

A Brief History of Breast Cancer

Part I: Surgical domination reinvented

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تاريخ موجز لسرطان الثدي
الجزء الأول: إعادة اختراع هيمنة الجراحة

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THE FEMALE BREAST HAS ALWAYS BEEN A symbol of beauty, fertility and femininity. In disease, however, it has challenged physicians since antiquity. Surgery, which ruled the roost for cancer therapy, inevitably caused disfigurement when the knife was applied to the breast. The history of breast cancer is a complex maze of attempts to understand the wily nature of this hormone-responsive cancer and the will of physicians to conquer it by physical removal (surgery), cell destruction (chemo-radiotherapy) or targeted therapy to cell receptors (biomodulation). It is also a saga of intense exploration to find the tools to enable early diagnosis. The story of the domination of surgery over two millennia and its evolution from fatalistic choices to minimal damage is told in the succeeding paragraphs. The pathobiological basis of breast cancer that changed chirurgical practice from crudity to finesse is woven through the narrative.

Beliefs and Practices Through Antiquity

It is not surprising that written records and illustrations of breast cancer date back to antiquity since the location of the organ permitted easy identification. The Edwin Smith Surgical Papyrus, dating back to 3,000–2,500 B.C., and possibly attributable to Imhotep (the Egyptian physician-architect), provides authentic accounts of breast cancer. A case was deemed incurable if the disease was “cool to touch, bulging and spread all over the breast”.¹ In ancient Greece, a divinity was exhorted to offer relief from breast maladies, as evidenced by votive offerings in the shape of breasts in Greek temples that housed Asclepius, the god of medicine.² Carcinoma (*karkinoma*), scirrhus (hard, Greek *skirros*) and cacoethes (malignant disease, Greek *kakoethes*) in the medical lexicon owe their

origins to Hellenistic writings. Hippocrates’ theory in c. 400 B.C. of the imbalance of humours (blood, phlegm, and yellow and black bile) as a cause of disease, and his classic descriptions of the progressive stages of breast cancer, represent early hypotheses on the cause of cancer.³

Leonides of Alexandria, in 1st century A.D., preserving the Greek traditions, boldly and skillfully detailed his approach of incision and cautery.⁴ His stipulation of leaving a wide margin of excision and only removing tumours of limited extent, foreshadows the oncological principles of contemporary surgical practice.⁵ Galen, attributing breast cancer in A.D. 200 to the accumulation of black bile in the blood, concluded that it was a systemic disease.⁶ These ancient physicians postulated that the cessation of menstruation was somehow linked to cancer; in fact it probably had to do with the association of cancer with old age. In line with this theory, Galen allowed surgical wounds to bleed freely to get rid of the black bile and frowned on the use of ligatures. The word ‘crab’ for cancer was coined by him to illustrate the dilated veins radiating from the tumour.⁵

Surgical Stagnation in the Middle Ages

Between 476 and 1,500 A.D. medical progress was inextricably intertwined with the emerging religious philosophies. Early Christian beliefs favoured faith healing and miracles over surgery, which was perceived as barbaric. Islamic emergence revived Greek medicine and, through meticulous translations, saved medical knowledge for posterity. Avicenna (Ibn Sina, Persia) and Albucasis (Abu Al-Qasim Al-Zahrawi, Spain) in the 10th century and Maimonides (Spain) in the 12th century were Arab physicians of renown, forming a

trio of exemplars who spread medical excellence to the boundaries of the expanding Islamic conquests;² Albucasis was a strong advocate of the use of cautery in surgery.⁷ The use of caustic pastes to annihilate the tumour and render it operable, is reminiscent of the same logic for using chemotherapy for large breast cancers today. Unique instruments to aid in the rapid removal of breast tumours were introduced into the surgical armamentarium by Albucasis, Henri de Mondeville ('father' of French surgery, 13th century) and Guy de Chauliac (France, 14th century).

