Proceedings of ICBioMed 2026 Symposium: Biomedical Engineering and Public Health: Real-Time Wearables for Disease Detection
DOI: 10.54254/2753-8818/2026.ES37820

Hydrogels in Breast Cancer Therapy: Applications and Recent Advances

Kerui Yang

Naval Medical University of Basic Medicine, Shanghai, China
3326384732@qq.com

Abstract. Breast cancer, which is the most common malignancy in the world for women, has been an enormous burden on human's health. The traditional multimodality therapy, including chemotherapy or radiotherapy are challenged with drug resistance, recurrence, metastasis and systemic toxicity. Hydrogels are 3D cross-linked polymeric network having a high water contents and combines injectability, ECM-mimicking structure, and smart response to pathological microenvironment, offering versatile platforms for treating breast cancers. Herein we summarize the recent progresses on using hydrogels in breast cancer treatment. Firstly, the classification of hydrogels by materials origins and environment response is given out, together with a discussion about the strategy in designing functions or controlling drug loading. We next review the four main therapeutic applications, namely: Localized and Sustained Chemotherapy for achieving high local concentration of drugs without causing much toxicity; combined photothermal-photodynamic therapy for the spatiotemporal-controlled tumor ablation; immunomodulation and tumor microenvironment reprogramming for enhancing systemically antitumor immune response; and combined postoperative tumor control, tissue repair, and reconstruction. Last but not least, we summarize some key benefits from using hydrogels for spatiotemporal drug control, multimodal therapeutic synergy, and functionally integrated, when talking about present-day challenges, such as exact matching of the degradation and drug release kinetics and individualization. Future directions, including gene–drug–cell co-delivery systems and intelligent theranostic hydrogels, are also discussed.

Keywords: hydrogels, breast cancer, drug delivery, anti-tumor

1. Introduction

Breast Cancer is the most common cancer diagnosis in Women around the world, and it is one of the main global burden to the human's health. Global cancer statistics 2022 shows breast cancer contributed to 11.6% of total new cancer cases and 6.9% of cancer deaths, and it was the primary cause of cancer death among women in 112 countries, notably, for having a major global disease burden and geographic disparity [1]. Multimodality treatment in the clinic today for breast cancer includes surgery, chemotherapy, radiotherapy, endocrine therapy, targeted therapy and immunotherapy. Nevertheless, drug resistance, recurrence and metastasis are still the main problems restricting its long-term therapeutic effect [2].

© 2026 The Authors. This is an open access article distributed under the terms of the Creative Commons Attribution License 4.0 (https://creativecommons.org/licenses/by/4.0/).

DOI: 10.54254/2753-8818/2026.ES37820

Hydrogels are 3D cross-linked polymeric structures consisting of hydrophilic macromolecular chains. Due to the high water-holding ability, injectability, and ECM-mimetic scaffolds, hydrogels present distinct advantages to delivering therapeutics as well as cells. Their pore size, swelling behaviour, mechanical property and rate of degradation could be tuned for facilitating encapsulation and controlled release of therapeutic cargo in a way that protects it against adverse physiological environment, thus improving the local therapeutic effect [3]. Specifically, their capability of forming drug depots at the tumor site and responding to pathological microenvironmental signals render hydrogels attractive platforms for localized and multimodal cancer treatment [4, 5]. Herein we provide a review of the most recent progresses toward hydrogel based strategies to treat breast cancers and highlight its functional design, applications in therapy, and perspectives towards the clinical use.

2. Classification and functional design of hydrogels

According to the origin of their materials, hydrogels could generally be divided into natural and synthetic polymer-based hydrogels. The former includes gelatin, collagen, hyaluronic acid, and alginate. These tend to be highly cytocompatible and enzymatically degradable, yet typically suffer from low mechanical strength and high batch-to-batch variation. They are widely utilized for the encapsulation of macromolecular therapeutics (e.g., proteins and growth factors) by means of a physical entrapment, where the main mechanism of drug release is mainly controlled via diffusion and enzyme degradation. The synthetic polymeric hydrogels such as polyethylene glycol (PEG), acetate-based copolymers, and polyacrylamide. They provide exactly controllable chemical structure and tunable mechanical properties but usually have no intrinsic bio-signals. Thus they may be further functionalized with degradable crosslinking sites/reactive groups to allow for covalent drug conjugation and better control of the rate of drug release [4].

