sagentia
MEDICAL

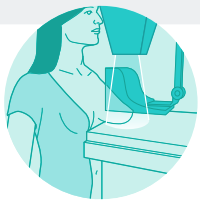
WHITE PAPER

Breast cancer screening: a patient-centric approach to innovation

AUTHOR
Erica Kantor, Head of Women's Health, Sagentia Medical

As the standard breast cancer screening technology, mammography plays a major role in early detection, improving patient outcomes and survival rates. Nevertheless, there is room for improvement, especially in tumour detection for women with dense breast tissue. This paper explores the potential for new technologies to enhance breast cancer screening programmes.

As the most prevalent cancer, particularly amongst women, breast cancer receives a lot of attention in healthcare systems worldwide. Screening is central to the breast cancer care continuum and for decades, mammography has been the cornerstone technology (see Figure 1). Its ability to enable early detection improves patient outcomes and saves lives. However, it is not without limitations.

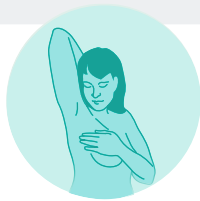


Mammography (MMG)

- The most common and widely practiced breast cancer screening modality
- Visualisation of breast tissue by the use of low dose X-rays

Limitations

- False negatives
- False positives
- Risk of radiation
- Limited spatial resolution
- Less accurate for dense breasts



Breast self-exam (BSE)

- Physical examination done by the female herself to find lumps or other abnormalities in the breast

Limitations

- Not effective as a standalone screening method
- User variability

Clinical breast exam (CBE)

- Includes detailed history, physical examination, palpation of breast, and lymph nodes examination by the clinician

Limitations

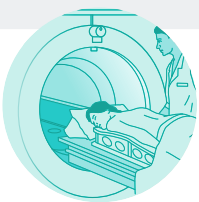
- Not effective as a standalone screening method
- Operator variability

Ultrasonography (US)

- Uses sound waves to develop a picture of the breast tissue
- Often recommended in younger women with dense glandular tissue

Limitations

- Lacks spatial resolution
- Cannot detect most calcium deposits
- Operator-dependent
- Requires skilled sonologist



Magnetic resonance imaging (MRI)

- Uses radio waves and strong magnets to develop detailed pictures of the breast
- Recommended in conjunction with MMG for high risk patients

Limitations

- Limited availability
- 10-fold higher cost compared to MMG
- Needs contrast enhancement
- Difficult to interpret
- False positives

Digital breast tomosynthesis (DBT)

- Digital mammography: thin cross-sectional images combined with conventional X-rays to develop 3D images
- Approved by FDA in 2011 for breast cancer screening

Limitations

- Prolonged time
- Increased radiation exposure (twice that of standard MMG)

BRCA gene detection

- Women with mutations in the BRCA1/2 genes have a 50-80% risk of developing breast cancer
- In the UK, genetic testing is only available if a relative has a positive test for a BRCA1/2 mutation

Limitations

- Genetic testing for BRCA1 and BRCA2 is not considered a part of the standard workup for breast cancer screening

Figure 1: A comparison of breast cancer screening methods

A major challenge cited by clinicians is that presented by dense breast tissue. This makes the detection of tumours on a mammogram more difficult, and it is also associated with higher breast cancer risk. Since around 40 percent of women have dense breast tissue, this is a significant limiting factor for screening programmes dependent on mammography. In this white paper, we interrogate the innovation potential in this space. Is there scope to develop new breast cancer screening technologies that could complement, or eventually replace, mammography?

Opportunities for innovation in breast cancer screening

We've identified four key areas where breast cancer screening strategies could be improved to better serve women with dense breast tissue:

Triaging:

Addressing the need for a cost-effective technology that accurately quantifies breast density earlier than current routine mammograms.

Risk stratification:

Creating better systems to risk stratify women with a higher chance of developing breast cancer. These should be integrated, automated and easy to use.

