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Review Article

Harnessing innovation for the future of breast cancer management

Tamer A. Addissouky[1,2,3,*], Ibrahim El Tantawy El Sayed[2], Majeed M. A. Ali[1], Mahmood Hasen Shuhata Alubiady[1], Yuliang Wang[4]

[1]Al-Hadi University College, Baghdad, Iraq

[2]Department of Biochemistry, Science Faculty, Menoufia University, Menoufia, Egypt

[3]MLS ministry of health, Alexandria, Egypt. - MLS ASCP, USA.

[4]Joint International Research Laboratory of Metabolic and Developmental Sciences, Key Laboratory of Urban Agriculture (South) Ministry of Agriculture, Plant Biotechnology Research Center, Fudan-SJTU-Nottingham Plant Biotechnology R&D Center, School of Agriculture and Biology, Shanghai Jiao Tong University, Shanghai, China

*Authors for correspondence:
Email: tedesoky@gmail.com; tedesoky@science.menofia.edu.eg

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Abstract

Background: Breast cancer remains a major global health burden despite therapeutic advances, necessitating further innovations to address persistent challenges like therapeutic resistance, adverse effects, and mortality in subgroups. Emerging technologies offer promising opportunities in this regard through data-driven, precise, and personalized approaches.

Main body: Omics-guided therapies leverage genome, epigenome, and other profiling to enable better characterization of complex cancer molecular alterations driving selection and monitoring of tailored treatment regimens. Gut microbiome manipulation via probiotics, prebiotics or fecal transplantation aims to counter dysbiosis linked to breast cancer progression. Nanotechnology-engineered platforms offer smart drug delivery selectively to tumors and integrated diagnostic-therapeutic functions. Artificial intelligence algorithms analyze complex datasets and images to extract detailed quantitative signatures guiding prognostic decisions and personalized care. Traditional Chinese medicine encompassing herbal remedies and acupuncture demonstrates anticancer effects in preclinical models, with early trials exploring integration with chemotherapy.

Conclusion: Substantial progress has been made in breast cancer management, yet significant unmet needs persist. Emerging modalities have shown tremendous translational potential through molecularly targeted, immunomodulatory, data-driven approaches improving upon conventional methods regarding precision, effectiveness, and quality of life. Incremental integration of these innovative technologies promises to transform breast cancer care.

Keywords: Breast cancer, Precision oncology, Omics microbiome, Nanotechnology, Artificial intelligence, Traditional Chinese medicine

Background

Breast cancer is the most commonly diagnosed cancer and the second leading cause of cancer-related mortality in women worldwide. Incidence rates continue to rise globally. Breast cancer encompasses a heterogeneous group of tumors with varying molecular features, clinical behaviors, and responses to therapy. While survival rates have improved, challenges persist such as invasive cancers, recurrent metastatic disease, and mortality among subgroups [1-2].

The current clinical management of breast cancer involves surgery combined with systemic chemotherapy, radiation, endocrine and targeted therapies. These interventions have substantially improved prognosis, yet intrinsic and acquired resistance remains problematic. Chemotherapies and radiation are associated with adverse effects impacting quality of life. Additionally, optimal protocols for breast cancer subtypes and high-risk groups warrant further research. Substantial drug costs also limit access to cutting-edge treatments. Overall, there is impetus to develop more precise, effective, and well-tolerated approaches through emerging technologies that build upon foundational breast cancer therapies [3-6].

This review thoroughly examines latest high-potential modalities including omics profiling, immune-directed vaccines, microbiome alteration, nanotherapeutics, artificial intelligence, and traditional medicines for future breast cancer solution development. Synthesizing across these cutting-edge areas elucidates promising near-term prospects to tackle disease heterogeneity, therapeutic resistance, adverse effects, accessibility, and precision demands - bridging gaps left by current gold standards to guide next-generation treatment and monitoring.

Emerging Vaccine Approaches

Cancer antigen vaccines

Vaccines targeting tumor-associated antigens (TAAs) or neoantigens have shown promising results in early preclinical and clinical studies for breast cancer. TAAs are antigens produced by tumor cells that can elicit an immune response. Neoantigens arise from somatic tumor mutations and are unique to an individual's cancer. Animal models have supported the immunogenicity and protective capacity of TAA and neoantigen-directed vaccines. Early phase clinical trials in breast cancer patients have demonstrated safety and the ability to generate antigen-specific T-cell responses after vaccination [7-11].

