

Breast Cancer from Different Clinical Perspectives

¹Faris Abdulaziz Habib, ²Najlaa Marzoq Alzaidi, ³Ahmed Saleh Alzahrani, ⁴Ahmed Hamed Alghamdi, ⁵Mohammed Dhafer Alshehri, ⁶Faris Muslih Althaqafi, ⁷Reyof Saeed Alharthi, ⁸Nawaf Mohammed Alamri, ⁹Ahmad Mohammed Saleh, ¹⁰Sultan Abdullah Alqarni

Abstract: The OBJECTIVE of this review is to overview breast cancer, from different clinical aspects such as; epidemiology, emphasizing etiological factors associated with breast cancer, screening and diagnosis, and then discussing the important treatment approaches to breast cancer which have been established relatively recently. Electronic databases (Medline, PubMed, and Embase) were searched up to May 2017, for relevant articles concerned with breast cancer within clinical aspects.

The etiology of breast cancer is multi-factorial, as well as several factors have been linked, which may act independently or in mix, particularly in high risk people. It is very important to recognize the etio-pathogenesis of this typical disease, which is associated with high morbidity and mortality, especially if not spotted early. The treatment of breast cancer is advancing in the direction of an individualized formula. MRI is being used with raising regularity and also appears to have one of the most importance in patients with occult breast cancers, recognized BRCA anomalies, and/or dense breast tissue. Indications for MRI have not yet been standard. Remarkably, both breast conservation as well as prophylactic mastectomy have actually grown in appeal for the management of diagnosed breast cancer.

Keywords: Breast cancer, BRCA anomalies, MRI.

1. INTRODUCTION

Breast cancer (BC) is the globe's leading cause of death among females globally ⁽¹⁾. Occurrence prices are high in even more established countries, whereas prices in much less established nations are reduced but increasing. As well as it's the most usual noncutaneous cancer in U.S. ladies, with an approximated 61,000 situations of in situ disease as well as 246,660 situations of invasive disease in 2016 ⁽²⁾. Roughly 1.38 million brand-new breast cancer situations were diagnosed in 2008 with virtually half of all bust cancer instances and also virtually 60% of fatalities happening in reduced revenue countries ⁽³⁾. There is a large variant in breast cancer survival prices all over the world, with an estimated 5-year survival of 80% in high earnings countries to below 40% for reduced income nations ⁽⁴⁾.

These causative factors consist of age, genetics, family history, diet, alcohol, weight problems, way of living, physical lack of exercise, along with endocrine factors (both exogenous and also endogenous) ⁽⁵⁾. Triple adverse breast cancer (TNBC) has just recently been recognized in particular sub-groups of patients, as well as has a higher reappearance rate, faster growth as well as poorer prognosis ⁽⁶⁾. Other connected factors for bust cancer are mammographic density and also previous benign disease ⁽⁷⁾.

The bust is made up of two main types of tissues i.e., glandular cells and stromal (supporting) tissues. Glandular cells house the milk-producing glands (lobules) and also the air ducts (the milk flows) while stromal cells include fatty and also fibrous connective cells of the bust. The bust is also comprised of lymphatic tissue-immune system cells that eliminates mobile fluids and waste (**Figure 1**) ⁽⁸⁾.

There are numerous kinds of tumors that may create within different areas of the bust. Most tumors are the outcome of benign (non-cancerous) modifications within the breast. Fibrocystic adjustment is a non-cancerous problem in which ladies create cysts (built up packets of fluid), fibrosis (formation of scar-like connective tissue), lumpiness, as well as areas of thickening, tenderness, or bust pain ⁽⁹⁾. The majority of breast cancers start in the cells that line the ducts (ductal cancers). Some begin in the cells that line the lobules (lobular cancers cells), while a handful beginning in the various other cells ⁽¹⁰⁾. Improved testing plays a role in this decrease. National Comprehensive Cancer Network (NCCN) suggestions for breast cancer consist of locoregional treatment with surgical treatment and also radiation, plus systemic treatment with radiation treatment, endocrine, and biologic treatments ⁽¹¹⁾.

