

A Brief History of Breast Cancer

Then, Now and Maybe

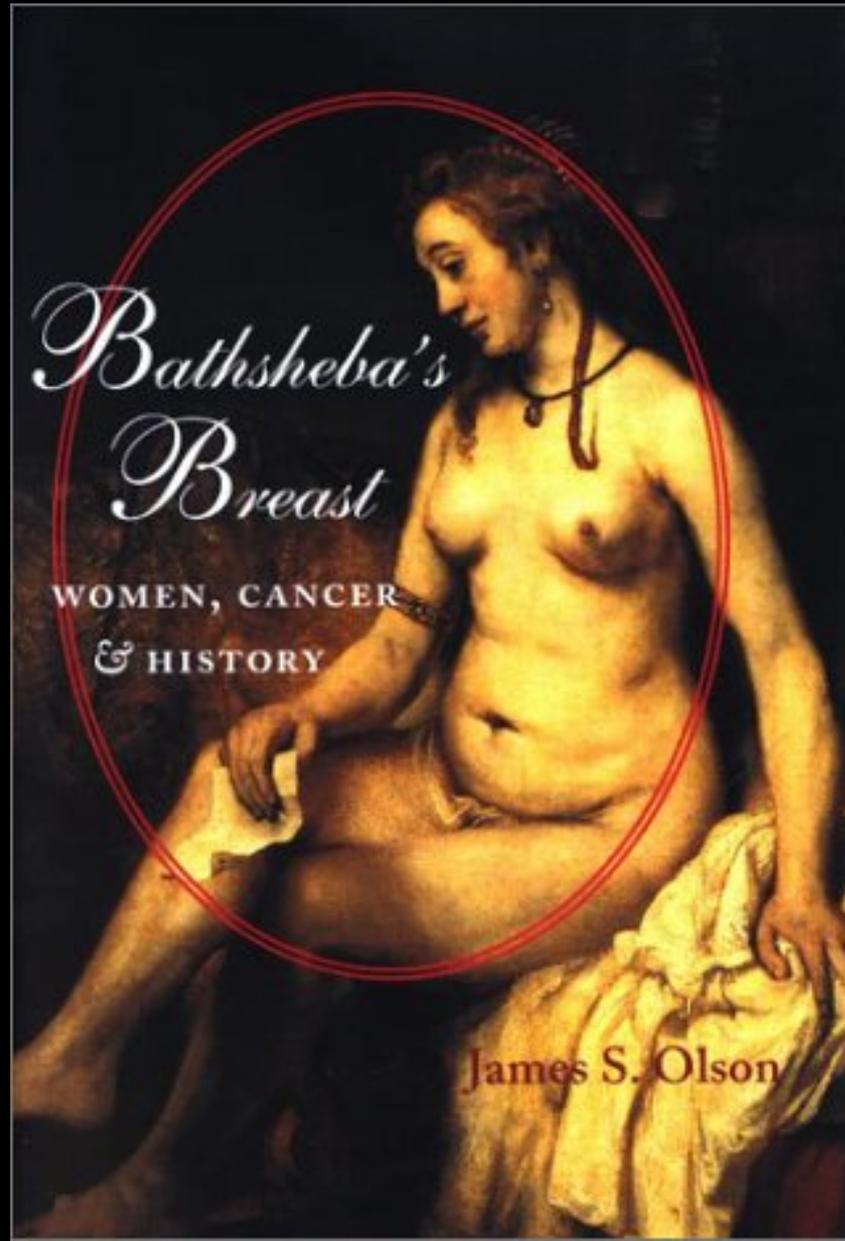
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With Thanks To:

- My Colleagues at UTHSCSA and at the Cancer Therapy and Research Center (CTRC) in San Antonio
- The Residents and Fellows at UTHSCSA, who helped with this presentation.
- All the Researchers, Writers, Editors and Compilers responsible for the fantastic resources on the Web.
- Mr. Cogburn, for offering me the privilege of addressing this gathering.

James S. Olson



The Mystery of Disease

- To this day, all disease is difficult to truly understand, scientifically and personally.
- In early history, without centuries of recorded observations, and without a modern understanding of disease processes, all disease was a terrifying mystery.
- This was particularly true of infectious disease and malignancy, which seemed to arise from nowhere.

Breast cancer has probably been with us as long as we've been human. In fact it is a known pathology in many lower animals, including dogs, cats, rats, cows and even hedgehogs.



Breast Tumors Were Different

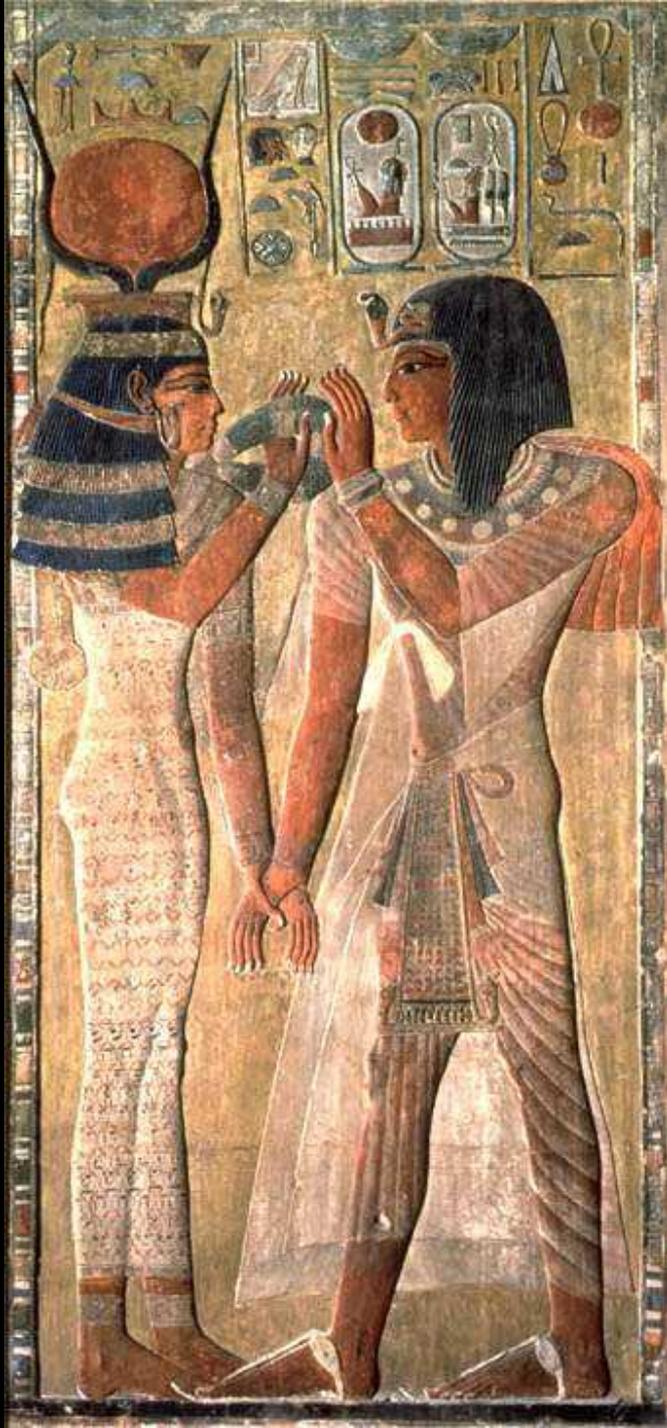
- People have always suffered and died of cancer. But before the days of X-rays and autopsies, most cancers: colon, ovarian, brain, lymphoma, leukemia, melanoma, were invisible. The decline was obvious but the cause was not.
- Breast tumors were different. The initial, tiny palpable mass could be observed growing and then destroying, first the breast and then the body.



The first known medical texts are from ancient Egypt.

The earliest is on the ailments of women (Kahun Gynecological Papyrus, ~1800 B.C.).

Curiously, the surviving document has no mention of breast ailments.



The first known description of breast disease is from a surgical text from ancient Egypt. The surviving pages give instructions on the treatment and the prognoses for a variety of mostly traumatic injuries.

Surgical techniques, herbs and potions, spells and magic were listed for the treatment of multiple conditions.

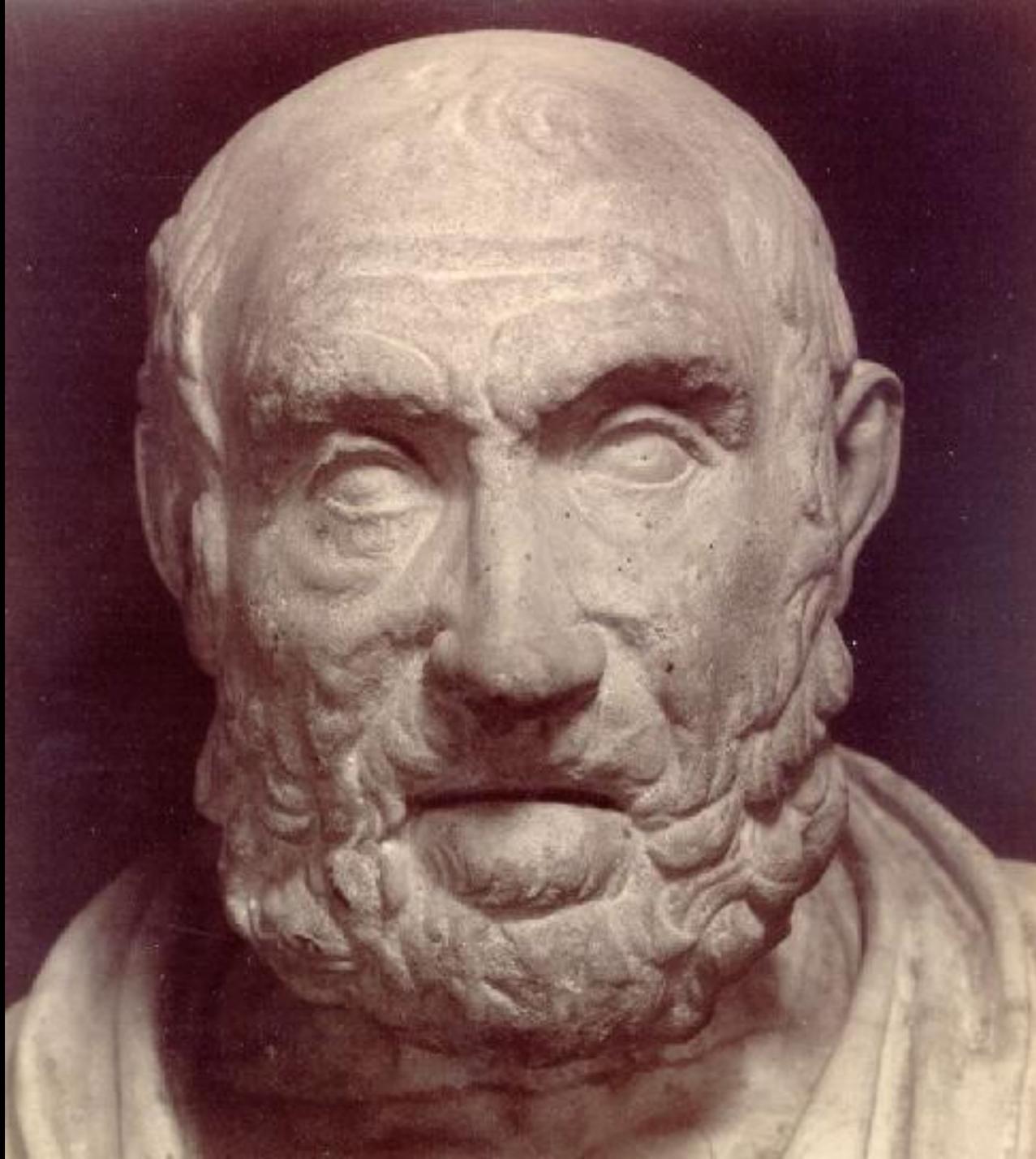
Ominously, when describing the “bulging tumors of the breast”, the presumed author, Imhotep stated simply, “There is no treatment”.

