

HIGHLIGHTS IN THE DIAGNOSIS OF BREAST NEOPLASMS

ISTAKNUTI MOMENTI U DIJAGNOZI TUMORA DOJKI

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SUMMARY

Breast malignancies are one of the most prevalent and major causes of morbidity and mortality among women worldwide. According to the available data, neoplastic lesions of the breast are one of the main causes leading to heavy costs for both the healthcare system and the society. Based on these realities and the fact that different aspects of these malignancies remain unknown to date, and are essential to be determined, these issues make a vast area of research in medicine. Just like the present time, breast neoplasms were under the focus of scientists lived in the past, from all over the world. Accordingly, these malignancies are a group of disease with a long-standing historical background. As a result, it can be claimed that modern-day knowledge of these matters has burgeoned on the extraordinary discoveries and the development of diagnostic and therapeutic methods made through the ages, especially those of the post-medieval era. Recognizing the previous efforts that have been made in this regard will show our future way for us. For this reason, in this paper, we will review the key milestones and vital discoveries in the field of breast neoplasms and some other diseases involving this body organ.

Key words: Breast Neoplasms; Diagnosis; History of Medicine.

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INTRODUCTION

Because of the consequent morbidity, mortality, medical costs, and need for long-term care associated with breast neoplasms, these diseases have been and remain a main point of attention in the medical community. As old as the art of surgery, breast neoplasms trace their history back to ancient times. In spite of the long history of neoplastic lesions of the breast, an important part of the present knowledge regarding them and their diagnosis and management was acquired through many years of effort and experience during the post-medieval era [1-4]. This paper summarizes key milestones in the development of modern knowledge of breast neoplasms (as the main point) and some other conditions affecting this body part.

A SYNOPSIS OF ADVANCEMENTS IN THE DIAGNOSIS OF BREAST DISEASES

BENIGN LESIONS

Fat necrosis: Fat necrosis is a benign and non-suppurative inflammatory process of adipose tissue. It is responsible for 2.75% of all benign breast lesions [5]. It was first described by *Burton J. Lee* and *Frank Adair* from the Memorial Hospital, New York, in 1924 [6].

Granular cell tumor: Granular cell tumors are a rare and usually benign neoplasm which may occur in any part of the body. Approximately 5% to 8% of granular cell tumors occur within the breast [7]. It was first described by *A. Abrikossoff*, a Russian pathologist, in 1926 [8].

Fibroadenoma: Fibroadenoma is a common and benign breast lesion which usually presents as a single breast mass in young women [9]. Eccrine syringofibroadenoma is a rare eccrine tumor first described by *JM Mascaro* in 1963 [10]. Complex fibroadenomas were first described by *William D. Dupont* and his colleagues from the Vanderbilt University School of Medicine, Nashville, USA, in 1994 [11].

Adenoma: Syringomatous adenoma of the nipple was first described by *Paul Peter Rosen* in 1983 [12]. Ductal adenoma was first described by *J. G. Azzopardi* and *Richard Salm* (from Royal postgraduate Medical School, UK) in 1984 [13].

Pseudoangiomatous stromal hyperplasia: Pseudoangiomatous stromal hyperplasia of the breast is a benign proliferative lesion of the mammary stroma which rarely presents as a localized mass [14]. This type of breast neoplasm

was first described by *Milan F. Vuitch* and his colleagues, a group from the Memorial Sloan-Kettering Cancer Center, USA, in 1986 [15].

Myofibroblastoma: Breast myofibroblastomas are rare, benign tumors which occur predominantly in men in their 6th to 7th decade of life [16]. It was first described by *Eric S. Wargotz*, a pathologist from the George Washington University Medical Center, USA, and his colleagues in 1987 [17].

PRE-MALIGNANT LESIONS

Mucocele-like tumor: A mucocele-like tumor is a benign lesion of the breast which can be associated with ductal atypical hyperplasia, intraductal carcinoma, and infiltrating mucinous (colloid) carcinoma [18]. This pathologic entity was first described in 1986 by *Paul Peter Rosen* as a benign lesion of the breast consisting of multiple cysts of mucinous material that have ruptured and discharged their contents into the surrounding stroma [19].

