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Use of 3D printed scaffolds in breast cancer studies (review study)

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Introduction

Breast cancer (BC) is characterized as a condition were breast cells multiply uncontrollably. According to the NIH, it is the second most diagnosed cancer after skin cancer. It is an incurable and malignant type of cancer found in breast tissues, typically discovered by feeling a lump and diagnosed through some procedures. Its origin can be due to genes, family history, or drugs. Forecasts indicate that within the United States, there will be approximately 297,790 new cancer cases in 2023, accounting for 15% of all new cases, and approximately 43,170 estimated deaths, accounting for 7.1% of all cancer mortality Many studies repeatedly emphasize that BC is a highly diverse disease at both the molecular and histological levels. Throughout the years, several molecular markers have been identified to categorize BC according to aspects such as genomic instability, genetic changes, and gene expression. For studying tumor physiology and validating treatments, animal models are widely used. Yet, they have significant limitations: approximately 90% of drugs that succeed in preclinical tests fail in clinical trials, with an 85% early-phase failure rate. Factors contributing to this include interspecies differences, overestimation of treatment success, and experimental biases. These limitations highlight the need for alternative models that more accurately recapitulate human tumors.

Methods

This narrative review was conducted through a comprehensive search of PubMed, Scopus, Web of Science, and Google Scholar for studies published between 2010 and 2025 using the keywords “Breast Cancer,” “3D Printing,” “3D Scaffold,” “Tissue Engineering,” and “Tumor Models.” English-language articles that directly addressed the use of 3D-printed scaffolds in breast cancer modeling were included, while irrelevant studies or those lacking sufficient data were excluded.

Results

The ECM is a 3D framework made up of proteins (including collagen, laminin, and fibronectin) and glycosaminoglycans (GAGs) such as hyaluronic acid, which offers support and signaling cues for cell adhesion, growth, and movement. It acts as a storage site for growth factors essential for cell survival, which are released when the ECM is broken down by matrix metalloproteinases (MMPs). The characteristics of the ECM, such as its composition, rigidity, and microarchitecture, affect cell behavior and may play a role in tumor development Individual cancer cells have a lower stiffness compared to benign cells, whereas breast tumor tissue exhibits a much higher stiffness (elastic modulus of 1000–4000 Pa) about normal mammary glands (150–200 Pa). The stroma associated with tumors is also stiffer (400–1000 Pa) than that of normal stroma (200 Pa). This increased rigidity within the tumor microenvironment could be attributed to elevated collagen production, enzymatic crosslinking (involving lysyl oxidase and transglutaminase), and interstitial pressure arising from tumor expansion and the growth of blood vessels. 3D cell cultures vary significantly from traditional 2D cultures in terms of cell interactions, mechanics, and nutrient availability. These 3D models are increasingly popular for more accurately mimicking in vivo environments. While many epithelial systems, like lung airway epithelia, can be effectively modeled in 2D cultures, these monolayer systems often fail to replicate the complex cellular behaviors observed in vivo. This difference likely stems from the simplistic nature of 2D cultures, which affects aspects like cell proliferation, differentiation, apoptosis, and movement 3D printing is a commonly utilized additive manufacturing technique that builds materials layer by layer to create intricate 3D structures. To date, no single bioprinting technique enables the production of all scales and complexities of synthetic tissues.

In this review, we analyze the 3D bioprinting models of BCT. While 3D environments present significant benefits over traditional cell cultures, such as delivering more accurate and reliable data, improved cell viability, greater proliferation, the ability to concurrently exhibit processes linked to protein expression and other biomolecules, understanding how cells react to drugs, and the potential for realistic evaluations of metastatic behaviors, there are major challenges in 3D bioprinting scaffolds that must be tackled to improve the effectiveness of future research by overcoming these issues