Handwritten text in Egyptian hieroglyphs and Demotic script, likely a medical or surgical text. The text is arranged in approximately 15 horizontal lines. Some words are written in red ink, possibly indicating specific medical terms or instructions. The script is dense and characteristic of ancient Egyptian writing.

Handwritten text in Egyptian hieroglyphs and Demotic script, continuing the medical or surgical text. The text is arranged in approximately 15 horizontal lines. Like the left page, it features dense script with some red ink used for emphasis or specific terminology. The overall appearance is that of an ancient medical manuscript.

Edwin Smith Papyrus, oldest known surgical text, ~ 3000-2500 BC mentions breast tumors

- Even today, the prospect of breast cancer is terrifying. In early history, the possibility of the agonizing progression of the disease must have caused unspeakable terror.
- The social stigma of any disease added to the burden.
- And the status of women in the ancient world was often dependent on their ability to work or their physical appearance, both profoundly changed by breast cancer.



Hippocrates, 460-370 B.C.

- Hippocrates is considered the founder of modern medical thought.
- While his theory of the humoral basis of disease (The four humours were blood, black bile, yellow bile and phlegm) is now thoroughly discredited, it was at least an organized way to address disease, and emphasized the clinical aspects of treatment and prognosis, rather than magic.
- Breast cancer was thought to result from an imbalance of black bile.

Galen, 129-217 A.D.



Library of Congress

- Hippocrates' theories were embraced for centuries, advanced by the Roman physician Galen.
- While breast tumor treatments included salves, herbs and bloodletting to balance the humours, primitive surgery and cautery were also used.
- Prognosis remained dismal.

Why is this important?

- While breast tumor treatments remained brutal and mostly ineffective, these early physicians changed a fundamental way of thinking about disease.
- Empiric evidence about the effectiveness of treatments was first considered.
- The very nature of disease was questioned and a variety of local and systemic treatments were considered.

Queen Atossa, 550-475 B.C.

- Queen Atossa was one of the most powerful women in the ancient world. She was the daughter of the king of Babylon, Cyrus the Great, the consort of Darius who united Persia and the mother of Xerxes, the Persian king who nearly conquered the ancient Greeks. While breast disease affects women of all classes, her story is one of the first recorded.



- When Atossa discovered a growing, painful breast mass, she was terrified. When the mass burst, yielding foul discharge, she went into isolation. The most powerful women in the world was reduced to summoning a Greek slave for treatment. If he could cure her, she promised the slave Democedes any wish. He lanced the mass and bathed the wound with herbs, curing a probable infection.
- Atossa granted his wish, to accompany a Persian scouting party to Greece, where he finally escaped to home.



Theodora, Empress of Byzantium

- Theodora is one of the most fascinating figures of the late Roman empire.
- Born poor and raised by her widowed mother, she became one of the most famous prostitutes in Constantinople.
- Justinian, the most successful emperor of the late Roman empire fell in love with Theodora and against all advice married her.
- She became one of the most important imperial advisors and the devotion between the couple was legendary.

Theodora, Empress of Byzantium

- At around age 47, Theodora discovered a breast mass.
- The advice of the court physician was radical surgery followed by cauterization, repeated often.
- When faced with this advice, and knowing the likely outcome, the self-aware Theodora declined treatment.
- With the use of pain killers, Theodora attended to her duties, made peace with her past and died in 548 A.D..





Do what the doctor says?

- Two Queens of the ancient world reacted very differently when faced with the prospect of a fatal disease.
- Today, women are faced with the same choices and physicians are faced with similar questions.
- Should we do something just because we can, without considering all outcomes?
- Is what we consider important and acceptable the same for the patient?
- Should we try to convince the patient that what we think is appropriate is the right thing to do?

The Middle Ages

- Over the next 1000 years, the treatments for breast tumors changed little.
- The suffering from breast cancer was often thought of as a penance, for past vanities.
- Those who sought treatment were subjected to extensive and brutal surgeries, with the final objective to excise the entire, often extensive tumors.
- But during the middle ages, some important observations on the epidemiology of breast cancer were noted.

Nun's Disease



GILBERTINE NUN

English Monastic Life by E.A. Gasquet
Methuen & Co. London. 1904



BENEDICTINE NUN

English Monastic Life by E.A. Gasquet
Methuen & Co. London. 1904



FRANCISCAN NUN, OR MINORESS

English Monastic Life by E.A. Gasquet
Methuen & Co. London. 1904

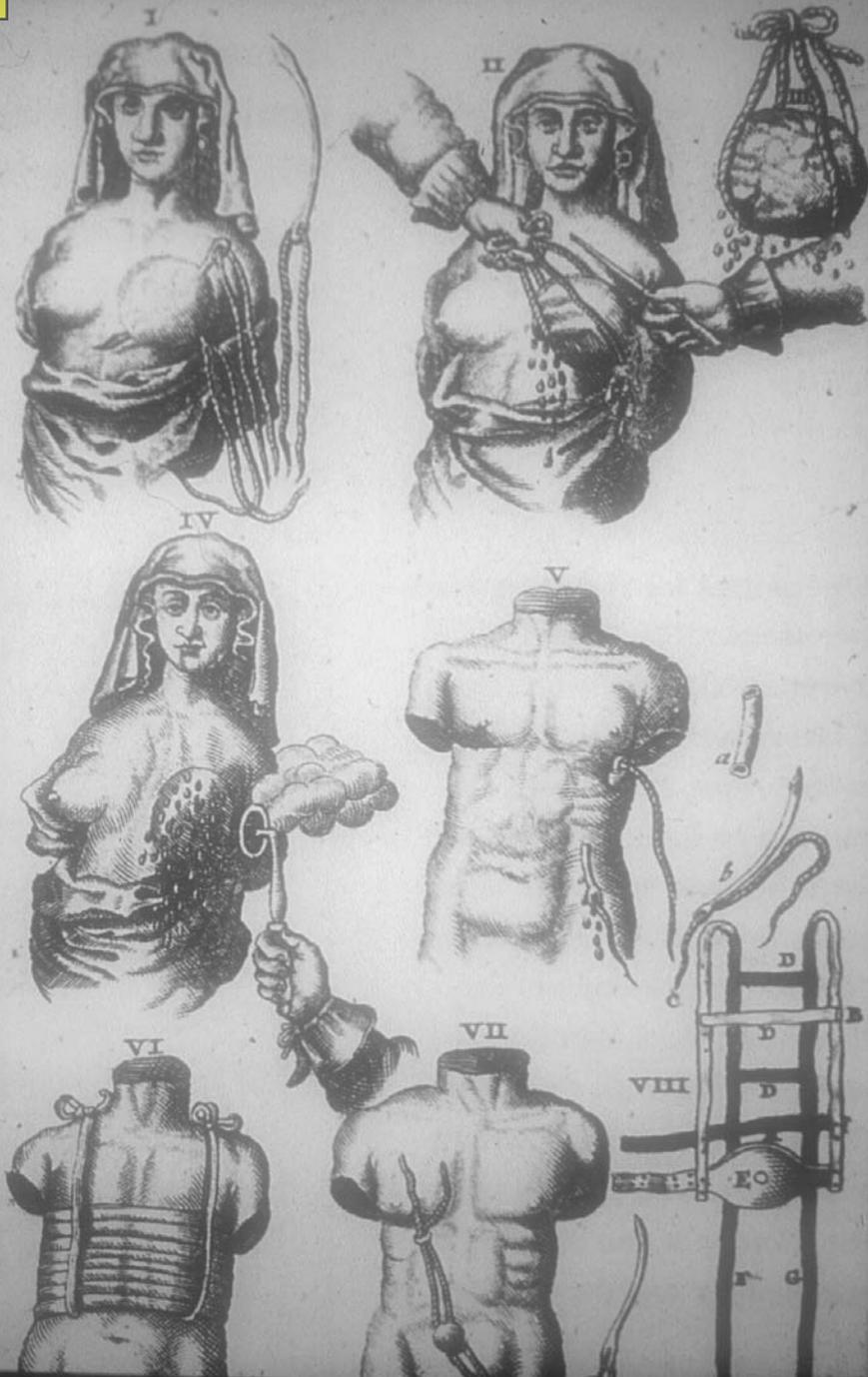


Saint Agatha

- In the days before hospitals, people died at home, cared for by family.
- Nuns cared for the poor, those alone and for their own.
- Both the dying and the caregivers gained comfort through prayer.
- The accounts of the nun's compassionate end of life care remain models for today's caregivers.

Early Epidemiology

- Convents were in every community in medieval Europe, and nearly every convent had a nun dying of breast cancer.
- While this was first thought to be a product of celibacy, we now know that increased risk is associated with the absence of child bearing.
- Then as now, nuns tend to live longer, and age increases risk.
- The greater incidence of breast cancer in certain communities and individual families was also observed.



For those who chose treatment, fast surgery was necessary in the days before general anesthesia. New surgical instruments were devised to make the ordeal as quick as possible.

However, patients often did not survive the procedure or it's common aftermath of infection.

Malignant disease nearly always recurred, at the surgical margins and in the axilla. And symptoms likely related to distant metastases occurred.



