INOSR APPLIED SCIENCES 14(2):1-5, 2026 ©INOSR PUBLICATIONS

International Network Organization for Scientific Research ISSN: 2705-165X
https://doi.org/10.59298/INOSRAS/2025/14.2.15000 INOSR14.2.00.000

Clinical Validity and Utility of Spatial Omics in Breast Cancer: Lessons for Population Screening and Policy

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ABSTRACT

Breast cancer remains a leading cause of cancer morbidity and mortality worldwide, necessitating advances in risk stratification, early detection, and personalized treatment strategies. Spatial omics technologies encompassing spatial transcriptomics, proteomics, and histopathological profiling offer unprecedented insight into tumour architecture, microenvironmental interactions, and intratumoural heterogeneity. This study critically examines the clinical validity and utility of spatial omics in breast cancer, with particular attention to its implications for population screening and health policy. While spatial omics holds promise for improving diagnostic precision and identifying novel biomarkers, current evidence of clinical validity remains limited, with few studies demonstrating robust associations between spatial signatures and patient outcomes. The paper further evaluates the feasibility, accuracy, and equity considerations of integrating spatial omics into population screening programmes. Key challenges include high costs, limited accessibility, lack of standardization, and insufficient validation across diverse populations. From a policy perspective, the integration of spatial omics requires careful consideration of regulatory frameworks, ethical safeguards, data governance, and cost-effectiveness. The study argues that, although spatial omics represents a transformative advancement in cancer research, its translation into routine screening and clinical practice demands coordinated investment in validation studies, infrastructure, and equitable implementation strategies. Ultimately, spatial omics should be viewed as a complementary tool that augments existing screening paradigms rather than a standalone solution.

Keywords: Spatial Omics, Breast Cancer, Population Screening, Clinical Validity, and Health Policy

INTRODUCTION

Breast cancer remains the most frequent cancer in women and the leading cause of cancer mortality worldwide [1]. To improve breast cancer risk stratification and enable more targeted early detection and prevention strategies that better balance risks and benefits of population screening programmes [2], spatial omics technologies have emerged to characterise the cancer genome at unprecedented resolution. Spatial omics encompass multiple analytical modalities such as transcriptomic, proteomic, and histopathology spatial profiling, and provide insight into the tumour microenvironment, intratumoural heterogeneity, and spatial relationships that bulk approaches cannot reveal [1]. Moreover, the increasing interest in the spatial distribution of cancer biomarkers arises from the awareness that their spatial pattern may hold complementary information with respect to tumour behaviour, yet the definition of the pattern and the underlying modelling remains poorly defined, hindering systematic investigation of its relevance to population screening [2]. This article reviews the state of spatial omics in breast cancer, discusses its implications for population screening and policy, and identifies challenges and opportunities for progress.

Spatial Omics: Concepts, Technologies, and Analytic Frameworks

For a variety of cancers, including breast cancer, the ability to determine pathobiological characteristics of tumor cells through analysis of formalin-fixed, paraffin-embedded tissue samples is essential to disease management [3].

Conventionally, assays of this type are performed using bulk nucleic acid extraction and characterization, with analysis of the average target sequence across all cells, or on single cells, requiring tissue dissociation that destroys spatial information [4]. An expanding range of techniques enables relying on archived samples to assess tumor/pathogen nucleic acid, protein, protein–protein interactions, and other analytes within the tissues' spatial context [3]. Technologies for spatial omics include microscopy-based (in situ hybridization and transcriptional barcoding) and non-microscopy-based (laser capture microdissection and mechanical macrodissection) methods; some have transitioned from development to commercial availability [5]. Procedures quantitatively space gene expression (transcriptomics), and protein–protein interactions (protein–protein interaction profiling), generate multi-omics data (combined output of different spatial-omics methods), unravel cell–cell interactions through molecular profile deconvolution, study evolution or conditions, determine spatial location coordinates of biomolecules within cells, and carry out spatial analysis of pathogens and cell culture; gene expression profiling assessed by the capture of mRNA through an output platform not associated with tissue-agnostic approaches (ligation and nonreverse transcription) enables mechanistic elucidation of breast cancer dedifferentiation[5]. Spatial omics is the examination of biological analytes in a spatially resolved manner within tissue preparations. Tumor cells and their surrounding microenvironments (extracellular and biotic) are often heterogeneous and exhibit intracellular aberrations [5]. The production at the chromatin level of certain analytes (RNA and protein) is only evident if specific conditions occur. Within tumor tissues, physiologically distinct regions are frequently present. Still, spatial information is generally disregarded when bulk or conventional single-cell approaches are employed [6]. Furthermore, such usual approaches assume that tissue sampling is randomly chosen across whole specimens either because samples originate from different patients or because intra-tumor heterogeneity is ignored when they represent tumor tissues of a specific patient [7].