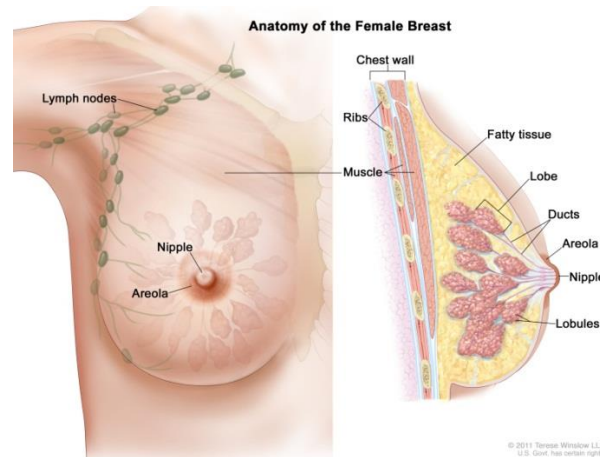


Figure 1: Anatomy of female breast

The OBJECTIVE of this review is to overview breast cancer, from different clinical aspects such as; epidemiology, emphasizing etiological factors associated with breast cancer, screening and diagnosis, and then discussing the important treatment approaches to breast cancer which have been established relatively recently.

2. METHODOLOGY

Electronic databases (Medline, PubMed, and Embase) were searched up to May 2017, for relevant articles concerned with breast cancer within clinical aspects, our search strategy used a Mesh terms as following; “breast cancer” OR “breast tumor” combined with “Treatment”, “Diagnosis”, “screening”, “Etiology” and “Risk factors”. Furthermore, references from included studies were screened for more relevant articles that could support our review study about breast cancer.

3. RESULTS

○ Etiology and risk factors of breast cancer:

Childbearing can be as risk factor for breast cancer:

It has actually been recognized for years that a lady's risk of bust cancer is lowered by bearing children, as suggested by high rates in religious women and also low rates in wedded relative to single women. There was additionally the belief that the sensation could be explained by a protective impact of breastfeeding, bust cancer risk being low in areas of the world where long term breastfeeding was normal, and boosting in the West where breastfeeding was decreasing. At once when ideas of chemical carcinogenesis projected, the concept likewise had some charm in the idea that lactation could rinse the poor things (whatever it was) together with the excellent. Some early research studies appeared to sustain this sight ^(12,13). In the 1960s, we intended to eliminate this particular piece of under-brush to see whether or not it concealed a pheasant, as well as arranged a case-control study in 7 parts of the world, including locations of high, reduced and also intermediate bust cancer risk ^(14,15).

Menopause as risk factor for bust cancer:

Evidence of the duty of the ovary in breast cancer is additionally seen in observations that boosted risk is connected with early beginning of menses and late natural menopause, which there is bountiful proof ^(16,17). With respect to menopause, the form of the age-incidence curve for bust cancer is interesting. In Western countries prices enhance sharply with age

approximately the moment of menopause, but at a slower rate afterwards. As kept in mind by Boyle, the pattern ends up being more intriguing in international data ⁽¹⁷⁾.

Age & Genetics background as a risk factor:

The risk of establishing breast cancer increases with age. Using the Surveillance, Epidemiology, and End Results (SEER) database, the chance of a woman in the United States creating breast cancer is a lifetime risk of 1 in 8; 1 in 202 from birth to age 39 years old, 1 in 26 from 40-59 years, and also 1 in 28 from 60-69 years ⁽¹⁸⁾.

About 20% -25% of breast cancer patients have a favorable family history yet only 5% -10% of breast cancer situations show an autosomal dominant inheritance ⁽¹⁹⁾. Hereditary predisposition alleles have actually been explained in terms of scientific importance ⁽²⁰⁾. High-risk predisposition alleles providing a 40% -85% lifetime risk of developing breast cancer include BRCA1 as well as BRCA2 anomalies, anomalies in TP53 gene resulting in Li-Fraumeni syndrome, PTEN resulting in Cowden syndrome, STK11 creating Peutz-Jegher's syndrome, Neurofibromatosis (NF1) and (CDH-1) E-Cadherin ⁽²¹⁾.

Breast previous diseases:

Proliferative breast disease is associated with a boosted risk of breast cancer. Proliferative breast lesions without atypia, including typical ductal hyperplasia, intraductal papillomas, sclerosing adenosis and fibroadenomas give just a little boosted risk of breast cancer development, about 1.5-2 times that of the basic populace ⁽²²⁾. Atypical hyperplasia consisting of both ductal and also lobular, typically incidentally located on testing mammography, confers a significant raised risk of breast cancer. Ladies with atypia have an approximately 4.3 times better risk of developing cancer compared with the general populace ^(22,23).

