BREAST CARE MAGAZINE

Women's Health at heart

The New Thinking On Breast Imaging

LEVERAGING INNOVATIVE TECHNOLOGIES:
FROM CESM TO CESM GUIDED BIOPSY

WHAT IS AT STAKE FOR AI IN BREAST IMAGING?

BREAST CARE JOURNEY:
MULTI MODALITY CLINICAL CASES

YEAR 5 ANNIVERSARY

SENOGRAPHE Pristina™ MAMMOGRAPHY

Magazine#2

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Dear Reader,

We believe we have a mission. In 2020, 2.3 million women were diagnosed with breast cancer, and 7.8 million women are alive, diagnosed with breast cancer in the past 5 years, making it the world's most prevalent cancer. Five years survival rate is 99% when detected at early stage and the disease is localized in breast. We are committed to bring to you the latest innovations to improve early detection, reduce time from suspicion to diagnostic, improve patient experience to encourage women not skip their mammogram. In this magazine, you will discover through peers testimonials, how the latest innovations - such as contrast-enhanced mammography and contrast-enhanced guided biopsy - can change the game for the patient as well as for the medical team.

Because mammography is only one piece of the overall women's imaging program, you will also find in this second edition, experience sharing and clinical cases from multi-modalities, from Abbreviated MRI to PET-MR, and Ultrasound.

Our hope is that this GE Healthcare Breast Care Magazine will draw your attention, answer questions or stimulate ideas.

We wish you good reading and remain your partner in elevating personalized breast care.

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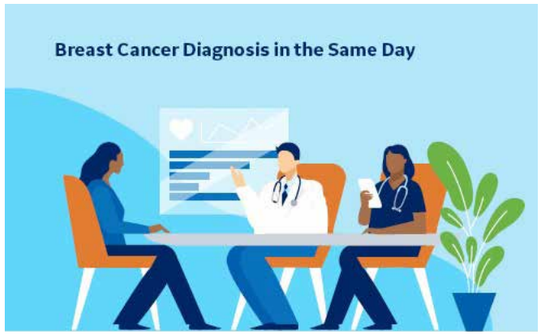

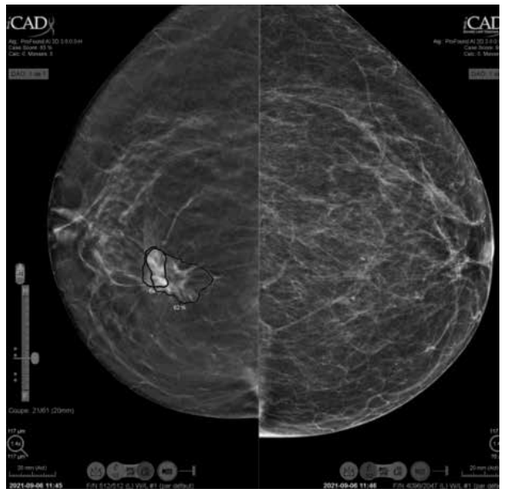

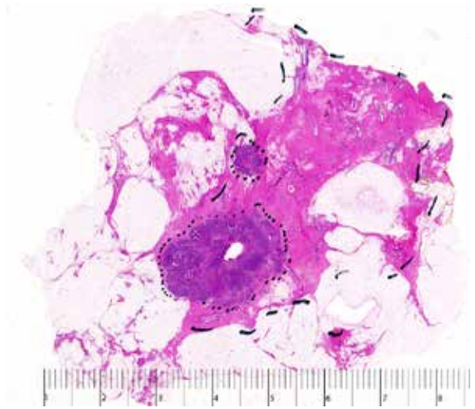

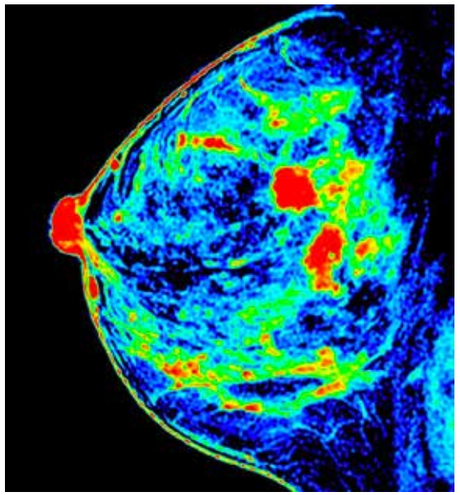

Rapid breast cancer diagnosis clinics.

- A game changer for patients and clinicians
- One-Stop Clinics Infographic
- Improving Breast Cancer Care in Colombia with One-Stop Clinics

One of the most frightening things a woman can experience is a call telling her there's something suspicious on her mammogram. Now imagine that same woman having to wait weeks before getting a firm diagnosis and treatment plan.

"*The problem is daunting*," said Benjamin O. Anderson, MD, professor of surgery in Global Health at the University of Washington in Seattle during GE Healthcare's digital meet-up "*From Weeks to Hours: Accelerating Breast Cancer Care with One-Stop Clinics.*" "*By the time the patient has talked with the referring physician and scheduled a follow up, significant time has passed*," he said. "*That means increasing anxiety.*"

"*This is a fundamental issue in breast cancer whether one is in the United States or Europe, or in Sub-Saharan Africa*," said Dr. Anderson, who pioneered guidelines for breast cancer early detection, diagnosis, treatment, and palliative care in low- and middle-income countries as the chair of the Breast Health Global Initiative. Indeed, the length of time between a screening mammogram and the first surgical consultation in the US can average 26 days, up to 43 days for women of color[1,2]. That wait can be much longer for women in other countries[3]. In Spain, for instance, a recent study of 500 women found average wait times of 57 days to undergo a biopsy after symptoms or evidence of abnormality on mammogram, and 92 days for surgery[4].

The COVID-19 pandemic is making the situation even worse. An estimated 285,000 American women missed their screening mammogram between March and June 2020 alone, and experts predict thousands of undiagnosed cancers[5,6]. With the second and third waves of the pandemic in the fall and winter, these numbers are expected to continue growing.

Indeed, said Dr. Anderson, the challenges of providing medical care during a global pandemic requires "*systems that are functional and meet a woman's emotional as well as physical needs.*"

Which is exactly what the One-Stop Clinic is designed to address.

One-Stop Clinics Redefine Patient Care Globally

Dr. Delaloge launched the One-Stop Clinic in 2004 with a specific set of algorithms to ensure rapid diagnosis. At the time, the median time between a screening mammogram and a cancer diagnosis in France was about 60 days. That, she said, "*is a very, very long delay.*"

Less than 10 years later, an analysis of the nearly 11,000 women seen at Gustave Roussy during that time found that 75 percent received same-day results with highly accurate diagnoses. 21 percent of patients had their diagnosis and treatment strategy changed due to Contrast-Enhanced Spectral Mammography (CESM) and another 10 percent of all the patients who underwent CESM avoided biopsies[7].

When Dr. Diaz started his One-Stop Clinic in Medellin, waiting times could be as high as six months for a diagnosis. His hospital initially created a woman's clinic that reduced the time to 35 days. But it still wasn't enough. Last year, he and team began working with the Gustave Roussy team to bring the One-Stop model to Medellin. Since implementing it, waiting times for diagnosis have dropped to 18 days, a timeline Dr. Diaz expects will continue to fall as the team gathers more experience.

Meanwhile, in the US, St. Luke's is working closely with GE Healthcare to develop a pilot site prior to expanding throughout the country. "Any time I tell a woman she needs further evaluation, her first question is, "*When can I do it?*" Dr. Russo said. "*She wants to come as soon as possible. So we developed our systems with that thought in mind.*"

It is already successful, with the diagnostic imaging flow down to five days. "*Once the One-Stop Clinic is fully operational, the goal is to reduce this time to 36 hours or fewer,*" said Dr. Russo. While women in the area can get their screening mammogram at any of 20 sites, if a second-level screening or diagnostic workup is required, she comes to the consolidated center where clinicians, technologists, and nurses work together to offer same-day biopsy to the highest risk patients. "*It's a truly patient-centered process,*" he said.

The clinic also benefits the physicians, said Dr. Diaz. "*In the same day we can get all the information we need: the images, the biopsy, the clinical exam. We have everything.*"

Indeed, said Dr. Delaloge, the greater complexity of the lesions her group sees these days is "*something that is perfectly addressed by this kind of multi-disciplinary clinic.*" For instance, the clinicians and the radiologist, often with the pathologist, view the images together and decide as a team on the next steps.

But, the three panelists agreed, the primary reason to start a One-Stop Clinic, is the patient. "*Once a woman has that callback or that recommendation for a biopsy,*" said Dr. Russo, "*the same-day biopsy is really the most valuable thing you could do for an anxious patient.*"

"*It's difficult facing a diagnosis," said Dr. Delaloge. "But facing it with a treatment plan with all the specialists together is very, very transformative.*"

Provide rapid diagnosis to patients in Egypt

In July 2019, Egypt President Abdelfattah Al Sissi launched the Women's Health Initiative, a program to improve early detection of breast cancer, hypertension, diabetes, osteoporosis, and heart disease and aimed at nearly 30 million women across the country.

To accelerate this initiative, the Egyptian Ministry of Health just signed a preliminary agreement with GE Healthcare and Europe's top cancer hospital Gustave Roussy to create rapid diagnosis clinics for breast cancer in Egypt.

As part of the collaboration in Egypt, Gustave Roussy will train clinical and administrative staff, and support the implementation of standard operating procedures and clinical algorithms to help set up One-Stop Clinics in the country. The aim is to improve the speed and quality of diagnosis and to reduce the costs of care, from consultation and diagnosis to treatment.