Tumor-associated antigens, neoantigens: Tumor cells express antigens that are either normal self-antigens overexpressed in tumors or novel antigens created by mutations. Both categories can be leveraged as targets for cancer vaccines. Preclinical studies have identified various TAAs that could serve as vaccine targets in breast cancer. Neoantigens tailored to a tumor's mutation profile also represent highly specific targets [12,13].

Animal models, early clinical trials: Animal models including mice and non-human primates have been utilized to establish proof-of-concept for vaccines targeting TAAs such as HER2. Findings have indicated vaccines can induce antigen-specific immunity that impacts tumor growth. Early clinical evaluation has progressed to phase I and II trials exploring safety and immunogenicity. Small randomized trials have suggested clinically meaningful benefits in patients with breast cancer [14-18]. As depicted in **Figure 1**, stem cells have emerged as a promising source for engineering 3D organoid models

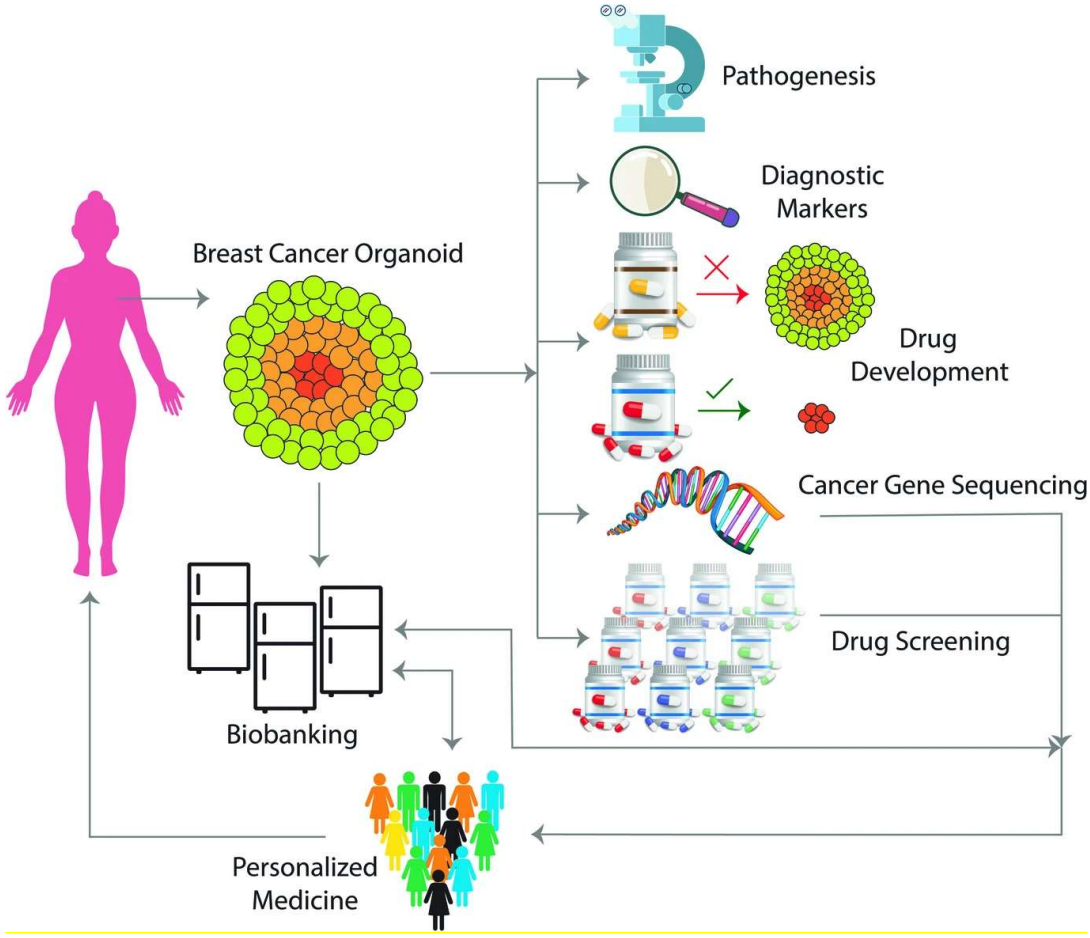

Figure 1: personalized drug screening and precision oncology applications [19].

that recapitulate the complex structure and function of organs with high fidelity. Studies demonstrate that stem cells are more stable than differentiated cells, enabling the formation of heterogeneous populations containing stem, differentiated, and functional cell types that accurately model tissue physiology and pathology [19].

