mexico Mammography Project
- San Francisco Mammography Registry
- Vermont Breast Cancer Surveillance System.

The investigators working across these sites are a multidisciplinary team that includes radiologists, primary care clinicians, pathologists, epidemiologists, statisticians, physicists, and advocates.

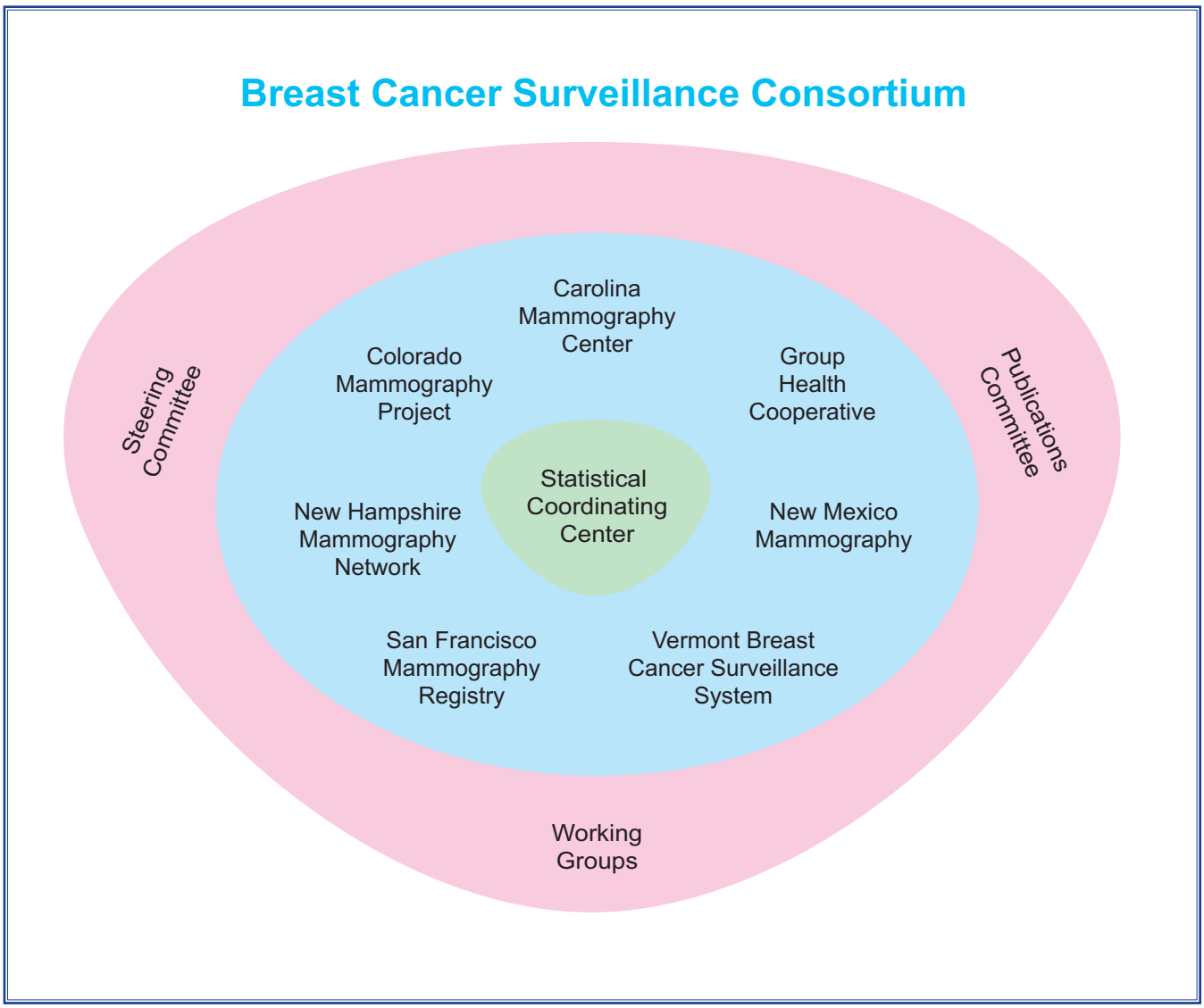


BCSC: Principal Investigators and NCI Staff

Carolina Mammography Registry Bonnie C. Yankaskas, PhD	Department of Radiology University of North Carolina Chapel Hill, NC
Colorado Mammography Project Gary Cutter, PhD Mark Dignan, PhD	University of Nevada at Reno Reno, NV Kentucky Prevention Research Center Lexington, KY
Group Health Cooperative Stephen Taplin, MD, MPH 1994–2003 Diana Buist, PhD 2003–Present	Group Health Cooperative, Center for Health Studies Seattle, WA
New Hampshire Mammography Network Patricia Carney, PhD	Department of Community and Family Medicine Dartmouth Medical School Hanover, NH and Lebanon, NH
New Mexico Mammography Project Charles Key, MD, PhD 1995–1997 Robert Rosenberg, MD 1997–Present	Department of Radiology Health Sciences Center University of New Mexico Albuquerque, NM
San Francisco Mammography Registry Virginia Ernster, PhD 1995–2000 Karla Kerlikowske, MD 2000–Present	Department of Medicine, Epidemiology and Biostatistics University of California at San Francisco San Francisco, CA
Vermont Breast Cancer Surveillance System Berta Geller, EdD Don Weaver, MD	University of Vermont Office of Health Promotion Research Burlington, VT
Statistical Coordinating Center William Barlow, PhD	Group Health Cooperative, Center for Health Studies Seattle, WA
National Cancer Institute Rachel Ballard-Barbash, MD, MPH Robin Yabroff, PhD, MBA Kathleen Barry Stephen Taplin MD, MPH 2003–Present	Applied Research Program Division of Cancer Control and Population Sciences Rockville, MD

Structure of the BCSC

The Consortium has three co-chairs (the NCI project director, a site principal investigator, and the SCC principal investigator). Additional oversight is provided by a Steering Committee (composed of the principal investigators of all the sites, a pathologist co-investigator, and the NCI project director), a Publications Committee, and Working Groups. Working Groups are formed for specific projects and disband when no longer needed.



Collecting Data Within the Context of Routine Clinical Practice

Unlike a multicenter clinical trial, which uses a common protocol and common data collection instruments, the BCSC sites conduct research within existing health systems and within the context of routine clinical practice.

The BCSC: A Unique Resource

As of October 2003, the Consortium had collected data for more than 1.7 million women and more than 5 million mammograms. Within this group, about 38,000 breast cancers have been detected.

The size of the BCSC database, the longitudinal nature of these data, and the multidisciplinary teams of participating investigators make the BCSC a unique resource for understanding breast cancer screening practices and outcomes in the U.S.

Each BCSC site has developed voluntary partnerships with mammography facilities in its geographic area. In some cases, 100% of facilities in the area partner with the site. In other cases, fewer facilities participate. Participating facilities represent a wide range of health care settings, including traditional fee-for-service solo and group radiology practices; managed care organizations; mobile mammography vans; freestanding mammography programs; hospital-based services; and nonradiology practices, such as pathology laboratories, surgical practices that perform breast biopsies, and other medical practices where mammography is performed (e.g., obstetrics and gynecology, internal medicine, and family medicine practices).

Each participating facility collects several distinct types of data about women and their mammographic exams. The data collected about women include basic information about their demographics, health history, screening history, and current health status. Information collected about the exam includes the indication for the exam, breast density, exam assessment, and follow-up recommendation. As part of ancillary studies, some sites also collect data about

"I feel lucky to be a part of the BCSC group that has been working together pooling their information and answering questions of value for women all over the U.S. My presence makes me feel a part of the research process, and I think it also is a reminder to the researchers and doctors that patients are real people who are waiting for answers."

Bambi Schwartz
Patient Advocate, San Francisco
Mammography Registry

radiologists, such as their specialty, practice patterns, and perceptions about screening and breast cancer risk. All data collection procedures have been approved by each site's Institutional Review Board (IRB) and are compliant with the Health Insurance Portability and Accountability Act (HIPAA).

A defining characteristic of the BCSC is that the data it collects from women and radiologists/facilities are linked to cancer outcomes data from population-based cancer and pathology registries. This linkage occurs at each site. Three sites—Group Health Cooperative, the New Mexico Mammography Project, and the San Francisco Mammography Registry—are linked to registries within NCI's Surveillance, Epidemiology, and End Results (SEER) Program. The Colorado Mammography Project is linked to its statewide pathology registry. The Carolina Mammography Registry, New Hampshire Mammography Network, and Vermont Breast Cancer Surveillance System collect benign and malignant breast pathology reports from laboratories in their defined regions and additionally link to their respective state cancer registries.

One of the Consortium's first tasks after it was established was to determine how to organize these various types of clinical data so that they could be used for research. This required Consortium investigators to identify the critical data elements

SEER: A Vital Source of Population-Based Cancer Data

The Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute is an authoritative source of information on cancer incidence and survival in the United States. The SEER Program currently collects and publishes data on all types of cancer from 11 population-based cancer registries and three supplemental registries. Approximately 26% of the U.S. population is covered by the SEER Program. Information on more than 3 million *in situ* and invasive cancer cases is included in the SEER database, and approximately 170,000 new cases are documented each year within the SEER catchment areas. The SEER Registries routinely collect data on patient demographics, primary tumor site, morphology, stage at diagnosis, first course of treatment, and follow-up for vital status. SEER is the only comprehensive source of population-based information in the United States that includes stage of cancer at the time of diagnosis and survival rates within each stage. The mortality data reported by SEER are provided by the National Center for Health Statistics.

necessary for evaluating screening performance and to develop a consensus on a standard set of core variables, response categories, definitions for analysis, and standard definitions of screening and diagnostic mammography. Within this common data structure, the sites agreed to maintain their own data collection procedures, developed with their participating mammography facilities, cancer registries, and pathology databases. These procedures have evolved over time as electronic data collection methods have gradually supplanted paper-based systems.

How Representative are BCSC Data?

Two important goals of the BCSC are that the data collected reflect mammography practice as it is performed in the community and that the population of women in the BCSC reflect the distribution of women in the U.S. who undergo mammography.

A comparison of women represented in the BCSC against 2000 Census data shows that Consortium sites are located in counties that contain slightly more than 5% of the Nation's population. As the following table shows, data in the BCSC reflect the national population in several important respects.