"We are extremely proud that Egypt has chosen to deploy to women the one-stop diagnosis concept invented at Gustave Roussy." comments Prof. Fabrice Barlesi, CEO of Gustave Roussy. "Women's health and the early diagnosis of cancer are causes that mobilize us and for which we deploy a lot of energy in order to develop new solutions. We are convinced that the hope of curing cancer in the 21st century lies largely in the fields of personalized prevention and rapid diagnosis."

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3. Pineros M, Sanchez R, Perry F, et al. Delay for Diagnosis and Treatment of Breast Cancer in Bogotá, Colombia. Salud Publica Mex. 2011;53(6):478-85.
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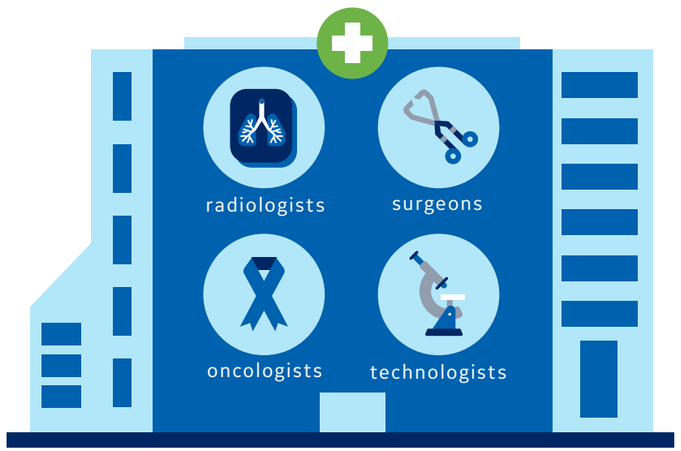
Uniting for Breast Cancer Care: A Roadmap for Building an Effective Cross-Disciplinary Team

In an ever-fragmented healthcare landscape, it can seem an impossible task to combine multidisciplinary forces in an expedited manner for the good of patient care. In breast oncology—a field dependent on multi-input sources, from imaging to surgery, chemotherapy, radiation, and beyond—it can seem all the more challenging.

But with the right mix of specialists, equipment, operational excellence, and wholehearted compassion, it is indeed possible. And at the One Stop Clinic on the Gustave Roussy Cancer Campus in France, oncology experts have done just that.

BUILDING A ONE STOP CLINIC: WHAT IS IT?

Driven by a same-day diagnostic model, a One Stop Clinic integrates multifaceted care for breast cancer from many sources for a coordinated patient journey, under one roof:



Patients can arrive in the morning with questions about prior screenings and leave that afternoon with next steps about their individual treatment plan.

IS IT REALLY POSSIBLE?

Yes, with the right **team**, **technologies**, and **process**.

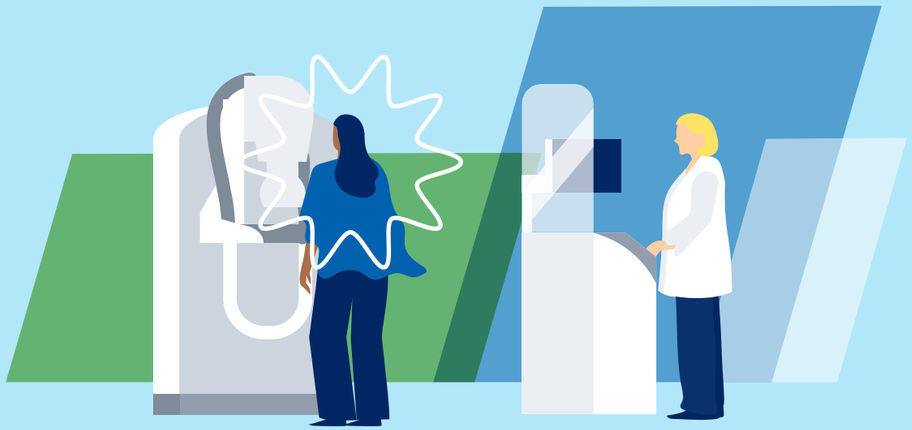
TEAM

Gustave Roussy's One Stop Clinic houses a multidisciplinary team of:

- 3 radiologists
- 1 breast surgeon
- 1 oncologist
- 1 cytologist
- 1 coordination nurse
- 1 pathology technician
- up to 5 nurses
- up to 5 imaging technicians
- 1 receptionist
- 3 medical assistants

TECHNOLOGIES

Gustave Roussy's One Stop Clinic features leading-edge technologies from GE Healthcare:



- Senographe Pristina™ Mammography Systems
- Senographe™ Essential
- SenoClaire™ 3D
- Ultrasound
- SenoBright™ Contrast-Enhanced Spectral Mammography (CESM)
- Stereotactic Biopsy

PROCESS

When coordinating care, efficiency is key, but compassion is all the more important. At Gustave Roussy's One Stop Clinic, patients are guided through their day-long visit by a compassionate patient navigator as clinicians work together to traffic patients in and out while ensuring enough time is spent with each patient:

1 Patients are referred to the center for suspect lesions.

2 Patients arrive in the morning on their appointment day, where they're greeted by a receptionist who goes over the day's schedule.

3 Once greeted, patients are seen within a triage structure and guided to consults with oncologists, surgeons, and radiologists based on their individual needs.

When needed, patients undergo same-day imaging, including:

- 2D and 3D Mammography
- Ultrasound
- Contrast-enhanced spectral mammography (CESM)
- Breast magnetic resonance imaging (MRI)

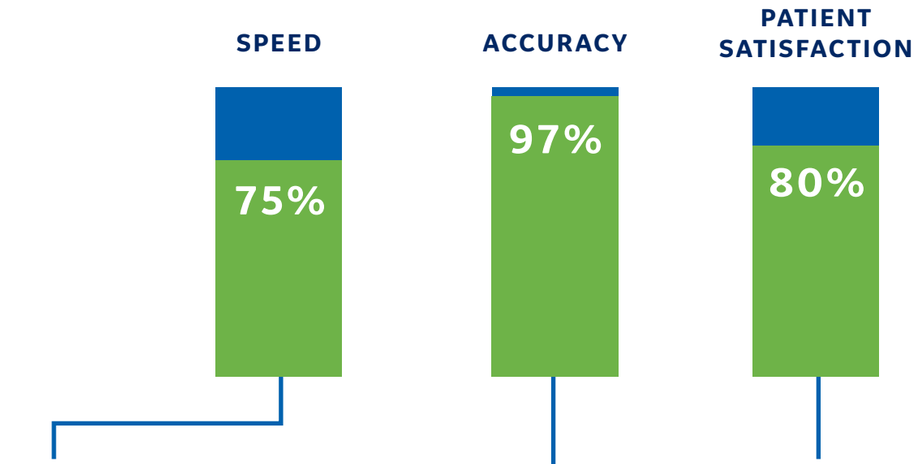
When needed, patients undergo same-day sample testing, including:

- Stereotactic biopsy (in cases of microcalcifications)
- Fine needle aspiration (in cases of solid tumors)
- Ultrasound-guided biopsy (in cases of determined malignancy)

4 At the end of the day, most patients leave with a definitive diagnosis, treatment plan, answers to their questions, and the confidence of knowing they have a path forward.

HAS IT BEEN SUCCESSFUL?

According to a study of approximately 11,000 women over an 8.5-year period, the One Stop Model has yielded unprecedented patient benefits:



Speed: In 75 percent of cases, patients received a same-day diagnosis. In some cases, test results may take longer.

Same Day Results: mammography, ultrasound, fine needle aspiration (FNA), CESM, tomosynthesis

Results Within Days: ultrasound-guided biopsy, stereotactic biopsy, breast MRI

Accuracy: Diagnoses measured 97 percent sensitivity and 99.7 percent specificity. Additionally, biopsies were avoided in 10 percent of all patients who underwent CESM.

Patient Satisfaction: More than 80 percent of patients were very satisfied with their interactions with the One Stop Clinic.

PUTTING IT ALL TOGETHER

In many places, women have to wait as long as two months or longer to see specialists after an abnormal screening—and then wait even longer for diagnostic answers. But by working from a one-stop model, clinicians can work together to make it feasible for a patient to consult with multiple experts in a single day, based on her unique needs. With the whole team working together for faster answers, it amounts to a more seamless treatment plan experience overall.

With Gustave Roussy Cancer Campus, a study was performed with ~11,000 women over 8 years and proved One Stop Clinic provides unprecedented patient benefits. JB71301XX

Sebastian Diaz, MD
National Director of Breast Diseases, SURA

"In Colombia, many women diagnosed with breast cancer have advanced disease at diagnosis."

Unlike the United States and most other Western countries, Colombia and other South American countries are experiencing not a declining rate of breast of cancer deaths, but one that is increasing.1,2

Improving Breast Cancer Care in Colombia with One-Stop Clinics

Unlike the United States and most other Western countries, Colombia and other South American countries are experiencing not a declining rate of breast of cancer deaths, but one that is increasing.[1,2] In 2018, one out of four women in Colombia diagnosed with cancer were diagnosed with breast cancer and 3,702 died. Overall, breast cancer is the most commonly diagnosed cancer in Colombia and the leading cause of cancer- related death in women.[3]

One reason for the high death rate is that nearly half of breast cancers (45 percent) are diagnosed at a late stage. Even though the government mandates coverage of screening mammograms, less than half of women who should have one receive one.[1,4] "I*n Colombia, many women diagnosed with breast cancer have advanced disease at diagnosis,*" said Sebastian Diaz, MD, National Director of Breast Diseases – SURA.

Indeed, one study of 1,106 Colombian women with breast cancer found that 81 percent were diagnosed because they exhibited symptoms rather than through a screening mammogram, and most were diagnosed with advanced stage disease. Twenty percent of the women waited more than three months before consulting a health professional.[5] Another study in the same population found that it took an average of 91 days from the time they saw a doctor to diagnosis, and 137 days before treatment began.[6]

Many years ago, Dr. Diaz said, the wait was as long as 200 days from the time a woman discovered a lump to diagnosis and treatment. Not anymore.