Ductal carcinoma in situ: Ductal carcinoma in situ, or intraductal carcinoma, is a non-invasive form of breast cancer which has a 25% incidence rate among American women with breast malignancies [20]. This type of pathology was first described by *Albert Compton Broders* (1885-1964) (Fig. 1), an American surgical pathologist, in 1932 [21]. In addition, this pathologist created a microscopic system for grading cancerous lesions in 1920 [22, 23].

Lobular carcinoma in situ: Presently, lobular carcinoma in situ can be an indolent precursor of invasive lobular cancer of the breast [24]. This diagnosis was first described in 1941 by *Frank W. Foote* (1911-1989) and *Fred W. Stewart* (1894-1991), two American surgical pathologists, as a

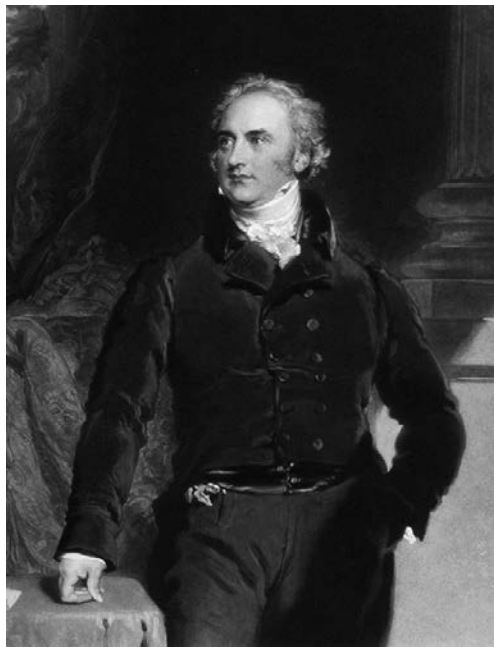


Fig. 1. Albert C. Broders (1885-1964). (Reproduced with permission from the Wright JR Jr (2012) *Albert C. Broders' paradigm shifts involving the prognostication and definition of cancer*. Arch Pathol Lab Med 136:1437-1446.)

noninvasive lesion arising from the terminal ducts and lobules of the breast [25].

Hypersecretory ductal carcinoma in situ: Hypersecretory cellular changes in lesions of the breast may represent the evolution of in situ forms of the disease toward cancer [26]. This pathologic diagnosis was first introduced by *Paul Peter Rosen* and *Marian Scott* (Memorial Sloan-Kettering Cancer Center, USA) in 1984 [27].

MALIGNANT LESIONS

Liposarcoma: Liposarcoma of the mammary glands is a rare malignant tumor that has an incidence of 0.3% of all sarcomas of the breast [28]. This type of breast pathology was first reported by *Ernst Neumann* (1834-1918), a German pathologist, in 1862 [29].

Myeloid sarcoma: The presentation of myeloid sarcoma as a breast mass is very rare and usually occurs in cases with a prior history of acute myeloid leukemia or other myeloid disorders [30]. This condition was first described by *Allan Burns* (1781-1813), a Scottish surgeon and physician, in 1811 [31].

Tubular carcinoma: Tubular carcinoma of the breast is an uncommon histological subtype of invasive breast cancer that accounts for approximately 1% to 5% of invasive breast carcinomas. It has an excellent prognosis [32].

This pathologic entity was first described by *Victor Cornil* (1837-1908) and *Louis-Antoine Ranvier* (1835-1922), two French pathologists, in 1869 [33].

Paget's disease: Paget's disease of the nipple is an uncommon type of breast neoplasm which usually presents itself as a pruritic and eczema-like rash involving the nipple-areolar complex [34]. Mammary Paget's disease was first described in 1874 by the English surgeon and pathologist *Sir James Paget* (1814-1899) (Fig. 2) [35].

