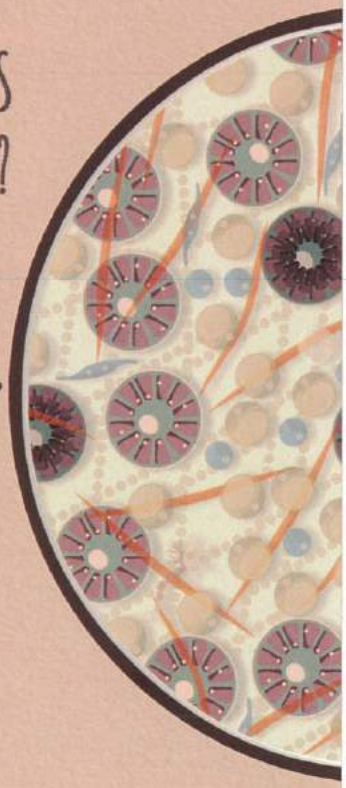
WHAT DOES MY NUMBER MEAN?



A BASIC RESEARCH PRIMER ON MAMMOGRAPHIC DENSITY

INTRODUCTION

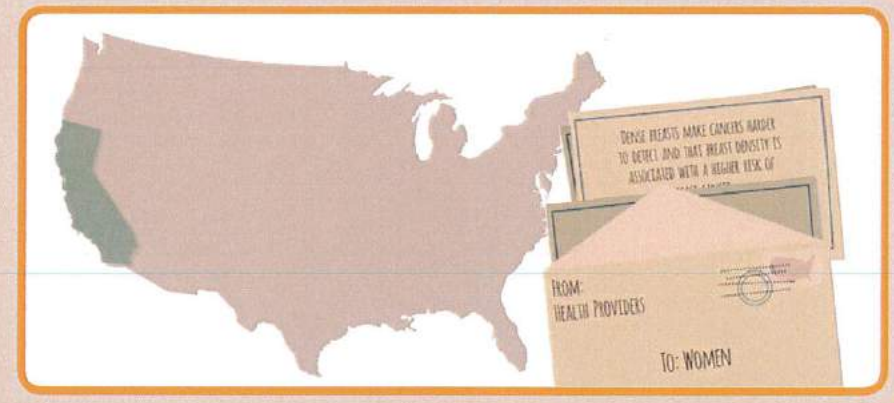
The What Does My Number Mean? video and comic book were developed by the Breast Cancer and the Environment Research Program (BCERP) to explain many unanswered questions about breast density. It utilizes microscopy images and animation to highlight methods of and theories from biology and physics about breast density and its relationship to breast cancer risk. Scholarly, yet direct, comprehensive and accessible, it offers clarification and a fresh way of thinking about a complex and controversial topic.

What Does My Number Mean? is a result of the collaboration between **Lori Schkufza**, an animation consultant; the BCERP basic science researchers **Dr. Zena Werb**, **Dr. Valerie Weaver**, and **Dr. Irene Acerbi** at the University of California San Francisco; **Alexandra Anderson** and **Janice Barlow** at Zero Breast Cancer and breast cancer advocate **Susan Samson** at the University of California San Francisco, the BCERP Community Outreach & Translation Core; and **Kim Huff** at Kimber Communications.

The goal of the video and comic book is to serve as an educational tool for health care providers and professionals as well as breast cancer advocates and organizations to explain one of the theories regarding the biology behind breast density and its relationship to breast cancer risk.

BACKGROUND

Several states, most recently California, have passed laws requiring health providers to tell a woman in writing if her mammogram reveals she has dense breasts. The letter is required to explain that dense breasts make cancers harder to detect and that high breast density is associated with a higher risk of breast cancer.



Breast density is one of the strongest risk factors for breast cancer.

Independent of other breast cancer risk factors, a woman with extremely dense breasts (10% of all women) has roughly twice the risk of developing breast cancer as a woman with scattered densities (40% of all women) and the majority of women with non-dense breasts.

However, breast density is not well understood.
There are many unanswered questions.

- WHY ARE THERE DIFFERENCES IN BREAST DENSITY?
- WHAT CAUSES THE DIFFERENCES?
- WHY DOES BREAST DENSITY CHANGE OVER TIME?
- IS BREAST DENSITY MODIFIABLE?
- HOW CAN BREAST DENSITY BE MEASURED RELIABLY?
- WHAT INFORMATION DO CURRENT MEASURES OF BREAST DENSITY PROVIDE?