Faster Treatment to Save Lives

Today, thanks to the One-Stop Clinic opened with the support of GE Healthcare two years ago, women are diagnosed and begin treatment 14 days or less after their initial visit. The clinic is modeled after the One-Stop Clinic at Gustave Roussy Cancer Center in Villejuif, France, one of the leading cancer centers in the world. There, women with abnormal or unclear findings from screening may receive a diagnosis and, often, additional tests required for treatment, in just one day.

Now, in conjunction with GE Healthcare, Gustave Roussy's founder, Suzette Delaloge, is expanding the concept internationally. The Medellin facility is the first to open.

The One-Stop Clinic model is easily replicable, said Delaloge. "When you combine the right people, process, and technology, you can deliver excellent clinical, operational, and financial outcomes with increased value."

The Gustave Roussy team traveled to Medellin in March 2017 to meet the Colombian team at Ayudas Diagnósticas SURA and assess its existing clinic model. Two months later, some members of the same Ayudas Diagnósticas SURA team traveled to France to tour the Roussy clinic. There, they also received training on the organizational and clinical algorithms Gustave Roussy uses in its clinic.

Then they returned to Colombia and got to work

Today, the Colombian diagnostic clinic at Ayudas Diagnósticas SURA in Medellín operates two cycles of appointments five days a week with two breast surgeons, two radiologists, and two pathologists. About 34 patients a day pass through the clinic – double the number seen just a year ago. Since opening its doors two years ago, the clinic has screened and/or treated almost 7,000 women.

Patients who have an abnormal breast image (BIRADS 4 or 5) are automatically referred to the clinic and seen within two to three days for a multidisciplinary approach with the specialists, as well as additional exams, including a biopsy. They are then referred to the appropriate specialist to begin treatment.

"*The patients love it,*" Dr. Diaz said. "*They are in one center receiving everything they need to get a diagnosis: the breast surgeon consultation, the radiology, the pathology. The time involved is getting shorter all the time and the patients are obviously very happy with that.*"

Now, he said, "*they don't have to go from one building to another for testing and other appointments and to get approval for them, which used to mean days of missed work and additional costs for transportation and childcare.*" Instead, he said, "*when I see those patients with a positive cancer diagnosis in the clinic, they can receive a treatment decision with all needed exams.*"

Patients are guided through their journey by nurse navigators who contact them, send texts and emails, and help coordinate their care.

The physicians also love it, he said. "*We are interacting all the time in person. We're not sending emails. If I have something I don't understand or the radiologist or pathologist doesn't understand, we go and talk and take a multidisciplinary approach to making a decision.*"

The model is now spreading to other Ayudas Diagnósticas SURAs, with One-Stop Clinics opening in 2020 and 2021 in Barranquilla, Bucaramanga, Bogota, and Cali.

Dr. Diaz has this advice for other hospitals in other countries seeking to start their own One-Stop Clinic: "*Just do it. It's perfect for us, for the patient, and for the insurance company.*"

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2. Sibioa AD, Abriata G, Forman D, Sierrab MS. Female breast cancer in Central and South America. Cancer Epidemiology. 2016:44(Supp 1): S110-S120
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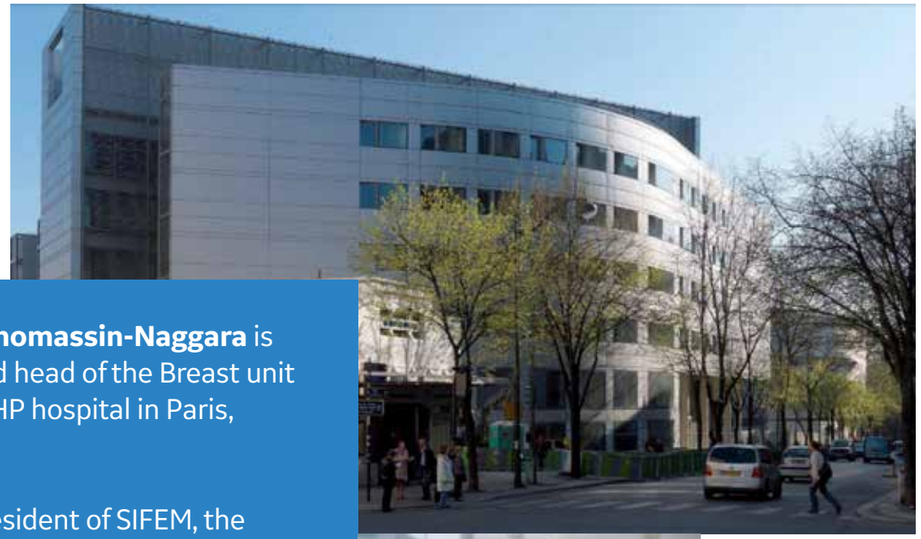
Mammography - Artificial Intelligence

Artificial Intelligence and Breast Cancer Screening

Over the past 10 years, the number of publications on artificial intelligence (AI) in radiology has increased exponentially by up to 700–800 per year. And breast screening is one of the main application in radiological imaging. Why ?
Breast cancer is a public health issue based on a clinical exam and on mammography. But one of the main limitations of mammography is the wide variability of interpretations, justifying the need to double-read each mammogram. AI could therefore be a support in image interpretation. Mammography has in fact a long history with Computer Aided Detection (CAD), and was widely implemented in the United States twenty years ago but is nowadays left aside due to a high level of false positives. This led to a certain degree of skepticism among breast radiologists with respect to the CAD concept. But CAD based on AI could be a game changer. In this article, Pr. Thomassin-Naggara will tell us what is at stake and review the performance of AI models in Breast Cancer detection



Pr. Isabelle Thomassin-Naggara is radiologist and head of the Breast unit at Thenon APHP hospital in Paris, France

She is Vice President of SIFEM, the French Women's Imaging Society and is very active in developing the future of Breast Imaging, including Artificial Intelligence to support decision-making in Mammography.

What is at stake for AI in Breast imaging?

"They are multiple areas where AI can support breast imaging. This obviously includes image interpretation, but also when it comes to improving image quality and decreasing radiation doses. Radiation dose is an important factor to consider when screening healthy women. What's more, AI could help predict the risk for Breast Cancer and personalize the screening programs".

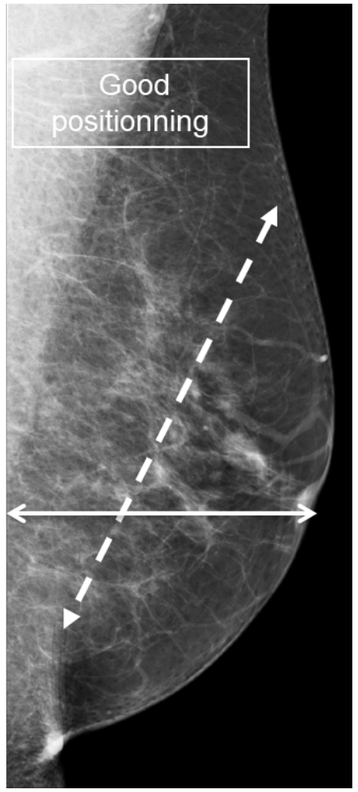
Concerning image interpretation, is AI performing better than radiologists with respect to Breast Cancer Detection?

"When comparing the performance of radiologists versus AI, radiologists perform better than AI models alone[1,2,3]. But the best approach is not to compare radiologists alone versus AI alone; it is more meaningful to combine Radiologist and AI, thus enhancing the performance of radiologists.

Studies demonstrate that these radiologists perform better than "standard" radiologists (without AI), increasing both their sensitivity (86% vs 83%) and specificity (79% vs 77%)[2]".

Does AI impact radiology workflow?

"When using AI on Standard mammography exam, there is no real impact on workflow. But, when using AI on Tomosynthesis, this leads to a decrease in reading time, regardless of the breast density".



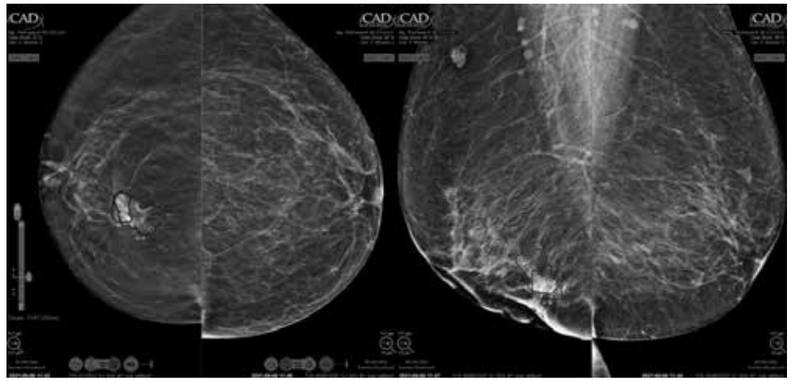


Fig. 1 Use of AI in tomosynthesis: indication of the optimal cut to improve reading time

Does breast density have an impact on the performances of AI models?

"No, studies have shown that breast density does not impact the performance of AI[3].

What is impactful is the number of views: having 2 views (Left & Right CC for example) allows improved specificity compared to 1 view[4]. This is understandable as 2 views will give information on potential asymmetry.

Interestingly, including anteriority does not impact the performance of AI[5]. But what makes a difference is having a different population to train the model on and to test it".[3]

Apart from image interpretation, how can AI provide support during examinations?

"Having an AI algorithm during image acquisition could help technicians achieve optimal positioning, define the correct compression and optimize exposure parameters.

Some software applications already allow this. After each exposure, anonymized data are sent to an external cloud database to analyze the final image quality of each diagnostic image and give advice on all acquisition parameters.

This is very powerful. If the technologist has the information when the patient is still in the room, he can re-do the acquisition if necessary. This significantly improves the workflow.