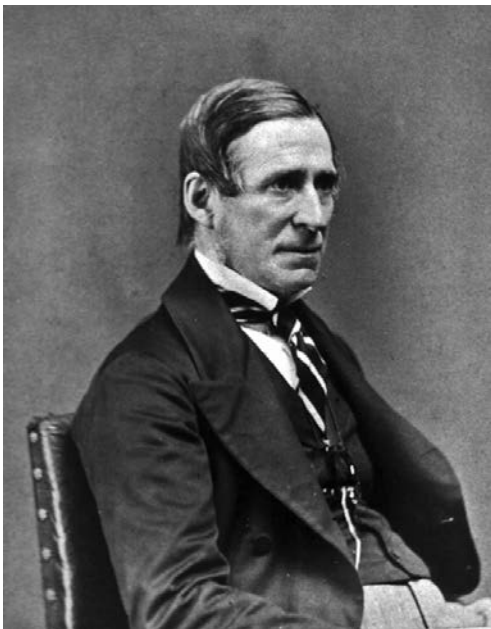


Fig. 2. Sir James Paget (1814 - 1899)

Angiosarcoma: Angiosarcoma of the breast is an infrequent and highly malignant form of breast sarcoma that has a poor prognosis because of the frequency of metastasis and recurrence [36]. It was first described by *Georg Benno Schmidt* in 1887 [37].

Invasive apocrine carcinoma: Invasive apocrine carcinoma of the breast is a rare, unique, and morphologically distinctive type of invasive ductal carcinoma [38]. This type of breast pathology was first described by *E. Krompecher*, a German pathologist, in 1916 [39].

Carcinoma erysipeloides: Carcinoma erysipeloides is an uncommon but distinctive form of cutaneous metastasis. It is most frequently associated with carcinoma of the breast, but may occur with other primary tumors [40]. In 1924, for the first time, *Burton J. Lee* and *N. Tannenbaum* from the Memorial Hospital of New York reported the association of breast cancer with inflammatory changes in the overlying skin [41]. This pathology was given its current name by *Carl Emanuel Flemming Rasch* (1861-1938), a Danish physician, in 1931 [42].

Adenoid cystic carcinoma: Adenoid cystic carcinoma (ACC) of the breast, previously called “cylindroma”, is a rare form of primary breast cancer which is responsible for less than 0.1% of all primary breast malignancies [43]. Although *Theodor Billroth* (1829-1894) (Fig. 3), an Austrian surgeon and the founding father of modern abdominal surgery, introduced the clinical and pathologic features of ACC of the trachea in 1859 and coined the term “cylindroma” for this diagnosis, *Charles Freeman Geschickter* (1901-1987), an American pathologist, and *Murray Marcus Copeland* (1902-1982), an American cancer specialist, were the first to report ACC of the breast in 1945 [44, 45].

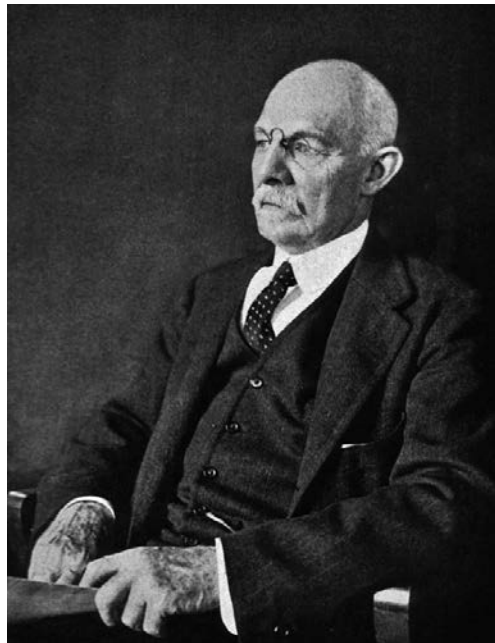


Fig. 3. Theodor Billroth (1829 - 1894)

Invasive lobular carcinoma: Invasive lobular carcinoma of the breast is responsible for 10% to 15% of all newly diagnosed breast cancers [46]. It was first described by *Frank W. Foote* and *Fred W. Stewart* in 1946 [47].

Medullary carcinoma: Medullary carcinoma of the breast is an invasive and uncommon form of breast cancer and has a prevalence of less than 5% of breast malignancies [48]. This class of breast pathology was first described by *Oliver S. Moore* and *Frank W. Foote* from the Memorial Hospital, New York, in 1949 [49].

Lipid-rich carcinoma: Lipid-rich carcinoma of the breast is a very rare variant of breast malignancies which is responsible for less than 1% of all breast cancers. The morphology of this carcinoma was first described by *Michel H. Aboumrada* and his colleagues at the Henry Ford Hospital, USA in 1963. The relation of lipid-rich carcinoma and neuroleptics (prolactin releasing drugs) was first described by *Tsubura* and his colleagues in 1992 [50-52].