DNA vaccines

DNA vaccines involve direct injection of genetically engineered DNA to produce target antigens. This approach allows *in vivo* production of antigens to activate the immune system. DNA vaccines are relatively stable, cost-efficient, and safer compared to other vaccine platforms. Evidence for DNA vaccines comes from animal models and human clinical trials are ongoing [20,21].

Vector-based anti-cancer vaccines

Viral vectors including adenovirus, vaccinia, and others have been engineered as anti-cancer vaccines. They can induce robust T cell responses due to natural adjuvanticity. Vector-based methods demonstrate protection against tumor progression in preclinical breast cancer models. Several phase I/II trials indicate safety and immunogenicity, with evidence of clinical responses [22-24].

Omics-Guided Therapies

The development of advanced "omics" technologies that permit high-throughput analysis of the genome, epigenome, transcriptome, proteome, and metabolome have enabled better characterization of the complex molecular alterations driving breast cancer. Leveraging omics approaches has facilitated more precise therapy selection, monitoring of treatment response, and identification of new therapeutic targets and agents.

Genomics: mutation profiling, microarrays

Genomic analysis examining mutations, polymorphisms and expression changes associated with breast cancer has uncovered molecular subtypes, prognostic gene signatures for personalized treatment, and actionable alterations matching targeted drugs. Genome sequencing and DNA microarrays now allow comprehensive examination of the genetic basis of a patient's cancer [25-27].

Epigenomics: miRNA, DNA methylation, histone modifications

The study of epigenomic modifications regulating gene expression has revealed new biomarkers and therapeutic opportunities in breast cancer. Aberrant miRNA levels, altered DNA methylation, and histone modification patterns are linked to tumor progression and response to certain therapies. Epigenetic signatures are emerging to guide management and counter drug resistance [28,29].

Proteomics/metabolomics: Biomarkers, insights into pathogenesis

Advances in proteomic and metabolomic profiling have enabled detection of protein and metabolic signatures associated with breast cancer initiation, diagnosis, staging, and treatment outcomes. Novel proteomic approaches can identify circulating tumor cells and tumor-educated blood platelets revealing protein biomarkers. Metabolomics examines metabolic reprogramming in cancer cells. Together, these strategies provide insights about pathological changes as well as biomarkers detectable in liquid biopsies [30-35].

Applications for therapy selection, monitoring, novel targets.

Omics information can assist in matching patients with tailored treatments, monitoring therapeutic response, and revealing new drug targets. For example, genomic tests identify candidates for HER2-targeted therapy. Signatures are emerging to predict immunotherapy efficacy. Metabolomics reveals stem-cell dependent metabolic pathways against which drugs could be directed. Integrative analysis of multi-omics data may have the greatest utility for precision oncology applications [36.37].

Microbiome Manipulation

The human microbiome has emerged as a modulator of anti-cancer immune responses. There is growing evidence that the gut microbiota influences breast cancer risk and progression, representing a new target for prevention and therapy. Modifying the microbiome through probiotics, prebiotics, bacteriotherapy or fecal transplantation may confer anti-tumor effects.

Gut microbiota dysbiosis in breast cancer

Compared to healthy women, breast cancer patients exhibit gut microbiota imbalance or dysbiosis characterized by decreased bacterial diversity and alterations in the abundance of certain bacteria. Dysbiosis disrupts microbiome interactions with host immunity. Animal models support direct pro-tumorigenic microbial effects promoting breast cancer growth and metastasis [38-39].