Anne of Austria, 1601-1666

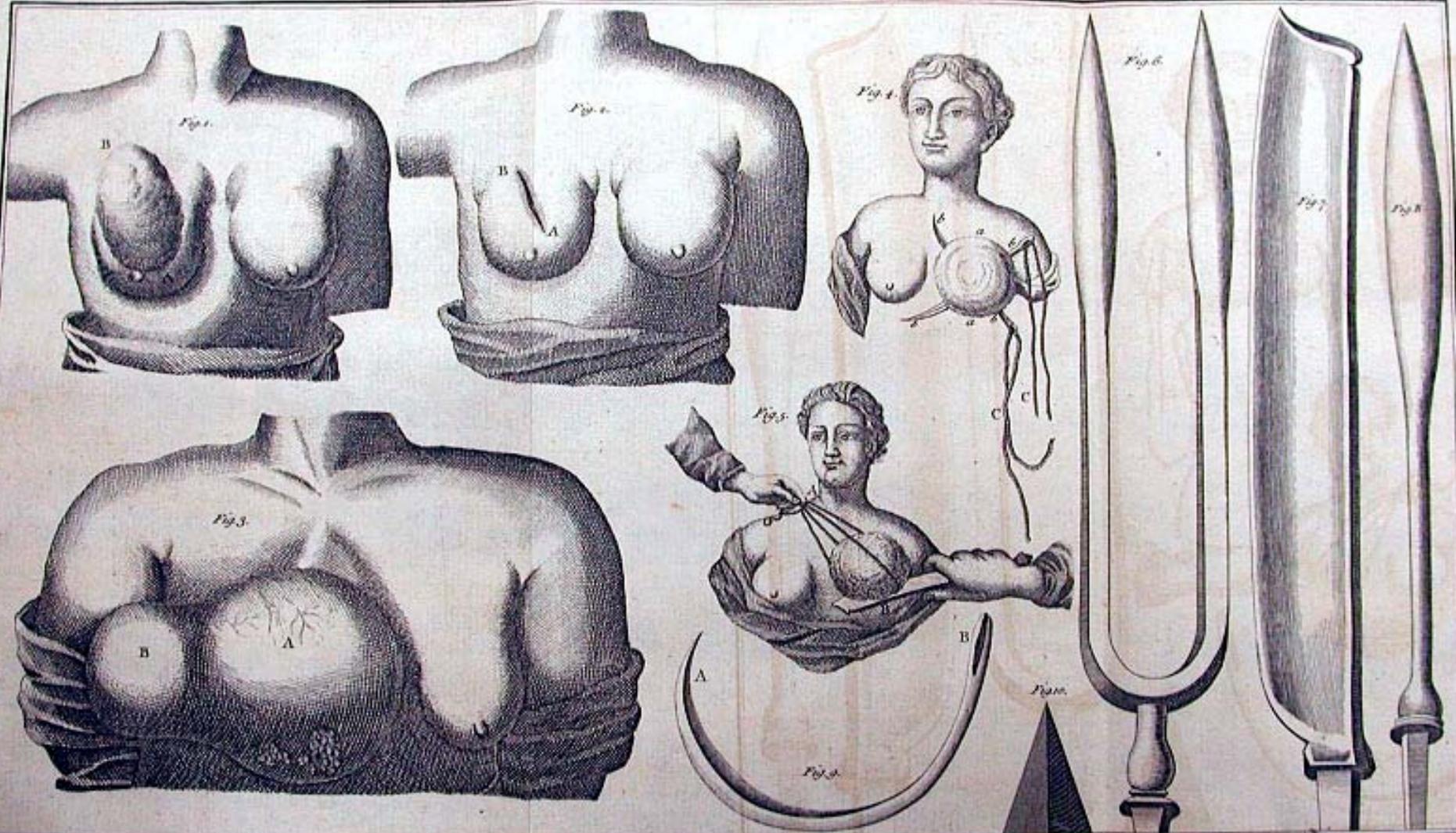
- Anne was the Queen Mother of the French royal dynasty. Her son and grandson ruled over the most lavish courts in Europe.
- The course of her breast cancer, from the discovery of a small left breast lump in 1663, to her death is well recorded.
- The course of her illness was like that of prior centuries, with horrible advanced local disease.
- But soon new and rediscovered ideas began to change the course of local disease treatment.

The Renaissance

- The works of the classical physicians of Greece and Rome were rediscovered, by way of translations from Arabic, centuries of medical knowledge from the Islamic world became available. Books became more common.
- Human dissections were performed, allowing better understanding of normal anatomy and the distinctions between benign lesions and the “karkinos, (crab like) cancers were described.
- Physicians and patients began to believe (prematurely) that medical treatments could make a difference in the course of disease.

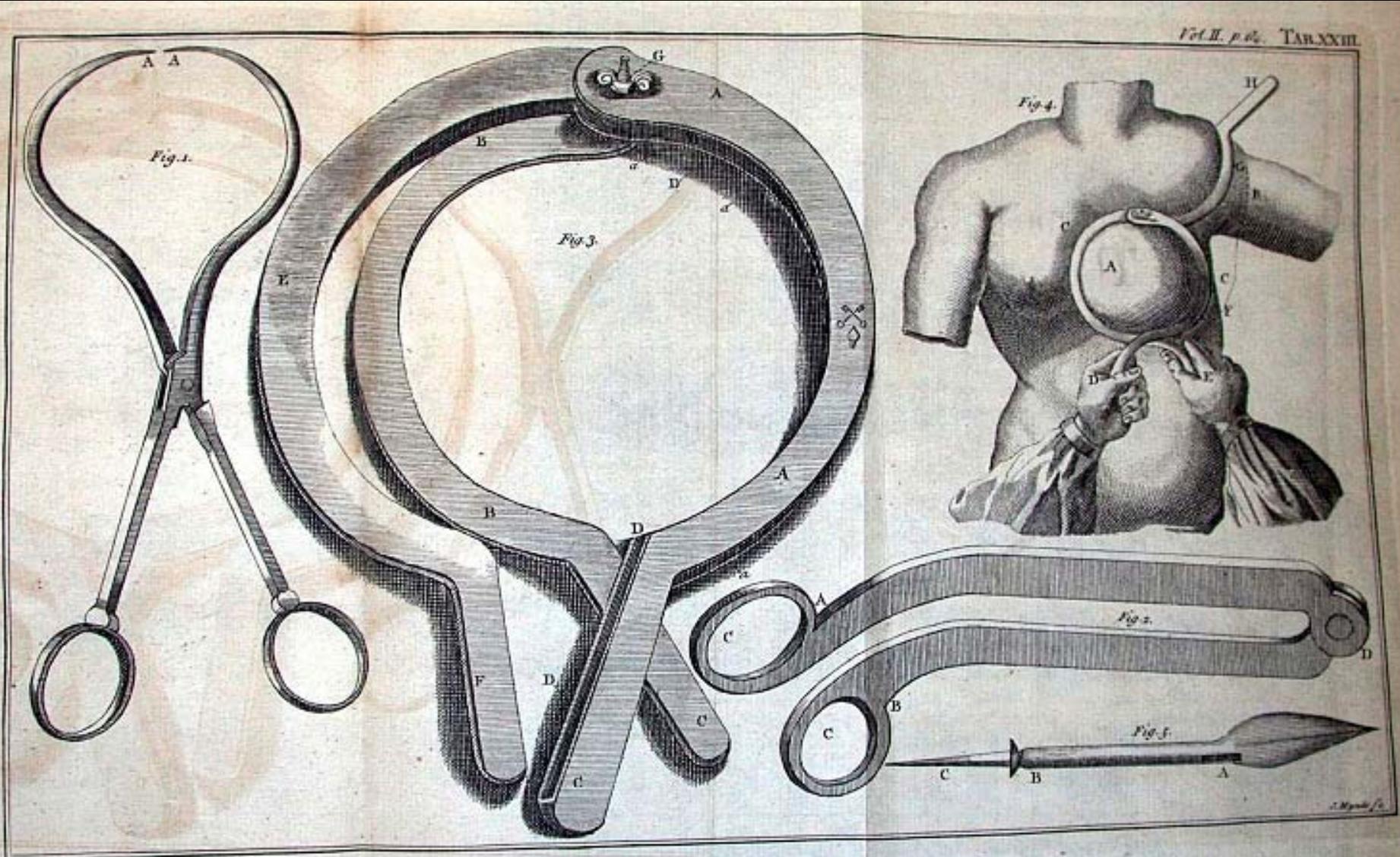
Descriptions, appearances and treatments were published

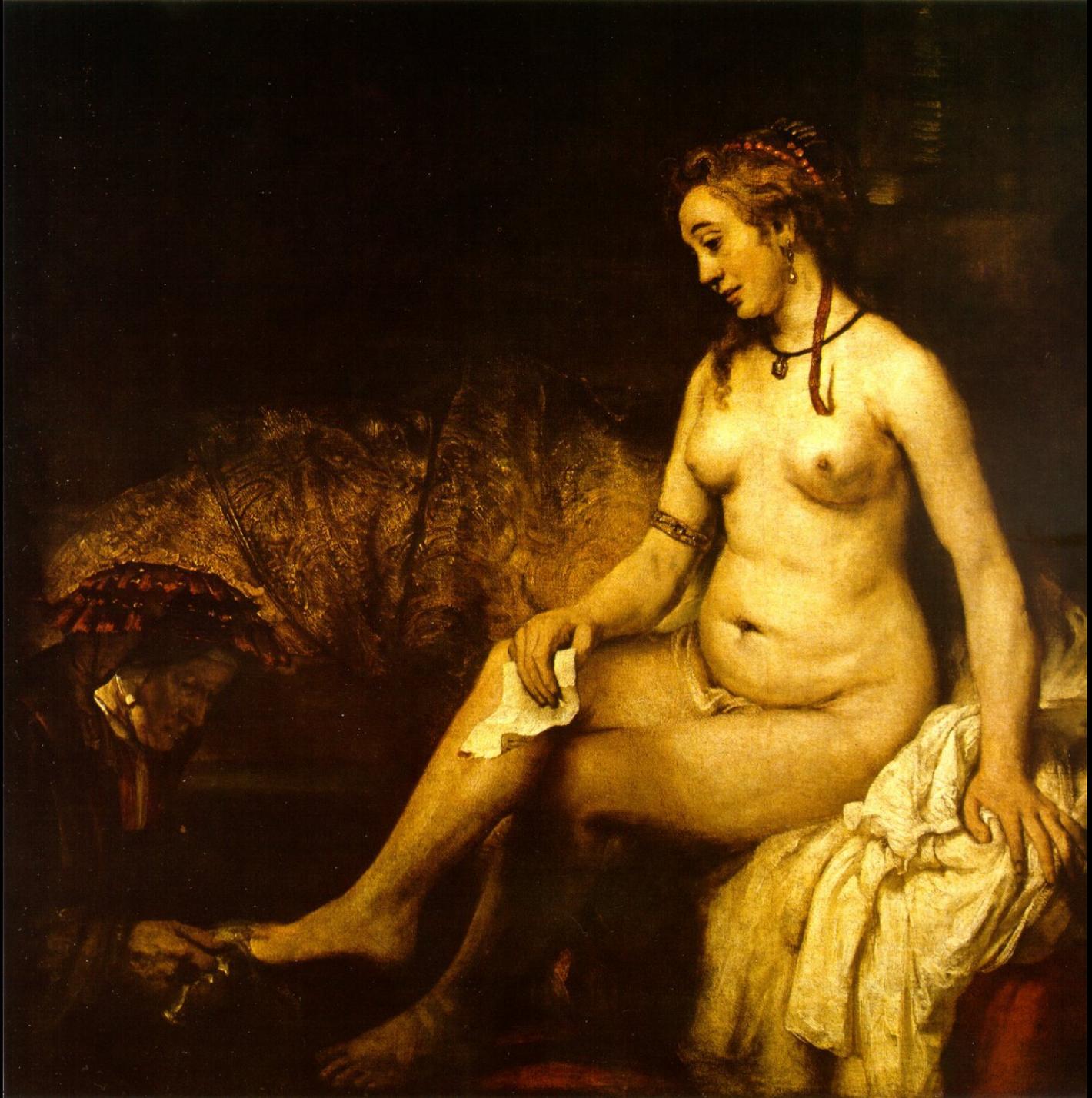
Vol. II. p. 63. TAB. XXII.