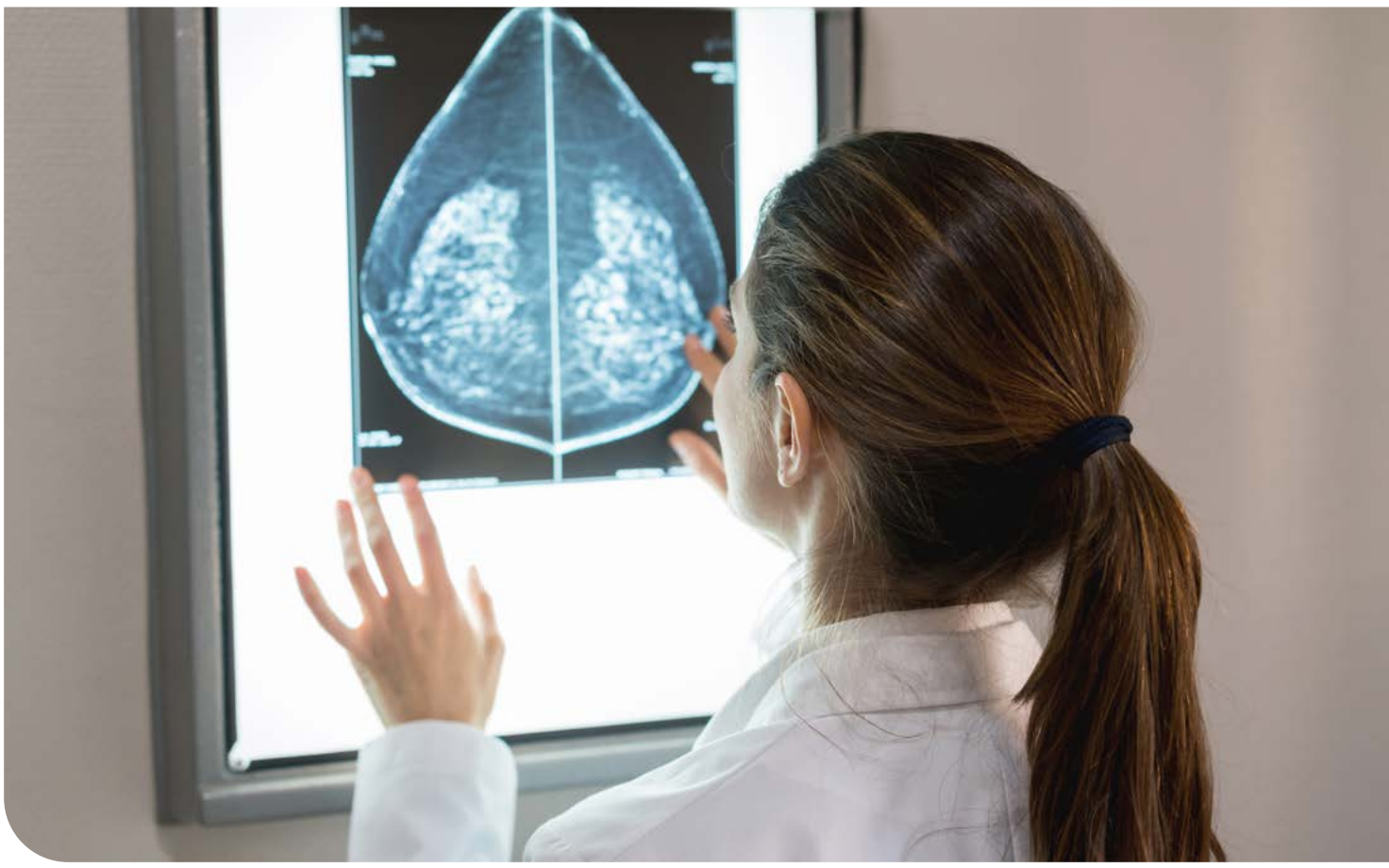
Screening technology:

Developing an alternative to mammography that addresses the current limitations, including patient discomfort, radiation exposure, and lack of specificity.