Renaissance: A celebration of arts and the emergence of surgery

The 16th to 18th centuries not only bred artistic creativity but proved to be the golden age for the emergence of surgery. The craft of surgery was unshackled from its previous conjoint status with the barber's trade and grew on the shoulders of a strong anatomical exploration of the human body by Andreas Vesalius in 16th century Belgium. In 18th century England and France, respectively, Cooper's eponymous ligaments of the breast and Sappey's subareolar *plexus* of lymphatics ushered in an era that revisited the origins and spread of breast cancer.^{8,9} In the same era, John Hunter (the Scottish 'father' of investigative surgery) replaced 'black bile' with lymph as the cause of breast cancer. A multitude of theories ranging from inspissated milk, trauma, personality type, exposure to air and infection were fed into the cauldron of carcinogenesis. The observation of the disease within families was naturally attributed to infection. Amidst this chaotic search for the truth, accounts of heroic surgeries from simple lumpectomies to radical removal of the *pectoralis*, enliven medical records.⁴ These are rendered more vivid and admirable when it is recalled that in the absence of anaesthesia, skill and speed were the sole attributes of a successful surgeon. It is also a grim reminder that surgery was the solitary modality for hope of relief with anecdotal incidences of cure. More conservative compatriots used ligatures or lead plates to strangulate the tumours, preferring them to the horrors of breast amputation.

Nineteenth Century: The golden age of surgery

The surgical discipline rapidly grew on the bedrock of a spate of discoveries that rendered it safer with a good outcome for the patient. Disinfection and sterilisation and the use of sterile gloves were the first landmark

events. General anaesthesia revolutionised the surgeon's ease (and indeed the patient's too!). Although in 1818 James Blundell attempted blood transfusion in postpartum haemorrhage, safe transfusions would be achieved only at the dawn of the 20th century with the discovery of blood groups by Karl Landsteiner. Against this background, seminal contributions to cancer came from the microscopic identification of normal cells and their cancerous brethren all the way from Hooke in 17th century England to Müller and Virchow in 19th century Germany. Müller dismissed the humoral theory of the origin of cancer, declaring that cancers were composed of living cells and suggesting that metastasis was due to spread of these cells.⁶ The demonstration that breast cancer spread along the lymphatics to the guardian axillary nodes was to form the basis of a variety of excision techniques. Unique forms of spread leading to the clinical manifestations of carcinoma *en cuirasse* or *peau d'orange* and Paget's disease would demand alternative ways of approaching treatment.

The middle years of the 19th century celebrated the newly acquired surgical freedom with bold and radical surgeries. The *en bloc* resections of Charles Moore in London,¹⁰ and Kuster and Volkmann in Germany ran a parallel course.¹¹ Axillary lymph node dissections as part of the philosophy of extermination were performed in 1882 by William Banks in Liverpool, UK.¹² While they may appear particularly mutilating today, they provided a unique opportunity to study the disease spread. Breast cancer surgery at the turn of the century came to be synonymous with the name of William S. Halstead, Professor of Surgery at Johns Hopkins hospital in Baltimore, USA. His radical mastectomy (first reported in 1894) with its emphasis on removing tissues in one piece to prevent spread and removal of the *pectoralis major* to prevent recurrence, became the undisputed path that generations of surgeons trod with diligence.¹³ "The suspected tissue should be removed in one piece, (1) lest the wound become infected by the division of tissues invaded by the disease or of lymphatic vessels containing cancer cells, and (2) because shreds or pieces of cancerous tissue might readily be overlooked in the piecemeal extirpation."¹⁴

These strict rules for non-violation of the tumour area precluded a preoperative biopsy to confirm whether the patient had a cancer at all: such was the strength of a skilled clinical diagnosis! Another age-old practice that came to a close was to leave the excised surgical wound open to granulate. The use of ligatures now allowed better wound healing through low infection rates.

Twentieth Century: *Surgery reinvents itself*

The hormone dependency of breast cancer was initially hypothetical, through the observation that the disease was aggressive in younger women. Beatson ignited the era of endocrine surgery in 1906¹⁵—long before the discovery of estrogen receptors by Jensen in 1967¹⁶ and oophorectomy and adrenalectomy (to achieve castration) came in vogue. These rather drastic methods were gradually overtaken by estrogen receptor modulators, luteinising hormone-releasing agonists and aromatase inhibitors.