This video offers one scientific perspective for understanding breast density and it highlights ongoing research using methods of, and theories from physics and biology.

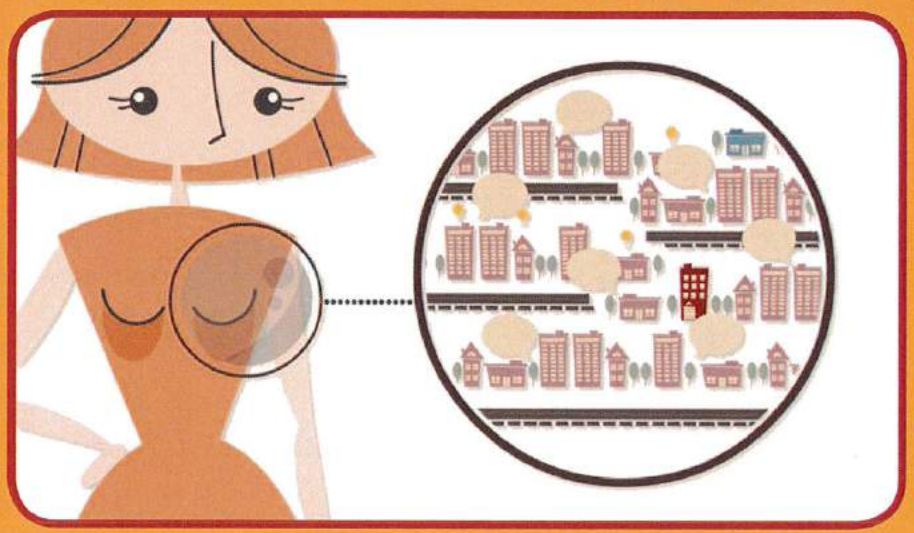
GETTING TO KNOW YOUR BREASTS

We live in a neighborhood that exists within a larger community that contributes to our well-being. The well-being of the neighborhood is maintained through:

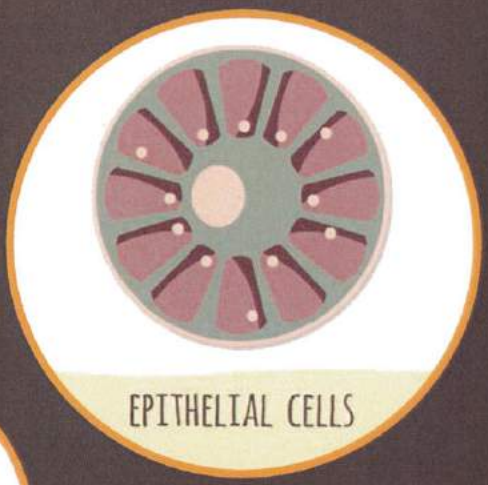
- facilitating communication among residents by providing telephones to talk to each other,
- streets that allow people to visit each other,
- needed services, such as garbage disposal,

These services create a well-organized, functioning community that allows residents to live healthy, happy and productive lives.

Likewise, your breast is a miniature 'community' whose health depends on its infrastructure that promotes communication and protection for all of the cells of the breast to maintain its long-term health and to do its job.

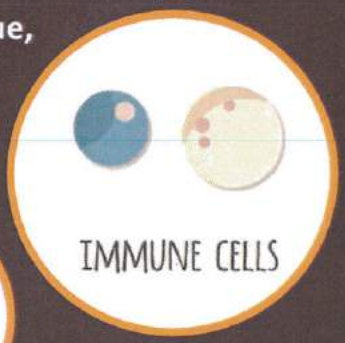


The breast community consists of many different types of cells. These include the breast epithelial cells, which produce the milk that feeds babies,