Based on the sensitivity of response to the environment, hydrogels could be categorized as common or stimulus-sensitive hydrogels. Common hydrogels show a drug-releasing pattern which is almost independent from any change in the surrounding environment; this releasing process is controlled mainly through free diffusion. In contrast, stimuli responsive hydrogels are able to detect endogenous/exogenous signals (temperature, pH, enzyme, light, ionic strength, and magnetic field to enable ondemand therapeutic release [5]. Swelling may be induced by changes in such stimuli: collapse, i.e., collapse of the hydrogel network or its phase transition. These transformations are mainly controlled by interactions between polymer chains as well as between polymers and solvents; the chemical structure of the network constituents determines the strength and sensitivity of such interactions [6].

The hydrogel material is also quite flexible when it comes to drug-loading approaches: firstly, there is physical encapsulation which exploits both the high water content as well as the mild gelation conditions for entrapping a therapeutic agent during network formation. Here again no chemical modification of the cargo needs to be performed; moreover this strategy may even assist in preserving the structure and biological activity of some sensitive biomolecules [7].Second, chemical conjugation attaches the therapeutics onto the hydrogel backbone via a degradable covalent bond (e.g., an ester linkage or an enzyme-sensitive peptide), which could be cleaved under certain pathological stimuli, such as acidity or high reactive oxygen species (ROS) level of tumour environment for a sitespecific and controlled drug release [8].

Hydrogels may also modulate sustained release kinetics through the adjustment of network mesh size, crosslinking density, and degradation rate [9]. Stimuliresponsive systems may also be used to detect pathologies: such as lowered pH, high temperature, or over expression of certain enzymes,

DOI: 10.54254/2753-8818/2026.ES37820

and can act as molecular switches that trigger the therapeutic release at desired locations and times [10].These features of programmable release can potentially be extended to include pulsatile or even sequential drug release and thus offer the potential of synchronized cancer therapy over time [5].

3. Major applications of hydrogels in breast cancer therapy

3.1. Localized and sustained chemotherapy

Conventional intravenous chemotherapy results in extensive systemic drug distribution, which may lead to insufficient drug exposure at the tumor site while causing systemic adverse effects, including bone marrow suppression and cardiotoxicity. When hydrogels are used as drug depots and directly implanted into postoperative cavities or injected intratumorally, therapeutic agents can be continuously released over several days to weeks through diffusion, matrix erosion, or degradation. This approach can substantially increase local drug exposure while reducing systemic toxicity [5].

Injectable stimuli responsive hydrogels also constitute an important platform for local chemotherapy. For instance, Gu et al. reported an injectable pH-responsive hydrogel with DOX and the BRD4 inhibitor JQ1 for combinational chemo-immunotherapy. The hydrogel facilitated prolonged drug release in response to the acidic tumour microenvironment and modulated local as well as systemic drug exposure, thus improving the therapy of poorly responsive tumors by immune checkpoint blockade, but also decreasing its systemically toxic effects [11].

In a separate research, they fabricated injectable and self-healing gelatin – PEG /Laponite hybrid hydrogel for local cancer therapy. DOX loaded Laponite NDs were introduced in to the hydrogel network, and the resulting system displayed pH-responsive drug release, with significantly increased cumulative DOX release in acidified conditions relative to that at physiological pH [12]. Our results thus show that hydrogel based drug depots can be used to harness the acidic tumor microenvironment in order to deliver locally acting, prolonged chemotherapy.

3.2. Combined photothermal and photodynamic therapy

Photosensitizers used for photodynamic therapy (PDT), are able to produce singlet oxygen and other reactive oxygen species when irradiated with light, thus inducing oxidative damage and tumor cell death [13]. PTT on the other hand relies upon photothermal agents that can absorb NIR light and transform it into local heat, leading to thermally damaged tumour cells and tumour associated vasculature [14].

Hydrogels could also enable combinatorial photothermal-photodynamic therapy through the encapsulation of photosensitizer, photothermal agent, and chemotherapy agents in the tumour locus for prolonged local retention and reduced early clearance; their high hydration volume can further enhance drug/dye dispersion and enable stimulus-responsive release. Thus, the hydrogels offer a useful platform to combine chemotherapy with photothermal and photodynamic therapy in a spatio-temporally coordinated fashion.