Monitoring:

Devising an accessible solution for regular, longitudinal monitoring of women with a higher risk of developing breast cancer, particularly younger populations.

Our scientists and technologists have explored potential solutions in each of these areas (see Figure 2). The following sections draw on first-hand insights from both patients and clinicians, gained via our own primary and secondary research, as well as detailed technology analyses.



Triaging

Breast density defined

Breast density is categorised into four levels according to the relative proportion of fatty tissue and dense tissue:

A: Almost entirely fatty

B: Scattered areas of fibroglandular density

C: Heterogeneously dense

D: Extremely dense

Levels C and D are considered dense, and almost half of women fall into these categories.

At present, breast density is classified by a radiologist, based on the visual assessment of a mammogram. Most women who have dense breast tissue only learn that this is the case at their first routine screening. Some countries, such as the US and China, recommend women begin regular screening from the age of 40. In the UK, women are invited to attend NHS breast screening every three years from the age of 50.

Dense tissue appears as a solid white area on a mammogram, as do tumours, making them difficult to distinguish and increasing the risk of 'false negative' diagnosis.

Women with dense breasts are also considered to be at higher risk of developing cancer. They could potentially benefit from beginning regular screening at a younger age, but current screening protocols don't enable this.

Innovation potential

In order to identify women with dense breasts early, a novel tool is required, ideally for use at the point-of-care. Microwave imaging is a viable alternative to mammography for measuring breast density. Since it doesn't involve radiation, it could be offered to women at a younger age.

Low cost, portable microwave breast imaging systems are already being explored by researchers. The challenge lies in the complexity of the computation, and the coupling between the patient and the sensors. Companies that address these issues could devise new ways for breast density to be classified quickly and easily in point-of-care settings. This could be used routinely for younger women, enabling effective triaging of those who are more likely to develop breast cancer.

Risk stratification

Age is currently used as the primary, and often the only, risk factor driving population-based screening for breast cancer. Extending this to draw on multiple relevant factors would enable earlier and more regular screening for women at greater risk. It could also bring greater overall efficiency to breast cancer screening programmes.

Identifying the 40 percent of women with dense breast tissue at an earlier age would be pivotal here. Widespread point-of-care breast density classification could provide valuable information to consider alongside other factors such as personal and family health data for more effective risk analysis. As genetic testing to identify people with a predisposition for certain cancers becomes increasingly mainstream, this could also form part of the risk stratification framework.

Innovation potential

More intelligent risk stratification could unlock ways to improve on current breast cancer screening programmes. However, this will require new solutions for patient-specific data aggregation. For instance, family health data is usually gathered based on a patient's knowledge and memory, but the ability to connect familial health records would provide more detail and accuracy.

Automated machine learning systems could also play an important role. By drawing on multiple data sources to improve risk stratification they could enable more focused decision making and better resource allocation. So, women at low risk of developing breast cancer might be invited for screening every two to three years from the age of 50 whereas those at high risk could be screened annually from the age of 30.

Screening technology

Our research indicates that while most women understand the importance of breast cancer screening, there are many factors that discourage them from attending. These include physical discomfort or pain caused by the temperature and pressure of mammography machine plates. Clinicians also report practical challenges related to breast positioning and achieving optimum balance of compression and image quality.

Nevertheless, mammography has a proven history of enabling the early detection of tumours that are too small to feel. Any alternative technology must exceed its level of accuracy, particularly with dense breast tissue. Ideally, it should offer greater comfort for patients as well as offering ease of use and interpretation for clinicians. Cost-efficiency and speed of throughput are also important considerations.

Innovation potential

Low-field MRI is an emerging field that could offer new possibilities for breast cancer screening. It is cheaper and occupies a smaller footprint than traditional MRI machines as well as consuming less energy. Recent research has proved that it is capable of accurate imaging across a wide range of magnetic field strengths, from 5mT-0.5T. For example, McDaniel, P. et al demonstrated the feasibility of a low cost, lightweight brain MRI system small enough to be used in point-of-care settings[1]. If this could be translated to breast cancer screening, it holds great potential.