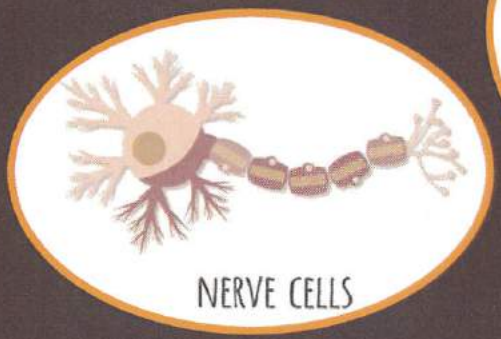


As well as fat cells that store nutrients,

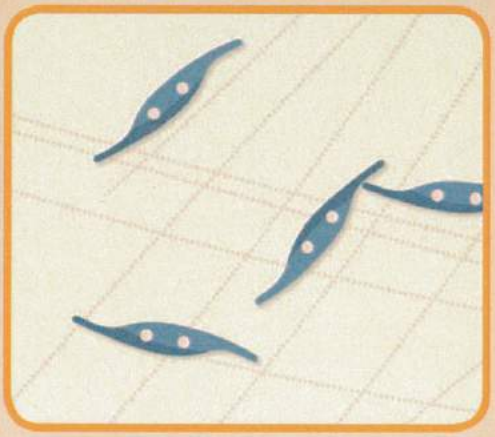
Immune cells that protect the tissue,



Nerve cells that relay messages to and from the brain

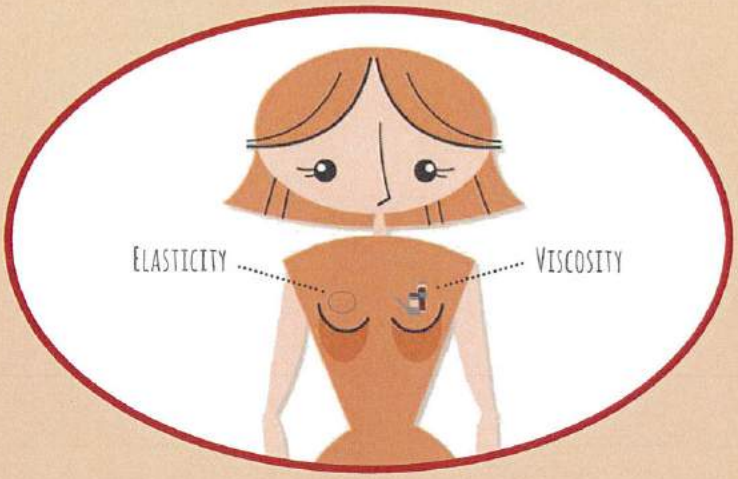


And fibroblasts which help to relay messages between the epithelial cells and the immune cells.



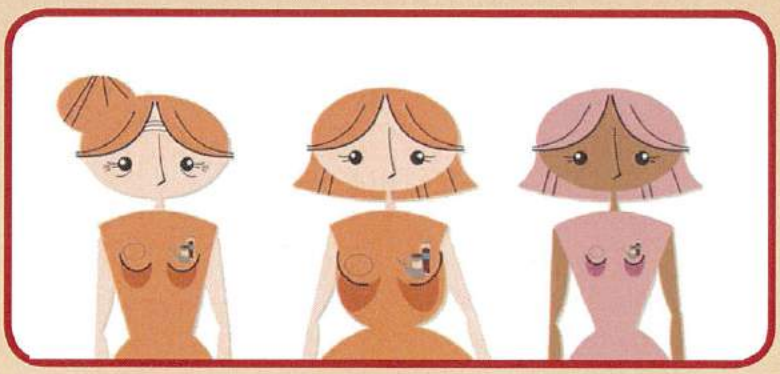
These breast fibroblasts also make and remodel the connective tissue, which is a jelly-like substance that consists of a meshwork of large, stringy protein molecules organized in a large fishing net-like structure.

The connective tissue is defined by its viscoelasticity, a combination of two physical properties, elasticity and viscosity.

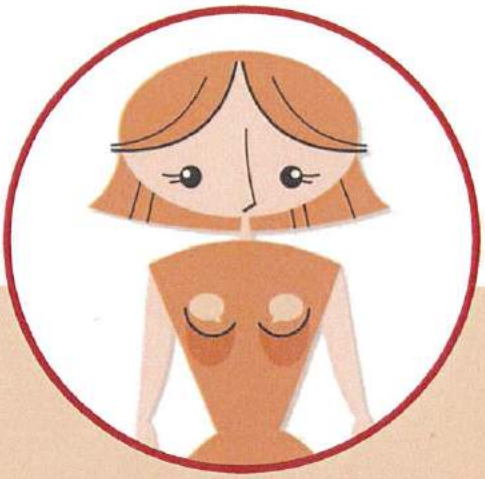


The elasticity of the breasts provides the breast with its strength and firmness so that it resists when pulled and tugged and retains its shape when subjected to gravity.

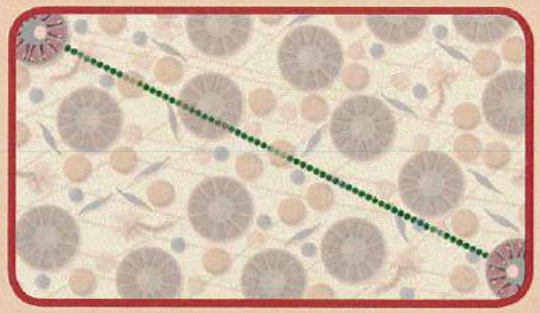
The viscosity of the breast gives the tissue its softness and allows it to be physically compressed.