Weight problems lifestyle and physical lack of exercise & Family history:

In addition to diet regimen, exercise could disrupt plasma levels of hormonal agents, which might affect breast cancer growth ⁽²⁴⁾. Aguas et al. ⁽²⁴⁾ observed that these two factors separately or in mix affect the body weight as well as obesity raises the risk of breast cancer in post-menopausal ladies. Dumitrescu et al. ⁽²⁵⁾ supported this observation in their paper and also noted that breast cancer risk is especially evident among obese females who do not use hormonal agent replacement treatment (HRT), and for every 5 kg of weight gain, breast cancer risk rises by 8% ⁽²⁵⁾. This is explained by the truth that fat in fat is an essential resource of oestrogens, which are synthesised from cholesterol.

A lady's risk of breast cancer is enhanced if she has a family history of the disease. In the Nurses' Health Study follow-up, females with a mother diagnosed before age 50 had an adjusted relative risk of 1.69 as well as females with a mother identified at 50 or older had a family member risk of 1.37 compared with ladies without a family history of breast cancer. A background of a sis with breast cancer also demonstrated an increased family member risk of 1.66 if the diagnosis was made prior to age 50 and also a family member risk of 1.52 if identified after age 50 compared with patients without a family history ⁽²⁶⁾. The greatest risk is connected with raising variety of first degree relatives detected with breast cancer at a young age (under age 50). Compared with women who had no damaged loved one, ladies who had one, two or three or even more affected first degree loved ones had risk proportions of 1.80, 2.93 and also 3.90, respectively ⁽²⁷⁾.

o Screening methods and diagnosis of breast cancer:

Clinical breast examination:

Energy of the breast self-examination (BSE) is controversial as the advantage in regards to reduced death has not been shown ⁽²⁸⁾. A lot of clinicians encourage women to perform regular monthly BSE to become acquainted with their normal makeup as well as empower them with regards to their own healthcare ⁽²⁹⁾. The 2013 NCCN guidelines advise annual medical breast evaluation (CBE) for females of ordinary risk > 40 years of age as well as BSE to create and show breast self-awareness ⁽³⁰⁾.

Mammography as an appropriate for screening and diagnosis of BC:

Among one of the most crucial developments in the treatment of breast cancer is early detection of non-palpable masses. In the 1960's, the very first randomized control tests comparing regular mammography screening vs medical assessment showed a reduced mortality by approximately one 3rd in the experimental group. Nevertheless, there is still dispute concerning death from breast cancer in the subset of females aged 40-49 years ^(31,32). Contemporary randomized control tests have demonstrated the take advantage of evaluating mammography in women aged 40 to 70 years ^(33,34). A 2013

Cochrane Review suggests that death is an end result biased toward testing, routine mammography causes excessive anxiety and unpredictability in the face of false-positive results with rise in complete varieties of lumpectomies and mastectomies however no decline in death ⁽³⁴⁾.

Mammography remains the pillar in breast cancer discovery ⁽³⁵⁾. Analysis mammograms are performed in women who have an apparent mass or other sign of breast disease, a history of breast cancer within the coming before 5 years, or have been recalled for extra imaging from an abnormal testing mammogram. Diagnostic mammograms consist of special views such as focal compression of one area of the bust cells or magnification photos. The breast imaging reporting and also data source system (BI-RADS) is the standard technique for coverage of mammographic findings ⁽³⁶⁾. Cancers present as asymmetries, calcifications, as well as masses (**Table 1**). By definition, a mass is a space-occupying lesion seen in 2 various aircrafts. This is distinguished from a thickness, which is seen just in a solitary plane. The form of masses is referred to as round, oval, lobular, or irregular, while the margins are determined as circumscribed (with well-defined margins), indistinct, and spiculated (with densities emitting from the margins). Calcifications related to benign disease are generally larger than those seen with malignancy and also usually are crude (round, lucent centered, or "layering" on median lateral or side median photos). Clustered amorphous, indistinct, pleomorphic (or heterogeneous), or penalty, straight, or branching calcifications are a lot more normal of carcinomas ⁽³⁶⁾.