Halstead's legacy was, for a while, preserved by Margottini and Veronesi in Milan who additionally removed internal mammary nodes and others who extended the scope of 'radicality' to supraclavicular and mediastinal nodes. However, the late 19th and early 20th centuries gradually heralded the demise of the adage: *big surgeons make big incisions* (and hence perform big surgeries). Patey and Handley from London and Auchincloss Jr. of New York ushered in a movement that 'modified' the radical mastectomy and preserved the *pectoralis major*.¹⁷ Rapid advances in medical radiation as a means of killing cancer cells and new forms of chemotherapy that did the same, but also achieved medical castration or targeted mutated tumour receptors, forced a rethink of cancer management strategies. These were coupled with the burgeoning knowledge of the biological behaviour of breast cancer and the less-than-guaranteed success of surgery alone. Early cancer detection of smaller lesions by mammography added a new dimension to surgical management.

The clarion call to reorient to limited surgery came from the surgery fraternity. Bernard Fisher, Professor of Surgery at the University of Pittsburgh, revived Galen's ancient belief that breast cancer was a systemic disease. Large randomised controlled clinical trials like the National Surgical Adjuvant Breast and Bowel Project (NSABP), published in 1989, provided scientific support.¹⁸ It is ironic that the disbandment of the radical Halstedian approach, the institution of trials and the acceptance of neoadjuvant therapy were the brainchildren of a surgeon! Veronesi from Italy and many others supported the notion of limited surgery complemented by adjuvants.¹⁹ Surgery reinvented itself to join hands with the other modalities. Since the close of the 20th century breast conservation and breast reconstruction—combined, where necessary, with sentinel node dissection—have held sway.^{20–22} The removal of only selected 'sentinel' nodes (those to which the tumour had spread) would relegate the swollen lymphoedematous arm, a distressing

manifestation of axillary lymph node dissections, to the annals of surgical history.

Once surgeons lead the revolution towards minimising extirpation, the first faltering steps towards restoring cosmesis were taken by Verneuil, a French surgeon who transferred autologous tissue from the normal breast to the diseased one in 1887.²³ This released the floodgates for a variety of innovative autologous and synthetic materials offering a restored shape that could even outdo nature's original creation. Muscle, myocutaneous flaps, lipomas and omentum were natural choices. The transverse *rectus abdominis* myocutaneous flap (TRAM) introduced in 1979 by Holmstrom has stood the test of time, undergoing several modifications in its evolution.²⁴ Prosthetic and synthetic options brought industry and commerce into the fray: petroleum jelly, glass balls, ivory, rubber, polyvinyl alcohol sponge and silicone—the list is ever growing!

Surgical domination over the treatment of breast cancer held sway for the millennia, ever since the first recorded medical literature. The hope for a cure by the radical removal of a diseased organ was always counterbalanced by fascinating and fearsome accounts of surgery *sans* anaesthesia as a physically and psychologically mutilating therapeutic option. While nowhere near its nadir, surgery remains at the heart of management in a multimodality setting. Instead of annihilation it now provides succour to the breast cancer survivor thus balancing cure and cosmesis.

Lessons from the History of Surgery in Breast Cancer

There are three lessons to be gained from the history of surgery in breast cancer. First, to delve into history is to rediscover buried insights: Galen's perceptive assessment that breast cancer is a systemic disease was echoed two millennia later in Fisher's 20th century observations. Second, the evolution of therapeutic weaponry raises the fortunes of medical disciplines (as antisepsis and anaesthesia did for surgery) or minimises their supremacy as stand-alone choices for *panacea* or cure (as chemoradiotherapy did for surgery). Third, stooping to conquer is the mark of survival in contemporary medical practice. Surgery has won the day by adapting and playing a complementary role in modern cancer management as a stylised, scientific and patient-friendly craft.

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