		BCSC Counties	All other U.S. Counties
Sociodemographic Characteristics	Median Family Income	$55,189	$50,984
	Percent Unemployed	3.4%	4.1%
	Percent With High School Degree	84.5%	80.2%
	Percentage of women aged 40+	22.0%	22.7%
Sociodemographic Characteristics in Women Aged 40+	Percent Hispanic	6.9%	7.3%
	Percent Black	8.9%	10.9%

Data Source: 2000 Census

Data Collected by BCSC Sites

From Women

Demographic Variables

- Unique anonymous identification number
- Zip code
- Date of birth
- Race (white, black, Asian or Pacific Islander, Native American, other); ethnicity (Hispanic)
- Education (1-11 years, 12, 13-15 years, 16 years, 16+ completed years of education)

Health History

- Age at birth of first child (year)
- Age at menarche
- First-degree family history of breast cancer (mother, sister, daughter) and age: <50, >50
- Personal history of breast cancer (yes, no)
- Personal history of breast biopsy, surgery, or radiation (yes, no)
- Procedure history per breast (implants, needle biopsy, surgical biopsy, lumpectomy, mastectomy, radiation therapy, and reconstruction)

Screening History

- Ever screened by mammography (yes, no)
- Time since last mammogram (within last year, 1-2 years, 3-4 years, 5 or more years)
- Time since last clinical breast examination

Current Health

- Menopausal status at examination (pre-, peri-, postmenopausal)
- Hormone replacement therapy use at time of examination (yes, no) and type (e.g., estrogen, estrogen/progestin, over-the-counter supplements)
- Presence of symptoms in last three months (nipple discharge or lump; right or left breast)
- Main reason for current visit (routine screening, routine follow-up, concerns about breast problems)

From Radiologists and Technicians

Radiologic Site and Interpreting Mammographer Identification (encrypted)

Dates of Current Examination and Comparison Film

Use of Comparison Mammogram at Time of Evaluation (yes, no)

Indication for Examination

- Screening (asymptomatic), evaluation of breast problem (symptomatic), additional evaluation of recent mammogram, short interval follow-up

Type of Examination(s) Performed

- Standard screening views, additional diagnostic views, sonography, other breast imaging

Breast Density (American College of Radiology BI-RADS™ categories)

- Entirely fat, scattered fibroglandular densities, heterogeneously dense, extremely dense

Assessment per Woman (American College of Radiology BI-RADS™ categories)

- Incomplete assessment, normal, normal with benign finding, probably benign, suspicious abnormality, highly suggestive of malignancy

Recommendation (American College of Radiology BI-RADS™ categories)

- Mammography in normal interval follow-up, additional views, sonography, short-term follow-up, fine-needle aspiration, core biopsy, biopsy or surgical evaluation, further diagnostic evaluation

From Tumor Registries and Pathology Databases (not all variables collected by all registries)

Procedure Performed (summarized per woman)

- Date and result (right versus left breast separately recorded)
- Type: total mastectomy, partial mastectomy, core biopsy, fine needle aspiration
- Guidance: clinical palpation, ultrasonography, stereotaxis, needle localized, mammographic

Pathologic Variables

- For invasive carcinoma findings:
  - Date and type of procedure, reporting source, laterality, guidance
  - Histologic type: ductal, lobular, other special types; grade, estrogen and progesterone receptor status
  - Staging: tumor size, number of positive lymph nodes, distant metastasis (American Joint Committee on Cancer TNM stage), extent of disease (SEER)
  - Therapy (initial treatment): surgery, radiation, chemotherapy, hormonal, biologic modification
  - Follow-up status: date of last follow-up, vital status last follow-up, cause of death
- For *in situ* carcinoma findings:
  - Date and type of procedure, reporting source, laterality, guidance
  - Histologic type: ductal, lobular, other
- For benign findings:
  - Date and type of procedure, reporting source, laterality, guidance
  - Histopathology: atypical hyperplasia (ductal and/or lobular), ductal hyperplasia, fibroadenoma, phyllodes tumor, other benign, normal, inconclusive)

BI-RADS™ in Practice: Assessing Mammograms and Guiding Clinical Management

In 1992, the American College of Radiology developed the Breast Imaging Reporting and Data System (BI-RADS™) to standardize the reporting and interpretation of breast imaging findings. This coding system is now widely used by radiology facilities and providers as well as by investigators. The system consists of six assessment categories that encompass a finding and a follow-up recommendation:

Assessment Category	Finding	Recommendation
0	Needs additional imaging evaluation	Perform additional mammography, ultrasound, magnetic resonance imaging, or other imaging
1	Negative	Follow-up at normal interval
2	Benign	Follow-up at normal interval
3	Probably benign	Follow-up at short interval (< 1 year)
4	Suspicious abnormality	Consider biopsy
5	Highly suggestive of malignancy	Take appropriate action (generally biopsy)

BCSC investigators have conducted several studies to determine whether, in fact, the BI-RADS™ codes are being applied as intended. One analysis, which examined 51,673 diagnostic mammographic examinations conducted between January 1996 and December 1997, showed that the expected management recommendation was given 85%-90% of the time for mammograms classified as 1, 2, 4, or 5. Category 3 mammograms had the most variability in associated recommendations. Management recommendations for category 0 also had inconsistencies. Overall, reporting of symptoms, particularly breast lumps, was associated with BI-RADS™ codes 4 and 5 and younger age.

A second analysis looked at whether the expected management recommendation was given for 292,795 screening mammograms conducted during January-December, 1997. This study had somewhat different results in that assessments and recommendations were highly consistent for the overwhelming majority of mammograms, which received assessment categories 1, 2, and 0. Recommendations were less consistent for the less than 10% of mammograms that received assessment categories 3, 4, and 5. These results suggest that although the implementation of BI-RADS™ has largely been successful, there is room for improvement and further education about the codes and their application may be useful.

The Reality of BCSC Data Collection

To date the BCSC has successfully recruited women, mammography facilities, radiologists, and mammographic technologists to participate in this research effort. However, conducting research within clinical settings does present a number of challenges:

- Many participating mammography facilities welcome the opportunity that this research effort gives them to compare their data with those from a considerably larger pool. At the same time, facilities are primarily in the business of providing care to patients. Consortium sites must always be careful that their data collection efforts do not interfere with the conduct of health care at the facilities.

- At each visit to a participating mammography facility, a woman is asked to fill in a form that asks demographic and other questions. For women who return to the same facility year after year, this means providing the same information repeatedly. A number of sites also conduct research projects that require additional data collection. Ensuring the continued willingness of women to participate in data collection means that the process must be as efficient and easy as possible. It also means that facilities must be sensitive to language and literacy issues as well as to other barriers associated with visiting facilities that women may experience.

- Correctly matching women to their mammographic and pathology records to construct a longitudinal cohort is an ongoing challenge. This is not a trivial task because of the fact that names change over time, key data elements may be missing, and errors can occur in social security numbers. In addition, women may not always use a BCSC facility for every mammogram, and this may result in an incomplete sequence of mammograms.

- Maintaining the confidentiality of the information provided by women, facilities, and radiologists is a priority. The Consortium has instituted a number of procedures to protect the data it collects. These include using unique identifiers after removing all personal identifying information, securing all data with passwords, encrypting all identification codes, revis-

ing consent forms and business agreements with mammography facilities to enhance confidentiality provisions, and requiring faculty and staff from BCSC sites to attend training workshops on confidentiality and privacy aspects of HIPAA. The sites also hold U.S. Public Health Service Certificates of Confidentiality, which provide BCSC and SCC databases with the highest possible degree of protection for the women and the health care providers who participate in this initiative.

- Staff turnover at facilities and periodic legislative and regulatory changes require ongoing staff continuing education. BCSC sites provide this service to many participating facilities.

- Facilities join and leave partnerships with BCSC sites for numerous reasons. For example, they may decide to no longer participate, or they may close or merge with another facility. Sites do not necessarily lose a facility's cohort when it drops out or merges with another facility, and BCSC investigators make a concerted effort to link all available mammographic encounters to the women who receive them.

Opening the Doors to New Understanding: Progress on a Research Agenda

BCSC data are designed to shed light on issues related to the delivery of breast screening technologies, the performance of these technologies, and their resulting impact on short- and long-term outcomes. The Consortium's well-established data collection infrastructure has allowed it to build a database that contains longitudinal records on millions of women and millions of mammograms. The large size of this database has given investigators across the Consortium an unprecedented opportunity to examine a range of complex issues related to breast screening. The size and depth of the database has allowed for analyses of pooled data that would not otherwise be possible, including examinations of factors relevant to small subpopulations (such as women with augmented breasts) or of infrequent outcomes. Consortium investigators also have conducted a number of site-specific studies to further pursue a specific avenue of research.

To date, approximately 150 papers have been published in peer-reviewed journals by BCSC investigators (see page 57 for a list of BCSC publications). Much of this research has focused on mammography, and the following pages highlight some of the key questions that BCSC investigators are asking about mammography and the answers that are emerging from ongoing research. These questions focus on several broad areas:

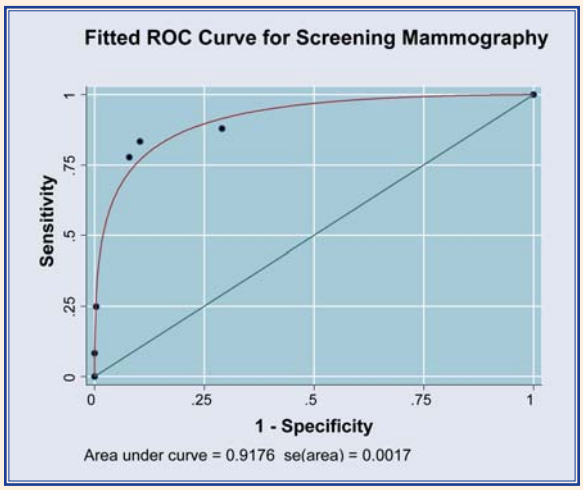
- What characteristics of women affect the performance of screening mammography?
- Do biological characteristics of breast tumors determine whether they can be detected by screening mammography?
- What characteristics of the mammogram, the radiology facility, or the radiologist affect the performance of screening mammography?
- What characteristics of the mammography equipment affect the performance of screening mammography?

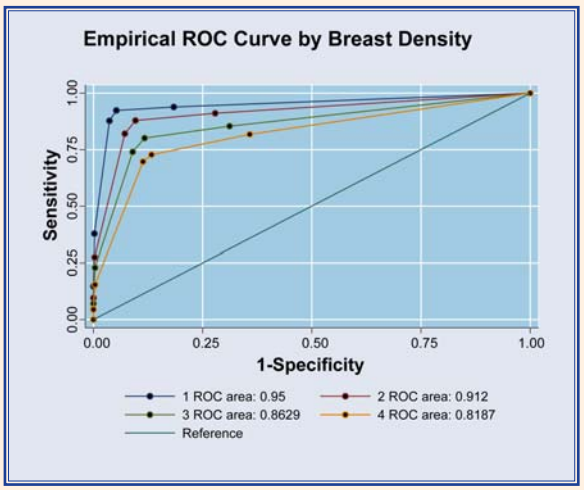
In addition, the BCSC has developed innovative statistical approaches to analyzing data, and these are briefly described.

Assessing the Performance of Screening Mammography

To understand how a disease develops and to provide appropriate prevention and care services, it is essential to be able to distinguish those in a population who have the disease and those who do not. Screening and diagnostic tests are used to make this distinction in individuals. A critical issue, therefore is determining how good these tests are at separating those with and without the disease in question. In mammography, as in all other screening and diagnostic tests, investigators use several key measures to accomplish this task:

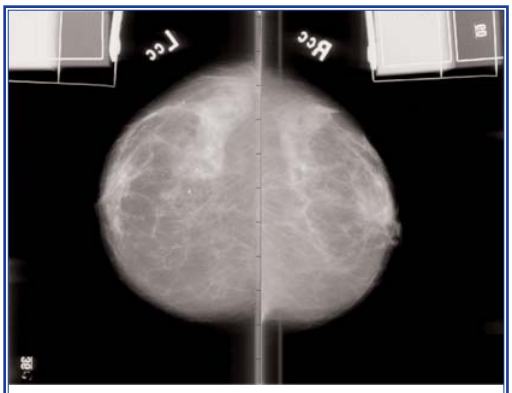
- **Sensitivity** represents the proportion of women who truly have breast cancer who have been identified as such by a positive mammogram ("true positives").
- **Specificity** represents the proportion of women who truly do not have the disease who have been identified as such by a negative mammogram ("true negatives").
- **Positive predictive value (PPV)** represents the likelihood that a woman has breast cancer, given a positive mammogram.
- **Recall rate** represents the proportion of women who are recommended for further follow-up evaluation because of an abnormality detected in a mammogram.
- **Cancer detection rate** represents the proportion of mammograms in which cancer is found through a positive mammogram among all women undergoing mammography.
- **Receiver operator characteristic (ROC) curve** provides a graphical lens through which to assess the ability of a screening test to discriminate between healthy and diseased persons. An analytic evaluation of the tradeoff between sensitivity and specificity, it allows investigators to distinguish between differences in accuracy and differences in the criteria for calling a mammogram positive. The graph on the left, below, shows an ROC curve for screening mammography across a large sample. A curve like this one, with a large area underneath, indicates that the mammograms are detecting a large percentage of true positives, and therefore the test is doing a good job at discriminating between those with breast cancer and those without. The graph on the right shows how differences in breast density can affect the ROC curve. Radiographically dense breasts (the orange line) are known to negatively affect the accuracy of mammography and that is shown here by a smaller area under the curve. The least dense breasts (the blue line) have the largest area under the curve and therefore the best accuracy.