Table 1: Breast imaging reporting and database system ⁽³⁶⁾

Category	Assessment	Follow up
0	Need additional imaging evaluation	Additional imaging needed before a category can be assigned
1	Negative	Continue annual screening mammograms (women older than 40 yr)
2	Benign	Continue annual screening mammograms (women older than 40 yr)
3	Probably benign	Initial short term follow-up (usually six month) mammogram (< 2% chance of malignancy)
4	Suspicious abnormality	Biopsy should be considered (2%-95% chance of malignancy)
5	Highly suggestive of malignancy	Requires biopsy (> 95% chance of malignancy)
6	Known cancer	Biopsy-proven malignancy

Role of Magnetic resonance imaging (MRI) in diagnosis of BC:

Mammography remains the gold criterion for breast imaging but magnetic resonance imaging (MRI) has actually become an important technique in the detection, analysis, hosting, and also administration of breast cancer in picked patients. Evaluating MRI is more delicate however much less certain for the detection of cancer in high risk women. The sensitivity of MRI is 0.77-0.79 compared with mammographic sensitivity of 0.33-0.39. Uniqueness of MRI is 0.86-0.89 as compared to mammographic specificity of 0.95 ^(37,38). In a methodical evaluation, MRI and also mammography showed a combined level of sensitivity and uniqueness of 0.94 and 0.77, respectively ⁽³⁷⁾. The 2013 NCCN guidelines recommend patients that have actually raised (> 20%) lifetime risk of establishing breast cancer undertake yearly mammography as well as MRI starting at age 25 or an age tailored to the risk of the patient on a specific basis. MRI is beneficial in the screening of choose high risk patients, patients in whom breast enhancement prevents efficient testing mammography, or in patients with ambiguous searchings for on various other imaging techniques

Ultrasound as a screening tool:

There are a number of research studies sustaining making use of adjunctive screening ultrasound in high risk patients with thick breast cells, which imparts a significant but approved variety of incorrect positives ⁽³⁹⁾. No randomized controlled trials have been conducted to evaluate the effect of screening ultrasonography on breast cancer death prices. Entire breast ultrasound could permit the clinician to display for breast cancers not identified by conventional mammography, especially in dense busts where mammographic level of sensitivity is lower ⁽⁴⁰⁾. Single facility researches have actually revealed that the incremental detection of breast cancer by ultrasound following screening mammogram provides only marginal added advantage in ladies of ordinary risk ⁽⁴¹⁾.

○ **Treatment approaches of breast cancer:**

Surgery (Mastectomy) for treatment of BC:

Relying on the stage as well as sort of the tumor, lumpectomy (elimination of the lump just), or medical elimination of the whole breast (mastectomy) is carried out. Requirement practice requires the surgeon to establish that the cells eliminated in the procedure has margins free from cancer, indicating that the cancer has actually been entirely excised. If the gotten rid of cells does not have clear margins, additional operations to remove even more cells could be essential. This could sometimes need elimination of part of the pectoralis significant muscular tissue, which is the primary muscle of the former upper body wall. Much more just recently, the strategy of sentinel lymph node (SLN) breakdown has actually ended up being preferred, as it needs the elimination of far less lymph nodes, resulting in less adverse effects. Breakthroughs in sentinel lymph node mapping over the past decade have actually boosted the accuracy of detecting guard lymph node from 80% using blue color alone to in between 92% as well as 98% making use of consolidated modalities^(42,43).

Surgery for breast cancer contains 2 major alternatives. In breast-conserving surgical procedure, just the tumor as well as a location of typical tissue bordering it are eliminated. Breast-conserving surgery includes the following:

Lumpectomy; A percentage of surrounding regular tissue is gotten rid of. **Wide excision;** Also called as partial mastectomy in which somewhat bigger amount of the bordering typical tissue is removed. **Quadrantectomy;** About one 4th of the breast is eliminated. In mastectomy, all breast tissue is eliminated.

