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Perspective

Fighting Breast Cancer with the Aid of Artificial Intelligence: A Big Challenge

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Introduction

According to BREASTCANCER.ORG (http://www.breastcancer.org/), "Breast cancer is always caused by a genetic abnormality (a "mistake" in the genetic material). However, only 5-10% of cancers are due to an abnormality inherited from your mother or father. Instead, 85-90% of breast cancers are due to genetic abnormalities that happen as a result of the aging process and the "wear and tear" of life in general".

Breast cancer, a global problem

According to official statistics, in the U.S. about 12% of women will develop invasive breast cancer over the course of their lifetime, and an estimated 246,660 new cases of invasive breast cancer are expected to be diagnosed in women in 2016. According to the World Health Organization, breast cancer is the top cancer among women, both in the developed and the developing world (19.3 per 100,000 women in Eastern Africa to 89.7 per 100,000 women in Western Europe) (http://www.who.int/cancer/detection/breastcancer/en/) According to the U.S. Department of Defense, Breast Cancer Research Program, February 2016 (http://cdmrp.army.mil/bcrp/pdfs/bc_landscape.pdf), worldwide, breast cancer accounts for nearly a quarter of all cancers in the female population. Besides the dramatic effect on people, breast cancer also has a huge impact on the health care system. Prevention is the key to reducing the emotional, physical, and financial burden of the disease.

Breast cancer incidence/recurrence/deaths

Statistically, according to CANCER TODAY- International Agency for Research on Cancer-IARC (http://globocan.iarc.fr), the data (estimated incidence, mortality and 5-year prevalence: women) show that: (*a*) there were about 1.7 million person diagnosed in 2012, and (*b*) there were about 522,000 deaths globally in 2012 (http://globocan.iarc.fr/Pages/fact_sheets_population.aspx). In 2035, with no major changes in prevention or treatment, it is estimated that 846,241 women will die from breast cancer worldwide. An estimated 20% to 30% of women diagnosed with invasive breast cancer will have a recurrence and may eventually die of their disease (http://cdmrp.army.mil/bcrp/pdfs/bc_landscape.pdf). Breast cancer can recur at any time or not at all, but most recurrences happen in the first 5 years after breast cancer treatment.

Survivorship

Most people diagnosed with breast cancer will live for many years. According to the American Cancer Society (http://www.cancer.org/cancer/breastcancer/detailedguide/breast-cancer-survival-by-stage), the 5-year relative survival rate for women with stage 0 or stage I is close to 100%, and the metastatic, or stage IV breast cancers, have a 5-year relative survival rate of about 22%.

Socioeconomic, race/ethnicity, cultural factors for breast cancer

Women are at higher risk of breast cancer if they have higher socioeconomic status (SES) or live in higher SES or urban communities [1]. In the past, breast cancer mortality was higher among African American women than among white women in the US. Cultural factors such as folk beliefs, fundamentalist religious beliefs, fatalism, etc. are significantly correlated with late-stage disease [2].

Fighting breast cancer

The large and increasing burden of breast cancer demands innovative research and bold new approaches to uncover the intricate combination of factors inside and outside the body that lead to the disease. There are currently approaches at national level in different countries to fight breast cancer. The U.S. Congress established in 2008 the

Public Law No. 110-354 "*Breast Cancer and Environmental Research Act*" (https://www.gpo.gov/fdsys/pkg/PLAW-110publ354/pdf/PLAW-110publ354.pdf). The U.K. Department of Health revealed the "*NHS Breast Screening Programme*" (https://www.gov.uk/guidance/breast-screening-programme-overview). The Direction Générale de la Santé (France) established a national screening program for breast cancer (http://www.has-sante.fr/portail/jcms/c_1741170/fr). The "*Nationalen Krebsplans*" (http://www.bmg.bund.de/themen/praevention/nationaler-krebsplan.html) for breast cancer screening was adopted in Germany. Last but not least, in Europe, the program "*European Partnership for Action Against Cancer* (EPAAC)" concluded in 2014 and was followed by "*Development of the European Guide on Quality Improvement in Comprehensive Cancer Control* (Cancon) (http://www.europeancancerleagues.org/ewac/european-partnership-action-against-cancer.html).