Monitoring

The risk/benefit equation for mammography requires careful consideration due to the radiation that patients are exposed to. For women aged over 40 or 50 attending screening every couple of years, the benefits of early breast cancer detection are thought to outweigh the risks. However, the balance changes for women who begin screening at a younger age or with greater frequency. Alternative technologies such as low-field MRI could be part of the solution. However, they may not be adequate in isolation, since women at the highest risk of breast cancer may develop interval cancers between screenings.

In the future, it could be feasible for women to undergo regular circulating tumour DNA (ctDNA) tests. This emerging diagnostic technique uses next-generation sequencing (NGS) technology to identify any tumour cells present in the bloodstream before they are detectable with imaging technologies.

Innovation potential

If ctDNA testing is deemed suitable for early detection of breast cancer, obtaining regular blood samples of sufficient volume could present a barrier to widespread use. However, the collection and analysis of menstrual blood could offer a solution. This non-invasive approach would allow longitudinal tracking and analysis of the evolution of any mutations. Sample collection could be performed easily and conveniently at home, without requiring appointments at a blood clinic.

Existing smart feminine hygiene products could provide a platform for further innovation. For instance, the Q-pad developed by QVIN which is already used to collect menstrual blood samples for analysis of HbA1c in diabetes risk assessment.

The most exciting opportunities for innovation in breast cancer screening

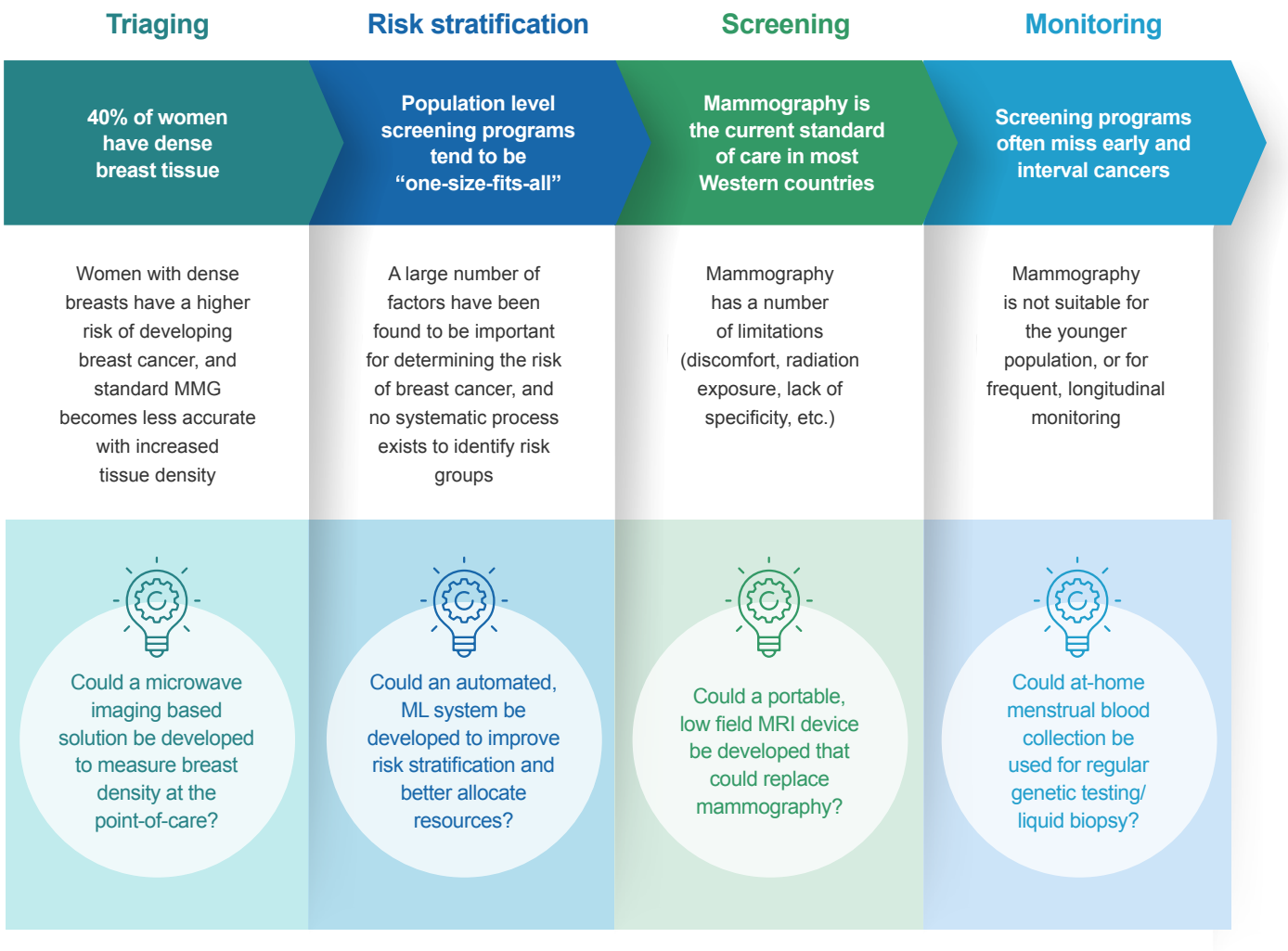


Figure 2: The innovation opportunity spectrum

Catching up after COVID-19

The disruption caused by the COVID-19 pandemic resulted in many women delaying or missing breast cancer screening appointments. US figures showed a 94% drop on previous years, with an estimated 285,000 screenings missed[2]. This could result in breast cancer being diagnosed at a later stage, with a poorer prognosis. New screening technologies and protocols, such as point-of-care screening, could play a vital role closing the gap.