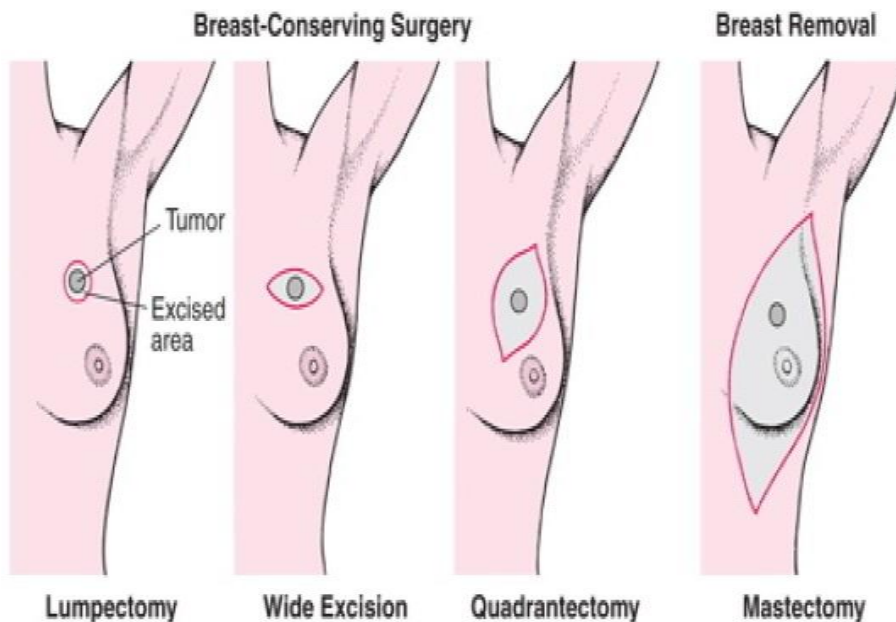


Figure 2: various types of surgery applied for breast cancer

Radiation Therapy for BC:

Radiation treatment includes making use of high-energy X-rays or gamma rays that target a tumor or post-surgical treatment tumor site. These radiations are very efficient in killing cancer cells that may continue to be after surgical treatment or repeat where the tumor was gotten rid of. Therapy implanted radioactive catheters (brachytherapy), similar to those utilized in prostate cancer therapy, could be utilized. This therapy choice has been superseded by electron light beam radiotherapy to the breast scar. Radiation therapy for breast cancer is usually carried out after surgical treatment and is an integral element of breast-conserving treatment. The dose of radiation must be strong enough to guarantee the removal of cancer cells. Therapies are generally given over a duration of five to seven weeks, carried out five days a week. Each treatment takes around 15 minutes^(44,45).

Chemotherapy for breast cancer:

Radiation treatment is making use of anti-cancer medications to deal with cancerous cells. Particular therapy for the breast cancer will be based upon; overall health and wellness, case history, age (whether menstrual cycle is there or otherwise), kind as well as stage of the cancer, tolerance for specific drugs as well as treatments and so on. Radiation treatment

treatments are usually given up cycles; a treatment for a period of time, adhered to by a recuperation period, then another treatment. Radiation treatment can be given prior to surgical treatment to shrink the tumor and in some cases make breast preserving surgery possible instead of a mastectomy. Lot of times, it is provided after surgical procedure and also may be given every three weeks or every two weeks in a "dosage thick" fashion ^(46,47).

4. CONCLUSION

The etiology of breast cancer is multi-factorial, as well as several factors have been linked, which may act independently or in mix, particularly in high risk people. It is very important to recognize the etio-pathogenesis of this typical disease, which is associated with high morbidity and mortality, especially if not spotted early. TNBC positions special analysis, treatment as well as prognostic difficulties, due to the fact that of the absence of the typically determined receptors, as well as connected bad survival in this team of patients. Consequently, the duties of very early testing in high risk or susceptible people, as well as appropriate security of cured instances in order to detect reoccurrence at the beginning have been advocated.

The treatment of breast cancer is advancing in the direction of an individualized formula. MRI is being used with raising regularity and also appears to have one of the most importance in patients with occult breast cancers, recognized BRCA anomalies, and/or dense breast tissue. Indications for MRI have not yet been standard. Remarkably, both breast conservation as well as prophylactic mastectomy have actually grown in appeal for the management of diagnosed breast cancer.