What Characteristics of Women Affect the Performance of Screening Mammography?

It has been known for some time that certain characteristics of women increase or decrease their risk of breast cancer. For example, age, family history of breast cancer, and the radiographic density of the breast all influence cancer risk. Evidence also suggests that these factors, either individually or collectively, may affect the performance and accuracy of screening mammography. In studies using both pooled and site-specific analysis, the BCSC has significantly expanded current knowledge about these issues.



Breast tissue varies in the relative amount of fat and epithelial and connective tissue. The fatty areas are radiolucent and appear dark on a mammogram. The other types of tissue are radiographically dense and appear light on a mammogram.

Physical Factors

- A prospective cohort study that examined the combined and individual effects of various physical characteristics on the accuracy of the test found that both breast density and age are important independent predictors of mammographic accuracy, whereas hormone replacement therapy (HRT) appears to affect accuracy only through its effect on breast density. This study, which used data on 329,495 women across all BCSC sites who underwent 463,372 screening mammograms, demonstrated that screening mammography is most accurate in older women with fatty breasts and least accurate in younger women with dense breasts who use HRT.

- Another analysis of data pooled from all seven BCSC sites explored the effect of family history of breast cancer on cancer detection rates. Although many guidelines recommend that younger women with a family history begin mammography screening at a younger age than those without a family history, few studies have examined this issue. In this study, investigators found that cancer detection rates for women who had a first-degree relative with a history of breast cancer were similar to those in women 10

years older without such a history. However, it appeared that the sensitivity of mammography was influenced primarily by age, not by family history. In other words, the ability of screening mammography to detect cancer in women who actually had cancer was less in younger women than in older women, regardless of family history. This study points to a need for further research to determine whether screening mammography is sufficiently accurate to support recommendations on screening in younger women with a family history.

- One hypothesis for why mammography is not as effective among younger women is that a higher proportion of young women have radiographically dense breast tissue, and dense breast tissue is known to reduce the sensitivity of mammography. A study involving women enrolled in the Group Health Cooperative examined the relationship of mammographic sensitivity, breast density, and menstrual cycle phase to determine whether the timing of a mammogram could affect the sensitivity of the test. The investigators found a small but statistically significant variation in density by time in the menstrual cycle. This variation was particularly evident for leaner women, who are already more likely to have dense breasts than are heavier women. These findings suggest that timing a mammogram to coincide with the portion of the cycle at which density might be less might improve the accuracy of mammography in women in their forties. This study has led several BCSC sites to collect data from premenopausal women on time since last menstrual period, to allow an assessment of sensitivity and specificity by phase of menstrual cycle in a larger sample of women.

Screening Mammography and Stage at Diagnosis

The primary goal of breast screening programs is to detect cancer in its earliest stages, when effective treatments have their highest chance of success. The BCSC has conducted a number of studies examining the impact of screening mammography on stage at diagnosis. Studies over the past 20 years have shown that black and Hispanic women have poorer breast cancer outcomes even though their breast cancer incidence is less than that of white women. In addition, studies have shown disparities in annual and biennial mammography screening rates across population

groups. As a result, racial and ethnic disparities are an important aspect of BCSC research in this area.

- A study of data from 1990 to 1998, conducted by Colorado Mammography Project investigators, assessed the effect of routine screening on breast cancer staging by race and ethnicity. After controlling for age, cancer history, and education, black women were still more likely to have late stage of disease at diagnosis compared with white women. Differences in late stage diagnosis between Hispanic and white women were not statistically significant. When restricted to incident cases, defined as those with at least one negative mammogram 10-25 months before their primary breast cancer diagnosis (excluding the detection mammogram sequence), racial and ethnic differences persisted. The percentage of early stage incident cases was higher in white women than in black or Hispanic women. A second study, conducted by Carolina Mammography Registry investigators, explored this issue further by comparing the accuracy of screening mammography among black and white women. This study found that mammography performed equally well in both groups of women, but that black women with symptoms had larger and more aggressive tumors than did white women. These results have implications for public health breast cancer screening programs and indicate that further research is needed to clarify the complex relationship between race/ethnicity, modifiable risk factors, and stage of disease at diagnosis.

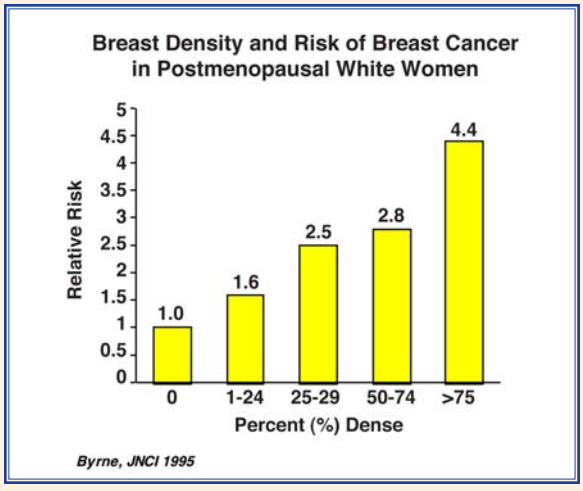
- Investigators with the Vermont Breast Cancer Surveillance System combined data collected between 1995 and 1999 with earlier data from 1975-1984 and 1989-1990 to document the changes in tumor size and lymph node metastasis that have occurred over the past 25 years in Vermont and to determine the extent to which screening mammography may have contributed to earlier detection of invasive cancer. They found that the trend toward earlier detection that occurred in the state corresponded with a significant increase in the use of screening mammography. The study also showed that tumor size and lymph node involvement also were related to the number of mammograms received and to the mammographic screening interval.

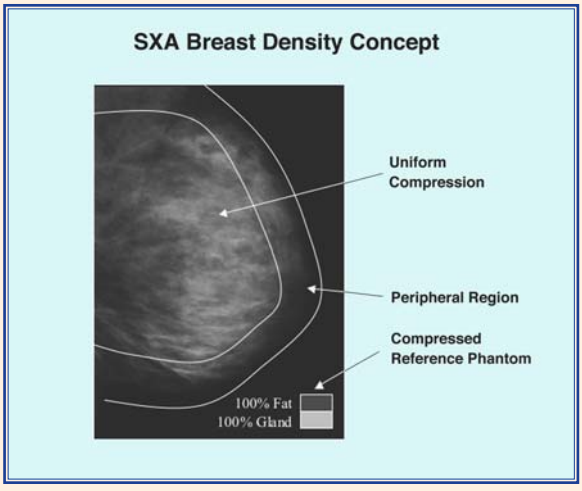
Using Screening Mammography to Identify Women at High Risk of Breast Cancer

Though it has improved markedly over the years, mammography is not a perfect test and results in false-positive tests. Physicians have limited means to assess risk factors at office visits, and available tools poorly discriminate the level of risk for individual women. If it were possible to determine who would benefit most from mammography, then it would be possible to focus mammography and preventive therapy on women who have a high enough risk to make prevention worthwhile. Such a predictive test also could be used to enroll women in trials of new preventive therapies, and primary care providers could use it to counsel women at high risk. BCSC investigators are examining this issue from several different perspectives.

An ideal risk factor to use in targeting mammography and prevention efforts toward women at high risk is one that would strongly indicate high cancer risk, be objective, and be easily accessed and inexpensive. Breast density is an obvious candidate because of its well-known association with increased cancer risk (see below, left). The current systems for categorizing breast density have limitations, however. Among the most important is that they depend on a subjective assessment by a radiologist reading the x-ray film. Variations in film development and the compression of the breast during the exam also can influence results. In addition, current systems for categorizing breast density have limited reproducibility.

These limitations have spurred the development of a number of potential alternatives that might improve the future clinical assessment of breast density as a measure of cancer risk. The San Francisco Mammography Registry is now testing one of these systems—single X-ray absorptiometry (SXA). This technique measures density only in the compressed area of the breast and works well in breasts with lower as well as higher density (see below, right). It appears to have several advantages in that it is objective, reproducible, and can be used on any standard mammography machine.





Do Biological Characteristics of Breast Tumors Determine Whether They Can Be Detected by Screening Mammography?

Although mammography is able to detect a large percentage of tumors, about 20% to 30% of breast cancers are found during the time interval between regular screening. Some of these interval cancers are due to technical or interpretive error, and some are tumors that truly arise in the time between screening exams. The breast's radiographic density also may mask a tumor and make it difficult to identify on a mammogram. Identifying the tumor or patient characteristics that are associated with increased risk of interval cancer is important if we are to accurately determine the relative contribution of these factors to the effectiveness of mammography.

- A case-control study of 578 women enrolled in the Group Health Cooperative showed that improving the understanding of tumor characteristics can help to explain why mammographic sensitivity is lower for certain groups and may help to improve screening technologies for specific groups of women. In this study, investigators assessed the characteristics of screen-detected and interval tumors that arose in participants after they had received a "negative" or "benign" BI-RADS™ code. The investigators found that interval cancers were more likely to occur in women younger than 50 than in older women. They also found in the younger women an association between interval cancer risk and several tumor characteristics, such as mucinous histology, high proliferation, and aggressive features, including lack of steroid receptors. These findings suggest that even if reader errors could be reduced to a minimum, a subset of rapidly growing, mucinous, or high-grade tumors would still arise during the interval between mammographic screening exams.

- Investigators at the New Mexico Mammography Project conducted a population-based case-control study of women diagnosed with interval breast cancer to explore the hypothesis that these cancers are, in part, due to rapid tumor growth. The investigators found that rapidly growing and aggressive cancers do explain a substantial portion of cancers not found on mammography, and that tumor proliferation rate and p53 expres-

sion are independent determinants of interval breast cancer. On the basis of their estimates, the researchers suggest that 75% of interval cancers appear to be rapidly growing tumors with 5% or more proliferating cells. Poorer outcomes in women with interval breast cancers may occur because of the tumors' biologic differences and rapid growth as well as delays in diagnosis and treatment. These results have important implications for breast cancer screening programs and decisions about the optimal timing for screening examinations, particularly for younger women, who have a high proportion of aggressive cancers.

➢ The success of mammography as a screening method depends on keeping the rate of interval cancers low. Understanding breast density's effect on the ability of mammography to detect a tumor is therefore of critical importance. A study of 576 women enrolled in the Group Health Cooperative showed that increased mammographic breast density was strongly associated with interval rather than screen-detected breast cancer. This finding was independent of the effects of age, menopausal status, use of HRT, or body mass index. The results of this study suggest that breast density may indeed obscure the tumor and contribute to a radiologist missing the signs of malignancy, thus increasing the importance of continued developments to improve the ability of breast imaging techniques to screen radiographically dense breasts.