Probiotics, prebiotics, bacteriotherapy

Strategies that increase levels of anti-inflammatory and anti-cancer phytochemical-producing bacteria may counter breast cancer-associated microbiota changes. Probiotic supplements can modulate gut dysbiosis and inhibit tumor progression in preclinical breast cancer models. Prebiotics promote the expansion of protective resident microbes. Bacteriotherapy involves oral consumption or injection of microbial strains with anti-tumor capabilities [40-45].

Fecal microbiota transplantation

Introducing fecal material from healthy donors into breast tumor–bearing mice delays tumor growth and enhances immune surveillance through normalization of gut microbiota. Early clinical research on fecal microbiota transplantation in cancer patients shows potential to attenuate common treatment side effects as well as modify anti-tumor immunity [46,47].

Nanotechnology-Based Precision Approaches

Nanotechnology-engineered devices and systems have shown tremendous potential to improve the precision of breast cancer diagnosis and therapy. Nanoparticle delivery platforms can transport therapeutics selectively to tumors, overcome drug resistance mechanisms, and integrate both imaging and therapeutic functions into unified "theranostic" systems.

Smart nanoformulations for chemotherapeutics

Conventional chemotherapies have limitations in water insolubility, lack of tumor specificity and dose-limiting systemic toxicities. "Smart" nanoformulations such as liposomes, dendrimers, nanogels and polymeric nanoparticles can encapsulate chemotherapeutics to improve pharmacokinetics and biodistribution, target tumors through surface modification, and enable controlled drug release at tumor sites through engineered biomaterials and

external triggers. This increases intratumoral drug delivery and antitumor efficacy while reducing off-target effects [48-50].

Theranostic nanoparticles

"Theranostic" nanoparticles with both imaging and drug delivery capabilities permit spatiotemporal monitoring and individualized optimization of therapy. By integrating modalities like fluorescence dyes, radioisotope labeling, Raman imaging and MRI contrast, nanoparticles can provide real-time insight into *in vivo* behavior. An early example is the FDA approval of Abextram, a liposomal nanoformulation harboring an imaging agent and doxorubicin for metastatic breast cancer treatment [51,52].

Applications in combination therapy, drug resistance

Nanotechnology platforms have potential to improve combinatorial treatments and counter breast cancer drug resistance. Co-delivery of synergistic chemotherapeutic combinations using a single nanoparticle carrier may maximize efficacy. Strategies are also being developed to target nanoparticles to breast cancer stem cells responsible for tumor regeneration and therapeutic recalcitrance. Overall, multifunctional nanoparticle technologies offer opportunities to overcome existing challenges in breast cancer management [53-56].

Artificial Intelligence and Breast Cancer Management

Artificial intelligence (AI) encompasses advanced analytical techniques enabling machines to perform tasks mimicking human cognition and decision making as depicted in **Table 1**. The application of AI is transforming all aspects of breast cancer care from risk assessment to treatment.

Medical imaging analysis

AI algorithms can rapidly analyze complex medical images and extract detailed quantitative data surpassing human capability. Machine learning has enabled automated breast cancer screening and improved diagnostic accuracy from mammograms and histopathology. AI applied to medical imaging data identifies subtle signatures correlated with genomics and clinical outcomes [57,58].

Predictive biomarkers and multiomics integration

Machine learning tools integrating complex molecular and clinical variables have defined prognostic signatures guiding precision treatment strategies. AI modeling of tumor genomic and transcriptomic profiles predicts response to targeted therapies and immunotherapies. Hybrid AI techniques show promise for reconciling multi-dimensional omics datasets to uncover biologically relevant patterns in breast cancer [59-62].

AI-based clinical decision support systems

AI-powered clinical decision support systems integrate patient health records with real-time data analytics to assist physicians with personalized treatment planning. Pilot studies indicate AI recommendation systems can promote evidence-based breast cancer therapy selection and comorbidity management. AI-based methods may enhance risk modeling for adequate patient screening and enable optimized medication dosing [63,64].

Traditional Chinese Medicine

Traditional Chinese medicine (TCM) encompasses a range of long-used therapeutic practices including herbal remedies, acupuncture and dietary measures that have shown promise as adjuvant treatments for breast cancer as depicted in **Table 2**. Commonly used Chinese herbs and formulations demonstrate antitumor effects in preclinical models. Ongoing studies are exploring the integration of TCM with conventional chemotherapy regimens.