AI is also applied in the field on ultrasonography mainly to help in the characterization of lesions and on MR imaging to improve cancer detection and predict the risk of cancer by analyzing the parenchyma".

How does this impact the Breast Screening Program?

"Several studies suggest that AI model may help to reduce the workflow of screening mammograms[1] as it can exclude the presence of cancer in about 20% of women without increasing recall rate.

Is it the end of the double reading? Not yet.

1/5 of mammograms can be read by a single reader. These scored 1 /10 or 2/10 using AI. But AI will not replace

radiologists. Radiologists remain ultimately responsible for patient care".

What about ethics ?

"The Radiologist community is starting to develop codes of ethics and practices for AI.

How will we document and notify patients about how their data are used? How should we document data used to train an algorithm? What are the patient and provider risks associated with this AI implementation, and what level of human oversight is necessary to mitigate these risks? How do we protect against malicious attacks on AI tools and data, for instance?

All these questions will need to be answered before moving on to widespread implementation of AI in clinical routines".

AI RESEARCH ISSUES

Organization issue

- **To identify reasons for non-participation in the breast screening program in the French national medical database.**
- **To analyze differences in the cancer detection rates at a local level (town, districts) to better select women at higher risk.**
- **To establish prediction parameters to improve cost effectiveness of organized breast screening programs.**

Reading issues

- **To predict comorbidities (vascular calcification correlated with heart attack).**
- **To improve screening performance of radiologists with different levels of experience.**
- **To better select patients for ultrasonographic evaluation.**

A world of possibilities

We have already discussed how AI can do what human already do. Hopefully, AI can do more and better. For example, a big challenge is to personalize breast cancer screening based on risk prediction.

Studies have shown that risk prediction results coming from deep learning based on mammography are superior to those from the typical model used to assess the risk, like Tyrer Cuzick model [1, 2, 3,4].

There are also new radiomic signatures predictive of breast cancer risk, such as the complexity score of breast parenchyma on mammography, which is independent of breast density. Or background enhancement on MRI, which is also probably an independent risk factors to predict breast cancer [3, 4]

This could help to better screen our patients.

Conclusion

Artificial intelligence with deep learning will likely profoundly change the role of imaging in the patient pathway.

However, AI in radiology should be appropriately transparent and highly dependable, limiting bias in decision making, ensuring that responsibility and accountability remain with human designers or operators.

Imaging-based risk prediction of breast cancer and biomarkers are potential fantastic ways to personalize medicine to make better recommendations for our patients.

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10. Le Bouch'land Thomassin-NaggaraDII 2020

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Contrast-enhanced spectral mammography

CESM to monitor patient response to Neo-Adjuvant Chemotherapy

In Reggio Emilia CESM has been used since 2012 when the trial to understand if it would be a good tool to monitor patients under Neo-Adjuvant Chemotherapy started.

CESM was at that time an emerging tool. No-one was comfortable with injecting iodine contrast medium outside the CT room!

The primary objective of this trial was to assess that CESM is non-inferior to MRI to monitor patient's response to Neo-Adjuvant Chemotherapy. MRI was (and still is) the most widely used and recognized technique in this context.

Contrast-enhanced spectral mammography in neoadjuvant chemotherapy monitoring: a comparison with breast magnetic resonance imaging

V. Iotti et al., Breast Cancer Research, 2017

CONTEXT: Neoadjuvant-chemotherapy (NAC) is considered the standard treatment for locally advanced breast carcinomas. It improves rates of breast-conserving surgery. Assessing the disease response is fundamental and is currently assessed by MRI. Contrast-Enhanced Spectral Mammography (CESM), because it also evaluates accurately the reduction of tumor size and because it's cheaper, more available and better accepted by the patient, appear to be a relevant substitute to MRI

OBJECT: The purpose of this study was to compare contrast-enhanced spectral mammography (CESM) and contrast-enhanced-MRI (MRI) in the evaluation of tumor response to NAC

MATERIAL: CESM images have been acquired on GE Senographe Essential

METHODS : For this prospective study, 54 patients have been enrolled. They underwent both CESM and MRI before, during and after NAC (Fig. 1). Response to therapy was evaluated for each patient, comparing the size of the residual lesion measured on CESM and MRI performed after NAC (Fig. 2 & 3) to the pathological response on surgical specimens (gold standard).

Fig. 1. FLOW CHART OF THE STUDY. MRI MAGNETIC RESONANCE IMAGING, CESM CONTRAST-ENHANCED SPECTRAL MAMMOGRAPHY

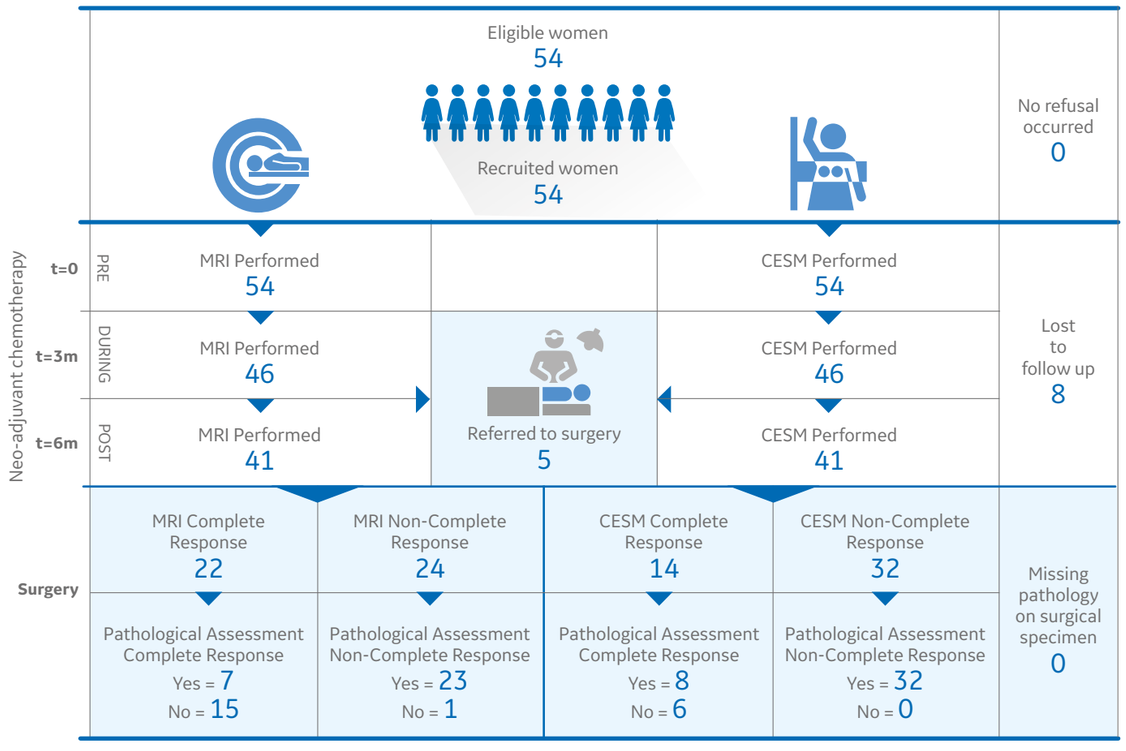
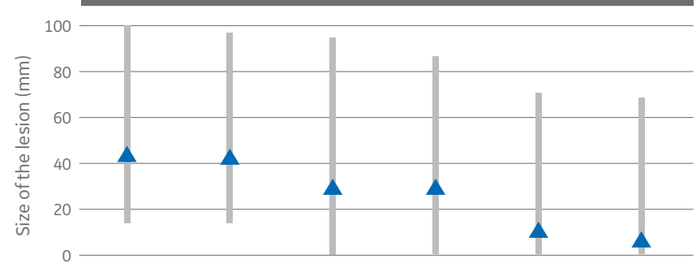


Fig. 2. MEAN TUMOR SIZES MEASURED ON CONTRAST-ENHANCED SPECTRAL MAMMOGRAPHY (CESM) AND MAGNETIC RESONANCE IMAGING (MRI). NAC NEOADJUVANT CHEMOTHERAPY

RESULTS



	pre-NAC CESM	pre-NAC MRI	during-NAC CESM	during-NAC MRI	post-NAC CESM	post-NAC MRI
Max (mm)	100	97	95	85	72	68
Min (mm)	15	15	0	0	0	0
▲ Mean (mm)	43	42	27	27	16	12

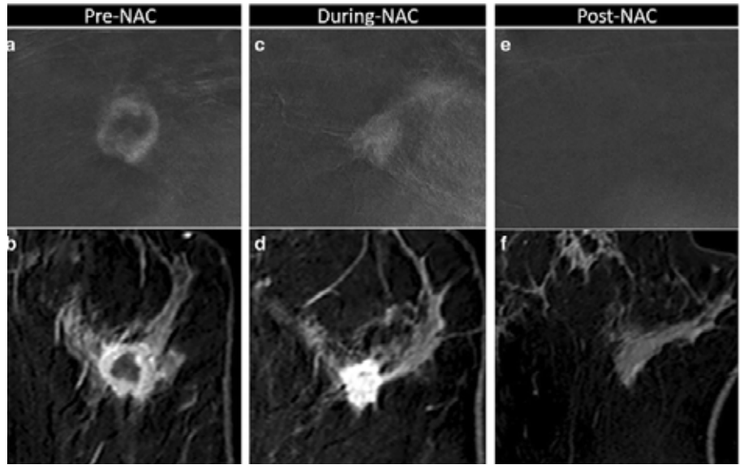


Fig. 3. Variation of enhancement during neoadjuvant chemotherapy (NAC). Complete response to NAC in a 41-year-old woman with 27 mm invasive ductal carcinoma (G3, triple negative) in the left breast, correctly assessed with contrast-enhanced spectral mammography (CESM) (a, b, c magnification of craniocaudal recombined image) and magnetic resonance imaging (MRI) (b, d, f axial post-contrast T1-w eighted at peak enhancement). Pre-NAC, evaluation showed the same round shape, well-defined margins and rim enhancement on CESM (a) and on MRI (b). During-NAC, both on CESM (c) and on MRI (d) we noted concentric shrinkage, and the tumor was no longer rimmed, with no significant loss of enhancement intensity. Post-NAC, no residual pathological enhancement was visible on CESM (e) or on MRI (f). Complete response was confirmed by the histopathological examination of the surgical specimen

CONCLUSION: CESM seems at least as reliable as MRI in assessing the response to NAC, and may be an alternative if MRI is contraindicated or its availability is limited.