➢ Since the early 1980s, the incidence of ductal carcinoma *in situ* (DCIS), a noninvasive cancer, has risen dramatically. This is usually attributed to increases in screening mammography, which have made diagnosis of DCIS much more likely than in the past. Because women diagnosed with DCIS undergo treatment, the fraction of untreated DCIS that would progress to invasive malignancy is unknown. However, it is thought that some women benefit from having their DCIS diagnosed by screening mammography because invasive cancers adjacent to the DCIS are detected when DCIS is detected. This study pooled data from all the BCSC sites to explore the rate of screen-detected DCIS. Investigators analyzed data on 653,833 mammograms performed throughout 1996 and 1997 on 540,738 women between 40 and

84 years of age. The study revealed that about 20% of all screen-detected breast cancers—or about one case detected in every 1,300 screening mammograms among the population studied—is DCIS. By providing investigators with opportunities to explore the distribution of DCIS in a population-based program and the long-term consequences of DCIS identification, BCSC data have contributed to the further understanding of this important area of breast cancer research.

➢ Postmenopausal hormone therapy (HT) has been associated with increased risk of breast cancer. Estrogen-plus-progestin regimens may be associated with a greater risk of breast cancer than estrogen-only regimens; however, results are not consistent or conclusive across studies. It is also unclear whether HT results in an increased risk of breast cancer with a favorable prognosis (low stage and grade), less favorable prognosis (high stage and grade) or both. This study pooled data from six BCSC sites to determine the risk of breast cancer and tumor characteristics among current postmenopausal hormone therapy users compared to non-users by duration of use. Investigators analyzed data on 373,265 postmenopausal women who underwent 683,435 screening mammography examinations between 1996 and 2000, of whom 3,202 developed breast cancer within 12 months of an examination. The study showed that postmenopausal women that use estrogen and progestin hormone therapy for five or more years are at increased risk of developing breast cancer, including both tumors with favorable prognostic features and tumors with unfavorable prognostic features.

What Characteristics of the Radiology Facility, Radiologist, or Mammographic Technologist Affect the Performance of Screening Mammography?

A number of studies have provided evidence suggesting that factors related to the imaging facility, radiologist, or mammographic technologist also may influence the accuracy and performance of breast screening, and BCSC researchers have begun to build a substantial area of research around these questions.

- BCSC-supported investigators examined various performance parameters for radiologists in a San Francisco practice that includes both breast imaging specialists and general diagnostic radiologists who interpret screening and diagnostic mammograms. The investigators analyzed the results of 47,798 screening and 13,286 diagnostic mammograms and found that the specialists detected more cancers and more early stage cancers, recommended more biopsies, and had lower recall rates than did the general radiologists (see below). However, general radiologists appear to benefit from using multiple-read systems of interpretation, in which at least two residents and one breast imaging specialist preview an examination and then present their results to the radiologist, who makes the actual interpretation. The investigators speculate that this difference results from the fact that the breast imaging specialists had considerably more initial and subsequent training in mammographic interpretation than did the general radiologists. They also interpreted 10 times more mammograms per year than the general radiologists.

Performance of Breast Imaging Specialists vs. General Radiologists

Abnormal Interpretations per 100 Examinations

Screening	Abnormal	Exams	Rate
Specialist	1,961	40,206	4.9%
General	537	7,592	7.1%

Radiology 2002; 224:861-869

Cancers Per 1,000 Examinations

Screening	Abnormal	Exams	Rate
Specialist	243	40,206	6.0%
General	26	7,592	3.4%

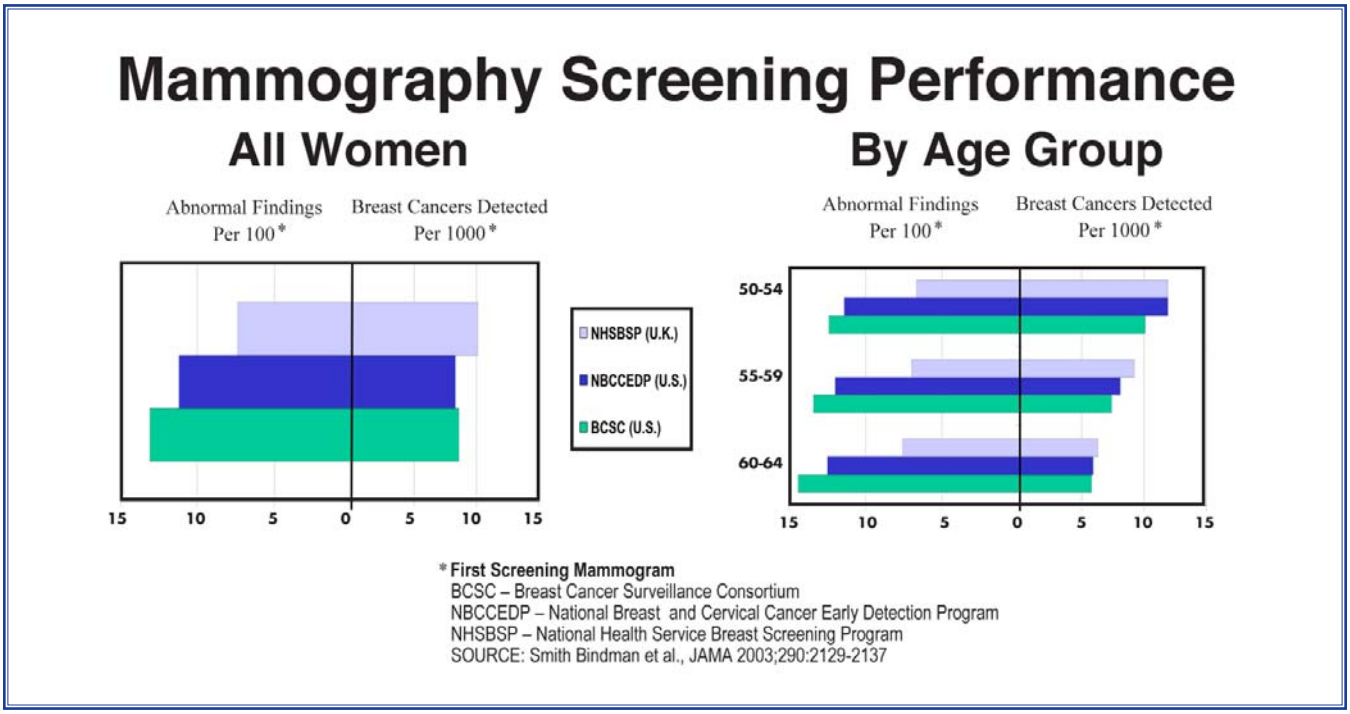
Radiology 2002; 224:861-869

- Not all cancers are detected at a screening exam because some are undetectable on mammography and some are missed because of human error. This study, conducted by investigators at the Carolina Mammography Registry, aimed at determining the percentage of false-negative findings from screening mammograms that might actually be detectable. Assessing this proportion of missed cancers might help determine a reasonable expectation for the sensitivity of mammographic screening in community practice. Over two years (1997 and 1998), four experienced radiologists reviewed 678 mammograms from 339 women. They estimated that 29% of the false-negative findings that emerged from these exams might be considered detectable. They concluded that a negative finding on screening mammography has a high probability of being correct, but occasionally is incorrect.

- The goal of cancer screening is to detect as many cancers as possible while avoiding unnecessary diagnostic evaluations, which are financially and psychologically costly. Recall rates, in combination with sensitivity and specificity, therefore, are an important indicator of the accuracy and performance of a screening test. BCSC investigators, working with colleagues from the Centers for Disease Control and Prevention's (CDC) National Breast and Cervical Cancer Early Detection Program (NBCCEDP) and the United Kingdom's National Health Service Breast Cancer Screening Program (NHSBCSP), explored this issue by comparing the performance of screening mammography and cancer detection rates in the U.S. and the U.K. The investigators found that cancer detection rates in the two countries were similar despite striking differences in recall rates. Recall rates were twice as high in the U.S. as in the U.K., and rates of open surgical biopsies were also higher in the U.S. The investigators proposed several explanations for their findings. U.S. radiologists must read at least 480 mammograms annually to comply with MSQA requirements, whereas U.K. radiologists must read at least 5,000 every year. Volume has been shown to be associated with health outcomes in other settings, and that may be the case here as well. Other possible explanations include the higher rates of mal-

practice lawsuits in the U.S., the greater extent of double reading in the U.K., the greater centralization of mammographic screening in the U.K., the existence of national quality assurance standards for the U.K.'s breast screening program, and an organized program of professional development for radiologists in the U.K.

➢ Another BCSC study also explored the relationship between recall rates and other performance measures. To date, no study has shown how recall rates affect other key measures, such as sensitivity and positive predictive value, although existing guidelines suggest that the trade-off between sensitivity and PPV can be maximized when a recall rate is less than 10%. This Carolina Mammography Registry study analyzed 215,665 screening mammograms obtained in 155,289 women to estimate the association of recall rate with PPV and sensitivity among community-based mammography facilities linked to a population-based tumor registry. The analysis showed that recall rates, which varied across facili-



ties, decreased with increasing age and decreasing breast density. The rates also increased as elapsed time since a previous mammogram increased, and they were greater for younger or black women and women with a history of breast cancer, breast surgery, or breast procedures than for women without such a history. The investigators concluded that these findings showed that practices with recall rates between 4.9% and 5.5% achieve the best trade-off of sensitivity and PPV.

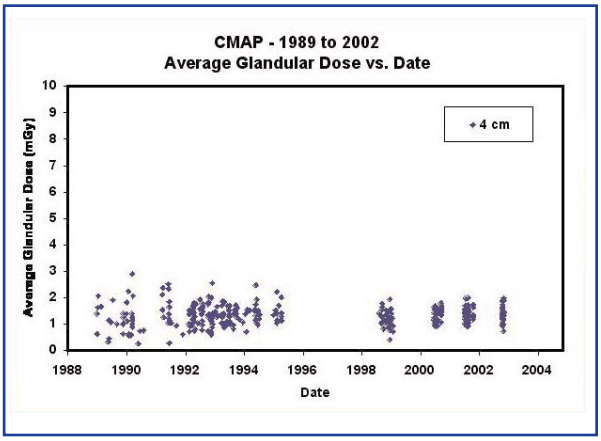
- Another factor that may be important in determining the performance and accuracy of screening mammography is the quality of the image itself. Investigators at the Group Health Cooperative evaluated several measures of clinical image quality of mammograms from 656 women with breast cancer who were screened between January 1988 and December 1993. These measures included positioning, breast compression, contrast, exposure, noise, sharpness, artifacts, and overall quality. The investigators found that sensitivity was highest among patients with proper breast positioning, but it fell significantly when positioning was not correct, suggesting that the detection of invasive breast cancer could be improved through attention to correct positioning during mammography.

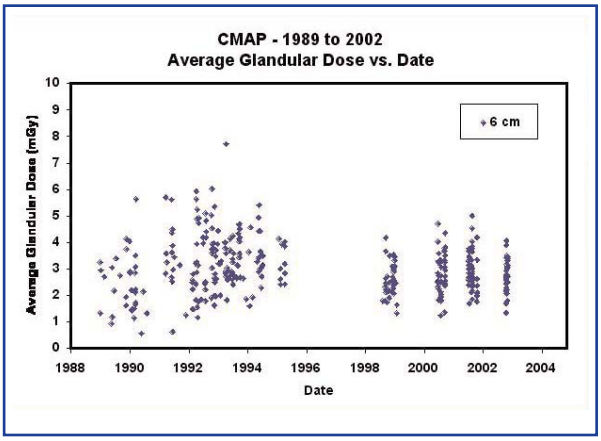
What Characteristics of Mammography Equipment Affect the Performance of Screening Mammography?