Commonly used herbs and formulations

Chinese medicinal herbs and mixtures with historical applications against malignancies are being investigated for breast cancer management. Notable single herbs include *Astragalus mongholicus*, *Tinospora cordifolia*, and *Scutellaria barbata*. Composite formulations such as Ren Shen Yang Rong Tang, *Yindan Jiedu* granules and Huachansu injection also exhibit anticancer activities in breast cancer models [65,66].

Anti-cancer effects and mechanisms of action

Laboratory studies indicate commonly used Chinese medicinal plants mediate cytotoxic, pro-apoptotic, anti-proliferative, anti-angiogenic, anti-inflammatory, and immunostimulatory responses in breast cancer cells and animal models. Extracts and isolated compounds modulate gene expression and signaling pathways associated with tumor progression and treatment sensitivity. Findings support both direct antitumor effects and immunomodulatory mechanisms [67,68].

Clinical trials of herbs with chemotherapy

Early phase trials demonstrate safety, positive impacts on

Table 1. Artificial intelligence technologies across the breast cancer management.

AI Technology	Application	Purpose	Development Stage
Deep learning image analysis	Automated screening mammography	Early breast cancer detection	FDA-approved algorithms, improved cancer detection over human review in studies
Convolutional neural networks	Histopathology image classification	Diagnosis and subtype categorization	Algorithms approaching pathologist-level accuracy, integration into hospital workflows
Multi-layer neural networks	Risk modeling with clinical datasets	Assessment of prognosis, recurrence risk	Validation ongoing in retrospective patient cohorts
Random forest models	Gene expression signature analysis	Prediction of relapse, treatment response	Commercially available prognostic tests guided by AI-derived biomarkers
Deep reinforcement learning	Treatment recommendation systems	Evidence-based guidelines for precision therapy	Pilot studies demonstrating feasibility to optimize regimens accounting for patient factors

Table 2. Traditional Chinese medicines exhibited antitumor effects in preclinical studies.

TCM Type	Herb/Formula Examples	Preclinical Anti-Cancer Effects	Clinical Trial Stage with Chemotherapy
Single Herbs	Astragalus, Tinospora cordifolia, Scutellaria barbata	Cytotoxic, pro-apoptotic, anti-angiogenic, immunomodulatory	-
Composite Formulas	Ren Shen Yang Rong Tang, *Yindan Jiedu* granules, Huachansu injection	Inhibit tumor growth, modulate signaling pathways	Early phase trials of Huachansu plus chemotherapeutics: improved response, survival
Acupuncture	-	Anti-inflammatory effects in breast cancer models	Phase II trials show reduced side effects of aromatase inhibitors
Dietary Therapy	Lingzhi mushroom	Stimulate immune cytokines, induce cancer cell apoptosis	-

quality of life, and potential anticancer activity of herbal additions to conventional chemotherapy. For example, Huachansu injection combined with chemotherapeutics was well-tolerated while appearing to improve tumor response and survival outcomes compared to chemotherapy alone. Larger randomized trials are still needed to conclusively evaluate combinations of Chinese herbal components with standard breast cancer regimens [69,70].

Future Directions and Limitations

Despite recent advances, significant challenges remain in breast cancer management warranting further research. More definitive phase III trials with larger patient cohorts are required to validate preliminary findings and conclusively determine clinical efficacy of emerging approaches like microbiome, nanotechnology, and AI-based interventions. Their real-world feasibility and health economics should also be established.

Predictive biomarker development and advanced bioinformatics analytics will be pivotal to realize precision oncology applications of multi-omics profiling. Integrative analysis of heterogeneous datasets remains difficult, and predictive signatures still require prospective clinical confirmation. Novel machine learning techniques show promise to distill meaningful biological patterns from noisy high-dimensional omics and imaging data [71,73].

Cancer antigen vaccines and immunotherapies face obstacles such as suboptimal immunogenicity, immunosuppressive mechanisms limiting efficacy, and risk of autoimmunity which should be key areas of focus. Both preclinical models and clinical trials must better recapitulate native immune microenvironments to enable translational success [74,75]. More research into microbiota dysbiosis and diet in breast cancer can help guide tailored therapeutic manipulation of the gut ecosystem [76]. Effects of traditional herbs require elucidation of bioactive compounds and mechanisms of action to allow pharmacologic optimization. Legal and regulatory hurdles also constrain the integration of complementary medicine despite early signals of benefit [77].