Identifying commercially viable opportunities

Despite their limitations, current breast cancer screening programmes based on mammography have played a vital role in the successful reduction of mortality rates. Innovative concepts that disrupt the status quo will need to demonstrate tangible benefits that complement or significantly improve upon the existing technology and protocols.

In the wake of COVID-19, achieving greater throughput of patients is likely to be a priority. Healthcare providers need to address high numbers of missed or delayed screening appointments and the potential repercussions. This could help drive the approval and uptake of new triaging, risk stratification and screening technologies.

In the medium to long term, emerging technologies – from machine learning to NGS – offer much potential to improve on current screening programmes. Overcoming challenges related to dense breast tissue could help drive further improvements in breast cancer survival. Here at Sagentia Medical, we are continuing to assess the commercial and technical feasibility of various solutions in this space.

Notes

1. McDaniel, P, (23 June 2019), The MR Cap: A single-sided MRI system designed for potential point-of-care limited field-of-view brain imaging. WILEY ONLINE LIBRARY. https://onlinelibrary.wiley.com/doi/10.1002/mrm.27861
2. Mast, C and Munoz del Rio, A (17 July 2020), Delayed Cancer Screenings—A Second Look. Epic Research. https://ehrn.org/articles/delayed-cancer-screenings-a-second-look

About Sagentia Medical

Sagentia Medical is a specialist independent advisory and leading-edge product development services focused on science and technology initiatives in healthcare. Working across diagnostics, surgical devices, and medical devices, Sagentia Medical works with start-up disruptors through to world leading brands in MedTech to extract maximum value from R&D and innovation investments.

sagentia.com/medical

For further information visit us at:
sagentia.com/medical or
email info@sagentiamedical.com

Sagentia Ltd
Harston Mill
Harston
Cambridge
CB22 7GG
UK

Sagentia Ltd
First Floor
17 Waterloo Place
London
SW1Y 4AR
UK

Sagentia Inc
1150 18th Street
Suite 475
Washington
D.C. 20036
USA

sagentia
MEDICAL