Contrast-enhanced spectral mammography

Dr. Valentina Iotti

Dr. Iotti graduated from the University of Modena and Reggio Emilia, Italy.
She was then Radiology Resident at AOU Policlinico, Modena, University of Modena and Reggio Emilia, Italy, focusing on Pelvic MRI (endometriosis, colorectal cancer), Breast MRI, and Senology.
Since 2014, she has been a radiologist in the Breast Unit of the Department of Diagnostic Imaging at Arcispedale Santa Maria Nuova (ASMN), I.R.C.C.S., in Reggio Emilia, Italy.
Dr. Iotti is the author of papers about the Tomosynthesis trial in Reggio Emilia and the comparison of visualization protocols in Tomosynthesis.
She is one of the early users of CESM and published a study comparing the performance of CESM and MRI in Neoadjuvant Therapy Response Monitoring.

Context of using CESM in Reggio Emilia: Neo Adjuvant Chemotherapy trial and extended use after the results

In Reggio Emilia, CESM has been used since 2012 when the trial to understand if CESM would be a good tool to monitor patients under Neo-Adjuvant Chemotherapy started.

CESM was at that time an emerging tool. No-one was comfortable in injecting iodine contrast medium outside the CT room!

The primary objective of this trial was to assess that CESM is non-inferior to MRI to monitor the patient's response to Neo-Adjuvant Chemotherapy. MRI was (and still is) the most widely used and recognized technique in this context.

Between 2012 – 2014, 54 NAC patients were enrolled.

Surprisingly, it has been observed that CESM was not only non-inferior but sometimes even slightly better than MRI. The results were very encouraging. CESM turns out to be easy to use and safe: no severe reaction has been observed so far.

So we became more confident and started using CESM not only for NAC, but also in daily practice.

Today, 1,000 exams have been performed. There is a slot twice a week to perform Contrast Mammography so we have 6/7 patients per week and the distribution of clinical indications is the following:

60% pre-operative staging
25% problem solving
15% NAC

What evolution of CESM do you see in clinical practice?

"For pre-operative staging, problem solving, and NAC, it is already a reality!

CESM also allows us to better study women who are unable to lie down for 20 minutes in an MRI because of psychological or physical constraints. And it is easier, cheaper, and faster than MRI.

Here in Reggio Emilia, we do have access to MRI (one morning per week). But there is still a need to keep some slots for other specialties who always require more slots (especially neurology). And reducing our number of requests for MRI allowed us to free slots for other. It's a win-win situation as we don't lose any information by performing CESM instead of MRI.

MRI still has a role to play for prostheses, implants, or for very peripheral cancers, that are not in the mammography field of view."

What about CESM in the context of screening?

"We are not ready for that.
In a screening setting, asymptomatic women are imaged. In Italy, as elsewhere, we should avoid causing any harm to asymptomatic women. CESM is a 2nd or 3rd level exam, so I would not personally use it unless there is a justification to do so.

We also must think about False Positives. There are studies showing that MRI finds a huge number of cancers in screening settings. But if I do find something, I need to take the time to perform a biopsy, to find the answer, and this generates significant anxiety for the patient. So it cannot be considered to be costless.

I look forward for the ongoing trials results and will take them into consideration in my daily practice."

Italy has just authorized the use of Omnipac for CESM. How will it impact the implementation of CESM in clinical routines?

"When going to an Italian congress and sharing my experience, the audience says that CESM is great for research but it still needs to be validated in daily practice, despite the increasing knowledge about CESM and its successful results.

Today, we use a protocol that has been validated at the very beginning of CESM.

But, most importantly, use a protocol that has been validated the very beginning of CESM. No-one really studied the timing, correct concentration of contrast-enhanced mammography, because everyone has concerns about using something that has not been fully approved.

Now we can move a step forward and study the perfect protocol and concentration, according to the clinical indication and the type of cancer. For example, lobular cancers have a different behavior compared to DCIS or Triple Negative, this is only for observations, it has not been clearly described to improve the protocol based on this.

I believe we should rely on what is used for CT. There is no reason why we should do something different for breast cancer."

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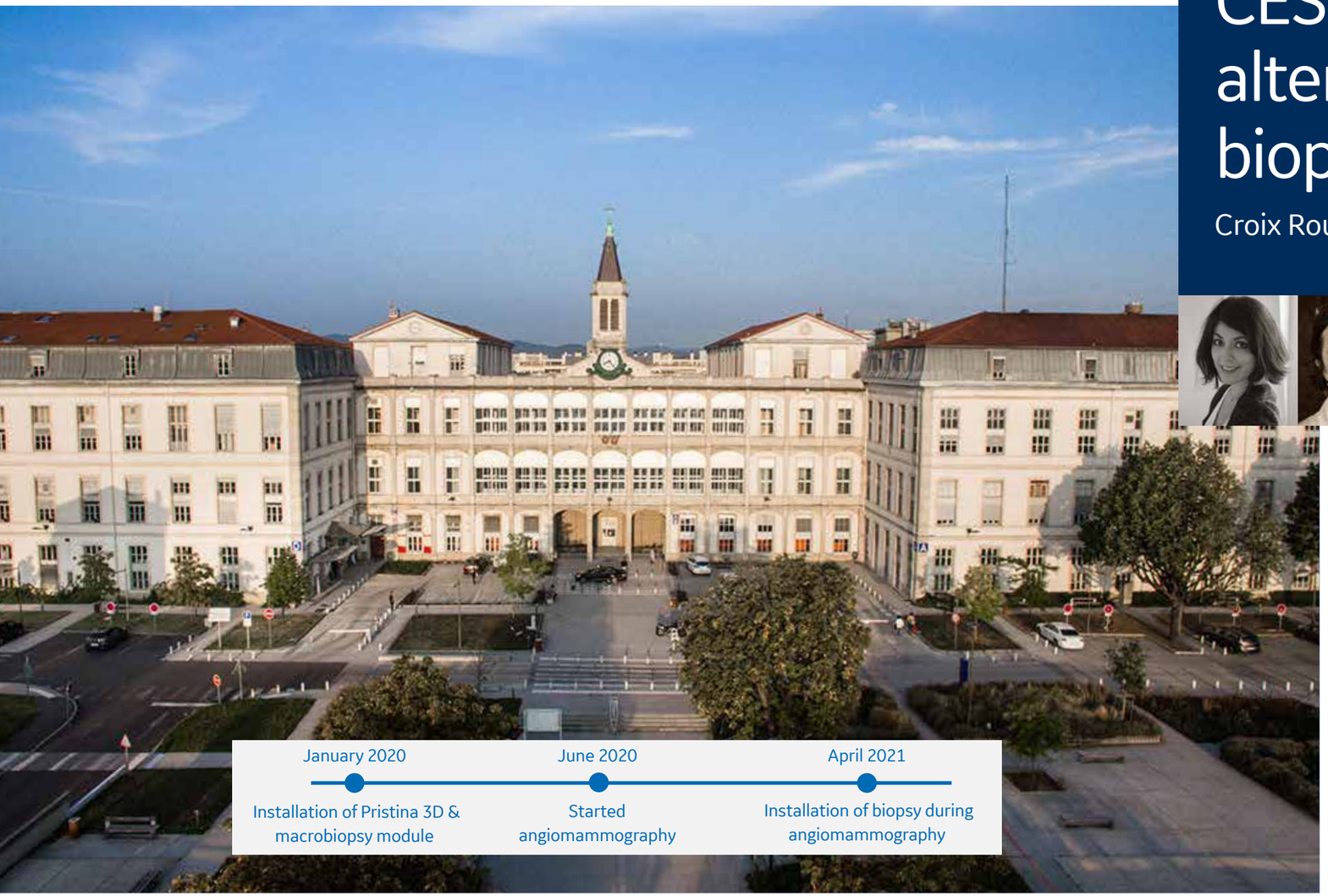
Contrast-enhanced spectral mammography biopsy

CESM biopsy, a new alternative to MRI guided biopsy in Lyon

Croix Rousse University Hospital, Lyon, France



Croix Rousse University Hospital in Lyon, has a dedicated breast imaging department, with four medical radiologists, one x 1.5T MRI scanner, one x 3T MRI scanner and ultrasound equipment. In January 2020, the team added a Pristina Mammograph with tomosynthesis as well as a biopsy robot. Then, in June 2020, the addition of a CESM module allowed them to start performing contrast-enhanced mammography (CESM) exams. Lastly, in April 2021, the CESM biopsy module was added to the team's routine care procedures, offering the ability to conduct biopsies on lesions visible on contrast-enhanced mammography but not depictable on routine mammography nor ultrasound. Dr. E. Maissiat and Dr. D. Taconet explain to us how the role of contrast-enhanced mammography has changed within the department since the introduction of the CESM biopsy procedure.

Tell us about the introduction of CESM in your institution

"We started performing contrast-enhanced mammography in June 2020. It was very easy to implement this new technique. We quickly realised what a simple, quick and intuitive diagnostic tool CESM would be. Besides the injection of iodine contrast agent, a contrast-enhanced exam is just like a routine examination. We just have to request a creatinine test (only for patients with history of kidney disease, diabetes, taking nephrotoxic drugs or above 60/65 years old) and check for any history of allergies.