Secretory carcinoma: Secretory carcinoma of the breast, previously called “juvenile breast cancer”, is a rare and low-grade type of breast cancer which can occur in the adult age group and can affect both male and female [53]. It was first described by *Robert W. McDivitt* and *Fred W. Stewart* in 1966 [54].

Adenomyoepithelioma: Adenomyoepithelioma of the breast is an uncommon and low-grade malignant neoplasm which has the potential of distant metastases [55]. This pathologic class was first described by *H. Hamperl*, a German pathologist, in 1970 [56].

Tubulolobular carcinoma: Tubulolobular carcinoma is a rare subtype of breast cancer which presents characteristics of both lobular and ductal differentiation [57]. This pathologic diagnosis was first reported by *Edwin R. Fisher* and his colleagues, a group of physicians from the University of Pittsburgh School of Medicine, in 1977 [58].

Breast carcinoma with choriocarcinomatous features: Mammary carcinoma with choriocarcinomatous features is a rare and distinct variant of metaplastic carcinoma in which focal choriocarcinomatous differentiation occurs [59]. It was first described by *Patricia E. Saigo* and *Paul Peter Rosen*, two American physicians, in 1981 [60].

Glycogen-rich clear cell carcinoma: Glycogen-rich clear cell carcinoma of the breast is an uncommon form of breast cancer which accounts for 0.9% to 2.8% of all breast cancer cases [61]. This pathologic finding was

first explained in 1981 by *Meredith T. Hull* and his co-workers, a group from Indiana University School of Medicine, USA [62].

Low-grade adenosquamous carcinoma: Low-grade adenosquamous carcinoma of the breast is a rare form of invasive mammary carcinoma [63]. It was first reported by *Paul Peter Rosen* and his colleague *Debra Ernsberger* (Memorial Sloan-Kettering Cancer Center, USA) in 1987 [64].

Invasive micropapillary carcinoma: Invasive micropapillary carcinoma of the breast is an uncommon and highly aggressive type of breast cancer [65]. This type of breast malignancy was first described by *Sumalee Siriaunkgul* and *Fattaneh Abbas-Zadeh Tavassoli*, two pathologists from USA, in 1993 [66].

Acinic cell carcinoma: Primary acinic cell carcinoma of the breast is a very rare condition that has pathology similar to that of acinic cell carcinoma of the salivary glands [67]. Acinic cell carcinoma was first identified by *Federico Roncaroli* and his colleagues, a group of scientists from two institutes in Italy and Slovenia, in 1996 [68].

OTHER BREAST PATHOLOGIES

Breast tuberculosis: Mammary tuberculosis is a rare form of tuberculosis which involves the breast [69]. It was first recorded in 1829 by *Sir Astley Cooper* (1768-1841) (Fig. 4), an English surgeon and anatomist, as what he called “*scrofulous swelling of the bosom*” [70]. Cooper’s one other great contribution to modern knowledge of the breast was his description of the suspensory support system of the breast (presently known as Cooper’s ligament). In addition, he authored two books about the breast, including *Illustrations of the Diseases of the Breast* (published in 1829) and *On the Anatomy of the Breast* (published in 1832) [71].

Phyllodes tumor: Phyllodes tumors are uncommon tumors of the breast that occur



Fig. 4. Sir Astley Paston Cooper (1768 - 1841)

in middle-aged women and can be classified into the categories of benign, borderline, and malignant based on histological features [72]. Phyllodes tumors were first described by the German scientist *Johannes Peter Müller* (1801-1858) in 1838 when he used the term “sarcoma” for this type of breast neoplasm because of its gross fleshy appearance [73].

Ectopic breast tissue: Ectopic breast tissue can present anywhere along the primitive embryonic milk lines (from the axilla to the groin) [74]. *Hartung* first introduced this diagnosis in 1872 when he reported a thirty-year-old woman with a fully formed mammary gland in the left labium majus [75, 76]. Later, in 1936, *Harry J. Greene*, an American physician, described the first known diagnosed case of adenocarcinoma arising in ectopic mammary tissue [77].