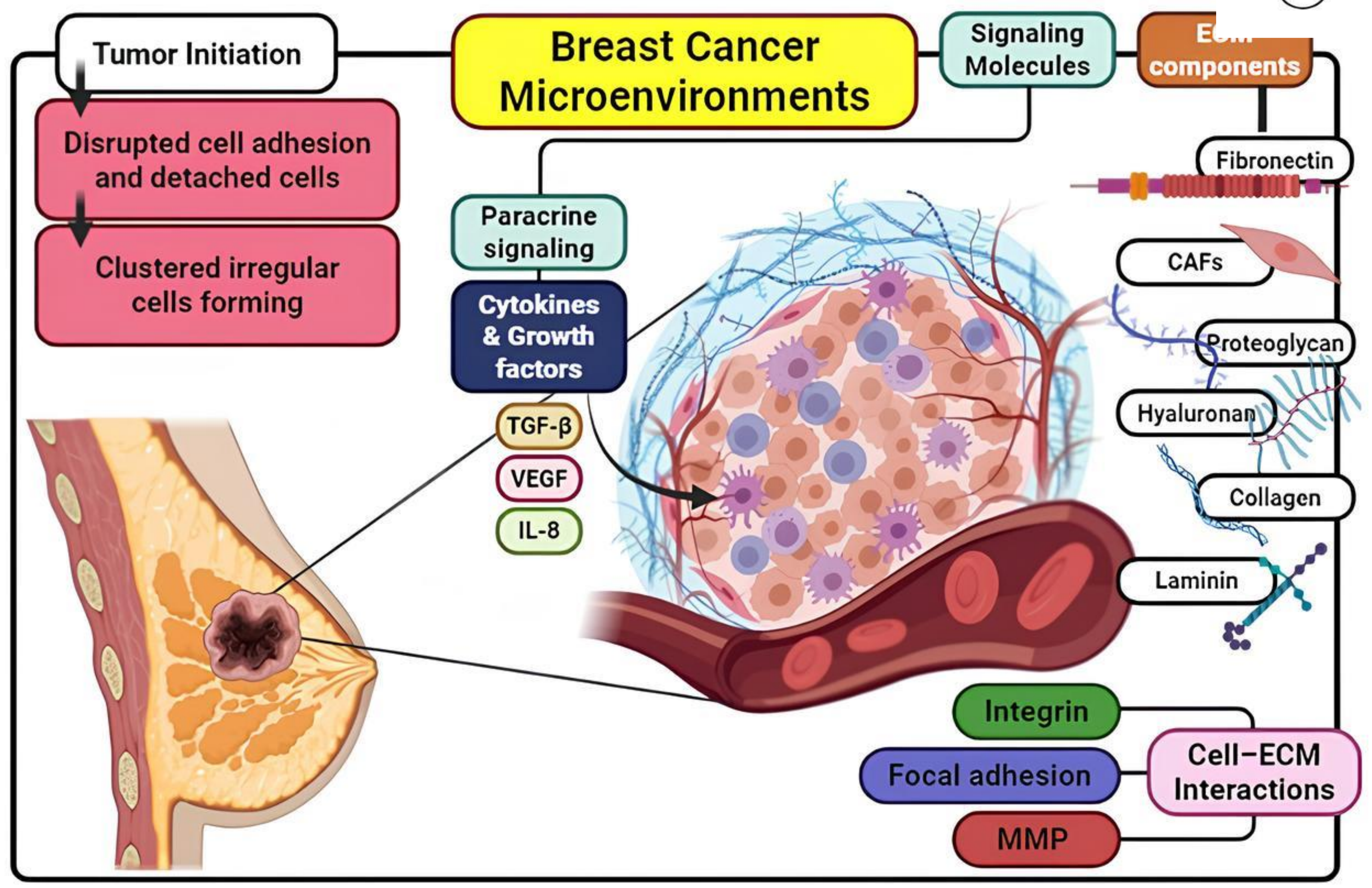

Fig 1.Complex cellular diversity, extracellular matrix structure, and molecular signaling pathways are all present in the tumor microenvironment