New instruments were developed to aid in the efficient performance of mastectomies

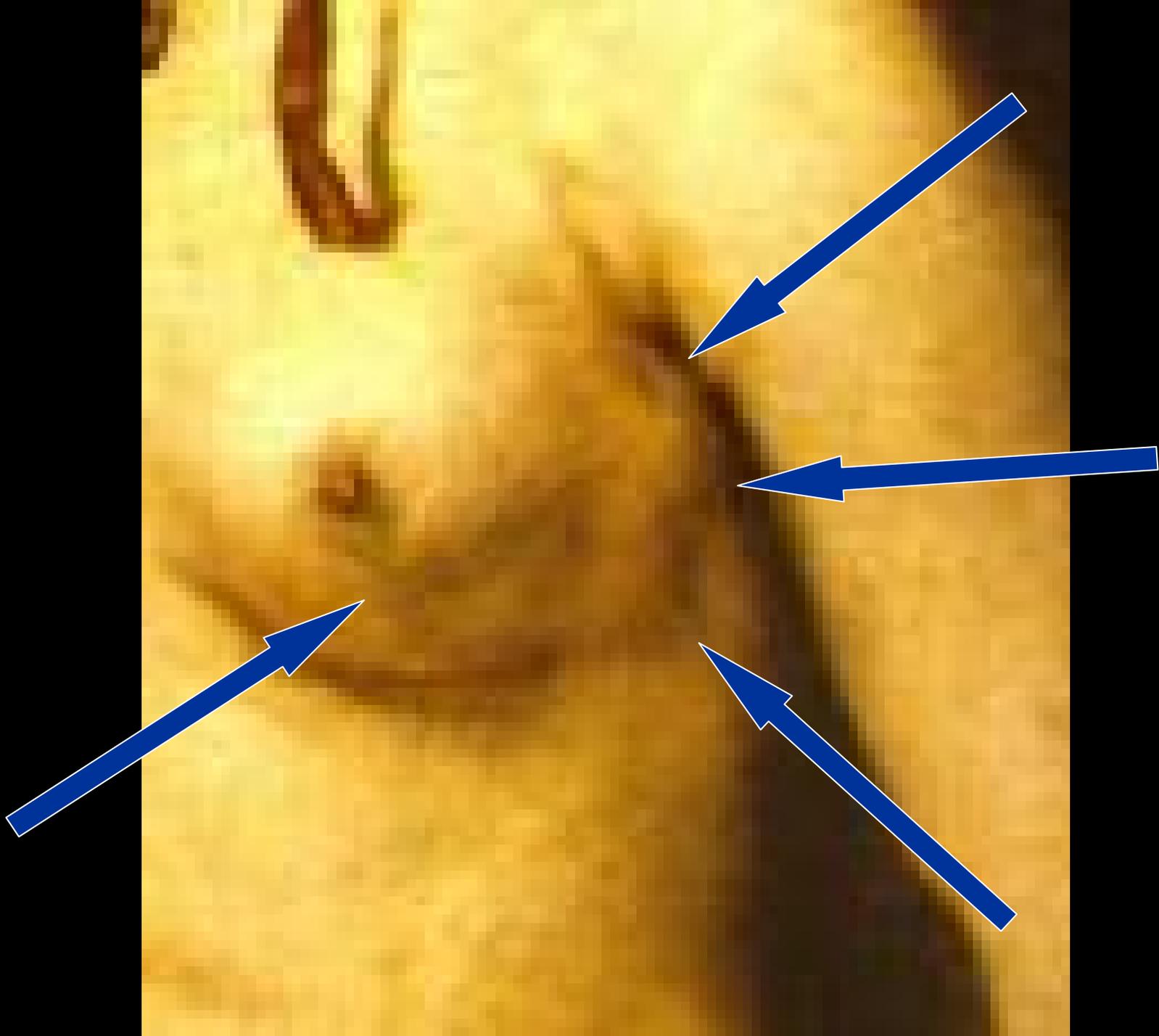




Bathsheba at her Bath

Rembrandt, 1654

- This painting inadvertently portrays physical exam findings of breast cancer.
- The model, Hendrickje Stoffels was Rembrandt's mistress. She died in a plague in 1663.
- While the face in the portrait is surely hers, we now know from advanced x-ray analysis that the face was changed in the painting process.
- The unfortunate woman who posed for the body in the portrait appears to have advanced breast cancer with axillary adenopathy.

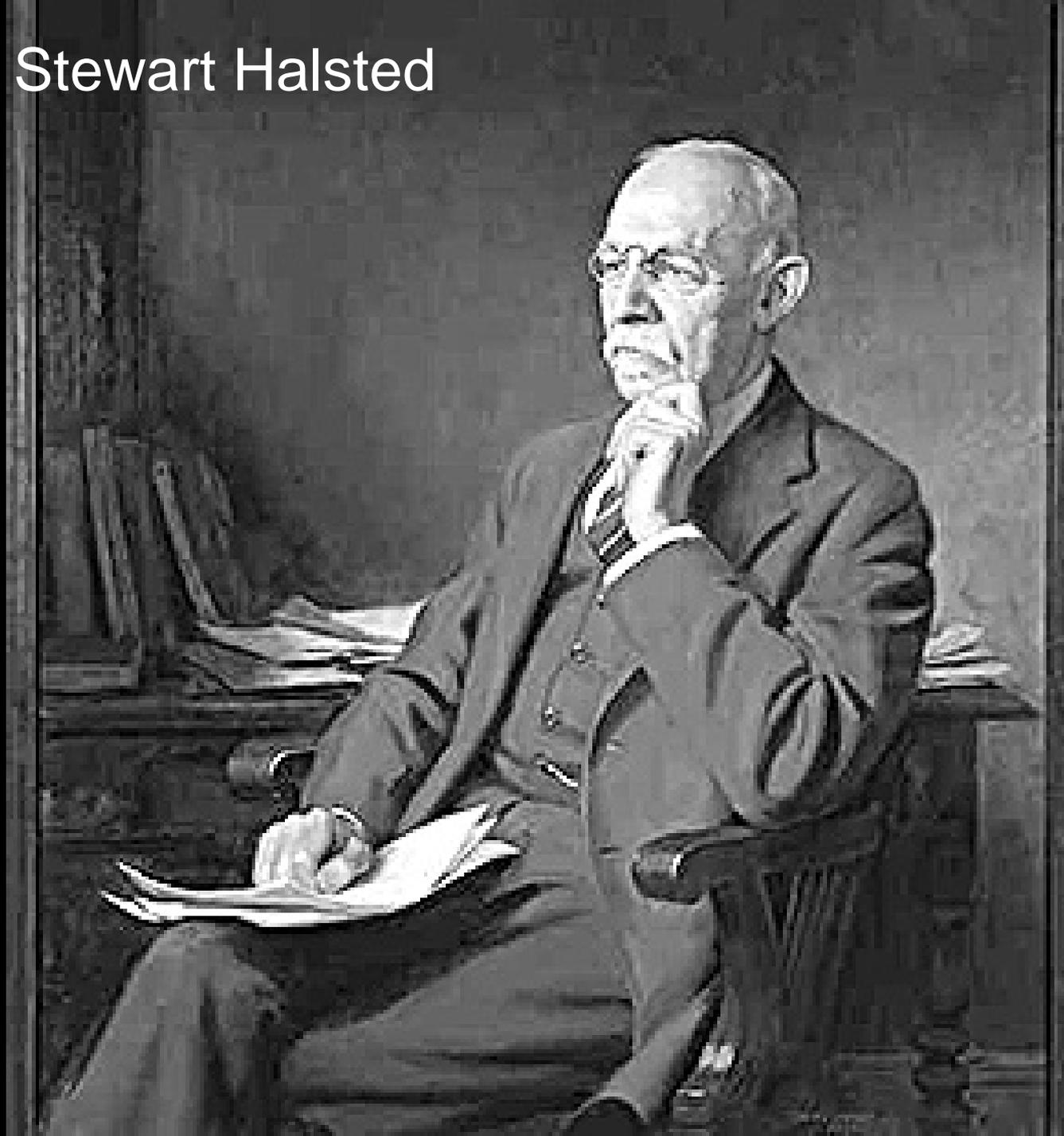




Nabby Adams, 1765-1813

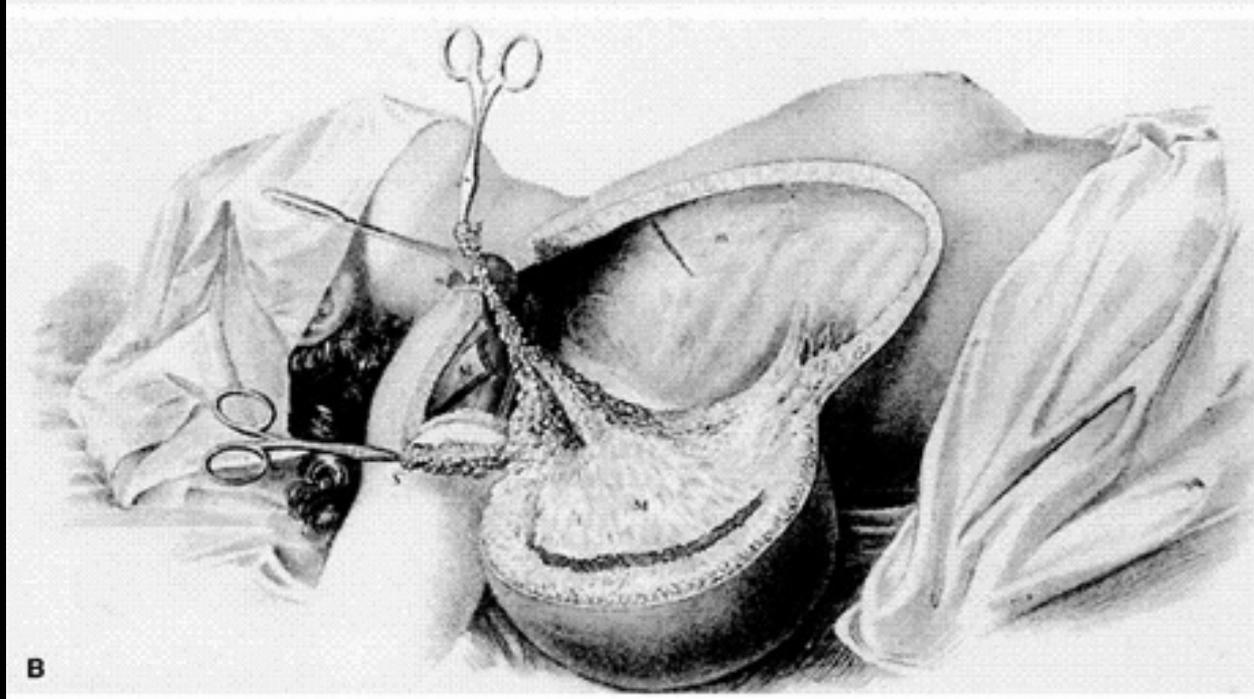
- The daughter of one president and the sister of another had a mastectomy and cauterization at her parents' home in 1811. But local recurrence and metastatic disease took her life two years later.
- While surgery techniques were improving, it seemed that outcomes were not.
- However, new techniques and new ideas in the later part of the 19th century would change the prospects of breast cancer patients.