Beforehand, technologists go through the patient's file with the radiologists in order to plan the laterality of the images to be taken post injection. Here, we start with the healthy CC view, then the pathological CC , followed by pathological MLO and healthy MLO and a profile view of the pathological side.

To make the patient's visit more seamless, we prepare the consultation room in advance (equipment for inserting the catheter and injector)

Since we started performing contrast-enhanced mammography at the end of June 2020, the number of CESM exams has increased significantly. 80 examinations were performed between June 2020 and July 2021. We could not have imagined doing so many in this time, given the reduced level of activity during the lockdown periods.

We use CESM for the following clinical indications (which are common to MRI, and which can be found in the bibliography):

- *Preoperative assessment : for outpatients, especially in dense breast, CESM brings relevant information*
- *Inconclusive mammogram (solving problem)*
- *Discrepancy between Mammography & US findings (especially in terms of lesion size) (figure 3)*
- *Chemotherapy follow-up (instead of MRI)*
- *2nd look post MRI*

After a while, given our rapid learning curve involved for CESM, its acceptance by the team and its clinical advantages for both radiologists and surgeons alike, we "transferred" some of our MRI indications over to CESM.

Of course, for some patients, particularly those at high risk or ACR3 MRI, or those being prepared for or coming out of plastic surgery, we always perform an MRI.

But we now easily use CESM if an exam with contrast injection is needed to complete the imaging assessment.

It's quicker for us and for the patient, and the extra procedure is performed using the same system and the same team that the patient is used to. Patients seem to prefer that.

For us, CESM gives a clear and easily interpreted image in a few minutes. This takes the pressure off the queue for an MRI."

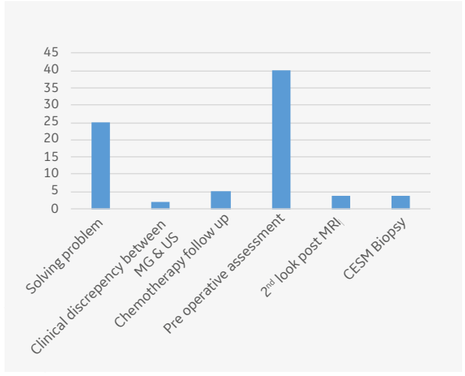


Fig. 1 CESM clinical indication at Croix Rousse University Hospital

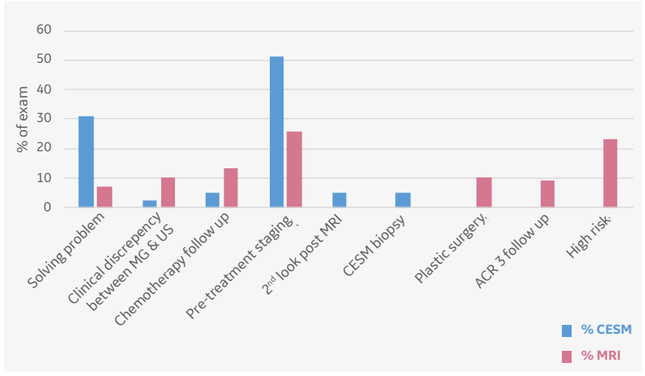


Fig. 2 Evolution of clinical indications : from MRI to CESM

Clinical cases

Patient, 58 years old, coming in for a screening, with a family history of breast cancer and a palpable nodule in the right upper outer quadrant. Biopsied nodule is a carcinoma in situ without microcalcification.

In the routine mammogram images, we can see a nodule measuring 32 mm, therefore much larger than what could be felt during the clinical examination.

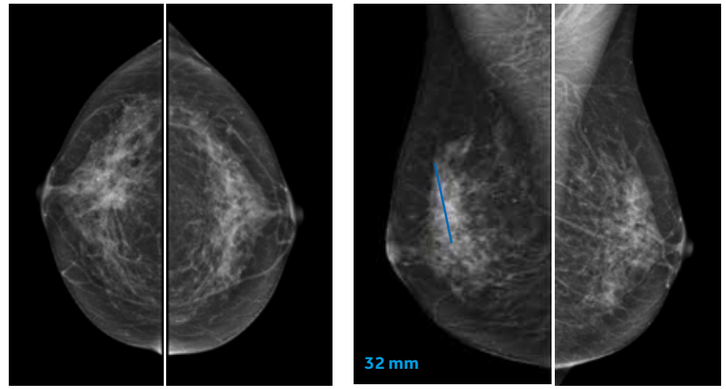
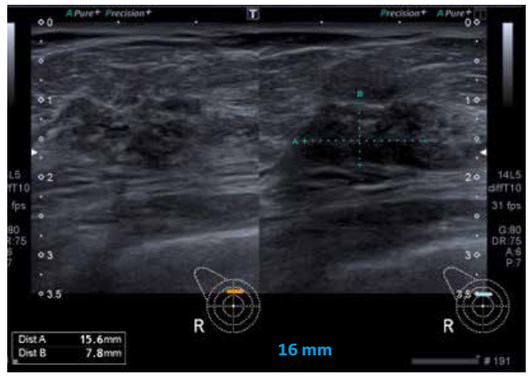
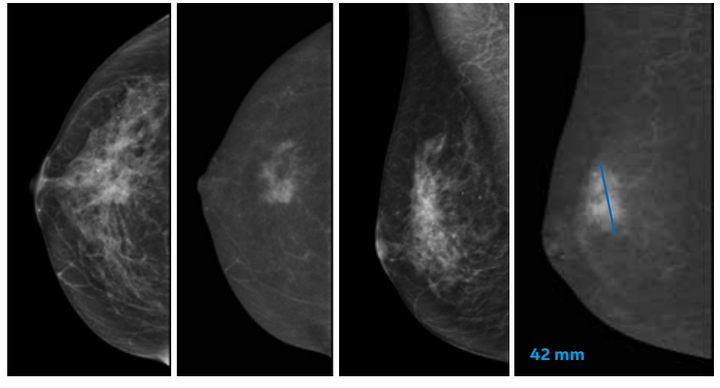


Fig. 3 Lesion size discrepency between Mammography and ultrasound images



On Ultrasound, the lesion results in a poorly visible heterogeneous hypoechoic patch, measuring 16 mm the on ong axis

We have a discrepancy between the clinical examination, mammogram and ultrasound images. We therefore proceed with a CESM exam.



The CESM recombined images give a better view of the extent of the lesion and showed an enhancement of 42 mm. The patient underwent surgery. The biopsy results confirmed a high-grade in-situ carcinoma of 48 mm in the excised tissue. CESM therefore displayed a better correlation between the size of the lesion in the recombined image and the anatomical pathology result.

You are among the first hospitals to use CESM biopsy equipment. How was this new technique received and how is it used?

"You are right, we've had this CESM biopsy capability since April 2021. As we've had already learnt to use the biopsy robot and the CESM technique, there was a rapid learning curve for both the radiologists and technologists. Here is our first case.

Mrs. M., 71 years, presented for a pre-treatment assessment for an infiltrating lobular carcinoma in the left breast showing a size discrepancy between the imaging and clinical results. A breast MRI has been carried out by another clinic. The MRI showed a much larger lesion on the left breast than initially suspected, with extension behind the nipple. It also shows a lesion in the right breast, at the union of the upper quadrants.

We performed a CESM exam. In the low energy images, we could see the left index spiculated lision.

The recombined CESM images concurred with the MRI, showing the extent of the lesion on the left and the additional contra-lateral lesion.

The index lesion of the left upper outer quadrant revealed an invasive lobular carcinoma. We also performed a second-line US guided biopsy, retro-areolar, after analysis of the CESM recombined images, which also revealed an invasive lobular carcinoma.

The right-hand lesion was however neither visible in 2D nor in tomosynthesis and went undetected in the ultrasound. Because the lesion enhanced on the routine CESM, we therefore decided to carry out a CESM guided biopsy.

The patient was injected with Xenetix 350 then, two minutes later, the breast was compressed. A lateral approach was chosen

The stereotactic localisation images (0, +15, -15) (Figure 5) helped to locate the lesion within the recombined images.

We positioned the target on the nodular lesion, at the union of the right upper quadrants. The lesion measured 7 mm."

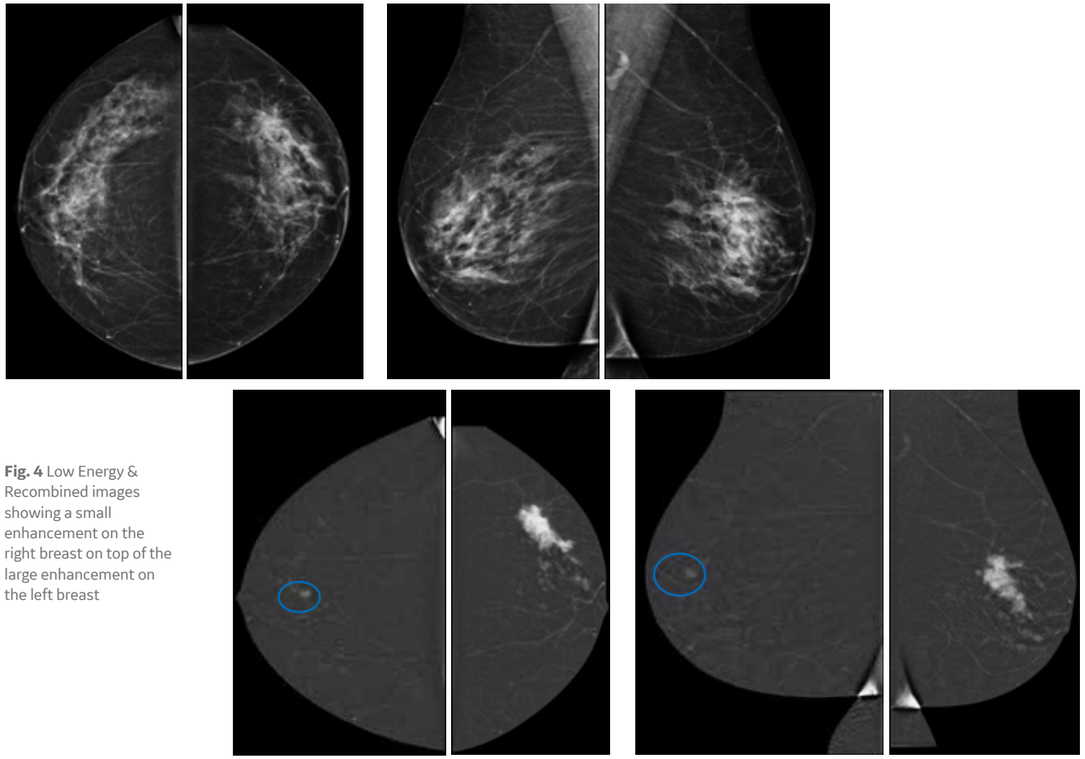


Fig. 4 Low Energy & Recombined images showing a small enhancement on the right breast on top of the large enhancement on the left breast