The elasticity and viscosity of the breast changes with age and varies from woman to woman.



Communication within the breast is very important and is also influenced by physical properties such as elasticity.

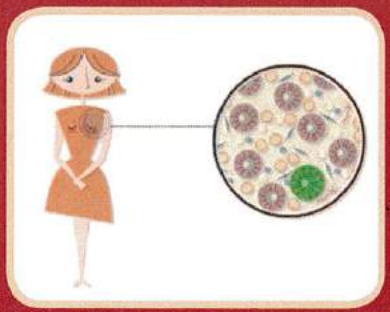


The cells in the breast talk to each other over short distances by sending out small chemical messages and by physically touching each other.

Breast cells pull and tug on the connective tissue network to communicate efficiently over longer distances and to coordinate their 'collective' behavior.

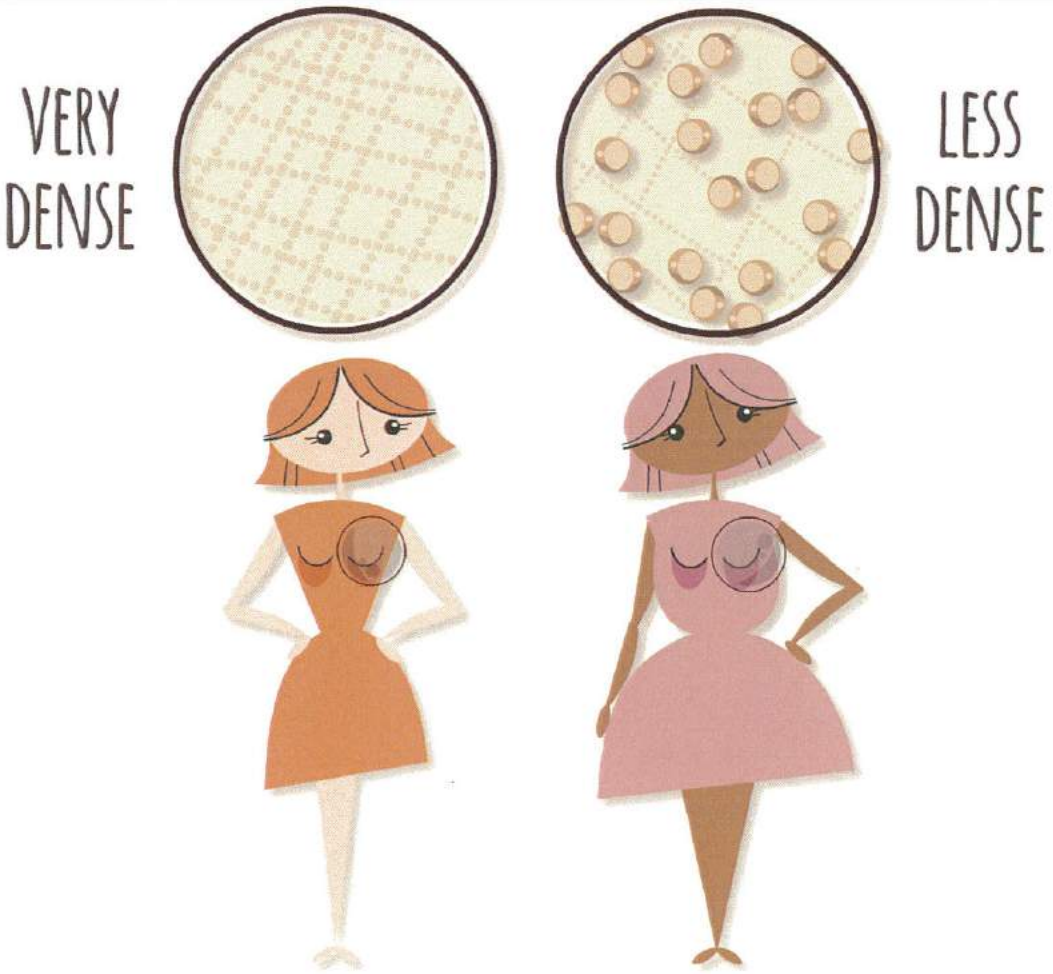
Imagine a group of friends all holding onto a large fishing net. When one person begins to pull on one end of the net, very quickly everyone in the group will 'feel' the tugging in the net. If the net is more elastic the response will be stronger and quicker.