 William Stewart Halsted

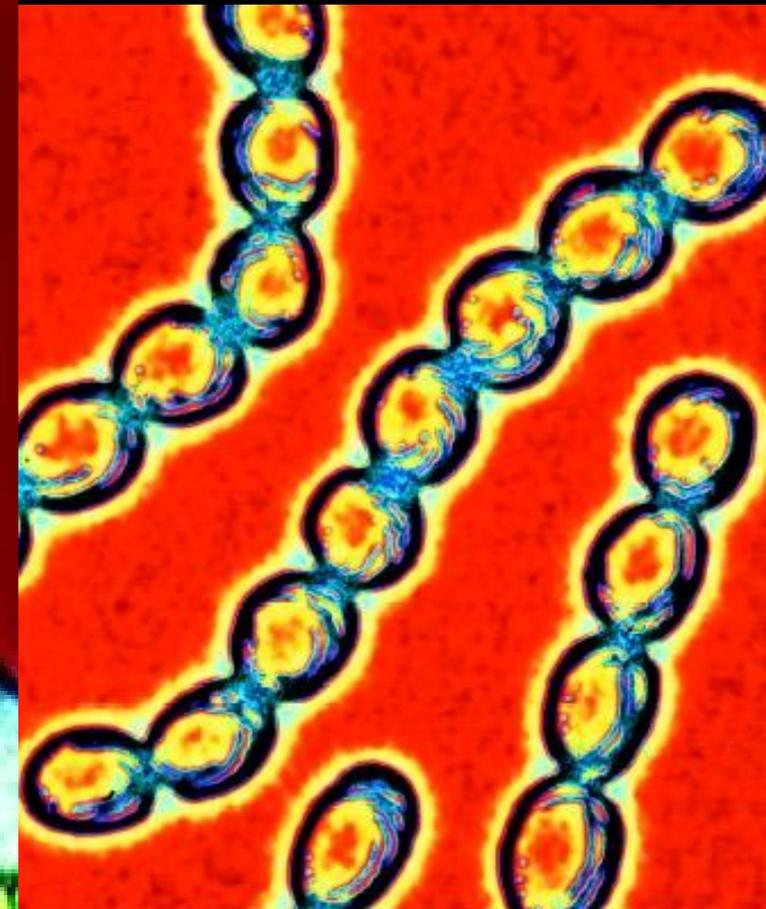
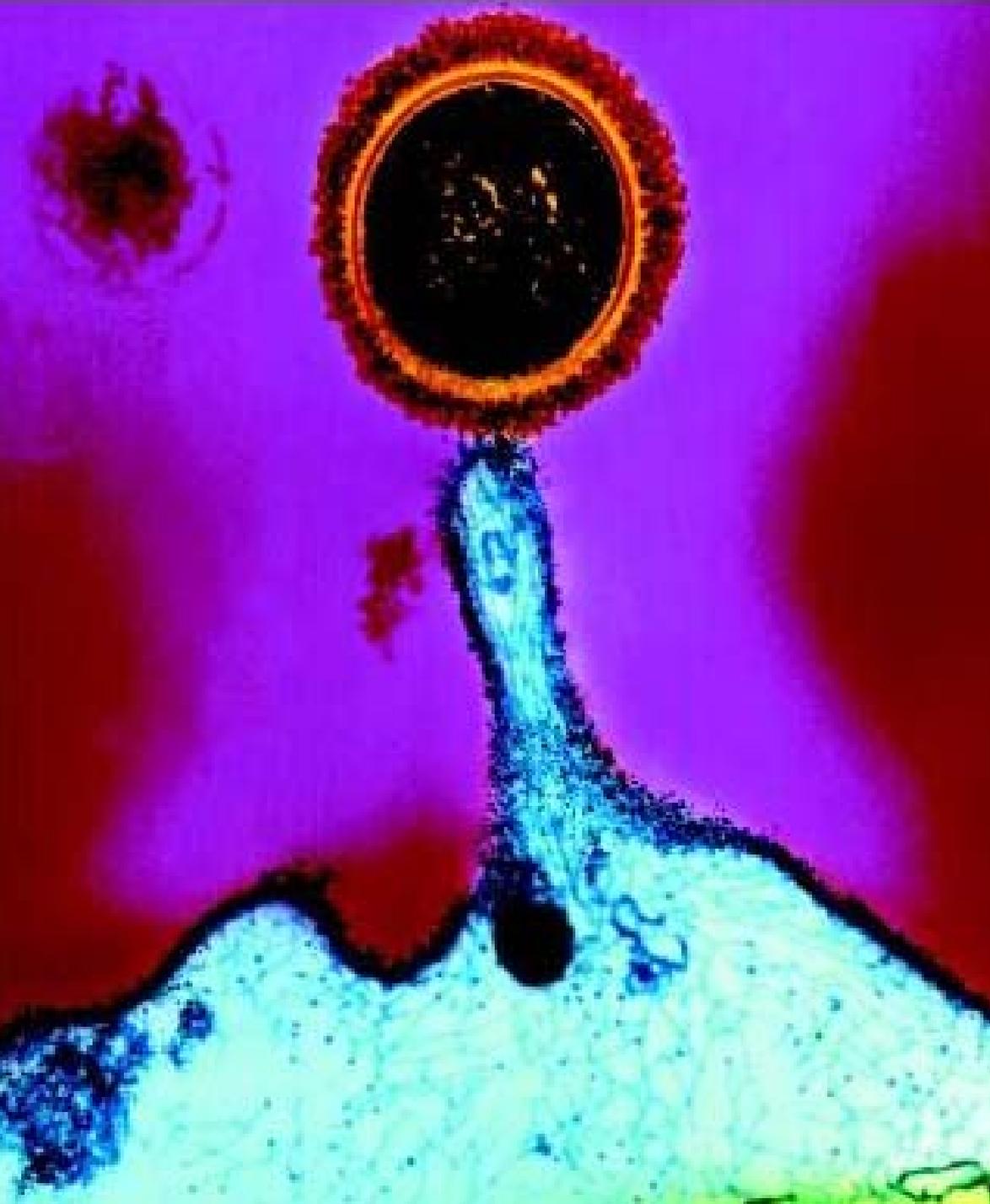


William Stewart Halsted and the Halsted Radical Mastectomy

- William Halsted was a brilliant American surgeon, who revolutionized breast cancer treatment in the late 1800's
- Mastectomies had been performed since the early 1600's and gradually came to include axillary dissections.
- Following the leads of European surgeons, he gradually developed en-bloc techniques that removed the breast, axillary nodes, pectoral muscles and skin, without cutting into the local tumor.
- His technique lowered local recurrences and metastatic disease.



Streptococcus Pyogenes



William Stewart Halsted and the Halsted Radical Mastectomy

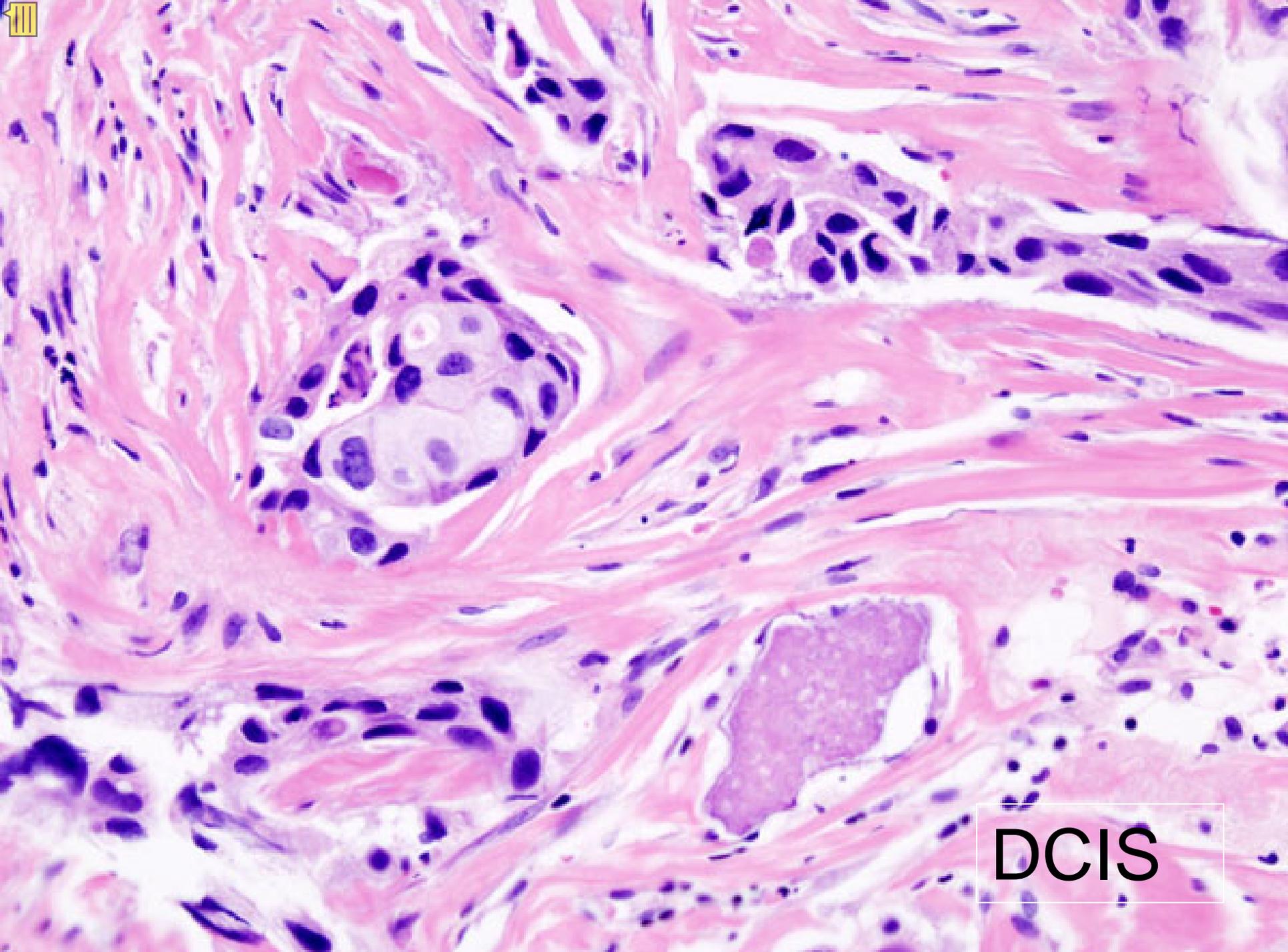
- Halsted's successes were founded on more than just aggressive surgical techniques.
- Aseptic surgery was then becoming the norm. Surgeons washed their hands between patients, eventually wore gloves and operated in clean hospitals, not homes.
- The infectious complications of such large surgeries, (especially strep / erysipelas) decreased markedly.

