

A tumour through time



200 MILLION YEARS AGO

Milk-producing skin glands evolve during the Late Triassic period in a group of egg-laying proto-dinosaurs called cynodonts. Instead of sweat or scent, these early mammarys produce a simple milk to supplement the diet of hatchlings. Over time, these glands grouped together under nipples and began responding to sex hormones such as oestrogen.

~ 2500 BC

A medical text from ancient Egypt contains the first known reference to breast cancer. It describes 48 surgical problems, including “bulging tumours on the breast”. The unknown author describes “swellings on [the] breast, large, spreading and hard: touching them is like touching a ball of bandages”. It would be some time before surgeons could offer anything beyond a diagnosis. The author’s take on treatment: “there is nothing”.

~ 1000

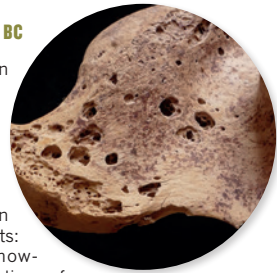
Doctors begin to embrace the possibilities — and limitations — of surgery for breast cancer. In eleventh-century Moorish Spain, the noted surgeon Abu al-Qasim al-Zahrawi writes that breast cancer could be cured when “complete removal [of the tumour] is possible, and especially when in the early stage and small. But when it is of long standing and large, you should leave it alone. I myself have never been able to cure such, nor have I seen anyone else succeed before me”.

1896

Emil Grubbe, an electronics enthusiast and medical student at the Hahnemann Medical College in Chicago, Illinois, assembles one of the earliest X-ray devices. A colleague remarks on the radiation burns on Grubbe’s hands and suggests that X-rays might be used against unhealthy tissue. The first recorded instance of radiation oncology occurs later that year when Grubbe’s machine is used to irradiate a breast carcinoma in a woman named Rose Lee. She reportedly received several hour-long treatments and died shortly thereafter.

BOX OF BONES -2200 BC

During a 2015 excavation of the Egyptian necropolis Qubbet el-Hawa near Aswan, a team led by Egyptologists and anthropologists from the University of Jaén in Spain discovered a coffin with remarkable contents: bones of a woman, showing the tell-tale deformations of metastatic breast cancer (pictured). She died some 4,200 years ago, making her the first known victim of the disease.



DEEP CUT 1590

French surgeon Barthélémy Cabrol suggests that advanced breast cancer could be cured by removing the underlying chest muscles along with the breast. Others will attempt variations on this idea for centuries, with often dismal results.



KNIFE SKILLS -1894

In the United States, William Halsted and Willy Meyer independently develop radical mastectomy to treat advanced breast cancer. The operation removes the entire breast, the pectoralis major and minor muscles directly underneath, and the axillary lymph nodes from the armpit. The surgery offers people with advanced breast cancer the first serious hope of a cure.

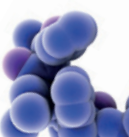
X-RAY VISION 1956

Robert Egan starts to develop effective mammography, an X-ray examination that can detect breast tumours that are too small to be felt. By the 1970s, mammography has become a popular screening test for women.

DOUBLE STANDARD 1975

The National Surgical Adjuvant Breast and Bowel Project shows that surgery combined with chemotherapy works better against breast cancer than surgery alone. Combined treatments become the standard of care.

CLOCKWISE FROM TOP LEFT: 914 COLLECTION/ALAMY STOCK PHOTO; ARCHIVO PROYECTO QUBBET EL-HAWA; WELLCOME LIBRARY, LONDON; NATIONAL LIBRARY OF MEDICINE/SPL



Breast cancer, one of the most common and deadly malignancies, has undoubtedly plagued humans since the dawn of our species. The history of the fight against the disease is one of lurching progress against a backdrop of misery. But recent decades have seen greatly improved treatments and increased survival. By Will Tauxe.

DRUG STOP 1977

The oestrogen-blocking drug tamoxifen (**pictured**) is approved in the United States as a treatment for advanced metastatic breast cancer. Today, tamoxifen is one of many hormone-blocking drugs used worldwide to treat — and in some cases prevent — certain types of breast cancer.

BUSTED FLUSH 1995

The US Nurses' Health Study reveals that hormone replacement therapy (HRT) increases the risk of developing breast cancer. At the time, HRT was popular both to treat and prevent menopausal symptoms among post-menopausal women. Today, HRT is no longer routinely recommended for long-term use in post-menopausal women.

LESS IS MORE 2002

Two large studies show that people with breast cancer live just as long after small lumpectomy surgery combined with radiation as they do after radical mastectomy. Further studies show that only a narrow 2-millimetre 'clean margin' of healthy tissue needs to be removed along with the cancer in a lumpectomy.

TIMES CHANGE 2009

The US Preventive Services Task Force recommends that women should be offered a mammogram first at age 50, and then every other year after — a departure from previous advice to start annual screening at age 40. The change sparks debate about the balance between the harm of unnecessary treatment and the risk of undiagnosed cancers.

1990

Mary-Claire King and colleagues (J. M. Hall *et al. Science* **250**, 1684–1689; 1990) use samples of DNA from families with a history of breast cancer to establish a link between mutations in a tumour-suppressing gene she names *BRCA1* and an elevated risk of breast and ovarian cancer. The discovery changed thinking about genetic influences on cancer. Further research showed that mutations in another gene, *BRCA2*, could also increase cancer risk. Today, some women who test positive for these mutations — including actress Angelina Jolie (**pictured**) — choose to have their breasts removed to reduce their cancer risk.



2000

Charles Perou and colleagues (C. M. Perou *et al. Nature* **406**, 747–752; 2000) show that breast cancers can be grouped into clinical subtypes on the basis of mutations in their DNA. Analysis of tumour-cell DNA enables doctors to choose treatments that are more likely to be effective. The subtype of 'triple-receptor-negative' breast cancer is particularly difficult to treat because these cancers do not respond to signals from any of the breast growth hormones: oestrogen, progesterone and human epidermal growth factor 2.

2013

In the case *Association for Molecular Pathology v. Myriad Genetics*, the US Supreme Court overturns molecular-diagnostics company Myriad's patents on the genetic codes of *BRCA1* and *BRCA2*. The court's decision states that "a naturally occurring DNA segment is a product of nature and not patent eligible", although tests to find specific harmful mutations are still considered patentable.

2015

In 2015, breast-cancer survival rates are at their highest ever. More than 6 million people worldwide are still alive 5 years after being diagnosed with breast cancer, although survival rates continue to lag in areas without reliable access to advanced medicine. Breast cancers are now treated with tailored combinations of surgery, chemotherapy and radiation, and continued research is making treatments more precise and minimizing side effects.

TOP: LEON NEAL/AFP/GETTY IMAGES; BOTTOM: LAGUNA DESIGN/SPL