Thus, the connective tissue network provides an infrastructure for the entire breast 'community' that facilitates rapid, long distance communication. This coordinated, rapid communication helps to maintain the long-term health and productivity of the breast.

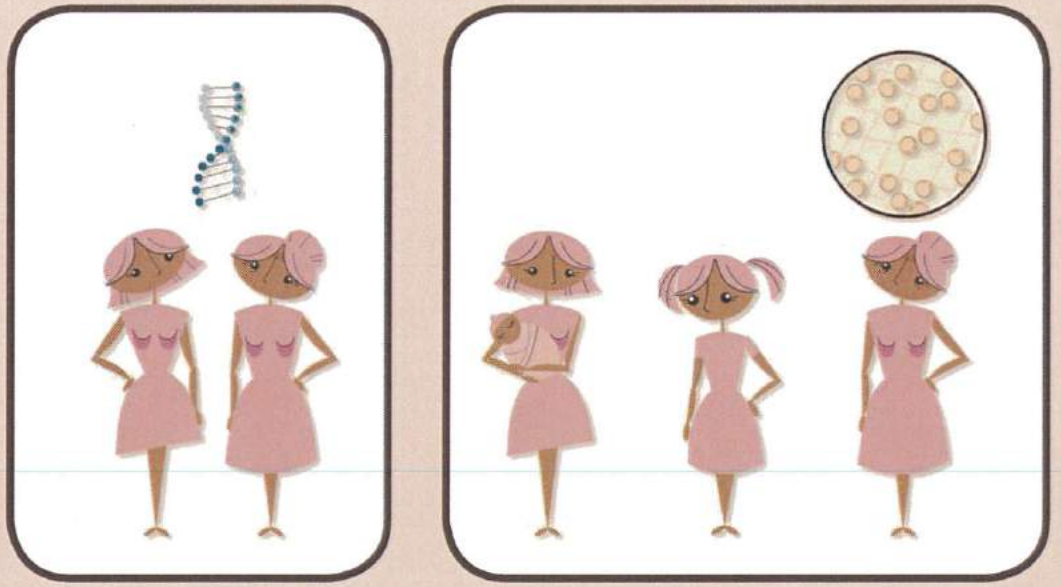


The physical properties, such as elasticity and viscosity, and the organization of the connective tissue network differ from person to person.

In some women there is more connective tissue in their breasts and the fibers are often thicker and more closely packed. This translates into a very 'dense' breast tissue. In other women the connective tissue is more loosely woven or the breast tissue may contain more deposits of fat. In this case, the breast is less dense.



Age, hormone status, whether you are pubertal, premenopausal or postmenopausal, and family history and genes influence breast density.



In general, all breasts start out denser in adolescence, a period of development when there is typically less fat deposits in the breast.

Breasts tend to lose density, particularly after pregnancy and breast feeding, as women age and more fat is deposited in the breast. Chances are that if your mother had dense breasts, you will too.

It is not possible to determine whether a breast is dense by palpation or feeling the breast during a physician or self-examination. Breast density is a way to describe the amount of dense tissue seen on a mammogram.

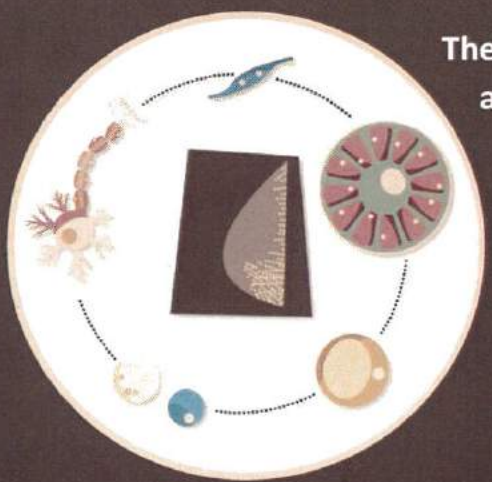
UNDERSTANDING MAMMOGRAPHIC DENSITY

Mammographic density is a score that is calculated for the breast tissue that is generated by an x-ray mammogram.

MAMMOGRAPHIC DENSITY

SCORE FOR WHOLE BREAST TISSUE

What Does Mammographic Density Measure?



The mammographic density score is a composite measurement of the whole breast tissue that includes all the breast cell types including the fat as well as the connective tissue network.