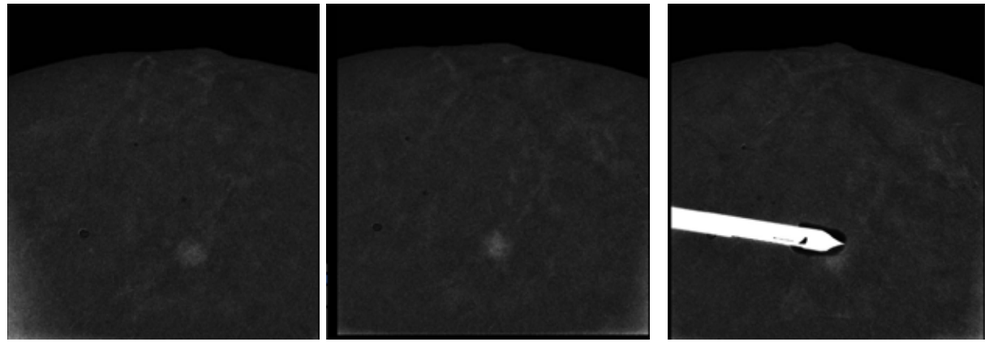


Fig. 5 Stereotactic localisation images (+15, -15) targeting the enhancement Seen with needle in a lateral approach.

Results

The biopsy showed an infiltrating ductal carcinoma associated with a DCIS of intermediate grade.

A mastectomy is planned for the left breast and a tumorectomy for the right breast.

Conclusion

Our recent experience of using CESM and CESM guided biopsie has shown us that this additional tool helps avoid performing MRI guided biopsy, which is a cause of stress for the patient. A biopsy under MRI is a long procedure where we are less sure of correctly targeting the affected area.

With CESM, we feel that the patient is getting a more comprehensive assessment. If there is no contrast in the images, we can simply send the patient home without any false sense of security.

With CESM, the technologists feel more involved in the patient's care. This improves their skills and gives them a greater understanding of the various types of cancers. Moreover, technologists working in tandem with radiologists is very rewarding.

For the patient, waiting times for a consultation are shorter than for an MRI, which means they are taken care of much more quickly, especially if they then require a consultation with the oncologist and surgeon. CESM helps take the anxiety out of the exam, as patients are reassured immediately after the examination by the doctor if there is no contrast in the images. And the procedure is also more comfortable procedure for the patient than with an MRI.

CESM Biopsy: Case Report

Dr Arenas, Hospital del Mar, Spain

Patient History

We have the case of a 52-year-old woman. She had a left breast neoplasm in 2005, who was initially treated with a conservative treatment comprising a tumorectomy, radiotherapy followed by chemotherapy. However, in 2014 the patient developed a local recurrence in the form of a carcinoma in situ, which led to a unilateral left mastectomy. Since then, the patient has been having her annual radiological check-ups with a mammogram and ultrasound and now in 2021 she is coming for her regular radiological check-up..

There are no relevant findings on the mammogram and the ultrasound does not highlight any suspicious focal areas either. However, the patient has been complaining of discomfort in the upper outer quadrant of the right breast for the last few months. Taking into account the patient's history, the high risk of recurrence and the risk of developing a contralateral neoplasm, we decided to further investigate with a contrast-enhanced mammogram.

Although in the low-energy images there are no relevant findings, in the recombined images, we see an extensive, non-mass and heterogeneous contrast enhancement. This is mainly located in the union of the upper quadrants and towards the upper outer quadrant of the right breast, coinciding with the symptomatic area reported by the patient. We also see that the radiological marker in relation to last year's biopsy does not show any pathological uptake. The patient has an intense background enhancement, which is, as with an MRI, a hormonal factor that also diminishes sensitivity to a certain degree.

We have a pathological enhancement which has no translation either on the standard mammogram nor on the ultrasound. So the only option to perform a biopsy is guided by functional technique.

Until very recently, the only option to biopsy lesions that manifested as real pathological lesions were MRI guided biopsies. What were the disadvantages of this procedure? One of them is the limited availability of MRI time in the hospital. MRI

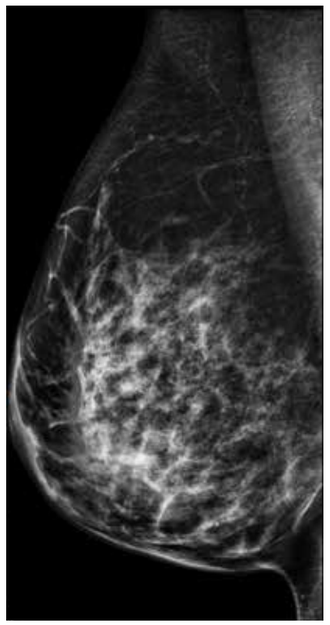


Fig. 1 Mammogram of the right breast : nothing suspicious

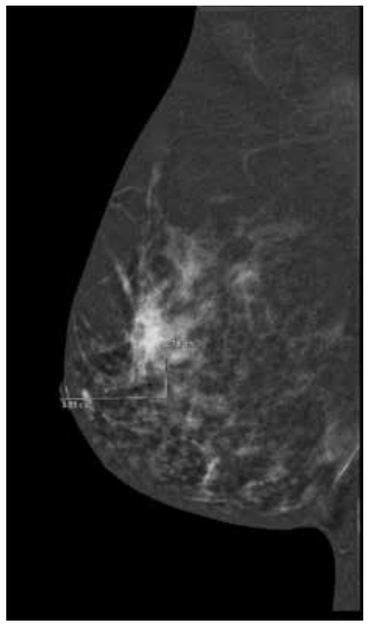
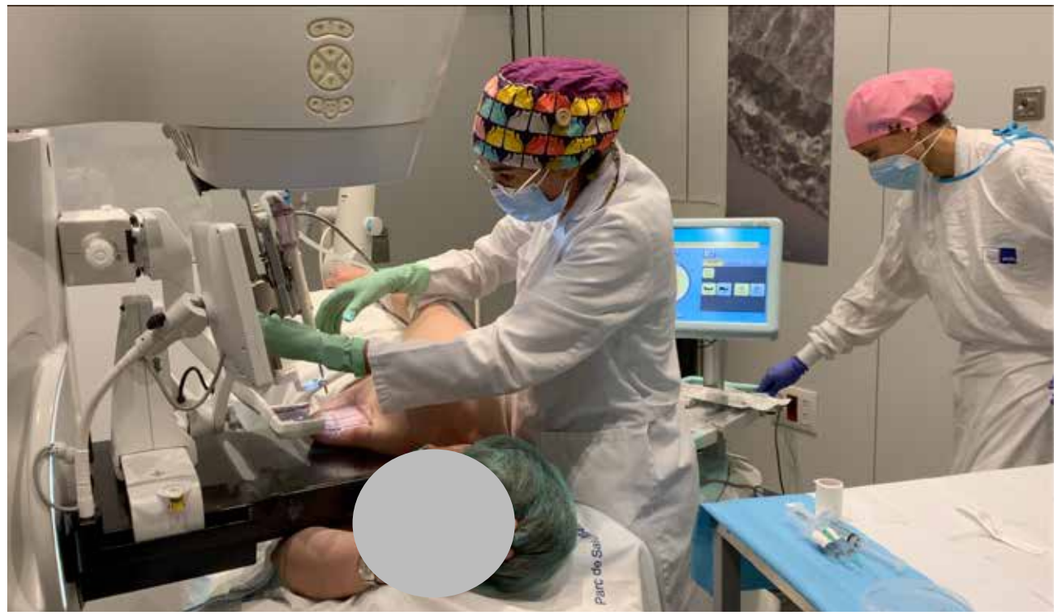


Fig. 2 CESM images show heterogeneous contrast enhancement



biopsy procedures take a considerable amount of time - it may take an hour, an hour and a half or even two hours to perform this biopsy procedure, depending on the hospital.

This means deprogramming for the duration of the procedure, as this requires blocking the MRI equipment, leaving several simple patient MRIs unperformed, which for a hospital is difficult to manage at an organizational level and often means postponing the scheduling of these procedures. The other alternative is the mammogram biopsy with contrast, which uses the dual energy technique that allows us to assess both the mammogram and the associated pathological enhancement.

This procedure is much quicker, usually not taking more than 15 minutes in total and is much better tolerable by the patients, as they remain still for almost an hour for an MRI biopsy. This makes it unfeasible for elderly patients with back problems for example. The shorter duration also blocks the equipment for a lesser period of time.

In general, for the hospital this means no inconvenience at the scheduling level for blocking a space for this biopsy, which facilitates everything. This means that the patient's diagnosis will be made in a very short time. In this case, the period between the mammogram and the biopsy result is no more than ten days. This is more like the time required for a pathology report than that for a radiology procedure.