REFERENCES

- [1] Jemal A, Center MM, DeSantis C, Ward EM. Global patterns of cancer incidence and mortality rates and trends. *Cancer Epidemiol Biomarkers Prev* 2010; 19:1893–1907.
- [2] American Cancer Society: Cancer Facts and Figures 2016. Atlanta, Ga: American Cancer Society, 2016. Available online.
- [3] Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer*. 2010;127:2893–2917.
- [4] Coleman MP, Quaresma M, Berrino F, Lutz JM, De Angelis R, Capocaccia R, Baili P, Rachet B, Gatta G, Hakulinen T, et al. Cancer survival in five continents: a worldwide population-based study (CONCORD) *Lancet Oncol*. 2008;9:730–756.
- [5] Ali S, Coombes RC. Endocrine responsive breast cancer and strategies for combating resistance. *Nat Rev Cancer*. 2002;2:101–12.
- [6] O'Toole SA, Beith JM, Millar EK, West R, Mclean A, Cazet A, et al. Therapeutic targets in triple negative breast cancer. *J Clin Pathol*. 2013;66:530–42.
- [7] Aiello EJ, Buist DS, White E, Porter PL. Association between mammographic breast density and breast cancer tumor characteristics. *Cancer Epidemiol*. 2005;14:662–8.
- [8] Breast cancer process india, Breast cancer cost india, Breast cancer, delhi India. Breast cancer information and resources. 2010. Apr 13, [14 May 2017]. <http://www.digfortheure.org/breast-cancer-process-india-breast-cancer-cost-india-breast-cancer-delhi-india.html> .
- [9] What is breast cancer? Imaginis. 2008. Jun 11, [15 May 2017]. <http://www.imaginis.com/breast-health/what-is-breast-cancer-2> .
- [10] What is breast cancer? American cancer society. 2009. Sep 18, [15 May 2017]. http://www.cancer.org/docroot/CRI/content/CRI_2_4_1X_What_is_breast_cancer_5.asp
- [11] NCCN. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology: Breast Cancer, version 2.2011.
- [12] Lane-Claypon JE. A further report on cancer of the breast with special reference to an association with antecedent conditions. London: Her Majesty's Stationery Office, 1926.

- [13] Lipworth L, Bailey A, Trichopoulos D. History of breast-feeding in relation to breast cancer risk: a review of the epidemiologic literature. *J Natl Cancer Inst* 2000;92:302–12.
- [14] MacMahon B, Lin TM, Lowe CR, Mirra AP, Ravnihar B, Salber EJ, Trichopoulos D, Valaoras VG, Yuasa S. Lactation and cancer of the breast. A summary of an international study. *Bull World Health Organ* 1970;42:185–94.
- [15] MacMahon B, Cole P, Lin TM, Lowe CR, Mirra AP, Ravnihar B, Salber EJ, Vakaoras VG, Yuasa S. Age at first birth and breast cancer risk. *Bull World Health Organ* 1970;43:209–21.
- [16] Hankinson S, Hunter D. Breast cancer. In: Adami H-O, Hunter D, Trichopoulos D, eds. *Textbook of cancer epidemiology*. New York: Oxford, 2002. p 301–39.
- [17] Boyle P. Epidemiology of breast cancer. *Baillie`re’s Clin Oncol* 1988; 2:1–57
- [18] Siegel R, Naishadham D, Jemal A. Cancer statistics, 2013. *CA Cancer J Clin*. 2013;63:11–30.
- [19] Margolin S, Johansson H, Rutqvist LE, Lindblom A, Fornander T. Family history, and impact on clinical presentation and prognosis, in a population-based breast cancer cohort from the Stockholm County. *Fam Cancer*. 2006;5:309–321.
- [20] Lalloo F, Evans DG. Familial breast cancer. *Clin Genet*. 2012;82:105–114.
- [21] Sharif S, Moran A, Huson SM, Iddenden R, Shenton A, Howard E, Evans DG. Women with neurofibromatosis 1 are at a moderately increased risk of developing breast cancer and should be considered for early screening. *J Med Genet*. 2007;44:481–484.
- [22] Hartmann LC, Sellers TA, Frost MH, Lingle WL, Degnim AC, Ghosh K, Vierkant RA, Maloney SD, Pankratz VS, Hillman DW, et al. Benign breast disease and the risk of breast cancer. *N Engl J Med*. 2005;353:229–237.
- [23] Dupont WD, Parl FF, Hartmann WH, Brinton LA, Winfield AC, Worrell JA, Schuyler PA, Plummer WD. Breast cancer risk associated with proliferative breast disease and atypical hyperplasia. *Cancer*. 1993;71:1258–1265.
- [24] Aguas F, Martins A, Gomes TP, de Sousa M, Silva DP. Portuguese Menopause Society and Portuguese Gynaecology Society. Prophylaxis approach to a-symptomatic post-menopausal women: Breast cancer. *Maturitas*. 2005;52(Suppl 1):S23–31.
- [25] Dumitrescu RG, Cotarla I. Understanding breast cancer risk - where do we stand in 2005? *J Cell Mol Med*. 2005;9:208–21.
- [26] Colditz GA, Kaphingst KA, Hankinson SE, Rosner B. Family history and risk of breast cancer: nurses’ health study. *Breast Cancer Res Treat*. 2012;133:1097–1104.
- [27] Collaborative Group on Hormonal Factors in Breast Cancer. Familial breast cancer: collaborative reanalysis of individual data from 52 epidemiological studies including 58,209 women with breast cancer and 101,986 women without the disease. *Lancet*. 2001;358:1389–1399.
- [28] Kösters JP, Gøtzsche PC. Regular self-examination or clinical examination for early detection of breast cancer. *Cochrane Database Syst Rev*. 2003;(2):CD003373.
- [29] McCready T, Littlewood D, Jenkinson J. Breast self-examination and breast awareness: a literature review. *J Clin Nurs*. 2005;14:570–578.
- [30] National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology v.1.2013. Breast Cancer Screening and Diagnosis.
- [31] Shapiro S, Strax P, Venet L. Periodic breast cancer screening in reducing mortality from breast cancer. *JAMA*. 1971;215:1777–1785.
- [32] Shapiro S. Evidence on screening for breast cancer from a randomized trial. *Cancer*. 1977;39:2772–2782.
- [33] Freedman DA, Petitti DB, Robins JM. On the efficacy of screening for breast cancer. *Int J Epidemiol*. 2004;33:43–55.
- [34] Nelson HD, Tyne K, Naik A, Bougatsos C, Chan BK, Humphrey L. Screening for breast cancer: an update for the