BREAST IMAGING REPORTING & DATA SYSTEM SCALE

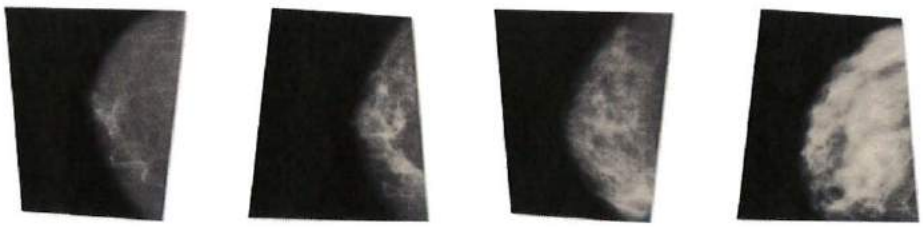
The mammographic density score is measured on the Breast Imaging Reporting and Data System (BIRADS)Scale and can be Category 1, 2, 3, or 4, with Category 1 considered least dense and 4, most dense.

CATEGORY 1 CATEGORY 2 CATEGORY 3 CATEGORY 4

MICROSCOPY IMAGES

LEAST DENSE MOST DENSE

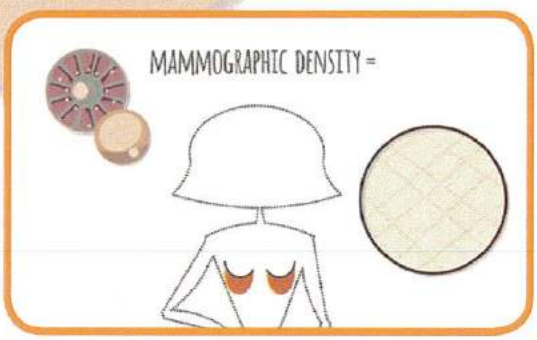
MAMMOGRAPHIC IMAGES



LEAST DENSE MOST DENSE

HOW IS IT CALCULATED?

Mammographic density is calculated based on the overall properties of the entire breast including epithelial cells, fat cells, and the connective tissue network.



For example:
The mammographic density score for a woman whose breast contains low levels of epithelial cells and soft, viscous connective tissue.

A second woman whose breast contains a lot of fat deposits and dense elastic connective tissue might also be scored as having high mammographic density.

A third woman whose breast contains little or no fat cells but has dense elastic connective tissue would be scored as having high mammographic density.

It is important to remember – having high density breasts does not mean you will develop breast cancer.

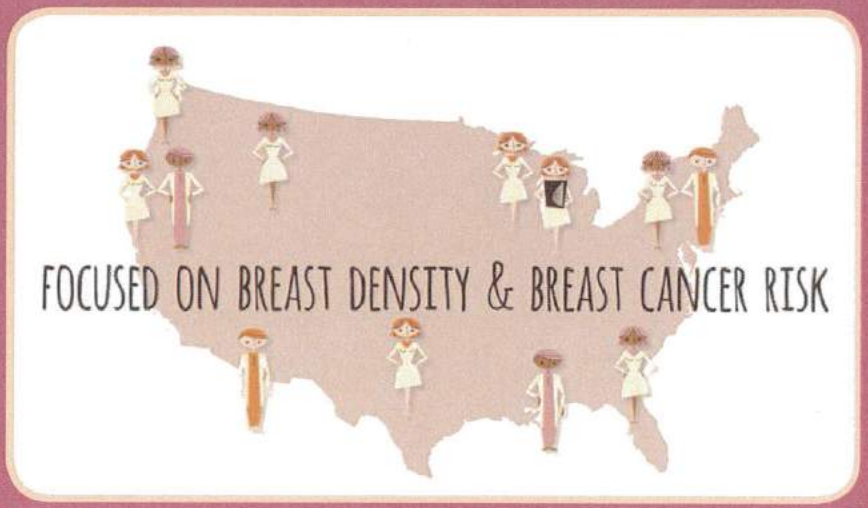
Likewise, having low-density breasts does not guarantee that you won't.

The challenge for researchers and clinicians is to increase our understanding of what breast density is and why it increases breast cancer risk.

WHY IS THE RESEARCH BEING DONE ON BREAST DENSITY SO IMPORTANT?

As mentioned earlier, breast density is associated with increased risk of breast cancer. The relation of breast density to breast cancer risk is unclear. Without a clear understanding of what breast density is and why it enhances breast cancer risk, it is not possible to develop prevention strategies, identify women who are at highest risk for developing breast cancer or developing therapies to modify breast cancer risk.