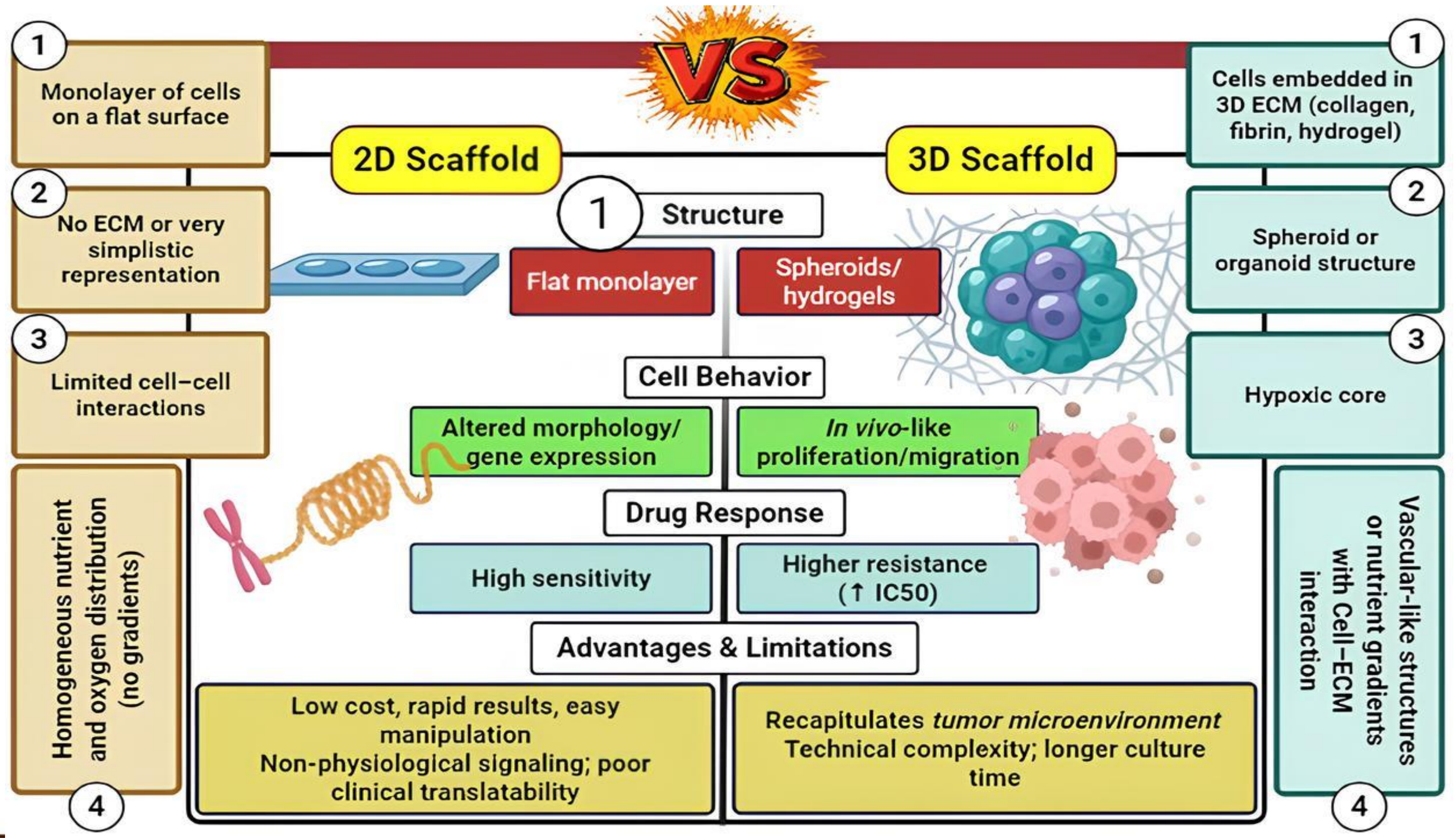

Fig. 2. Comparison of the key architectural and functional differences between advanced 3D cell culture models and conventional 2D monolayer culture

Conclusions

Despite advances in cancer research, the astounding rate of failure in anticancer drugs during clinical translation reflects the urgent need for more predictive and physiologically relevant preclinical models. The traditional animal models and 2D cultures cannot recapitulate the complexity of BC tissue and, therefore, have limited clinical utility. 3D bioprinting offers an innovative solution by allowing the creation of biomimetic BC models that can be precisely equivalent to the in vivo tissue architecture and cell-cell and cell-ECM interactions. This platform technology offers controlled spatial organization of cells and ECM components, offering a potent platform to study cancer growth, metastasis, and drug response. Although currently there are issues like limited standardization, biocompatibility of the materials, and scalability, ongoing innovation in the development of bioinks and printing technologies holds much promise.