Clinical Validity of Spatial Omics in Breast Cancer

Despite rapid technological and analytical advances, core biomarkers remain the foundation of multi-omic breast cancer research [3]. Evaluated in large, multicentric clinical trials spanning thousands of patients, the genomic, transcriptomic, and proteomic markers included in routine practice (e.g., the Oncotype DX test, the PAM50 signature, and protein expression of KI67, ER, PR, HER2) best predict recurrence and treatment response, and spatial omics data must be integrated with established omics datasets to approximate these performance benchmarks [4]. Only examining genuine omics signatures and truly spatial profiles such as those generated by multimodal, whole-tissue microimaging and spatial saliency maps overcomes the substantial confounding effects of tissue fixation, embedding, and sectioning that plague standard digital pathology [4]. Studies based on either conventionally profiled bulk RNA measurements or standard whole-tissue images, whether considering transcriptomic, proteomic, methylomic, or histopathological information, document a dearth of clinical validation and a tendency to claim genuine spatial resolution for data lacking a spatial dimension entirely. Existing evidence linking spatial spectra to histological ground truth and established tumor- and patient-level risk factors remains surprisingly thin, especially in breast cancer [5]. The breast cancer spatial omics landscape retains a modest level of exploratory breadth, even in relation to the broader cancer research domain. Few investigations into the spatial organization of disease have yet been undertaken, while the majority of studies examine a sole tissue feature or modality alone rather than multiple-image or multi-omic scenarios [4]. TILs, coupled to tissue specimens exclusively intermediate or terminally fixed in 10% buffered formalin, constitute the only spatial signal rigorously characterized in independent cohorts according to either safety- or efficacy-critical endpoints such as long-term survival or overall clinical response [5].

Clinical Utility and Impact on Patient Outcomes

In oncology, landscape changes over the past decade, science-driven therapies, comprehensive whole-genome magistral reforms, integrated analysis of clinical/biochemical data, have spurred enthusiasm for cure on the some of most paying cancer cases [3]. Among them, breast cancer remains an acute research area because it has the highest incidence and approval numbers among various cancers [4]. At the core of the clinical relevance is multilevel understanding of genomic profiles in individuals. In 2021, the prognosis of luminal breast cancer patients, concerning loss of heterozygosity (LOH) was proposed based on complete-genome sequencing. Literature has been accumulating to advocate diagnostic, prognostic, or predictive analysis as "one-for-all" solid clinical utility encompassing targeted mutation screening, transcriptomics, copy-number variations, epigenomics, or phosphorylation [5]. Metastatic breast cancer spreads through heterogeneous route. Tissue to tissue, the free cancer cells switches phases several times to obtain optimal fitness risking terra incognita before settling. Even within single lesions, variety of subclones co-exists [6]. Currently, the knowledge about primary-residual lesion transition, early-transit change, and intra-primary diversity during early-phase dissemination is stillt limited. Nevertheless, systematic study on a series of primary-transit-residual lesion samples highlighted the distinctive temporal transition of the metastatic colonization, suggesting new universal theoretical framework relevant for other cancer types [7]. Indeed, population screening was a major risk-reduction paradigm and yet the breast was

relatively far from other organs in the advancement [2]. Well-matured imaging, microscopical, serological, and computational algorithm allow accuracy-oriented early detection. At different phases of system implementation, the ground truth is unambiguously required to estimate the utility function of pre-targeted era [8].