Many scientists, from varied disciplines across the country, are working together on studies focused on breast density and breast cancer risk.

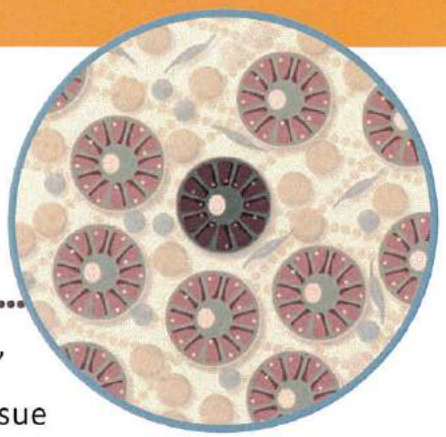


Dr. Zena Werb at the Department of Anatomy and Dr. Valerie Weaver at the Departments of Surgery, Anatomy, Bioengineering, and Therapeutic Science at UCSF, in collaboration with an interdisciplinary team of researchers, including basic cell and molecular biologists, biomedical and mechanical engineers, breast pathologists, mammographic and MRI breast imaging experts, as well as breast radiologists, breast surgeons and breast cancer advocates are collaborating together.

The research being conducted aims to understand the molecular basis of mammographic density and to determine why breast density enhances lifetime risk to breast cancer. The research focuses on the role of the connective tissue in the breast and the impact of connective tissue stiffness on breast cell behavior.

To date, studies at UCSF and elsewhere have produced innovative findings, which will generate additional hypotheses and additional studies.

SOME OF THE FINDINGS ARE:

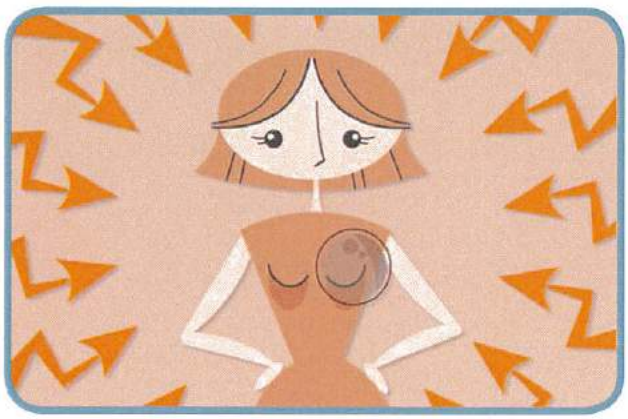


There are more epithelial cells in dense breasts. More cells increase the probability one of the cells may become cancerous.

Because epithelial cells within a "dense" breast are surrounded by connective tissue there are more opportunities for the cells to communicate with each other.

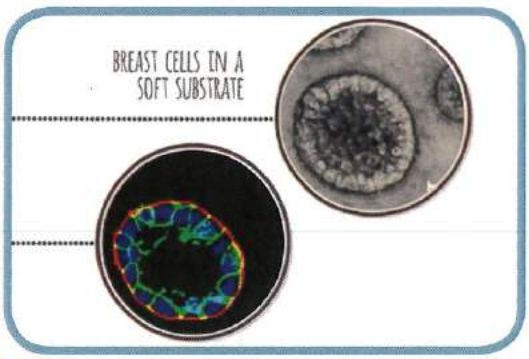
The connective tissue in "dense" breasts is more elastic so that communication should be more robust and efficient.

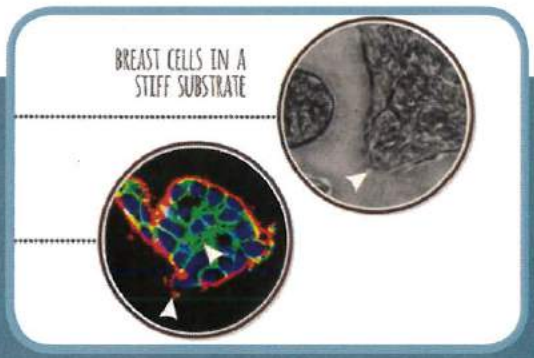
This means that when the breasts of a woman with dense breasts are exposed to environmental toxins or radiation or are subjected to negative lifestyle behaviors, there is a higher chance that the epithelial cells will become stimulated and this could increase the likelihood that these cells could be induced to grow, to migrate and eventually become corrupted.