U.S. Preventive Services Task Force. *Ann Intern Med.* 2009;151:727–37, W237-42.

- [35] Smetherman DH. Screening, imaging, and image-guided biopsy techniques for breast cancer. *Surg Clin North Am.* 2013;93:309–327.
- [36] American College of Radiology. Breast imaging reporting and data system (BI-RADS). 4th ed. Reston (VA): American College of Radiology; 2003.
- [37] Warner E, Messersmith H, Causer P, Eisen A, Shumak R, Plewes D. Systematic review: using magnetic resonance imaging to screen women at high risk for breast cancer. *Ann Intern Med.* 2008;148:671–679.
- [38] Kriege M, Brekelmans CT, Boetes C, Besnard PE, Zonderland HM, Obdeijn IM, Manoliu RA, Kok T, Peterse H, Tilanus-Linthorst MM, et al. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. *N Engl J Med.* 2004;351:427–437.
- [39] Berg WA, Blume JD, Cormack JB, Mendelson EB, Lehrer D, Böhm-Vélez M, Pisano ED, Jong RA, Evans WP, Morton MJ, et al. Combined screening with ultrasound and mammography vs mammography alone in women at elevated risk of breast cancer. *JAMA.* 2008;299:2151–2163.
- [40] Kelly KM, Dean J, Comulada WS, Lee SJ. Breast cancer detection using automated whole breast ultrasound and mammography in radiographically dense breasts. *Eur Radiol.* 2010;20:734–742.
- [41] Gartlehner G, Thaler K, Chapman A, Kaminski-Hartenthaler A, Berzaczy D, Van Noord MG, Helbich TH. Mammography in combination with breast ultrasonography versus mammography for breast cancer screening in women at average risk. *Cochrane Database Syst Rev.* 2013;4:CD009632.
- [42] Breast cancer treatment, the breast cancerInfo.com. [21 May 2017]. http://thebreastcancerinfo.com/breast_cancer_treatment.htm
- [43] Surgical oncology. UT health science center. 2009. Sep 24, [21 May 2017]. <http://www.surgery.uthscsa.edu/surgicaloncology/breast.asp> .
- [44] Rath G. K. Radiation Therapy in the Management of Cancer. 50 Years of Cancer Control in India. [21 May 2017]. <http://mohfw.nic.in/pg96to104.pdf> .
- [45] Detailed guide: Breast cancer radiation therapy. American cancer society. 2009. Sep 18, [21 May 2017]. http://www.cancer.org/docroot/CRI/content/CRI_2_4_4X_Radiation_Therapy_5.asp?sitearea .
- [46] Breast health chemotherapy for breast cancer treatment. [21 May 2017];University Virginia Health System. 2006 Aug 29; http://www.healthsystem.virginia.edu/uvahealth/adult_breast/chemo.cfm .
- [47] Cancer. Wellness.com. 2006-2010. [21 May 2017]. <http://www.wellness.com/reference/conditions/cancer/prevention-and-treatment>.