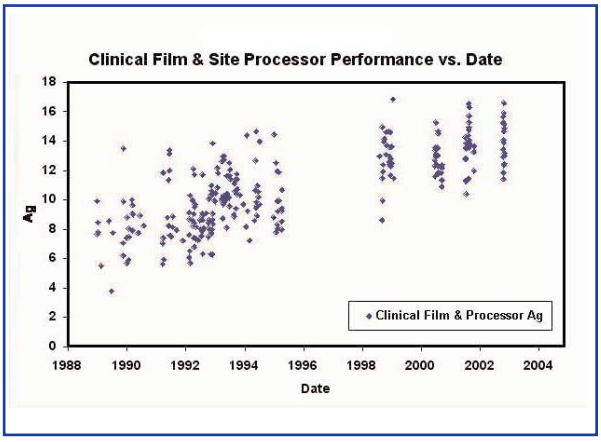
For the past 14 years, the Colorado Mammography Project (CMAP) has collected data on the performance of all mammography equipment at participating facilities. These data illustrate that the technical performance of the mammography equipment plays an important and often overlooked role in the performance of screening mammography. To evaluate the mammography system, a medical physicist from CMAP has conducted an annual survey to assess patient dose, film processor performance, radiologist viewing conditions, and other parameters that affect image quality. These data indicate that mammography equipment performance has improved significantly over the past decade, both in terms of improved image qual-

ity and improved film and processor performance. However, there remains a wide variation in how patients are imaged, the resulting image quality, and patient radiation doses, especially for women with thicker breasts. The CMAP technical performance results identify potential areas for technologic improvement.

In an effort to monitor and assess the performance of new technologies, the Colorado group has also begun to compare the performance of conventional screen-film mammography equipment with full-field digital mammography (FFDM) systems. The digital systems were first approved by the Food and Drug Administration in







These graphs show the dramatic improvements in glandular doses and film processor performance that have occurred over the past 14 years. For patient doses, the lower the value the better. For the clinical film and processor data, the higher the score the better. The 4 and 6 cm values on the graphs indicate breast thickness.

early 2000 and due to their ability to manipulate the digital image in ways screen-film cannot, they may have the potential to improve lesion detection, especially in women with radiographically dense breasts. Thus, it is hoped that FFDM will improve the performance of screening mammography.

- A study comparing 18 digital mammography systems and 38 conventional screen-film mammography systems showed that digital systems improves image quality for equal or lower breast radiation doses for all but the thinnest breasts. FFDM also provides tighter control (less variability) on exposure times, image quality, and patient doses.
- Optimized technique factors were determined for a full-field digital mammography system in terms of low-contrast lesions' detectability and then compared with results obtained from an optimized screen-film system. Results showed that using a softer x-ray beam for thin breasts and a harder x-ray beam for thick breasts improved digital mammography's ability to detect low-contrast lesions when the average glandular dose was kept constant. Under this constraint, optimum low-contrast lesion detection with digital mammography was superior to that of conventional screen-film mammography for all but the thinnest breasts.

Developing Innovative Statistical Approaches to Analyzing Data

As part of the BCSC's overall research agenda, the SCC has developed statistical techniques that permit new approaches to the data. One of these is ROC modeling that uses BI-RADS™ assessment codes as the outcome and cancer status and woman-level measurements as the covariates. This technique allows BCSC investigators to examine mammography performance adjusted for case mix. For example, sites have been able to explore the impact of covariates, such as family history, that affect the likelihood of a positive mammogram but do not actually affect the radiologist's ability to detect a breast cancer. The SCC has found that the strongest covariate affecting performance is breast density, with accuracy decreasing with increasing breast density even after adjustment for age and body mass index.

The SCC also has developed tools to address the correlation induced by women having multiple mammograms over time and by each radiologist reading several hundred or thousand mammograms each year. For example, the FAVOR project (described on p. 34) collects survey information from radiology facilities and radiologists. Individual mammograms from a woman are nested under a radiologist who is nested under a facility that is in turn nested under the regional site. Because the BCSC has covariates at all levels, a complicated mixed model hierarchical analysis has been developed to sort out the components of variation. Preliminary analysis shows that the experience of the mammographer and the number of mammograms read affect the criteria for calling a mammogram positive—in other words, changes the location of the radiologist's performance on the ROC curve. However, the area under the ROC curve does not change by these measures. Additional statistical topics the SCC has explored include the effect of missing outcome data on measurement of performance and the relationship of past mammogram results to current screening outcomes.

Beyond Research: Other BCSC Accomplishments to Date

Since its establishment in 1994, the Breast Cancer Surveillance Consortium has made major strides in accomplishing its mission. It has instituted a solid infrastructure for collecting and analyzing data and has, to a significant degree, clarified the performance parameters by which screening mammography is assessed. The Consortium has made a major contribution to the current understanding of women-level factors that influence the detection of breast cancer through screening mammography. Consortium investigators are also building a research base of information on facility, provider, and other health system factors that affect mammography and are contributing to the work of other investigators by monitoring improvements in existing screening technologies and tracking changes in the use of technology. These research accomplishments can be seen in the approximately 150 papers published by sites individually and collaboratively. BCSC investigators also have presented data at numerous national and international meetings.

Bibliometric Statistics Demonstrate BCSC Research Impact

- A recent analysis showed that the "expected citation rate" in the same journal, year, and article type—the most rigorous indicator of relative scientific impact—of a sample of 117 BCSC papers was significantly higher than the average. Papers from all BCSC sites combined received 1,801 citations, whereas the expected citation rate was 1,375 citations.

- Web site "hits" are another way to judge impact. The *Annals of Internal Medicine* Web site, which published the BCSC paper "Individual and Combined Effects of Age, Breast Density, and Hormone Replacement Therapy Use on the Accuracy of Screening Mammography," has received 2,326 requests for the full text and 1,991 requests for the abstract in the nine months since the paper was published in February 2003.

In addition to these research accomplishments, the BCSC has achieved success in several other arenas, described here.

Extending Research Use of BCSC Data

In addition to their primary purpose of serving the research needs of the Consortium, BCSC data are increasingly being recognized as a valuable resource for other studies related to breast screening. Non-BCSC investigators may use BCSC data for research following an application process that consists of submitting a request to the BCSC Program Director, who forwards it to the Steering Committee. If the project is approved by the Steering Committee, the investigators work closely with staff at the SCC, who supply coded anonymous data and assist with analyses as needed. (See the Appendix for descriptions of some of these studies.)

In other ways as well, BCSC data have had an impact on a wide range of scientific and policy arenas beyond the immediate work of the Consortium. For example, BCSC data have been used by the General Accounting Office (GAO) in two reports, *Mammography Services: Impact of Federal Legislation on Quality, Access, and Health Outcomes* and *Mammography Capacity Generally Exists to Deliver Services*. BCSC data represent U.S. breast screening in the work of the International Breast Screening Network (IBSN) and were cited in the World Health Organization's International Agency for Research on Cancer (IARC) 2002 *Handbooks for Cancer Prevention, Volume 7: Breast Cancer Screening*.

BCSC data also have been used in several key ongoing studies sponsored by NCI and other federal agencies. For example, the BCSC has collaborated with the NCI-sponsored Cancer Intervention and Surveillance Modeling Network (CISNET), a consortium of investigators whose focus is to use modeling to clarify the impact of cancer control interventions such as prevention, screening, and treatment on population trends in incidence and mortality. These models also are used to project future trends and to help determine optimal cancer control strategies. CISNET simulation models require realistic inputs on the relationship of screening to cancer stage by race, age, screening interval, and other factors, and the BCSC has been able to supply such data so that the models can reach scientifically meaningful conclusions.

Another arena in which BCSC data are contributing to research is the Factors Affecting Variability of Radiologists (FAVOR) study, an examination of the impact on screen-

ing accuracy of the settings and environment in which breast screening occurs. Several BCSC sites—the Group Health Cooperative, the New Hampshire Mammography Project, and the Colorado Mammography Project—are working with the University of Washington to assess sources of variability in mammographic interpretation that can be attributed to radiologists, practice settings, and the practice environment. The study, co-funded by NCI and the Agency for Healthcare Research and Quality (AHRQ), is examining location, available services, waiting times for both diagnostic and screening mammograms, use of computer-assisted diagnosis (CAD) and digital mammography, facility staffing, charges, market competitions, patient payment mechanisms, radiologist concerns about malpractice, use of double reading, and use of computerized mammography management systems. Preliminary results indicate considerable variability among radiologists across many of these factors, and this variability remains even after statistical models account for patient, radiologist, and facility factors.

Collaborating With the American College of Radiology

The American College of Radiology (ACR) licenses BI-RADS™ to 18 Mammography Information Systems software vendors. These vendors work with many radiology facilities that participate in the BCSC. Until recently, this presented several problems for BCSC sites who wanted to use data from ACR-licensed vendors because the system's lexicon did not present a common data collection structure, nor could vendors add to or change data fields to suit BCSC research purposes.

A BCSC and BI-RADS™ committee met throughout 2002 to discuss ways to increase vendors' ability to expand data collection and alter fields to meet the needs of BCSC as well as ACR. Representatives from the two groups matched ACR and BI-RADS™ data fields, talked with vendors, and decided on changes in both systems that would create one mutually agreeable data structure. As a result, common data forms have been designed to collect patient and radiology information. ACR is incorporating this suggested data collection form into its newest version of the BI-RADS™ manual. In its turn, BCSC has written a data dictionary to accompany the forms that will be publicly available. ACR and BCSC sites are working with software vendors to encourage them to adopt the new common data structure.

Disseminating Information and Collaborating With Other Groups

BCSC sites work hard to disseminate the results of their research and collaborate with other groups to improve breast cancer screening practices in their communities. This work is carried out through traditional channels, such as the published literature and professional workshops for radiologists. Other means include distributing newsletters and reports to radiologists, facility staff, and other interested parties; forming consumer advisory groups; and partnering with federal, state, and local groups. The sites also are actively engaged in enhancing their information systems and data collection technologies. The following paragraphs provide a few highlights from these activities.

Examples of Partnerships Established With Federal and State Groups

- The **Carolina Mammography Registry** has partnered with the Health Committee of the North Carolina Commission of Indian Affairs in a special project funded by a minority supplement to their grant. Two Native American epidemiology graduate students from the University of North Carolina at Chapel Hill have worked with the Commission to develop a breast health survey for Native American women that is being distributed with the partnership of each American Indian Tribe or Organization in the state. The results will be shared with each tribe for their own use, as well as analyzed on a statewide basis.

- The **Vermont Breast Cancer Surveillance System** works closely with the Vermont Department of Health to provide Ladies First, the CDC's National Breast and Cervical Cancer Early Detection Program in Vermont, with mammography and pathology data for their clients. All the mammography facilities across the state participated in the evolution of this process. The VBCSS and the Vermont Cancer Registry, which is housed at the Vermont Department of Health, annually conduct quality control on the breast cancer case finding and reporting.

Examples of Feedback Provided to Facilities and Radiologists

- **BCSC sites** provide monthly or quarterly feedback to the mammography facilities that use the forms they provide. These audit reports present numbers of mammograms read, by radiologist and exam type. For each radiologist, the reports provide the number and percent of recommendations by exam type, the number and percent of exams by ACR assessment, and a cross-tabulation of assessment by recommendation. They separately report exams that are double-read. Sites provide additional feedback to facilities as well. For example, facilities working with the New Mexico site receive a monthly follow-up report, which lists patients recommended for additional views, ultrasound, biopsy, or short-interval follow-up. In addition, all facilities contributing data to the New Mexico site, whether by scan form or electronically, receive an annual report of the match with the SEER registry. The site also has established an ongoing collaboration with Indian Health Service and tribal facilities to improve data collection and follow-up for Native Americans, and works with state and tribal Breast and Cervical Cancer Early Detection Programs to share data and improve the quality of the data collection.