Anesthesia

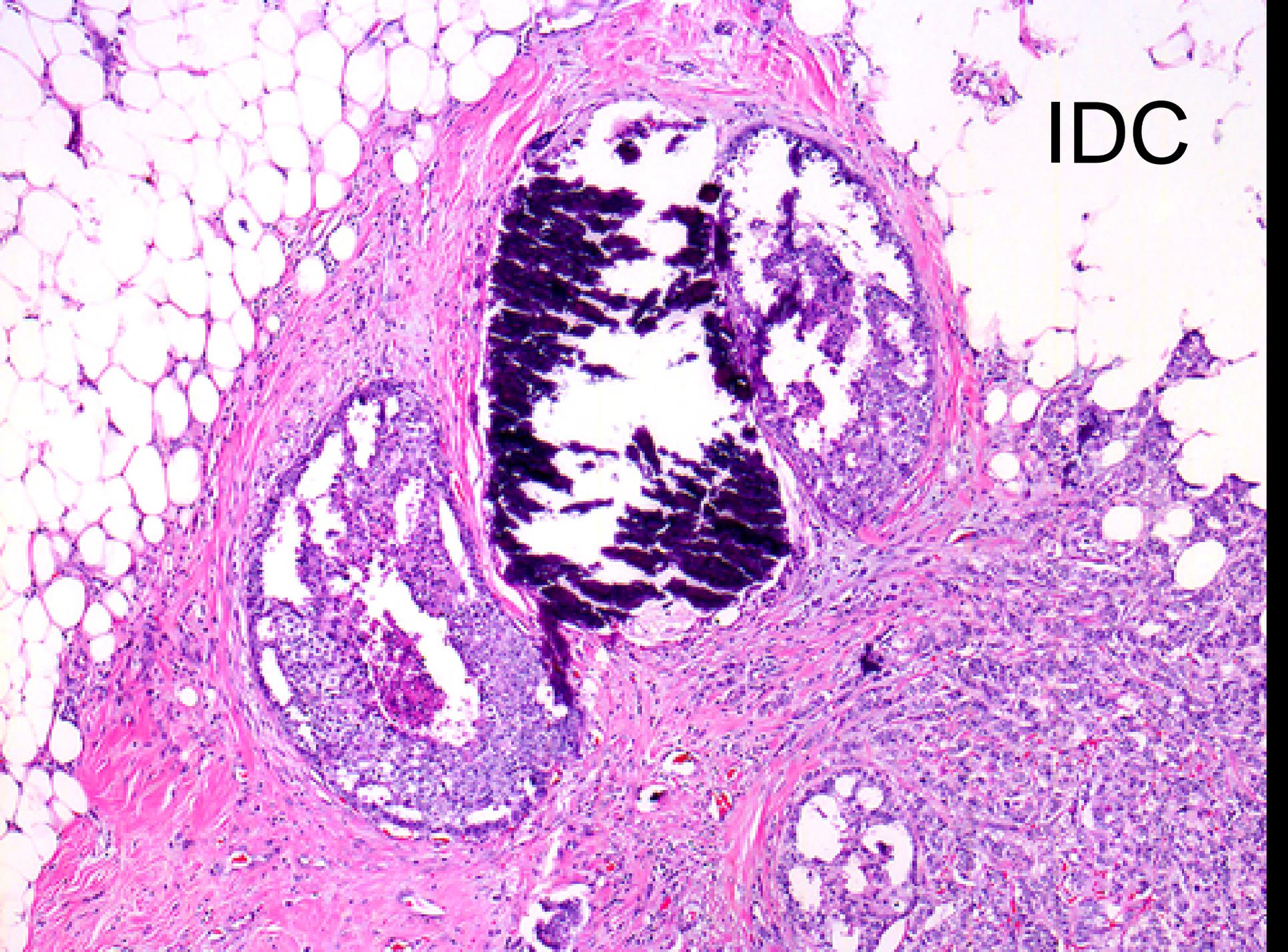


William Stewart Halsted and the Halsted Radical Mastectomy

- Halsted also had the advantage of new, general anesthesia, pioneered in Boston, in 1846.
- Surgery was faster with an unconscious patient, and safer, as blood loss was minimized.
- Fewer people could be involved in the procedure and there was less chance of staff and patients causing wound contamination.



DCIS



IDC

William Stewart Halsted and the Halsted Radical Mastectomy

- The many types of breast cancer, and their benign mimics were first characterized in the late 1800's.
- Finally, Halsted had the advantage of knowing what the pathology of the excised lesion was, through the new medical science of cellular pathology.
- An initial diagnostic biopsy could spare the patient the trauma and still significant danger of a major surgery.

William Stewart Halsted and the Halsted Radical Mastectomy

- Halsted's synthesis of techniques and new discoveries made a real difference.
- In 1898, his patients had a real chance of surviving what had been an almost universally fatal disease.
- Halsted's patient had a 57% chance of being alive after 3 years, and a 51% chance of being disease free.

William Stewart Halsted and the Halsted Radical Mastectomy

- Halsted noticed that patients with smaller tumors, sparing the nodes, had better outcomes.
- His early efforts at staging, i.e. providing a realistic prognosis, provoked a real change in patient behavior.
- Women came in for treatment sooner, rather than hiding what had been an almost certainly fatal, frightening, and often shame inducing condition.

William Stewart Halsted and the Halsted Radical Mastectomy

- The Halsted radical mastectomy became the standard of surgical care for the next 70 years.
- Over time, even more aggressive “super radical mastectomies” came to be performed.
- The advent of better anesthesia, frozen sections, antibiotics, and blood transfusions allowed longer, more extensive and terribly deforming surgeries, for better control of then poorly understood metastatic disease.
- These included removal of most of the chest structures, radical node dissections, amputations, oophorectomies, adrenalectomies and even pituitary surgeries (early hormonal theories).

Adjuvant Therapies

- Survival could not be much improved with aggressive surgical therapy alone.
- Therapies that improved quality of life, if not long term survival were quickly added to the therapeutic regimen of breast cancer treatment.
- The first, adjuvant radiotherapy began as a treatment within one year of the discovery of X-rays!

Wilhelm Roentgen (1845-1923)
discovered X-rays in 1895





Emile Grubbe, 1875-1960



Emile Grubbe

- Just 2 months after the discovery of X-rays, medical student Grubbe noticed that his hands peeled after exposure to new fangled X-rays.
- He talked his professor into letting him irradiate the tumor of a patient who had failed all other therapies, and she responded (at least temporarily).
- Grubbe can be considered the founder of radiation oncology.

Radiation Therapy

- In the early part of the last century, radiation therapy was quickly adopted as an adjuvant therapy after mastectomy.
- In the 60's, linear accelerators allowed high energy, megavoltage treatments which caused less skin reaction and later, intensity modulated radiation therapy allowed even more precise targeting.
- This steady progress has allowed much of the breast conservation therapy of today.



Local or Systemic Disease?

- While mastectomies controlled local disease, metastatic disease still cast a dark cloud over breast cancer patients.
- Even with the most extensive and deforming surgeries, about half of those treated died within 10 years, of distant metastases.
- Hormone control through oophorectomy, adrenalectomy and pituitary resection slowed disease but didn't stop it.
- However, a byproduct of war lead to new weapons against breast disease.



Chemotherapies

- American scientists observed the cell stopping aftermath in the victims of mustard gas attacks in late WWII. Derivatives of these chemical weapons were the basis of the first chemotherapeutic agents.
- Over time, multiple other drugs have been discovered by chance or been developed through targeted research. Multiple mechanisms to control or kill cancer cells are employed.
- All are used to control both local disease and distant spread.

Chemotherapies

- While chemotherapeutic agents exploit various strategies to control cancer cells, they have one characteristic in common.
- They are all poisons.
- The great benefits of chemotherapeutic agents were made possible by the parallel development of supportive care strategies.
- Central lines
- Anti-nausea drugs
- TPN
- Transfusions/Platelets

Strong Doctors, Weak Patients

- Although the chance of surviving breast cancer improved in the late 19th and early 20th centuries, the status of women remained subservient.
- At the same time as these treatments were evolving, so were ideas about gender and social equality.
- Some of the most aggressive and deforming techniques were first performed on poor women.
- Sexism is less a factor today. Poverty and race are still issues in breast cancer care.



Early Detection Strategies

- The earliest therapies for breast tumors were aimed at advanced disease. Care givers only became aware of the condition long after the patient knew of the existence of the disease. In fact most early victims presented when the symptoms of the disease became unbearable.
- Some of the accounts of early sufferers of breast cancer describe symptoms likely caused by distant metastases.
- Even today, advanced disease is a challenge to treat.



Physical Examination

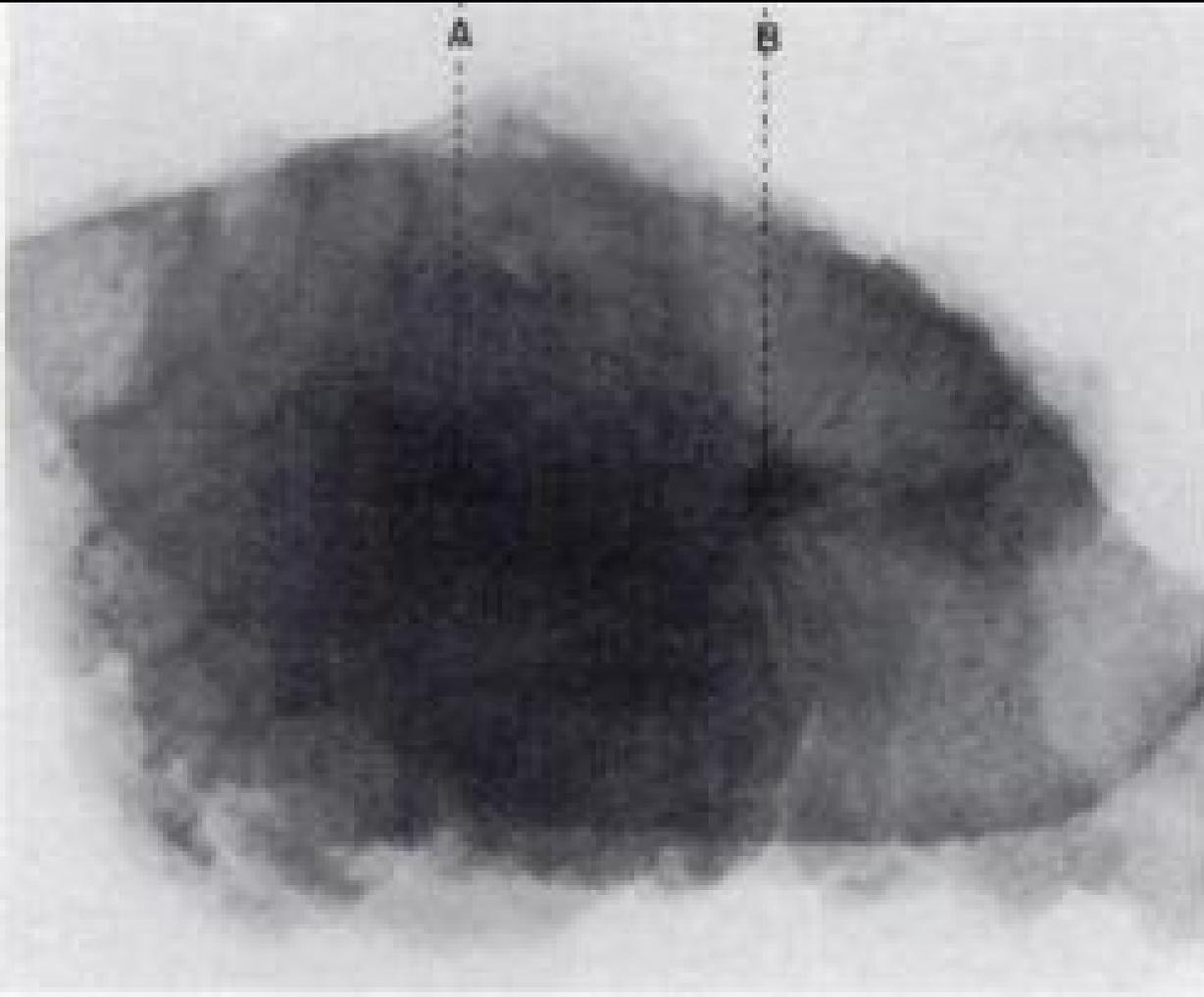
- Physical examination was the first method of breast cancer discovery.
- Self exams remain a mainstay of breast cancer detection, but are highly variable in accuracy and consistency. And small lesions are difficult to detect.
- Cultural and personal resistance to physical touch remains an obstacle to effective self examination.
- Exams by health care providers are often just as limited.
- The power of denial must be considered.