Implications for Population Screening: Accuracy, Feasibility, and Equity

Spatial omics signatures may assist risk stratification for population screening, with the potential to identify high-risk individuals who could benefit from alternative strategies such as increased surveillance or prophylactic interventions [4]. However, significant misclassification risk remains even for signals deemed informative and several boundary conditions must be satisfied before pursuing spatial omics as a screening test [5]. Spatial omics could ameliorate the challenge of screening within subpopulations at higher risk of breast cancer, yet these specific population needs may not be reflected in the underlying risk models used to identify broader cohorts for eventual deployment [6]. Substantial efforts are required to build the data-sharing infrastructure and conduct follow-on studies necessary to realize these and other accessibility needs [7]. Basic spatial omics implementations have yet to be performed in low-resource settings or on devices suited for low-resource contexts. As per the greater considerations surrounding equity discussions, these aspects must remain a focus of the ongoing debate [8]. Addressing these needs early in the implementation pathway is critical for mitigating the potential for spatial omics to inadvertently exacerbate existing inequities and ensuring that equitable access can be formally integrated into the overall proposition for population screening [9].

Policy Considerations and Health System Integration

The implementation of spatial omics in clinical practice hinges on evidence of analytical validity, clinical utility, screening implications, and policy adoption. Addressing these criteria can inform preliminary evaluation and maximally accelerate health system integration [5]. Spatial omics delineates tumor microenvironments, intratumoral heterogeneity, and transcriptomic relationships; its study design, analytical frameworks, and technical benchmarks are established [6]. Clinical utility concerns the prioritised roles of breast cancer diagnosis, prognosis, treatment selection, and surveillance, and the incremental value offered over standard tests. Screening implications encompass the accuracy thresholds needed for spatial omics to meet population screening standards, the extent of misclassifications in the absence of screening gain, and the timeliness and completeness of risk stratification improvements [7]. Policy considerations involve regulatory pathways, legislative compliance, data access for product development, integration into existing clinical workflows, and interoperability with other health system initiatives [2]. Facilitating health system uptake of spatial omics in breast cancer requires upholding standards for validation evidence, ensuring educational pathways for informing clinicians, and outlining strategies for embedding decision-support tools [7]. Maximising return over investment mandates modelling cost-effectiveness, reimbursement prospects, resource allocation dynamics, equity concerns, and concurrent population-level implications. Key ethical challenges encompass privacy issues surrounding sensitive health information, obtaining consent for various proposed uses, and accounting for incidental findings that present opportunities and dilemmas [7]. Discerning economic implications associated with distinct breast cancer populations necessitates deriving cost benefit estimates that capture anticipated health system resource demand, screening follow up interactions, and potential fiscal pressure on investment into competing national health priorities[8].

Economic and Ethical Considerations

Comprehensive economic modelling that incorporates the management of scarce healthcare resources suggests that the cost-effectiveness of spatial omics in breast cancer screening depends on both the availability of resources and the desired level of coverage [8]. Corridors of cost-effectiveness for widespread coverage have been identified, under limited-supply scenarios and with restricted reimbursement from payers, spatial omics would need to demonstrate substantial further gains in accuracy (detection of advanced rather than early-stage disease) to be deemed sufficiently effective to justify public funding, making it viable only for high-risk women who are recurrently screened[8]. Nevertheless, even with stringent supply constraints, access to spatial omics could still be envisaged for some substantial segments of the female population, permitting extensive onward investment in technology enhancement [8]. Concerns about privacy, consent, the handling of incidental findings, the potential criminalisation of data use, and whether systems reflect the preferences that women have elsewhere contributed to ongoing scrutiny of risks imparted by health surveillance [7]. The capacity for faithfully monitoring the evolution of screening outcomes, and hence avoiding the risks of double-counting progress, remains a serious potential hindrance to gaining adequate control over reporting error [6]. Exploiting the existing international alignment around the WHO's health-life expectancy indicator could instead present an opportunity to work towards far greater usable breadth of the analysis. The extent of incidental findings and other adverse impacts derived from misuse of the screening focus have also been assessed [6]. Despite breast cancer's heavy burden at a population level and significant investments on both clinical and commercial fronts, fundamental research efforts often occurring only in the public domain, and their coordination facilitated transparently through an appropriate

framework remain essential to unlocking sufficient convergence towards a shared understanding of normality of screening outcomes[7].