"I have been a strong proponent of quality mammography for some time. My relationship with the BCSC in New Mexico has been extremely beneficial to our practice. The audit data supplied to us about our practice from the New Mexico Tumor Registry have allowed us to improve the quality of our mammography practice. We process the data we receive to provide feedback to each radiologist about his or her performance. In turn, individuals can improve their performance by making any necessary adjustments in mammography interpretation. By doing so, our group has been able to demonstrate a continual improvement in performance parameters with each passing year.

I am constantly in touch with mammographers throughout the country who use the published results of studies performed by the BCSC to convince their colleagues of the improving demonstrated value of mammography. The work that the Consortium is doing is invaluable to the mammography community, as well as to the entire medical community. The Consortium is certainly providing the most important data we have on the status of mammography in the U.S. Those of us deeply involved in breast imaging continue to look to the Consortium to offer us the feedback we need to take us to the next level of success in our ongoing battle against breast cancer."

Michael N. Linver, MD, FACR
Director of Mammography, X-Ray Associates of NM, PC
Clinical Associate Professor of Radiology
University of New Mexico School of Medicine
Albuquerque, NM

- The **San Francisco Mammography Registry (SFMR)** provides annual summary reports or oral presentations of mammography and cancer outcomes to radiology facilities. In addition, site investigators present published BCSC results in lectures for University of California at San Francisco Postgraduate Programs for medical practitioners and radiologists, medical and radiology grand rounds, and research meetings of the UCSF Breast Cancer Special Projects of Research Excellence (SPORE). The site also uses its Web site (http://mammography.ucsf.edu/inform/index.cfm) to present mammography findings to a broad group of professionals and non-professionals. The Web site contains published information on age-specific risks of breast cancer, effectiveness and accuracy of mammography, and short-term consequences of an abnormal mammogram result (including diagnostic procedures and morbidity from the procedures).

Examples of Enhancing Information Systems and Data Collection Technologies

- The **San Francisco Mammography Registry** has developed a fully automated system for collecting and tracking personal history and radiologic information for each patient and each exam. Mammography facilities partnering with the site assign each woman a medical record number (MRN). On the day of examination, the woman completes a two-part questionnaire (in English, Spanish, Russian, Vietnamese, or Chinese) that has an examination identification barcode (mammogram ID) on it. One copy of the questionnaire stays with the film jacket; the other is sent to the site office to be scanned into the registry's database. Using the patient's MRN, the site's software system also obtains demographic information from the hospital system and stores it in a local database along with the mammogram ID. When the exam is completed, the radiologist scans the mammogram ID in an interpretation module in the system and provides interpretation results

using a barcode template. An automated MQSA-compliant physician report and patient letter are displayed for real-time verification and editing and later printed. In some cases, reports are transmitted to the hospital system for archival purposes. At the end of each day, each site's mammographic data are sent to the data research office and imported into the registry database to be consolidated with other data.

- The **Group Health Cooperative** has been working with its Information Services Division to develop a new information system. The system, part of the Group Health Cooperative's screening program and health care delivery system, provides the software infrastructure to record risk factors and mail recruitment and reminder correspondence. The system also interfaces with an IDXrad Mammography module that records and tracks radiology findings. As part of this work, the site has developed a new questionnaire to be given to women when they come to the radiology department. This questionnaire uses Teleform software to scan the data directly into the databases.

- The **New Hampshire Mammography Network** has contracted with OmniCare to revise its mammography management system to conform to data collected as part of this population-based program. The site provides this software to five mammography facilities in New Hampshire, who submit their mammography data electronically. This system also produces letters to patients and referring physicians reporting results of mammography as well as reminder letters for patients to return for their next mammogram.

Example of Including Community Experts on Advisory Boards to Strengthen Research Relevant to Practice

- The **Vermont Breast Cancer Surveillance System** has a Peer Review Committee comprised of radiologists, pathologists, and public health officials who meet to discuss breast imaging issues in Vermont. They have a Data Use Review Subcommittee whose function is to review and approve or disapprove all data requests. The site also has an advisory

board that includes cancer survivors and all the disciplines related to the diagnosis and treatment of breast cancer. The advisory board reviews current research and proposed new ideas for research.

Example of Newsletters

- The **Colorado Mammography Project** publishes a quarterly *CMAP Circular* newsletter, which consists of articles informing radiologists, facility staff, and other interested parties in Colorado about current breast cancer and mammography research questions and issues as well as the progress of the site and the BCSC. The *CMAP Circular* reports common results across facilities and provides information about other projects in breast cancer research.

BCSC Web Sites

The Consortium as a whole sponsors two Web sites, shown on pages 41-42. In addition, six of the individual sites have Web sites:

- The Carolina Mammography Registry, at www.cmr.unc.edu
- The Colorado Mammography Project, at www.cmap.cooperinstden.org
- Group Health Cooperative, at www.centerforhealthstudies.org/surveillanceproject/default.htm
- New Hampshire Mammography Network, at www.dartmouth.edu/~nhmn/
- San Francisco Mammography Registry, at http://mammography.ucsf.edu/SFMR
- Vermont Breast Cancer Surveillance System, at www.uvm.edu/~vbcss/

Public Web Site. The public Web site (http://breastscreening.cancer.gov) provides information and news about the BCSC to scientists and non-scientists. In 2002, the BCSC Web site received an NIH Plain Language Award for excellence in Web-based communication.

Internal Web Site. This password-protected Web site, maintained by the SCC, provides an invaluable forum for communication and news sharing among NCI and the Consortium investigators and staff. The site is a repository for BCSC documents, abstracts and papers, meeting minutes, data collection forms, and Consortium policy documents. Consortium investigators and staff can also use the Web site to access information about papers in progress, site-specific data idiosyncrasies, the current and past data dictionary, and data transfers.

Enhancing the Career Development of Junior Investigators and Students

One of the goals of the BCSC has been to enhance the career development of junior investigators and students in research related to early breast cancer detection. Sites within the BCSC have used several strategies to assist new scientists with career development, including mentoring, providing assistance with research grants and funding, providing opportunities for doctoral research, and encouraging participation in seminars and research meetings.

> "The data that are collected as part of the BCSC have allowed me to pursue the whole spectrum of breast cancer research. We can link breast cancer risk factor data with biologic characteristics of tumors. We can also examine how risk factors and biologic characteristics influence breast cancer survival. Being able to link population-based risk factor data with screening experiences and outcome data is a great strength of being a part of the BCSC. The interdisciplinary nature of the BCSC allows new researchers an opportunity to learn from and collaborate with experts in other fields, which ultimately strengthens our research products. Being able to use data that are collected as part of BCSC as preliminary data for grant applications has been important to me for obtaining a career development award as well as for other collaborative grants."
>
> Diana Buist, PhD, MPH
> Group Health Cooperative

BCSC investigators have mentored junior investigators and have helped them with grant writing and obtaining funding for breast cancer research. This assistance has taken several forms:

- Collaborating with junior faculty, doctoral, and pre- and post-doctoral students on research projects, master's theses, and doctoral dissertations using registry data that result in publications and presentations; investigators also serve as mentors on dissertation and residency projects
- Facilitating the submission of research abstracts by junior faculty to the BCSC, assisting in data analysis and advising on the development of manuscripts for publication
- Assisting with NIH K07 preventive oncology awards, American Cancer Society Career Development Awards, and NIH scholar awards

- Helping junior investigators submit minority supplements to the BCSC
- Developing multidisciplinary clinical fellowship support within medical school departments, including Internal Medicine, Women's Health, and Breast Imaging
- Using institutional NCI training grants to fund pre- and post-doctoral students in training and breast cancer research
- Assisting with development of research grants through other organizations, including the American Cancer Society
- Helping with small grants applications through state-based research funds, intramural awards within cancer centers, and R03 grants from the NCI
- Providing support for statistical analyses for manuscripts related to mammography performance using BCSC data
- Permitting junior investigators to use BCSC data as preliminary data for research grant applications.

BCSC investigators also have encouraged new scientists to participate in regular seminars and breast cancer research meetings by:

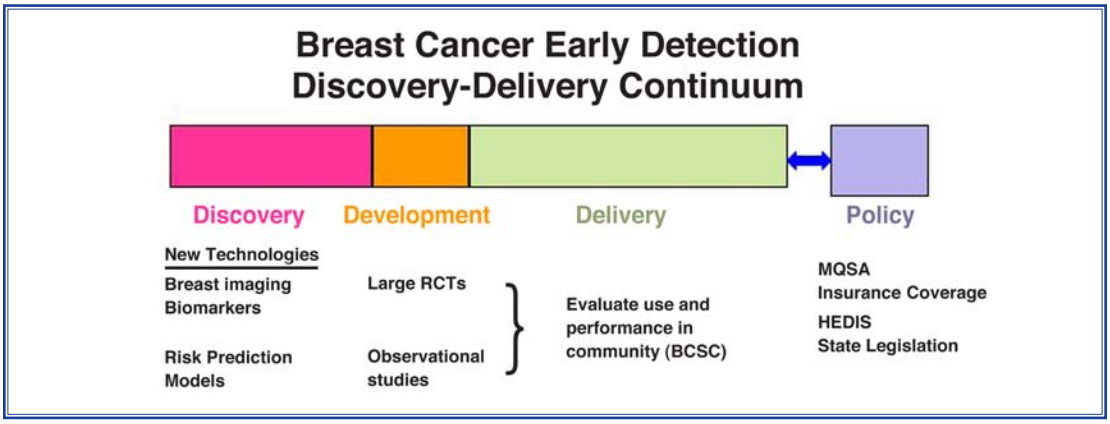
- Encouraging attendance at monthly scientific seminars at which junior investigators can present their research to and receive feedback from senior investigators
- Encouraging attendance at breast cancer seminar meetings with expert speakers, journal clubs, and other educational activities.

"Initially, my participation in the BCSC was as a co-investigator and has evolved into principal investigator of the San Francisco Mammography Registry, a transition that contributed to my promotion to Associate Professor at UCSF. Participation in the BCSC has given me the opportunity to collaborate with investigators from multiple disciplines across the country to address clinically relevant research questions and to publish seminal scientific papers. The collegial environment of the BCSC fosters productive working relationships. Importantly, I have been able to extend scientific opportunities to junior investigators through participation in the BCSC."

Karla Kerlikowske, MD
University of California
at San Francisco

Meeting the Challenges That Lie Ahead

The research and accomplishments described in this report have created a solid foundation that is enabling NCI and the investigators at BCSC sites to address a number of emerging practice, technology, and basic science issues. As the Consortium moves forward, it does so with the understanding that it takes years to fully and accurately ascertain changes in cancer rates and the impact of prevention, screening, and treatment strategies. Early work within the BCSC focused on evaluation processes of breast cancer screening. As this research resource has matured, it has allowed for in-depth examination of screening outcomes and identification of targets for improving care. In addition, research that has refined risk assessment through enhanced biologic measures suggests that the BCSC will be a major contributor to population-based efforts to refine our understanding of how best to target interventions for at-risk populations.



Challenges in Conducting Research

More than two dozen imaging techniques, or variants of imaging techniques, are now being developed for breast screening. In addition, new technologies that allow comprehensive analysis of molecular alterations in human tumors are being rapidly developed. These technologies have the capacity to screen large populations and could soon provide new opportunities for early breast cancer screening. These emerging technologies provide an opportunity for the BCSC to expand its research focus beyond

mammography to encompass research on the accuracy, performance, and impact of other types of breast screening methods. Another issue confronting investigators is that as breast cancer screening tests become increasingly sensitive, the problem of overdiagnosis will become more prominent and should be accounted for in the design, analysis, and interpretation of screening studies. Research within the BCSC has provided quantitative data on the extent of overdiagnosis in general populations of women, including the extent of follow-up care they undergo.