As an example, Han et al., constructed a NIR responsive drug-delivery nanoplatform that is based on UCNPs and mesoporous silica mSiO2. Under the influence of 980 nm NIR irradiation,hydrophobic 2-diazo-1,2-naphthoquinone (DNQ) to a hydrophilic 3-indenecarboxylic acid (ICA), which induced the opening of the nanovalve and enabled on-demand drug release [15]. While this system was not itself a hydrogel, it does provide an important design principle to incorporate NIR-triggered chemical switches in hydrogel-based delivery systems.

DOI: 10.54254/2753-8818/2026.ES37820

In another work, Liu et al. also fabricated an injectable and NIR-responsive DNA–UCNP–Au hybrid hydrogel with enhanced PTT via integrating DNA with inorganic NPs. This system demonstrated a high PTC efficiency (42.7%) and successfully inhibited tumor growth and recurrence upon 808 nm NIR irradiation [16]. All these works demonstrate that coupling stimuli-responsive delivery systems to a PTT-hydrogel platform can be used as an efficient strategy in order to obtain local, controlled treatment against cancer diseases.

3.3. Immunomodulation and tumor microenvironment reprogramming

Triple-negative breast cancer (TNBC) has the potential to create an extremely immunosuppressive environment by expressing molecules such as PD-L1 or recruiting regulatory T cells and/or tumour associated macrophages that are in a suppressive state (M2). This may prevent immune detection and clearance of malignant cells. Despite the fact that ICIs have shown to be clinically beneficial for a subset of patients, its effectiveness is still limited in many patients, and the systemic administration can lead to immune related side effects such as pneumonitis or colitis [17].

In these cases, a localized hydrogel-based delivery would have certain benefits since hydrogels could enable sustained release of ICIs (such as anti-PD-1/PD-L1 antibody), Direct administration of STING agonists/cytokines into the tumor bed to alter local immune microenvironment with minimal systemic exposure. In addition, the combination with radiotherapy, photothermal therapy or chemotherapy could lead to ICD, leading to the release of tumor-associated antigens and DAMPs, whose resulting inflammatory signals may promote DC activation and antigen presentation, thus promoting systemic anti-tumour T cell response and possibly better control of distant tumours [9].

Luo et al. fabricated a chitosan/β-glycerophosphate thermosensitive hydrogel loaded with MTO hydrochloride, at physiological temperature, the hydrogel was triggered with a phase change to achieve local release of MTO nanocrystals and MTO could produce PTEs as well as promote chemosensitivity under laser irradiation. MTO decreased thermal tolerance via DNA damage associated downregulation of heat shock protein 70, creating a chemo-photothermal synergistic effect to promote DAMP release and remodeling of immunosuppressive TME. Combined with anti-PD-L1 Ab, the treatment successfully suppressed both the growth of the primary tumour and that of its distant metastases [18].

Li et al. constructed a hydrogel as a co-delivery vehicle of CAR-T cell and a mitophagy agonist that remodelled local TME and improved mitochondrial function, thereby facilitating CAR-T cell expansion and anti-tumor response. Such a strategy greatly enhanced the effectiveness of immunotherapy for treating TNBC [19].

3.4. Postoperative tumor control, tissue repair, and reconstruction

Following breast-conserving surgery or mastectomy, residual microscopic disease remains an important concern because local recurrence can occur after surgical treatment [20]. At the same time, postoperative tissue defects and wound-healing processes create opportunities for developing local therapeutic platforms that can simultaneously control residual tumor cells and support tissue regeneration. Conventional tissue patches generally provide limited functionality and are unable to fully address the dual requirements of antitumor therapy and tissue repair.

As three-dimensional biomaterial scaffolds, hydrogels can physically fill tissue defects and support the structural integrity of postoperative cavities. Meanwhile, they can regulate the local wound microenvironment and provide prolonged retention of chemotherapeutic or

DOI: 10.54254/2753-8818/2026.ES37820

immunomodulatory agents through controlled release, thereby creating opportunities for simultaneous tumor control and tissue repair.