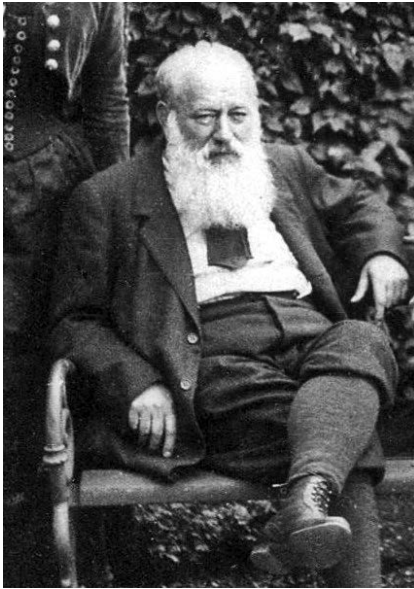


Fig. 5. William Stewart Halsted
(1852 - 1922)

Occult breast cancer: Occult primary breast carcinoma is an uncommon type of breast cancer which presents itself with axillary metastasis [78]. It was first described by the American surgeon *William Stewart Halsted* (1852-1922) (Fig. 5) in 1907 [79]. This physician made another major contribution to the field of breast cancer management, i.e., the development of the radical mastectomy as a treatment for breast malignancies [80].

Breast sarcoidosis: *J. Strandberg* was probably the first to present a case of breast sarcoidosis in 1921. His reported patient had suffered from systemic sarcoidosis with bilateral breast nodules. Although *Strandberg* believed that the presence of such nodules was representative of sarcoidosis, he was unable to confirm sarcoid involvement of the breast [81]. After him, in 1938, *R. Bodley Scott* described the first case of breast sarcoidosis with adequate clinical and histological findings [82].

Hamartoma: Hamartoma of the breast is a rare, benign, and tumor-like malformation of glandular, adipose, and fibrous tissue [83]. Mammary hamartomas were first described in 1971 by *Marco G. Arrigoni* and his co-workers

in a study of 10 patients whose breast tumors clinically and grossly resembled fibroadenomas [84].

Granulomatous mastitis: Granulomatous mastitis is a rare, chronic, and inflammatory condition of the breast with an unknown etiology that affects women of child-bearing age [85]. This diagnosis was first described by the two physicians *Edward Kessler* and *Yaakov Wolloch* in 1972 [86].

Diabetic mastopathy: Diabetic mastopathy is an uncommon kind of lymphocytic mastitis and stromal fibrosis which typically occurs in patients with longstanding type one diabetes [87]. It was first described by the two physicians *Norman G. Soler* and *Romesh Khardori* from the Southern Illinois University School of Medicine in 1984 [88].

CONCLUSION

Present-day knowledge of breast neoplasms, their screening, diagnosis, and their management is highly indebted to the previous and continuous efforts made in this field. Yet there are still many unknown aspects of neoplastic lesions of the breast. This means that there is still a strong need for further efforts to improve the current status of diagnosis and therapy for diseases of the breast, a task which could affect the lives of a large number of the population.

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SAŽETAK

Maligne bolesti dojki su jedan od najčešćih i glavnih uzroka pobola i smrtnosti među ženama diljem svijeta. Prema dostupnim podacima, tumorske lezije dojke su jedan od glavnih uzroka koji dovode do teških troškova i za zdravstveni sustav i za društvo. Na temelju tih danosti i činjenici da su različiti aspekti tih malignih bolesti i dalje nepoznati do danas, te se tek trebaju odrediti, ta pitanja čine ogromno područje istraživanja u medicini. Baš kao i u sadašnjem trenutku, karcinom dojke je bio i u prošlosti u fokusu znanstvenika iz svih krajeva svijeta. Prema tome ove zloćudne bolesti su skupina bolesti s dugogodišnjom povijesnom pozadinom. Možemo, kao rezultat, tvrditi da suvremena znanja o tim pitanjima je procvjetalo s izvanrednim otkrićima i razvojem dijagnostičkih i terapijskih metoda kroz stoljeća, a posebno u onim one nakon srednjeg vijeka. Prepoznajući prethodne napore koji su uloženi u tom pogledu pokazat će nam put za budućnost. Iz tog razloga, u ovom radu ćemo dati pregled ključnih prekretnica i važnih otkrića na području tmora dojke i nekih drugih bolesti koje uključuju taj organ.

Ključne riječi: karcinom dojke; dijagnoza; povijest medicine.