Current problems and limitations in breast cancer research

(1) lack of financial and practical resources, (2) poor collaboration between disciplines, (3) relatively insufficient knowledge on: genetic changes, initiation of breast cancer, progression of breast cancer, therapies, disease markers, strategies for prevention, and psychosocial aspects [3].

Costs of care

According to the U.S. National Cancer Institute (http://www.

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cancer.gov/), the expenditures for breast cancer in 2010 was estimated as $16.5 billion. The expenditures for breast cancer in 2012 was estimated as £1.5 billion in the U.K. (BBC: http://www.bbc.com/news/health-20222759). Breast cancer accounted in 2009 for the highest cost of all cancers in Europe (€6.73 billion) [4].

Fighting Breast Cancer with the Aid of Artificial Intelligence

Artificial intelligence (AI) is a powerful tool for detecting very early stages of breast cancer because it can "look" at all data collected from patients, data contained in huge medical databases, and can use the whole knowledge regarding the correct diagnosis of experienced physicians, also provided by the databases.

Breast cancer diagnosis improved with help from Artificial Intelligence

Relatively novel approaches developed within AI have brought new gateways in breast cancer diagnosing process. According to SCIENCEDAILY (https://www.sciencedaily.com/releases/2016/06/160620085204.htm), "A research team from Beth Israel Deaconess Medical Center (BIDMC) and Harvard Medical School (HMS) recently developed artificial intelligence (AI) methods aimed at training computers to interpret pathology images, with the long-term goal of building AI-powered systems to make pathologic diagnoses more accurate." The goal in most breast cancer AI-based diagnosis is to predict malignant vs. benign tumors to aid in biopsy decisions. Finding an algorithm to provide the highest possible accuracy for breast cancer diagnosis is the "holy grail" of all AI techniques.

Limits of the current approaches in the context of the state-of-the-art in the computer-aided cancer research

The effectiveness of computer-aided detection (CAD) systems in diagnosing early breast cancer has received a lot of attention over the years. The first U.S. Food and Drug Administration (FDA)-approved CAD system for mammography was the R2 Image Checker M1000 (P970058/1998, U.S. FDA). Since then, various computer technologies based on AI algorithms have been the subject of intense research. According to the recent PubMed results regarding the subject of AI and cancer, more than 7510 articles have been published until today, many of them focused on breast cancer [5]. A large variety of AI techniques (e.g., Artificial Neural Networks, Support Vector Machines, committee machines, hybrid algorithms, etc.) have been widely applied for detection, recurrence, survivability, and an improvement of 15-25% of cancer prediction accuracy has been observed [6]. The accuracy of the classification process has been reported most often either as percentage (of correct predictions) or as area under the curve (AUC). A very recent survey [5], based on two prestigious electronic databases, namely PubMed and Scopus, reported that, depending on type of data, dataset size and algorithm, accuracy ranged between 69%-97%, and 0.851-0.965 (AUC). However, the major limitations of current approaches consist of: (*a*) the small amount of data samples (dataset size), (*b*) the dataset quality, (*c*) the feature selection (FS) methods (setting of a reliable hierarchy of the most significant predictive features), (*d*) the possibility of validating the model's performance with external datasets from other sources, as alternatives to internal validation (*e*) the appropriate integration of different types of data (e.g., clinical, genomic, histological, imaging, demographic, epidemiological, proteomic data or different combinations).

Despite the relatively high number of studies on using AI techniques in the breast cancer research, very few have actually penetrated the clinical practice. Accordingly, more research is needed to overcome these limitations before the methodology can be useful in the clinics.

Future developments

In our opinion, future projects devoted to further and deepen the breast cancer research using the AI aid have to envisage two main objectives: (*a*) *R&D interdisciplinary studies* between clinical breast cancer research and AI, and (*b*) *Young researchers' collaboration and partnership*, building a solid framework of common scientific research between young researchers.

Impact of future developments

Intelligent decision support systems (IDSS) have been recently promoted as one of the key features leading to a real step forward in health care assisted by the latest AI technologies. The ideas presented above belong to a long-run multi-objective research challenge targeting both theoretical and practical points of view, and covering the breast cancer research through the development and implementation of efficient IDSS. The impact of such developments resides in: (1) *scientific impact*, (2) *healthcare impact*, (3) *economic impact*, (4) *social impact*, (5) *environmental impact*, (6) *human resource impact*.

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