Conclusions

While substantial progress has been made in breast cancer management with conventional therapeutic approaches, significant unmet needs persist including disease relapse, adverse effects, and mortality among high-risk subgroups. Emerging modalities such as omics-based biomarkers, cancer vaccines, microbiome/nutrition manipulation, nanotherapeutics, artificial intelligence, and traditional medicines have shown tremendous translational potential to address existing challenges through data-driven precision diagnosis/prognosis and molecularly targeted, immunomodulatory, personalized interventions with favorable safety profiles. Thoughtful integration of these innovative technologies with current breast cancer care strategies can facilitate incremental improvements in risk stratification, early detection, therapeutic selection for precision oncology, monitoring of treatment response, as well as discovery of fresh targets and agents as summarized in **Table 3**.

Table 3. Emerging modalities for enhancing breast cancer management.

Emerging Modality	Key Components	Mechanism of Action	Current Development Stage
Cancer Antigen Vaccines	Tumor-associated antigens (TAAs), Neoantigens	Stimulate immune response against antigens on tumor cells	Preclinical animal models show therapeutic potential, early phase clinical trials demonstrate safety and immunogenicity
DNA Vaccines	Engineered DNA injected to produce tumor antigens *in vivo*	Antigen production activates anti-tumor immunity	Preclinical efficacy established; phase I/II human trials ongoing
Vector-based Vaccines	Viruses engineered to express TAAs	Robust cytotoxic T cell response due to natural viral adjuvanticity	Protective capacity and safety evidenced in animal models, phase I/II evaluation of patient immunogenicity and clinical impact
Omics-Guided Therapies	Genomics, epigenomics, proteomics, metabolomics	Molecular profiling guides therapy selection and reveals targets	Commercially available tests match patients with targeted drugs based on genomic/proteomic signatures
Microbiome Manipulation	Probiotics, prebiotics, bacteriotherapy, fecal transplant	Restore anti-inflammatory commensal bacteria depleted in cancer	Preclinical studies demonstrate anti-tumor immune modulation, synergy with immunotherapy, early-phase patient trials

Nanotechnology Platforms	Smart nanoparticles, combination drug nanoformulations, theranostics	Selective tumor targeting, controlled drug release, integration of therapeutic & diagnostic features	Preclinical evidence of enhanced pharmacokinetics, biodistribution and antitumor efficacy, some nanoparticle formulations FDA-approved
Artificial Intelligence	Medical imaging analysis, multi-omics integration, clinical decision support	Advanced machine learning analytics extract clinically meaningful patterns	Pilot studies indicate improved diagnostic accuracy, prognostic predictions, and personalized treatment recommendations

Recommendations

Moving forward, it is recommended that the most promising emerging breast cancer technologies proceed to definitive clinical evaluation through larger, randomized controlled trials to validate preliminary findings, conclusively establish clinical added value over standard management, and assess real-world feasibility. Development of predictive biomarkers and advanced analytics will be key to unlock the potential of high-dimensional "big data" approaches. Regulatory infrastructure and scientific consensus should be proactively developed to enable responsible translation of new modalities. Importantly, next-generation solutions must remain human-centric regarding accessibility, financial burden, and quality of life. Keeping patients at the center of future innovations will ensure breast cancer care continues to advance towards more precise, effective, and compassionate practice.

List of Abbreviations

TAA: Tumor-Associated Antigen; HER2: Human Epidermal Growth Factor Receptor 2; miRNA: MicroRNA; MRI: Magnetic Resonance Imaging; FDA: Food and Drug Administration; AI: Artificial Intelligence; TCM: Traditional Chinese Medicine

Declarations

Ethics approval and consent to participate

Not Applicable.

Consent for publication

Not Applicable.

Availability of data and materials

All data is available, and sharing is available as well as publication.

Competing interests

The authors hereby declare that they have no competing interests.

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Authors' contributions

The authors completed the study protocol and were the primary organizers of data collection and the manuscript's draft and revision process.

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