As another example, Wu and colleagues designed a magnetic injectable supramolecular hydrogel (MSH) as postoperative cancer therapy. The gel to sol transition, magnetic nanoparticle-mediated heating released the encapsulated chemotherapeutic agent, as well as induced thermally mediated tumour-cell damage. This combination of MSH mediated chemotherapy and thermotherapy was shown to be effective for prevention of post-operative breast cancer recurrence [21].

Liu et al., designed an in situ thermosensitive mRNA-loaded hydrogel that could modulate the postoperative tumor immune microenvironment to prevent recurrence and metastasis, it promoted a good macrophage phenotype balance and modulated local immunity; thus improving postoperative tumor control [22]. This suggests that multifunctional hydrogels could be a one-stop solution to postoperative tumor elimination, recovery from injury, disease or surgery; and/or recurrence prevention, and/or tissue repair.

4. Conclusions and perspectives

Hydrogel-based treatment for breast cancer has developed from a single function of delivering drugs to an advanced platform that combines functions including drug delivery, microenvironmental regulation, immunomodulation, and tissue engineering. The recent progress in these areas could be summarized into the following three major aspects Firstly hydrogels offer considerable spatio-temporal dosing benefits. By means of postoperative implantation or intratumor injection, chemotherapy drugs, photodynamic dyes or immune modulators could concentrate in tumour location and keep therapeutical concentrations over a long period, thus enhancing the local potency and reducing the general toxicities .Second, multimodal treatment modalities can combine the systemic toxic effect of chemotherapy with the spatiotemporally controllable tumor ablation of photothermal/photodynamic therapy, and the systemic immune activation caused by immune checkpoint blockade. Such integration might be beneficial in terms of synergy between different treatment modalities during one minimally invasive intervention. Thirdly, the recent studies have focused more on functional integration with simultaneous removal of residual tumour cells as well as promoting tissue repair and regeneration. In general, hydrogels can be used as targeted therapeutic systems in the treatment of breast cancer.

Despite these advances, there are still a number of key issues that must be addressed prior to clinical translation. First is the challenge of accurately coupling hydrogel degradation with drug release kinetics. Ideally, one would have enough drug release when the likelihood for recurrence is high, but then slowly degrade as the patient moves into the phase where tissue repair occurs. This level of dynamic control will necessitate further refinement in controlling network architecture and stimulus response. Second, personalized adaptation is underdeveloped. Tumour microenvironments and recurrence patterns differ greatly in different molecular subtypes and individuals, complicates the ability of any one hydrogel formulation to achieve optimal therapy in all clinical populations. Pathological and molecular data collected prior to operation, in order to accelerate the personalization of the drugs' formulation, must be part of future precision-based approaches: release rates.

In the future, it is likely that gene–drug–cell co-delivery system will be one of the directions in the development of multifunctional hydrogel platform. For instance, future devices might integrate CRISPRCas9 gene editing tools, small-molecule pro-drugs, and engineered T-cells onto the same hydrogel scaffold, to allow for synchronized gene regulation, chemosensitization, and immunological tumoricidal activity [23]. These systems might offer programmable, spatially-

DOI: 10.54254/2753-8818/2026.ES37820

confined control over multiple therapeutic modalities. Furthermore, intelligent theranostic hydrogels could be a promising direction in enabling the clinical translation, e.g., a TEMPO-loaded DNA hydrogel that can be used for combined treatment and early diagnosis of OA was developed; this showed the possibility of combining therapy with imaging-based monitoring of the disease in one system (hydrogel) [24]. These ideas may also be applied to the treatment of breast cancer in order to provide combined loco-regional therapy, follow-up for relapse, and treatment-response monitoring. Taken together, these developments could offer new avenues for developing and clinically translating hydrogel-based precision therapies in breast cancer.

References

[1] Bray, F. *et al.* Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA. Cancer J. Clin., 74*, 229–263 (2024).

[2] Zannetti, A. Breast cancer: From pathophysiology to novel therapeutic approaches 2.0. *Int. J. Mol. Sci., 24*, 2542 (2023).

[3] FarasatiFar, B. *et al.* Hydrogel encapsulation techniques and its clinical applications in drug delivery and regenerative medicine: A systematic review. *ACS Omega, 9*, 29139–29158 (2024).

[4] Li, J., & Mooney, D. J. Designing hydrogels for controlled drug delivery. *Nat. Rev. Mater., 1*, 16071 (2016).