Early Detection Strategies

- While surgeons long recognized that the limited treatment success they had was in patients with small lesions, Halsted was the first to describe prognosis based on the extent of disease. In his patients, survival at 3 years was:
 - 85% if node negative
 - 31% if node positive
 - 10% if supraclavicular node positive
- If prognosis was to be improved, breast tumors had to be found and treated before nodal spread.



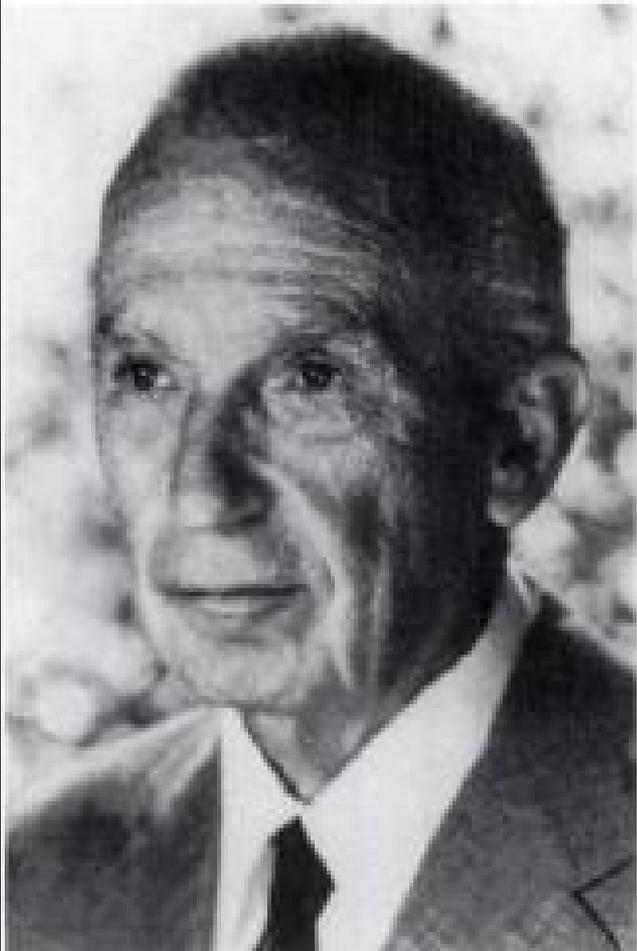
Albert Salomen X-rayed mastectomy specimens as early as 1913, to help localize tumors for pathology analysis



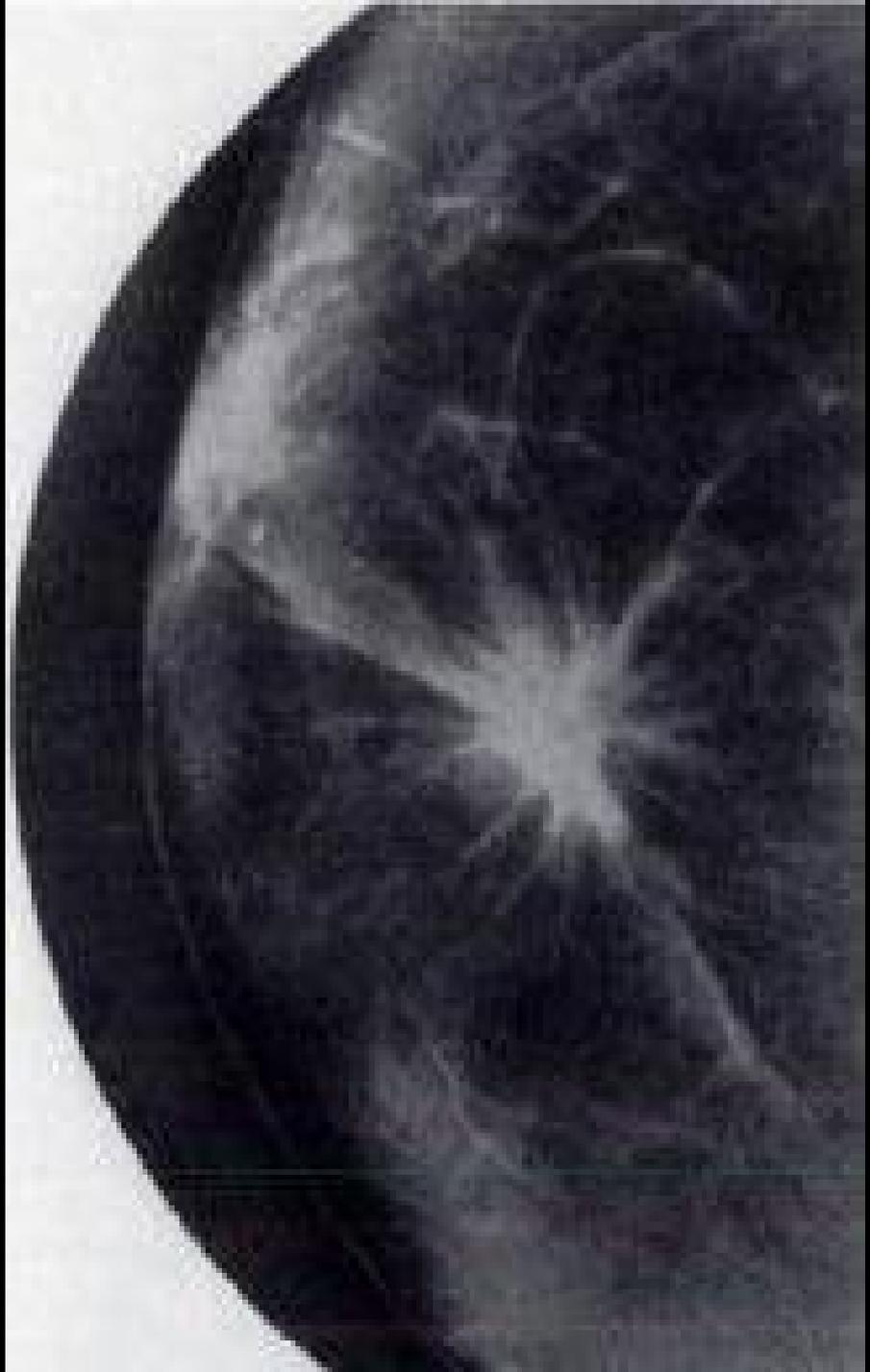
But it took another 30 years to transfer the technology to living patients with early mammography.



In the late 20's, surgeons such as Warren L. Stafford proposed the use of mammography as a localizing tool prior to major breast surgery.



Raul Lebourgne developed early mammography in Montevideo, Uruguay in the 40's and 50's





Breast Cancer is Common

- Physicians and scientists for over a century struggled to find new ways to treat breast cancer.
- Everyone acknowledged that treatments were most effective when addressing small and presumably early tumors.
- But how could we detect breast cancer before it became palpable, locally invasive and possibly wide spread?
- A screening tool was needed.



In the 50's and 60's, Robert L. Egan, a radiologist, proved that mammography could be used to detect breast lesions in asymptomatic women. Finally, breast disease too small to detect with palpation could be addressed.





The age of screening began in the early 1960's.

The first randomized trial of screening, organized by Philip Strax, showed that over 5 years, mortality from breast cancer was reduced by nearly 1/3, and that the benefit to those screened remained significant for 18 years.



In 1985, Laszlo Tabar published a randomized trial of 134867 women, aged 40-74.

The trial was started in 1977, and by 1984 showed a 31 % decrease in the mortality due to breast cancer and a 25% decrease in stage II or greater cancers.



More and Better?

- As confidence in screening as an early detection tool increased, so did other technologies.
- Minimally invasive techniques to sample lesions and confirm pathology were developed.
- As more early breast cancers were discovered, more mastectomies were performed.
- Lives were being saved, but the emotional and physical cost to the patients was profound.

Breast Conservation Therapy



Breast Conservation Therapy

- In 1973 and 1976, major randomized trials compared outcomes of lumpectomy and quadrantectomy with traditional mastectomy.
- No significant difference in survival between the groups was shown in earlier stage tumors, especially when conservation therapies were combined with XRT.
- Use of limited axillary dissection techniques and advances in implant and flap reconstruction technologies reduced the cosmetic devastation of breast cancer therapies.

Where We Are Now?

- Breast cancer is no longer a death sentence.
- Stage 0 and I cancers have a 100% 5 year survival rate.
- Mammography, sonography and now MRI have increased our chances of finding early stage disease.
- Breast surgery is less debilitating and cosmetic results are good if not great.
- Medical and radiation therapies are more tolerable.

Where We Are Now?

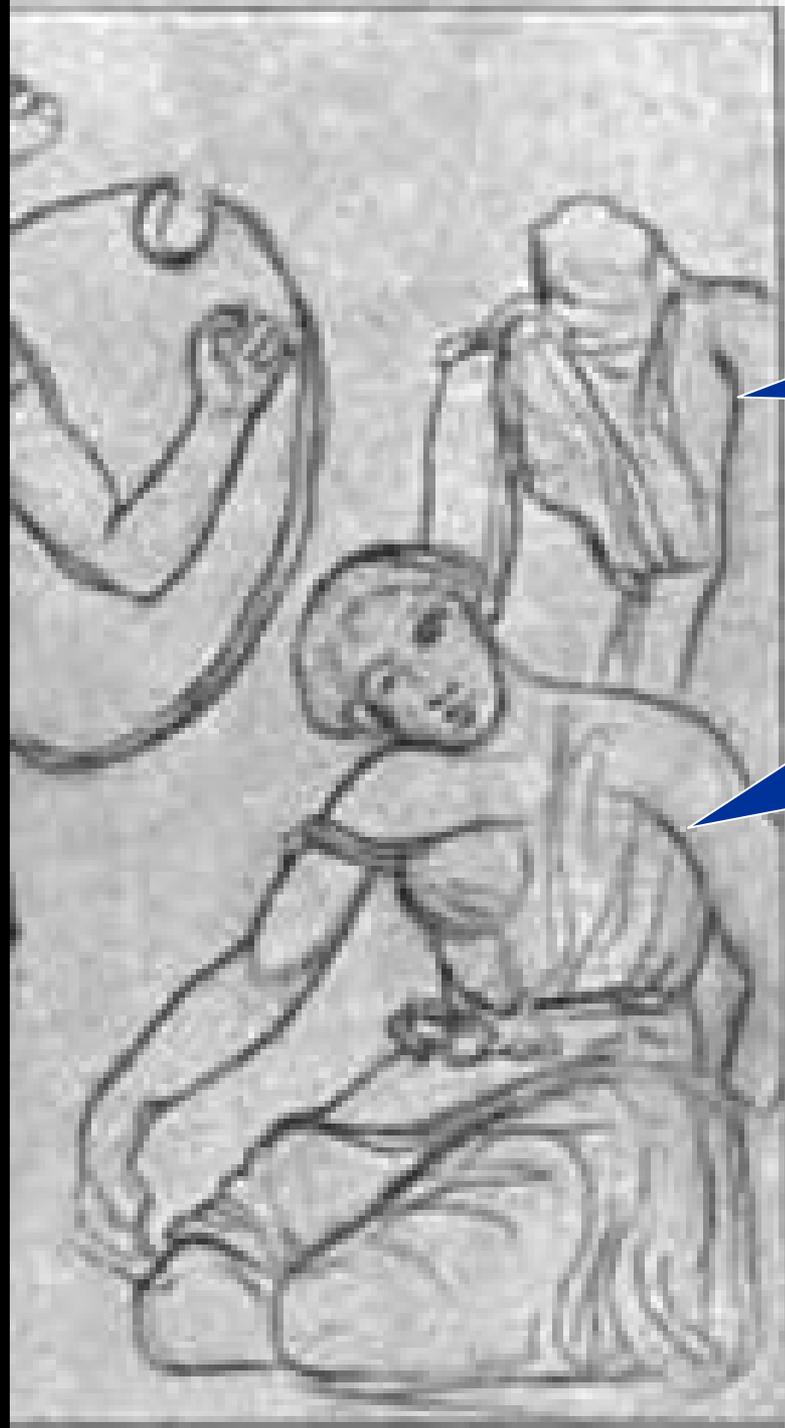
- In 2006, 191,410 breast cancer cases diagnosed.
- In 2006, 40,820 patients died of breast cancer.
- Stage IIA 92% 5 year survival
- Stage IIB 81% 5 year survival
- Stage IIIA 67% 5 year survival
- Stage IIIB 54% 5 year survival
- Stage IV 20% 5 year survival
- Overall survival is 88% at 5 years, 63% at 20 years