On a basic science level, studies aimed at better defining the molecular and biological underpinnings of DCIS and invasive tumors are likely to lead to the identification of novel markers. Current evidence from BCSC studies and others suggests that interval cancers are characterized by aggressive growth and most often prove to be invasive carcinomas. Therefore, research into the biology of interval cancers may prove to be especially fruitful because it is likely to lead to the discovery of biomarkers that can reliably distinguish indolent cancers from aggressive ones, thereby permitting the development of screening assays to complement mammography and allowing focused attention to women at high risk. Finally, a growing body of experimental evidence is showing that the microenvironment contributes to tumorigenesis in many, if not all, cancers. An increased understanding of the molecular mediators underlying the complex interactions between breast tissues is likely to lead to the identification of the microenvironmental changes that represent the earliest lesions in breast cancer development. Special studies within the BCSC have allowed in-depth examination of these basic science questions. If biologic measures of breast cancer risk are identified for screening, the BCSC provides a research resource for evaluating their utility in practice.

A third critically important aspect of research that BCSC sites have been and will continue to address are issues related to preserving the confidentiality of patient, provider, and facility data and responding to HIPAA requirements. The ramifications of these recent regulations are slowly becoming apparent and it will take some time for the scientific community to develop a common understanding of how to appropriately respond to them as it engages facilities, providers, and women in studies.

A final issue of critical importance to the BCSC research agenda is the Consortium's efforts to respond to the

ongoing evolution in screening technology. A number of sites are currently assessing the availability and use of new technologies including new types of imaging equipment (digital, MRI, screening ultrasound, optical imaging, laser), computer-aided detection, and enhanced risk evaluation using molecular markers, breast density, and genetic testing. The BCSC also has worked with the Food and Drug Administration and NCI staff to identify data elements relevant to tracking the use of digital mammography as it diffuses into clinical practice.

Several facility-level issues are also important to ongoing surveillance of screening implementation, such as real time reading and batch reading; double reading (2nd physician vs. computer-aided detection [CAD]); the experience, training, and specialization of technologists; the facility setting (hospital-based vs. outpatient, mobile vs. fixed); services offered; image quality; and facility capacity. Capacity issues, such as the waiting time for studies, could also be evaluated with surveys of BCSC sites.

Challenges in Using BCSC Data to Influence Clinical Practice

Data collected by the BCSC has the potential for influencing and improving clinical practice in various ways, and the sites will need to continue working closely with partnering facilities and patients to ensure continued progress in this area. For example, one component of the data systems support that sites have always provided to partnering facilities is regular facility, radiologist, radiology group, and state performance reports. These reports provide information on the facility's volume of screening and diagnostic exams performed, BI-RADS™ interpretive categories assigned and cancer outcomes, sensitivity and specificity rates, recall rates, and biopsy yield information. Facilities also receive patient tracking reports on all patients with pathology reports (including benign, where available), patients who received BI-RADS™ 0, 4, 5 assessments or a biopsy recommended/sur-

"Receiving an annual summary of our performance compared with all radiologists in New Hampshire has allowed us to think about how we proceed in working up suspicious findings. This would not be possible without the statewide infrastructure currently in place. In addition, getting such comprehensive assistance from the registry with MQSA requirements has allowed us to focus our time in looking at what we do rather than just collecting and tracking information."

Karen Jensen, MD
Radiologist
Berlin, New Hampshire

gical consult and who had a cancer outcome, and patients with BI-RADS™ 1, 2, or 3 with cancer outcome assessments. Providing these reports and assisting facilities in using them to evaluate and improve their performance will be a continuing BCSC priority. As part of this effort, the Consortium is developing an interactive Web site for radiologists that will provide mammography performance benchmarks calculated from BCSC data. Users would enter their own local data on measures such as abnormal interpretation rate and positive predictive value and compare these data with a distribution of BCSC data for the same measure.

Taking Data Collection into the 21st Century

A key issue for the BCSC is accommodating the research needs of the consortium within the business environment of participating radiology facilities. Collecting data can sometimes be problematic because the methods used are inconsistent, it can be inconvenient for patients (particularly if they are answering the same questions repeatedly), and it can delay the efficient processing of patients through the facility.

To circumvent these problems and make continued participation in research more appealing to women, the Group Health Cooperative site has been developing an automated data collection system prototype. This system is similar to a Palm Pilot, only it is closer to the size of a notepad. Before a women checks in for her appointment, facility staff load a questionnaire for her onto the tablet. If she has completed the questionnaire previously, these data can be loaded into the form so that she does not need to answer the same questions again. Once the woman completes the form, staff empty the data into a central database and then load a new form for a different person.

The tablet's user-friendly design has a number of advantages. For example, it allows users to navigate forward and backward within a questionnaire and it incorporates skip patterns, which allow users to ignore questions that do not apply to them. The tablet is resilient, which means that data are not lost if the power goes out or the tablet is dropped. The system automatically saves data every five seconds and the data are protected with security features. It also provides a summary page for technologists and radiologists, a key feature for them. A particularly important next step in the development phase is to create a way for women to sign the survey once they complete it so as to verify that it was really them who provided the information.

Group Health is also working with the North Carolina Mammography Project and the Vermont Breast Cancer Surveillance System to test various aspects of the system. North Carolina is particularly interested in studying whether the system can be adapted for Spanish as well as English, and in comparing usage and acceptance between small rural practices and large hospital settings. The site also wants to test the system's usability in settings where large commercial data collection packages are used. Vermont is particularly interested in studying whether it is possible to automate the creation of additional survey forms and is testing a complementary audio component.

Appendix A: Metrics for Programmatic Evaluation

Introduction

It is the responsibility of the awarding agency, in this case the National Cancer Institute (NCI), National Institutes of Health, to review progress achieved toward scientific goals in grant applications over specific grant periods and to provide scientific and logistical feedback to grantees to enhance the quality of their scientific efforts. To review progress toward achieving the objectives of the BCSC and its investigators, BCSC program officials gather information on the functioning of the Consortium in order to update the NCI leadership. This Appendix describes the evaluation metrics used to assess progress.

NCI Charge to the BCSC

At the Consortium's establishment, NCI leadership provided the following charge to the BCSC:

- Enhance the understanding of breast cancer screening practices in the U.S. through an assessment of the accuracy, cost, and quality of screening programs and the relation of these practices to changes in breast cancer stage at diagnosis, survival, or mortality
- Foster collaborative research among surveillance consortium participants to examine issues such as regional and health care system differences in providing screening services and subsequent diagnostic evaluation
- Provide a foundation for clinical and basic science research, especially basic research on biologic mechanisms that can improve understanding of the natural history of breast cancer.

Evaluation Metrics

Publication Productivity

Have the individual sites and the Consortium as a whole published papers on the objectives funded by the BCSC? How many and in what journals?

A bibliometric analysis of BCSC papers was completed in February 2004. This analysis reviewed a sample of 138 papers published between 1995 and mid-February 2004. Results of this analysis showed the following:

- More than two-thirds of the papers have been published since 1999. This is not surprising given the fact that it takes time for studies to be completed and results to be analyzed and published.

- The 138 papers received a total of 2,476 citations in peer-reviewed journals. The 14 most-cited received 1,230 citations, which is 49.6% of the total. The top-cited 28 papers (approximately the top 20%) received 1,729 citations, or 69.8% of total citations.

- The papers' Expected Citation Rate (the average for papers in same journal, year, and of same article type) was 1,923. The overall Actual Citation Rate (2,476) was about 29% higher than the journal average or the field average, with about 10 exceptions, and all these were either editorial items or letters.

- The 138 papers were published in 39 journals, representing a range of fields, including radiology (32%), cancer research (30%), medicine (22%), public health (17%), and other (3%). Fourteen of the 39 journals accounted for 78% of papers. The Journals included *JAMA*, *American Journal of Roentgenology*, *Radiology*, *Annals of Internal Medicine*, *American Journal of Public Health*, *Cancer*, *Radiology Clinics of North America*, *American Journal of Epidemiology, Journal of Clinical Epidemiology*, *Journal of the National Cancer Institute*, *Breast Cancer*, and *Medical Physics*.

Grant Funding Using the BCSC Research Resource

Have sites applied for additional peer-reviewed grant or contract funding? Has the site team been successful in gaining additional funds? Has the BCSC been helpful to the success of funding these new grants or contracts?

More than 40 ancillary studies are being conducted that use BCSC mammography registry populations. These studies use variables collected in the registry, including demographic information, breast cancer risk information, mammography interpretations, and cancer outcomes, to characterize study

populations. In addition, these studies commonly acquire additional NIH funding or funding from another source to collect supplementary information. Three common uses of registry populations are to:

- Identify a specific study population by age, race/ethnicity, level of breast cancer risk, mammography screening history, or cancer status in order to conduct observational studies or case-control studies, enroll participants in randomized controlled trials, or test novel imaging methodologies

- Combine mammography registry data with information in other databases not obtained by the registries

- Collect additional information from registry participants (women or radiologists) to combine with demographic and clinical information, mammography interpretation, and cancer outcomes.

The following are examples of projects that use registry data to conduct ancillary studies:

- "Breast Cancer Prevention: The Views of Women and Physicians" is funded by the California Breast Cancer Research Fund. This project is interviewing women about their knowledge, attitudes, and practices with respect to breast cancer prevention. Women are identified as potential participants according to their ethnicity and Gail score.

- "Compositional Breast Density as a Risk Factor" is funded by the California Breast Cancer Research Fund. This project is examining whether single x-ray absorptiometry and compositional densitometry are more accurate and precise measures of breast cancer risk than the BI-RADS™ categorical system. Women are identified as potential participants based on postmenopausal status, current hormone therapy use, and whether they have a history of breast cancer.

- "Soy and Tamoxifen for Breast Cancer Prevention in High-Risk Premenopausal Women" is funded by the U.S. Department of Defense. This study is a randomized controlled trial to determine the effect of soy and tamoxifen on breast tissue density. Women are identified as potential participants according to their menopausal status, mammographic breast density, and Gail score.

- "Physician Predictors of Mammography Accuracy" is funded by the NCI. This study is determining physician characteristics and practice patterns that influence the accuracy of screening mammography by linking data from four mammography registries with the American Medical Association's master file on individual radiologists.

- "Understanding Variability in Community Mammography" (referred to as FAVOR on p. 34) is co-funded by NCI and the Agency for Healthcare Research and Quality. This study is examining the degree of variability in mammography performance at a regional, facility, and radiologist level by surveying radiologists in three mammography registries and linking survey data with mammography registry data.

- "Relationship Between the Interval Between Screenings and Risk of Late Stage Breast Cancer" is funded by the NCI. This study is examining the relationship between the length of screening interval and risk of late-stage breast cancer. Women are identified as potential participants according to their number of previous mammograms in the mammography registry.

- "Hormone Replacement Therapy and Breast Cancer" is funded by the NCI. This study is examining the relationship between hormone therapy in postmenopausal women and breast cancer detection, risk, and tumor characteristics by surveying women for more detailed information on hormone therapy and linking survey information with mammography registry data. Women are identified as potential participants according to their menopausal status and current hormone therapy use recorded in the mammography registry.

- "Measuring the Quality of Cancer Care in the Community" is funded by the NCI. This study is developing metrics to measure quality of breast care in the community. Women are identified as potential participants according to their cancer status in the registry and by linkage with a breast problem questionnaire and census data.

- "The Sensitivity of Medicare Billing Claims Data for Monitoring Mammography Use by Elderly Women" is funded by the NCI. This study is examining the

proportion of mammograms submitted for payment to Medicare among women ages 65 and older by linking registry data with Medicare billing data.