Translation from Bench to Population: Challenges and Strategies

All genetic risk factors associated with breast cancer development remain to be discovered; current knowledge still has not led to widespread integration of germline genetic testing into screening programs [10]. In the absence of sufficient knowledge about the interplay of somatic and germline information, pilot population studies incorporating somatic-based spatial omics into breast cancer screening or risk assessment are not yet justified and no proposals are provided [9]. Genetic risk variants still need to be further elucidated for accurate risk stratification. Efforts to reduce delays and create awareness of the need for collaborative population studies that include spatial omics as a prioritized option are instead emphasized [10]. Prioritization is needed for population-based studies with adequate multi-modal data representation to address the early understanding of these aspects at the population level. Social media endeavours seek to enliven collaboration surrounding spatial omics considerations for population study design as early understanding of the utility following routine clinical practice on risk modelling indicatively remains a research gap [9].

Recommendations for Research Agendas and Validation Studies

Spatial omics remains underexplored in breast cancer research, and dedicated studies are needed to guide prioritization responses. Key areas warranting early investigation include [1] spatial profiling of transcriptomes, proteomes, or histopathology at single-cell resolution with integrative analysis across data types; [2] clarification of spatial-only breast cancer signatures; [3] formal comparison of protocols for multi-modal data generation, pre-processing, and timecourse modelling; [4] documentation of consistency across platforms or data subsetting; [5] exploration of commercially available systems enabling breast cancer tissue spatialomics or prototyping of custom set-ups; [6] evaluation of origin attribution methods for human samples and treatment naïve early lesions; and [7] characterisation of implementation determinants influencing the adoption of novel technologies and methods within clinical settings [8 , 9]. Reproducibility, transparency, and robustness bolster credibility and trust in scientific activities. Spatial omics projects should adhere to data-sharing and open-access obligations, retain a persistent DOI, and register on relevant platforms [10]. Special consideration should also be given to public repositories, documentation of data-generation provision, study-specific metadata, dataset linking within openly available resources, and any formatting or description standards. Reporting standards play an essential role in transparency and reproducibility; the community would benefit from guidelines establishing the minimum information established for spatial omics experiments. Pre-registering experimental analysis plans enables further specification of research questions, analytical approaches, sample sizes, and primary endpoints and promotes coherent reporting of scientific activities [10]. Highly heterogeneous datasets risk exclusion from the wider spatial omics community. Efforts to share unprocessed data or images, and metadata detailing acquisition and pre-processing history, alongside transparency of sample provenance, experimental design, and statistical modelling, facilitate sharing of insights on such complex datasets and enhance their accessibility [9]. Participation in and endorsement of relevant international consortia that issue minimum information standards, promote suitable community-wide practices, or provide similar guidance and support, supports reform initiatives within particular research domains[10]. Sample size and statistical power studies enable more accurate assessments of the minimal number of samples required to derive biologically relevant insights. Community-concerted efforts to map the experimental design-space and reporting standards for biological discovery studies across numerous disciplines would yield complementary guidance on sample size, dimensionality, and power parameters [10]. Choice of tissue source and production of high-quality biological material are vital drivers of ongoing national and international initiatives focused on the establishment of biobanks dedicated to breast and related tissues. Importantly, consideration of the breast cancer research community more generally is likewise required, recognising that other multi-omics biomarkers have already been deployed with arbitrary, often unknown, thresholds in clinical and adjuvant treatment decisions and space for further progression beyond such indicators remains. tissuOmics, a highly modular spatial-proteomics solution compatible with tissue microarrays and whole-tissue slides, offers rapid prototyping for spatial tissue-analysis projects and remains prominently placed within the commercial milieu[9]. Best practices garner substantial interest and demand focused on guidelines that assist optimal execution following technology acquisition. Spatial transcriptomic river diagrams elucidating straightforward integration options, with guidance on critical upstream and down-stream decisions, support a comprehensive overview of the multi-omics space without prescriptive recommendation as to any specific implementation [10].