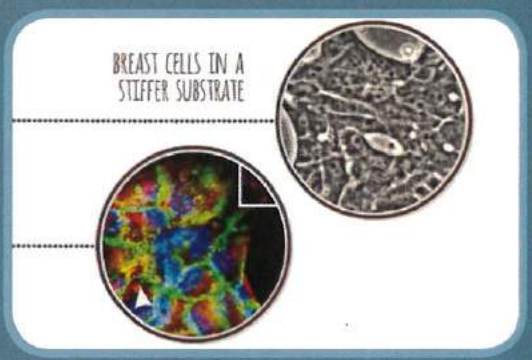


Women with high mammographic density frequently have breasts that contain increased levels of a type of collagen.

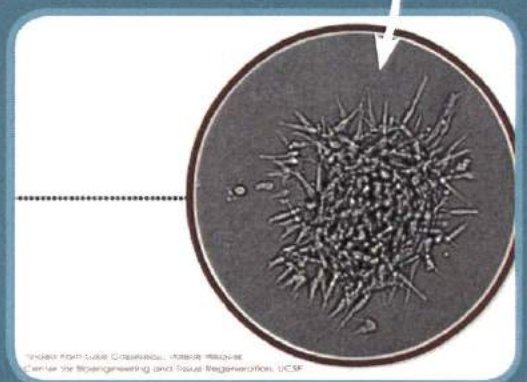
Women with dense breasts often have a high number of epithelial cells and their stiff connective tissue enhances overall cell growth and survival.







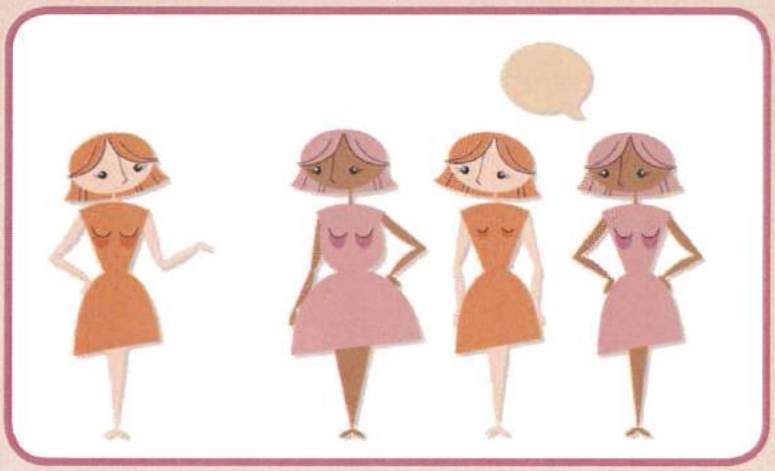
Connective tissue stiffness enhances the migratory behavior of pre-malignant epithelial cells.



CONCLUSIONS:

Through research being done at UCSF, scientists have increased understanding of the relationship between epithelial cells and the connective tissue as well as the impact of connective tissue stiffness on breast cell behavior.

With additional research, it may be possible one day to modify breast density or develop prevention strategies and treatments.



We encourage you to share this information with others interested in learning more about breast density, breast cancer risk, and scientific research.

Likewise, we urge you to be proactive in reducing your risk of breast cancer.

Engaging in healthy lifestyle behaviors such as:

being physically active, limiting alcoholic beverages, avoiding weight gain, minimizing your exposure to environmental chemicals and medical radiation, as well as breast feeding your baby and limiting your use of hormone replacement therapy.

WHAT DOES MY NUMBER MEAN?

ACKNOWLEDGMENTS

ART DIRECTOR & ANIMATOR
Lori Schkufza

NARRATOR
Cheryl Jennings

WRITERS & PRODUCERS
Janice Barlow, BSN, PHN, CPNP
Zero Breast Cancer

Alexandra N. Anderson, MPH
Zero Breast Cancer

Susan Samson, MA, MPH
Breast Science Advocacy Core
University of California, San Francisco

Irene Acerbi, PhD
University of California, San Francisco

Valerie Weaver, PhD
University of California, San Francisco

Zena Werb, PhD
University of California, San Francisco

COMIC BOOK DESIGNER
Kim Huff
Kimber Communications

SPECIAL THANKS

We extend a special thank you to the researchers and community members who were involved in the Breast Cancer and the Environment Research Program for their support and continuing contributions to advancing our knowledge about breast cancer.

This project was made possible by the support of funds from grants U01 ES019458 and U54 CA143836-01 from the National Institute of Environmental Health Sciences and the National Cancer Institute along with additional funding from Zero Breast Cancer.