- "Long-term Antibiotic Use as a Breast Cancer Risk Factor," funded by the Pfeiffer Foundation, takes advantage of the mammography surveillance database and links it to pharmacy data to evaluate the relationship between antibiotic exposure and breast cancer.

- "Breast Cancer Treatment Effectiveness in Older Women." This study, funded by the NCI, is evaluating the treatment of breast cancer in older women. The study will also look at the long-term sequelae of that treatment.

- "Optimizing Breast Cancer Outcomes: BMI, Tumor Markers and Quality of Care." This junior investigator Clinical Research Training Grant funded by the American Cancer Society allows the investigator to develop expertise in the evaluation of the effectiveness and consequences of breast cancer treatment in practice.

- "A Population-Based Randomized Trial to Assess the Effects of Short-Term Cessation of HRT on Mammography Assessment and Breast Density." This study was funded through the Department of Defense. Women continue to use HRT, and the question this study will address is whether cessation of HRT at two or three months before a mammogram will improve interpretive performance.

- "Developing Automated Alternatives For Eliciting Patient Information For Breast Cancer Surveillance—Phase 2." This NCI-funded study is using the clinical setting of Group Health Cooperative to develop an automated breast cancer surveillance questionnaire.

- "Maximizing Mammography Use." In this NCI-funded study, BCSC investigators conducted a randomized trial of motivational interviewing to test its effect on recruitment for screening mammography compared with reminder cards and reminder phone calls. The study showed no additional effect of motivational calls over reminder calls though both were better than reminder letters.

- "Towards Reducing Cervical and Late Stage Breast Cancer." This

study, funded by NCI, was part of the Cancer Research Network. It built on the surveillance system and knowledge of breast cancer screening implementation to evaluate where breakdowns may account for delayed diagnosis. The study is evaluating whether absence of screening, absence of detection, or potential breakdowns in follow-up are associated with invasive cervical cancer and late-stage breast cancer.

- "Driving Distance and Mammography Utilization in Vermont." In this NCI-funded study, investigators are evaluating the relationships among driving distance to mammography, mammography utilization, and initial presentation with breast cancer in Vermont.

- "Breast Cancer Survivors in Vermont: A Qualitative Study of Their Perspective of Post-treatment Primary Care Services." This study, funded by Fletcher Allen Health Care and University of Vermont, used focus groups of breast cancer survivors to identify health care needs and resources used in the post-treatment period. These data will be used to develop an experimental study testing an intervention to improve primary care services for breast cancer survivors.

In addition, several ancillary studies are investigating issues important to our understanding of health disparities:

- The Carolina Mammography Registry is conducting a five-year project to build mammography and breast cancer registries for Native American women, beginning with the Lumbee women of southern North Carolina, and to test the feasibility of a breast tissue bank for Native American women in North Carolina. A second one-year grant supplement was funded to provide the opportunity for a student to construct, pilot test, and conduct a survey for American Indian Women in North Carolina. This study will measure risk factors associated with screening mammography practice and breast cancer risk.

- In 2002, NCI awarded the University of Vermont a minority supplement to fund a three-year research project which aims to examine mammography screening practices of Native American women in Vermont. Qualitative

and quantitative research approaches will be used to collect data, generate theory, and develop a survey instrument based on the transtheoretical model.

Progress Reports, SCC Visits to Sites, and BCSC Investigator Meetings

The BCSC has instituted several mechanisms for regular reporting and updates on the sites' progress toward meeting Consortium goals and objectives.

Biannual Progress Updates

Each BCSC site produces biannual progress updates with information about site-specific efforts, including updates on the following parameters:

- Numbers of screening and diagnostic mammograms
- Number of women in the database
- Number of breast cancers linked to women in the database
- Number of facilities providing mammography data.

Information about the timing of the most recent linkages with tumor registry and data from pathology laboratories are also included in project updates.

Annual Written Progress Reports

Each BCSC site completes an annual report as part of the non-competitive renewal process. This report emphasizes progress toward scientific goals of the original grant application and progress toward the BCSC mission.

SCC Visits to Sites

The Statistical Coordinating Center and the BCSC Steering Committee conduct visits with each BCSC site twice within the five-year grant period. A major goal of these visits is to discuss stated scientific objectives, specific aims, and progress toward addressing these specific aims. Comparisons of site data with overall pooled BCSC data also are conducted. In addition, these visits review:

- Data collection procedures and data management
- Quality control procedures
- Confidentiality of data and related procedures

- Software
- Research methodology.

Biannual BCSC meetings

Principal investigators, statisticians, data managers, and other personnel from all sites meet biannually to discuss:

- Progress of collaborative studies
- Technical aspects of collaborative implementation
- Standards for data collection and management
- Prioritization of ongoing research
- Development of new studies.

Investigators present findings from ongoing and completed studies.

Appendix B: BCSC Publications

Collaborative Publications

Miglioretti DL, Rutter CM, Geller BM, Cutter G, Barlow WE, Rosenberg R, Weaver DL, Taplin SH, Ballard-Barbash R, Carney PA, Yankaskas BC, Kerlikowske K. Effect of breast augmentation on the accuracy of mammography and cancer characteristics. *JAMA* 2004;291(4):442-450.

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Rosenberg RD, Yankaskas BC, Hunt WC, Ballard-Barbash R, Urban N, Ernster VL, Kerlikowske K, Geller B, Carney PA, Taplin SH. Effect of variations in operational definitions on performance estimates for screening mammography. *Acad Radiol* 2000;7:1058-68.

Ballard-Barbash R, Taplin SH, Yankaskas BC, Ernster VL, Rosenberg RD, Carney PA, Barlow WE, Geller BM, Kerlikowske K, Edwards BK, Lynch CF, Urban N, Chrvala CA, Key CR, Poplack SP, Worden JK, Kessler LG. Breast Cancer Surveillance Consortium: a national mammography screening and outcomes database. *Am J Roentgenol* 1997;169:1001-8.

Publications From Individual Sites

Group Health Cooperative, Seattle, WA

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Appendix C: Data Forms

ptshort, version 5: 5-2-2000

PATIENT INFORMATION FORM

1. Have you had any of the following breast changes in the last 3 months? *(check all that apply)*

	Both	Left	Right
Lump	☐	☐	☐
Nipple discharge	☐	☐	☐
Pain	☐	☐	☐
Other, describe: _____	☐	☐	☐

No changes ☐

2. What is the <u>main</u> reason for your visit today?
(check one)
☐ Routine screening
☐ Follow-up to routine screening exam
☐ Concerns about breast problems

3. When was your last mammogram?
Date: __ __ / __ __ __ __ (month/year)
☐ I never had a mammogram

4. Has a health care provider examined your breasts in the last 3 months?
☐ No ☐ Yes ☐ Not sure

5. Have you ever been diagnosed with breast cancer?
☐ No
☐ Left breast ☐ Right breast ☐ Both breasts

6. Have you had any of the following breast procedures? *(check all that apply)*

	Left	Right	Both
Fine needle or cyst aspiration	☐	☐	☐
Biopsy	☐	☐	☐
Lumpectomy (for breast cancer)	☐	☐	☐
Mastectomy	☐	☐	☐
Radiation therapy	☐	☐	☐
Breast reconstruction	☐	☐	☐
Breast reduction	☐	☐	☐
Breast implants (still present)	☐	☐	☐

I have not had any of the above procedures ☐

Have any blood relatives been diagnosed with breast cancer?
Mother: ☐ No ☐ Yes ☐ Not sure
Sister: ☐ No ☐ One ☐ 2 or more ☐ Not sure
Daughter ☐ No ☐ One ☐ 2 or more ☐ Not sure

IF YES: Were any diagnosed before age 50?
☐ No ☐ One ☐ 2 or more ☐ Not sure

Today's date: __ __ / __ __ / __ __ __ __ (month/day/year)
Date of birth: __ __ / __ __ / __ __ __ __ (month/day/year)

(Consent)

8. Are you currently taking any of the following hormone medications? *(check all that apply)*
☐ Hormone replacement therapy (Premarin)
☐ Tamoxifen (Nolvadex)/Raloxifene (Evista)
☐ Hormones for birth control
☐ Other hormone:_____
☐ I am not currently taking hormone medication

9. Have your menstrual periods stopped permanently?
(check one)
☐ No
☐ Yes, natural menopause
☐ Yes, surgical procedure
☐ Yes, other reason
☐ Not sure

IF YES, *age* at last period: __ __ years old

10. Have you ever given birth?
☐ No ☐ Yes
IF YES: How old were you when your <u>first</u> child was born? __ __ years old

11. What is your current height? __ feet __ __ inches

12. What is your current weight? __ __ __ pounds

13. Are you of Hispanic, Spanish, or Latino origin?
☐ No ☐ Yes

14. What is your racial or ethnic background?
(check all that apply)
☐ White
☐ Black or African American
☐ Asian
☐ Native Hawaiian or other Pacific Islander
☐ American Indian or Alaska Native
☐ Other, describe: _____

15. What is the highest level of education you have completed? *(check one)*
☐ Less than high school graduate
☐ High school graduate or GED
☐ Some college or technical school
☐ College or post-college graduate

Thank you for taking time to complete this questionnaire.

RADIOLOGIST / TECHNOLOGIST EVALUATION — SHORT FORM

NOTES

1. INDICATION FOR EXAM: *(check one)*
- ☐ Screening (asymptomatic)
- ☐ Evaluation of breast problem (symptomatic)
- ☐ Additional evaluation of recent mammogram
- ☐ Short interval follow-up

2. TYPE OF EXAM(S) PERFORMED:
(check all that apply)

	B	L	R
Routine views (MLO, CC)			
Standard film screen	☐	☐	☐
Digital	☐	☐	☐
Both	☐	☐	☐
Diagnostic (additional) views (i.e., spot compression, magnification, other projections, etc.)			
Standard film screen	☐	☐	☐
Digital	☐	☐	☐
Both	☐	☐	☐
Ultrasound	☐	☐	☐
MRI	☐	☐	☐
Nuclear medicine	☐	☐	☐
Other breast imaging	☐	☐	☐

3. OTHER PROCEDURES PERFORMED:
Not on short form

4. BREAST DENSITY:
(check denser breast if left and right differ)
- ☐ Almost entirely fat
- ☐ Scattered fibroglandular densities
- ☐ Heterogeneously dense
- ☐ Extremely dense

5. INFORMATION AVAILABLE AT TIME OF ASSESSMENT AND RECOMMENDATION(s):
(check one)
- ☐ Comparison films only
- ☐ Physical findings only
- ☐ Both films and findings
- ☐ Neither

6. ASSESSMENT:	B	L	R
0: Needs additional imaging evaluation	☐	☐	☐
1: Negative	☐	☐	☐
2: Benign finding	☐	☐	☐
3: Probably benign finding	☐	☐	☐
4: Suspicious abnormality	☐	☐	☐
5: Highly suggestive of malignancy	☐	☐	☐

7. RECOMMEDNATION(S): *(check all that apply)*

Next mammogram:	B	L	R
Normal interval	☐	☐	☐
Short interval	☐	☐	☐
Immediate Work-up:			
Additional views	☐	☐	☐
Ultrasound	☐	☐	☐
Clinical exam for further evaluation	☐	☐	☐
Surgical consult	☐	☐	☐
Fine needle aspiration	☐	☐	☐
Biopsy	☐	☐	☐
Other _____	☐	☐	☐

8. DIGITAL MAMMOGRAPHY read by:
(check all that apply)
- ☐ Hard copy
- ☐ Soft copy

9. COMPUTER ASSISTED DIAGNOSIS TECHNOLOGY used to read: *(check all that apply)*
- ☐ Routine views
- ☐ Diagnostic views

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