Tracing from the Phigalaeian Frieze



The Amazons

- In ancient Greek legends, the Amazons were a tribe of warrior women.
- In a tough fight, you always wanted the Amazons on your side.
- The Amazon archers were so fierce that they would cut off their right breast so as not to interfere with the draw of their bows.



Attitudes have Changed

- The breast cancer community has become a force in the scientific, political and cultural world.
- This change in attitude has been driven by individuals touched by breast cancer. The scientific and medical community has followed.
- Support for those with breast cancer, both financial and emotional, is greater than for any other condition.
- These support structures have become a model for other causes.

MASTECTOMY

1 IN 8

**YOUR CHANCES OF
GETTING BREAST CANCER**

Breast Cancer
Striking Younger
Than Ever

**YOUR BREASTS:
NOT JUST
FOR LOOKS**

**BREAST
CANCER
EPIDEMIC:
What's Behind It?**

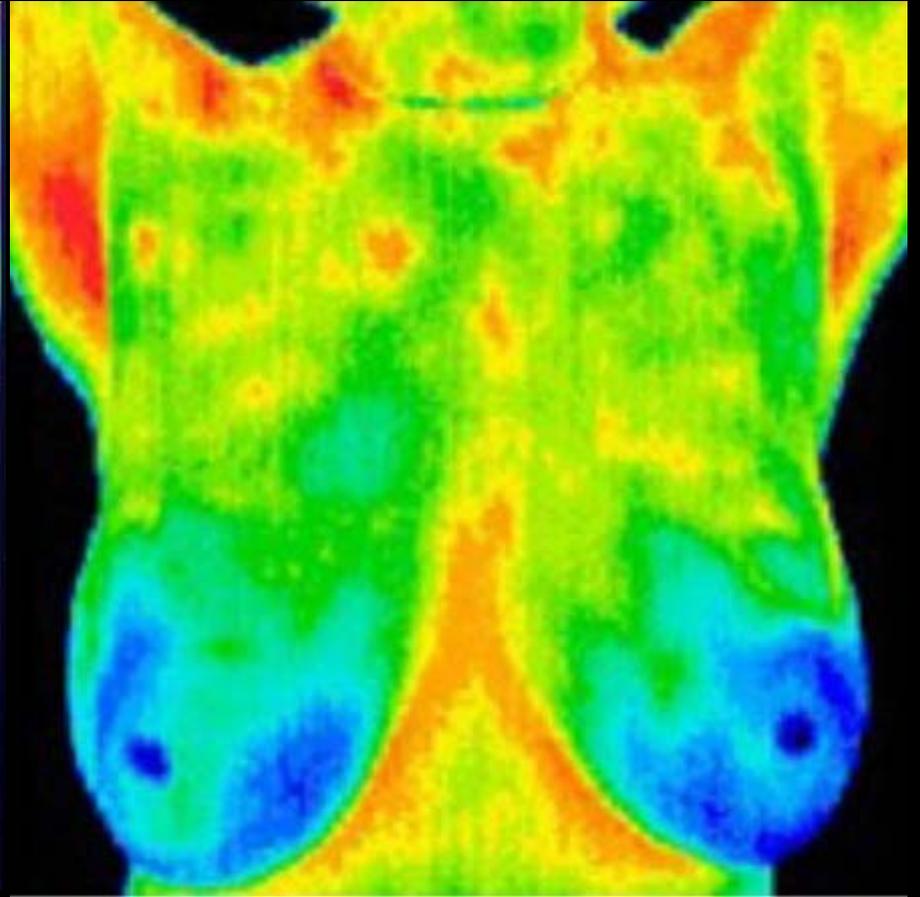
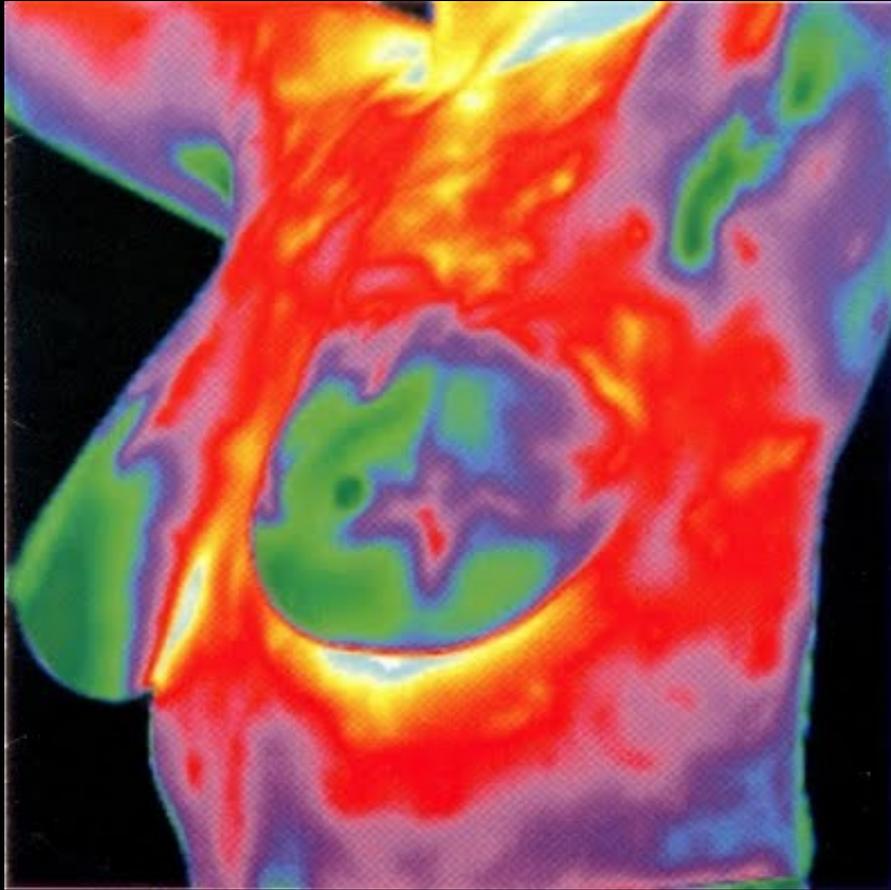
**PROFILE
OF A
KILLER**

**BREAST
CANCER QUIZ:
Are You At Risk?**





Where are we going?



Where are we going?

- Novel medical therapies including additional antibody medications and vaccines are being researched.
- New imaging techniques including laser, sono, infrared and MRI are being examined.
- New surgical techniques are being developed for better control and cosmesis.

Where should we be going?

Cancer Type	2007 Spending (in millions)	2008 Spending (in millions)	2009 Spending (in millions)	2009 ARRA Spending (in millions)
Lung	\$226.9	\$247.6	\$246.9	\$48.0
Prostate	296.1	285.4	293.9	47.0
Breast	572.4	572.6	599.5	85.5
Colorectal	258.4	273.7	264.2	44.5
Bladder	19.8	24.1	25.9	2.8
Melanoma	97.7	110.8	103.7	17.6
Non-Hodgkin Lymphoma	113.0	122.6	130.9	14.0
Kidney	35.2	43.4	45.2	7.2
Leukemia	205.5	216.4	220.6	33.9
Pancreatic	73.3	87.3	89.7	10.7

Where should we be going?

Annals of Internal Medicine



AHRQ
Agency for Healthcare Research and Quality
Advancing Excellence in Health Care • www.ahrq.gov



SCREENING FOR BREAST CANCER USING FILM MAMMOGRAPHY CLINICAL SUMMARY OF U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATION

Population	Women Aged 40–49 Years	Women Aged 50–74 Years	Women Aged ≥75 Years
Recommendation	Do not screen routinely. Individualize decision to begin biennial screening according to the patient's context and values.	Screen every 2 years.	No recommendation.
	Grade: C	Grade: B	Grade: I (insufficient evidence)

Risk Assessment	This recommendation applies to women aged ≥40 years who are not at increased risk by virtue of a known genetic mutation or history of chest radiation. Increasing age is the most important risk factor for most women.	
Screening Tests	Standardization of film mammography has led to improved quality. Refer patients to facilities certified under the Mammography Quality Standards Act (MQSA), listed at www.fda.gov/cdrh/mammography/certified.html .	
Timing of Screening	Evidence indicates that biennial screening is optimal. A biennial schedule preserves most of the benefit of annual screening and cuts the harms nearly in half. A longer interval may reduce the benefit.	
Balance of Harms and Benefits	<p>There is convincing evidence that screening with film mammography reduces breast cancer mortality, with a greater absolute reduction for women aged 50 to 74 years than for younger women.</p> <p>Harms of screening include psychological harms, additional medical visits, imaging, and biopsies in women without cancer, inconvenience due to false-positive screening results, harms of unnecessary treatment, and radiation exposure. Harms seem moderate for each age group.</p> <p>False-positive results are a greater concern for younger women; treatment of cancer that would not become clinically apparent during a woman's life (overdiagnosis) is an increasing problem as women age.</p>	
Rationale for No Recommendation (I Statement)	Among women 75 years or older, evidence of benefit is lacking.	
Relevant USPSTF Recommendations	USPSTF recommendations on screening for genetic susceptibility for breast cancer and chemoprevention of breast cancer are available at www.preventiveservices.ahrq.gov .	

Where should we be going?

- Probably everybody here is involved with breast cancer care. We're a biased audience.
- Controversies about evaluations, treatments and cost have always circulated in the breast cancer community, and that won't change.
- Commitment to the care and comfort of those with breast cancer is without controversy.

Thank you

I welcome your comments