[5] Correa, S. *et al.* Translational applications of hydrogels. *Chem. Rev., 121*, 11385–11457 (2021).

[6] Hoque, J., Sangaj, N., & Varghese, S. Stimuli-responsive supramolecular hydrogels and their applications in regenerative medicine. *Macromol. Biosci., 19*, e1800259 (2019).

[7] Albumin-based delivery systems: Recent advances, challenges, and opportunities. *Journal of Controlled Release, 380*, 375–395. (2025).

[8] Palmese, L. L., Fan, M., Scott, R. A., Tan, H., & Kiick, K. L. (2021). Multi-stimuli-responsive, liposome-crosslinked poly(ethylene glycol) hydrogels for drug delivery. *Journal of Biomaterials Science, Polymer Edition, 32*, 635–656.

[9] Park, S. H., *et al.* (2022). Injectable thermosensitive hydrogels for a sustained release of iron nanochelators. *Advanced Science, 9*, 2200872.

[10] Andrade, F., Roca-Melendres, M. M., Durán-Lara, E. F., Rafael, D., & Schwartz, S. (2021). Stimuli-responsive hydrogels for cancer treatment: The role of pH, light, ionic strength and magnetic field. *Cancers, 13*, 1164.

[11] Gu, J., *et al.* (2022). Injectable pH-responsive hydrogel for combinatorial chemoimmunotherapy tailored to the tumor microenvironment. *Journal of Nanobiotechnology, 20*, 372.

[12] Cimen, Z., *et al.* (2021). Injectable and self-healable pH-responsive gelatin–PEG/laponite hybrid hydrogels as long-acting implants for local cancer treatment. *ACS Applied Polymer Materials, 3*, 3504–3518.

[13] Aebisher, D., Przygórzewska, A., & Bartusik-Aebisher, D. (2024). The latest look at PDT and immune checkpoints. *Current Issues in Molecular Biology, 46*, 7239–7257.

[14] Li, Z., *et al.* (2023). Porous SiO2-based reactor with self-supply of O2 and H2O2 for synergistic photo-thermal/photodynamic therapy. *International Journal of Nanomedicine, 18*, 3623–3639.

[15] Han, R.-L., Shi, J.-H., Liu, Z.-J., Hou, Y.-F., & Wang, Y. (2018). Near-infrared light-triggered hydrophobic-to-hydrophilic switch nanovalve for on-demand cancer therapy. *ACS Biomaterials Science & Engineering, 4*, 3478–3486.

[16] Liu, B., *et al.* (2020). Injectable and NIR-responsive DNA-inorganic hybrid hydrogels with outstanding photothermal therapy. *Advanced Materials, 32*, e2004460.

[17] Zagami, P., & Carey, L. A. (2022). Triple negative breast cancer: Pitfalls and progress. *NPJ Breast Cancer, 8*, 95.

[18] Luo, Y., *et al.* (2025). Thermosensitive hydrogel-mediated chemo-photothermal combined immunotherapy for triple-negative breast cancer. *ACS Applied Materials & Interfaces, 17*, 63103–63115.

[19] Li, G. *et al.* Improved efficacy of triple-negative breast cancer immunotherapy via hydrogel-based co-delivery of CAR-T cells and mitophagy agonist. *Adv. Sci., 12*, 2409835 (2025).

[20] Fisher, B. *et al.* Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus irradiation for the treatment of invasive breast cancer. *N. Engl. J. Med., 347*, 1233–1241 (2002).

[21] Wu, H. *et al.* Injectable magnetic supramolecular hydrogel with magnetocaloric liquid-conformal property prevents post-operative recurrence in a breast cancer model. *Acta Biomater., 74*, 302–311 (2018).

[22] Liu, X. *et al.* In situ thermosensitive mRNA-loaded hydrogel modulates post-surgery tumor immune microenvironment to prevent recurrence and metastasis. *Biomaterials, 333*, 124188 (2026).

DOI: 10.54254/2753-8818/2026.ES37820

[23] Mo, F. *et al.* DNA hydrogel-based gene editing and drug delivery systems. *Adv. Drug Deliv. Rev., 168*, 79–98 (2021).
[24] Huang, H. *et al.* A TEMPO-loaded DNA hydrogel enabling integrated early diagnosis and treatment of osteoarthritis. *J. Nanobiotechnology, 23*, 695 (2025).