CONCLUSION

Spatial omics technologies represent a significant advancement in the molecular characterization of breast cancer, offering detailed insights into tumour heterogeneity, microenvironmental interactions, and spatially resolved biomarker expression. These capabilities hold substantial promise for enhancing diagnostic accuracy, refining prognostic assessments, and informing personalized treatment strategies. However, this review highlights that the

clinical validity and utility of spatial omics in breast cancer remain at an early and largely exploratory stage. Current evidence is insufficient to support its widespread integration into population screening programmes, particularly given the lack of standardized methodologies, limited large-scale validation studies, and uncertainties surrounding reproducibility and generalizability. Established biomarkers and existing screening modalities continue to provide more reliable and clinically actionable insights. The potential of spatial omics for population screening lies primarily in its future role as a complementary tool for risk stratification, particularly among high-risk groups. Yet, significant challenges must be addressed, including high implementation costs, infrastructure requirements, data-sharing limitations, and the risk of exacerbating existing health inequities. Ethical concerns related to privacy, consent, and incidental findings further complicate its deployment. From a policy standpoint, the responsible integration of spatial omics will require robust regulatory oversight, investment in interdisciplinary research, development of standardized reporting frameworks, and alignment with broader health system priorities. Emphasis should be placed on cost-effectiveness, equitable access, and the creation of scalable models suitable for diverse healthcare settings, including low-resource environments. In conclusion, while spatial omics has transformative potential, its current role in breast cancer care is best understood as investigational. Future progress will depend on coordinated efforts across scientific, clinical, and policy domains to establish its validity, define its utility, and ensure that its benefits are distributed equitably across populations.

REFERENCES

1. Evans, D. G. R., Harkness, E. F., Brentnall, A. R., van Veen, E. M., Byers, H., Astley, S. M., Sampson, S., Howell, A., Cuzick, J., & Newman, W. G. (2019). Breast cancer pathology and stage are better predicted by risk stratification models that include mammographic density and common genetic variants. *British Journal of Cancer*, *121*(7), 562–567. https://doi.org/10.1038/s41416-019-0566-7
2. Briggs, S., & Slade, I. (2019). Evaluating the integration of genomics into cancer screening programmes: Challenges and opportunities. *Public Health Genomics*, *22*(3–4), 111–121. https://doi.org/10.1159/000502665
3. Lee, S., Kim, G., Lee, J. Y., Lee, A. C., et al. (2024). Mapping cancer biology in space: Applications and perspectives on spatial omics for oncology. *Nature Reviews Clinical Oncology*, *21*(2), 85–103. https://doi.org/10.1038/s41571-023-00820-4
4. Eng, J., Bucher, E., Hu, Z., Sanders, M., et al. (2023). Robust biomarker discovery through multiplatform multiplex image analysis of breast cancer clinical cohorts. *Nature Communications*, *14*, 1023. https://doi.org/10.1038/s41467-023-36684-0
5. Shin, K., Kim, R., Park, H., Lee, W., et al. (2024). Clinical utility of whole-genome analysis as a one-for-all test for breast cancer: A case series. *NPJ Genomic Medicine*, *9*, 12. https://doi.org/10.1038/s41525-024-00390-1
6. Chowdhury, S., Dent, T., Pashayan, N., Hall, A., et al. (2013). Incorporating genomics into breast and prostate cancer screening: Assessing the implications. *Genetics in Medicine*, *15*(6), 423–432. https://doi.org/10.1038/gim.2012.165
7. Pashayan, N., Hall, A., Chowdhury, S., Dent, T., et al. (2013). Public health genomics and personalized prevention: Lessons from the COGS project. *Journal of Internal Medicine*, *274*(6), 572–580. https://doi.org/10.1111/joim.12113
8. McWilliams, L., Evans, D. G. R., Payne, K., Harrison, F., et al. (2022). Implementing risk-stratified breast screening in England: An agenda-setting meeting. *BMC Cancer*, *22*, 1150. https://doi.org/10.1186/s12885-022-10160-5
9. Glaab, E., Rauschenberger, A., Banzi, R., Gerardi, C., et al. (2021). Biomarker discovery studies for patient stratification using machine learning analysis of omics data: A scoping review. *BMJ Open*, *11*(12), e046301. https://doi.org/10.1136/bmjopen-2020-046301
10. van den Driest, L., Kelly, P., Marshall, A., Johnson, C. H., et al. (2024). A gap analysis of UK Biobank publications reveals SNPs associated with intrinsic subtypes of breast cancer. *Cancers*, *16*(3), 512. https://doi.org/10.3390/cancers16030512

CITE AS: Nambi Namusisi H. (2026). Clinical Validity and Utility of Spatial Omics in Breast Cancer: Lessons for Population Screening and Policy. INOSR APPLIED SCIENCES 14(2):1-5. https://doi.org/10.59298/INOSRAS/2025/14.2.15000