Histopathological Result

In that case, the pathological report of the biopsy confirms the presence of multiple scattered foci of hyperplasia, as well as an in situ lobular carcinoma. These kinds of lesions are known as B3 lesions or lesions of uncertain malignant potential, which correspond to a heterogeneous group of abnormalities that are in a histological spectrum, borderline to malignant lesions.

In this case, taking into account that the patient is high-risk because she has a history of contralateral breast cancer under the age of 50, she will be brought back to the Multiple Disciplinary Breast Cancer Committee to define whether an exegesis or simply monitoring will be needed.

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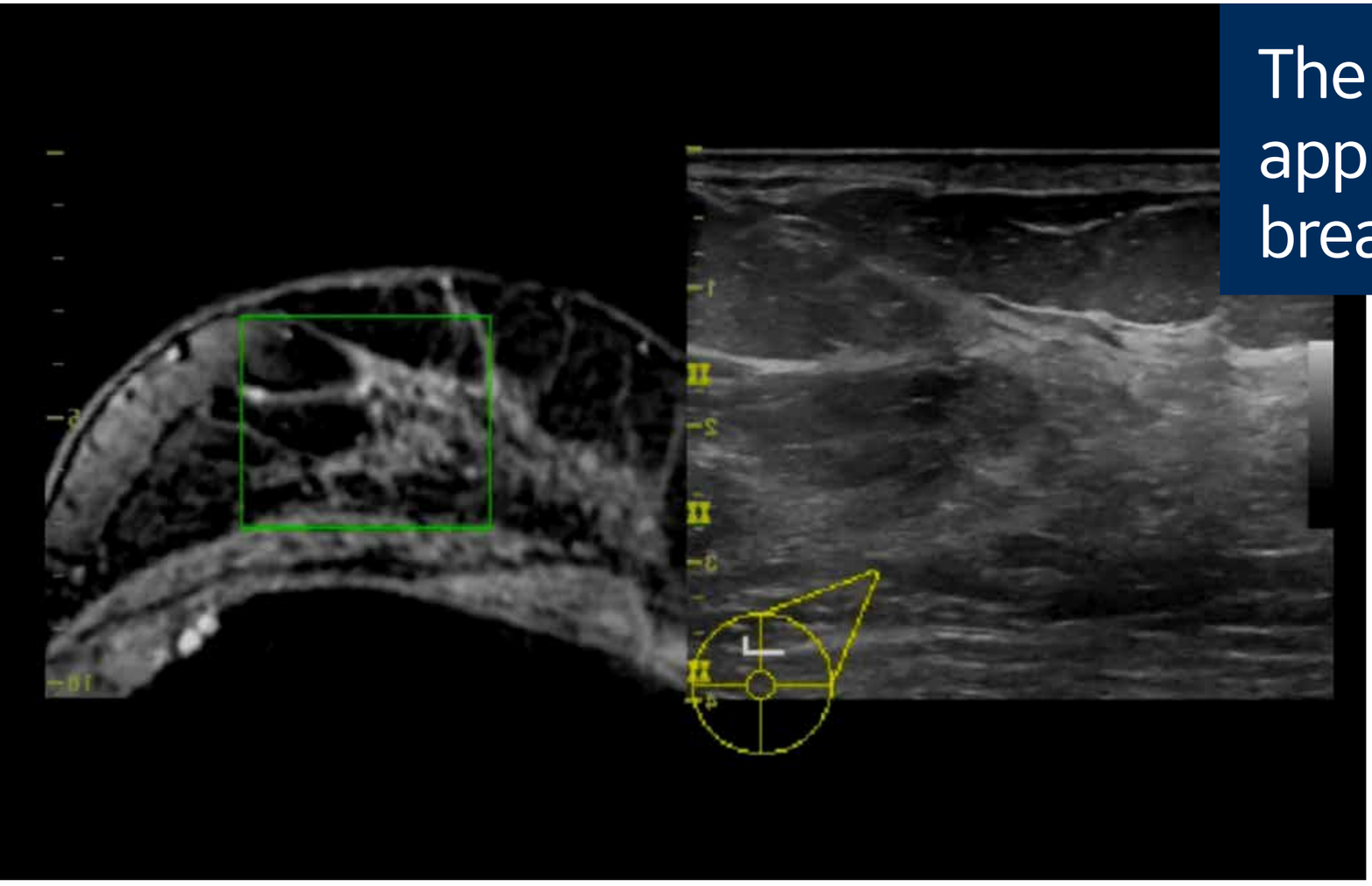


The value of a multi-modality approach for a personalized breast care.

There are many variables that we must address every day to obtain an effective and timely diagnosis for breast cancer. These include the different ways breast cancer can manifest itself in the breast, different breast structures and different imaging techniques. The solution is to find the best combination of treatments in a Personalized Breast Care program, which means applying the right combination of methods to these different situations. More importantly, this is a way of thinking using the knowledge we have of the many techniques available for breast diagnostics that are used in different people to enhance the quality of care. Below is an example of a clinical case which illustrates these challenges where a potential false negative was subsequently found to be positive due to careful multi-imaging and a thorough investigation.

Dr. Fausto
I have been working for the last eleven years in the Radiology Department of the Azienda Ospedaliera Universitaria Senese directed by Prof. L. Volterrani, a leading expert in computed tomography. Here I continue the work started in Gorizia by applying Fusion Imaging also to double energy CT and MR. Being able to use many more different techniques also available in the Breast Department, directed by Dr. F. Fantozzi. The diagnostic path starts alike for all patients but in dealing with specific cases the path often undergoes variations in order to customize the combinations of selected techniques and get the best result out of it. At the standard examinations for breast, mammography and ultrasound, in Siena I have the opportunity to add magnetic resonance imaging, dual-energy CT, mammography with contrast media and all types of biopsies guided by different imaging techniques (all from GEHC). The best combination is never accidental, but it comes as result of confrontation with colleagues having different experiences and memories of earlier mistakes.

From my father, a passionate tailor, I learned how on every occasion the right suit is sewn with the best fabric, depending on the dress model and the morphology of the client.

The outcome may be a result that does not take into account knowledge and so will not necessarily be the best result.

In the same way, in medicine I learned that we can and must offer each woman a different diagnostic path suitable for her own body and age, using different techniques and methodologies based on risk factors and a clinical history. Each decision is refined with the experience and knowledge of different investigators, multiple techniques and different types of breast disease.

Tell us something more about yourself

"I started my medical career in the air force, perhaps because I wanted originally to be a pilot. Later, I worked in general practice and contact with patients gave me a lot of satisfaction. However, following a meeting with some colleagues in a hospital setting, I was convinced that with graduate studies in radio diagnostics I would find my way.

Initially with Prof. F. Sardanelli and subsequently with Dr. G. Rizzatto, I understood that breast care would become my passion. They taught me to take a broad view of each of their own fields: MRI and ultrasound respectively. The love for research and the desire to experiment with new paths reached a peak in Gorizia with the use of the first LOGIQ E9 ultrasound prototype which allowed us to perform research in the purest sense of the word. We found a simple solution for a complex technology by combining two different techniques in a new modality: Breast Fusion Imaging with Volume Navigation. It was a real opportunity to grow professionally in a place where all cutting-edge technology was available with exceptional experts.

I have been working for the last eleven years in the Radiology Department of the Azienda Ospedaliera Universitaria Senese directed by Prof. L. Volterrani, a leading expert in computed tomography. Here I continue the work started in Gorizia by applying Fusion Imaging to double energy CT and MR. In this way, I was able to use many more different techniques also available in the Breast Department, directed by Dr. F. Fantozzi. The diagnostic path starts alike for all patients but when dealing with specific cases the path often diverges to customize the combinations of selected techniques and achieve the best result. In standard examinations for breast mammography and ultrasound in Siena, I have the opportunity to add magnetic resonance imaging, dual-energy CT, mammography with contrast media and all types of biopsies guided by different imaging techniques (all from GEHC). The best combination is never accidental, but comes as a result of conferring with colleagues with different experiences who have learned from past mistakes.

What would you recommend to your colleagues using the Breast Ultrasound approach?

"I would like to share a thought with those who have recently approached this profession: everyone can contribute in a unique way to improving knowledge. I feel lucky because in our field, technology allows us to obtain results that otherwise would not be possible. In any case, it is important to remember that the most important tool to use is our brain. This is where we understand how we can selectively and specifically adapt all the available tools to the different situations we encounter every day, making each medical procedure unique for specific patients."

What are your expectation of the Industry in Breast care?

"The industry has been making great strides in breast care... Today there is a vast amount of equipment available in different fields of applications and the biggest challenge is determining the different combinations to design a suitable diagnostic path to obtain the best diagnosis. Artificial Intelligence will certainly support this development. I am sure that the greatest support will not only be in providing the technology but also applying the training background accumulated over time which will shorten the learning curve of each individual diagnostician and lead to sharing of experiences."

Why and/or when should Fusion Imaging US/MRI of the Breast be used?

"Breast Ultrasound/MRI fusion imaging is a very important technique that we have practiced since 2009. Combining the sensitivity of MRI with the real-time imaging of ultrasound, Fusion Imaging of the breast provides a second look or guidance for simple interventions . We know that lesions are much more visible in MRI so it's very important to have a technique combining the advantages of both methods."

Which patients are eligible for breast MRI ultrasound fusion?

"We use the Fusion technique in patients where breast lesions are not visible in ultrasound but are clearly detected with MR imaging. In these cases, we can consider using fusion imaging to take a second look or obtaining a pathological answer from a biopsy. In these cases, biopsies can be performed under US/MRI guidance. We first need to be sure that the patient is eligible for the procedure as this depends on breast size. This type of technique is not suitable for large breasts and the patient will need an MR-guided biopsy. All other patients with a small or medium breast can undergo a biopsy under volume navigation guidance, reducing the need of MR guided biopsies. This helps decrease overall procedure costs and

patient discomfort."

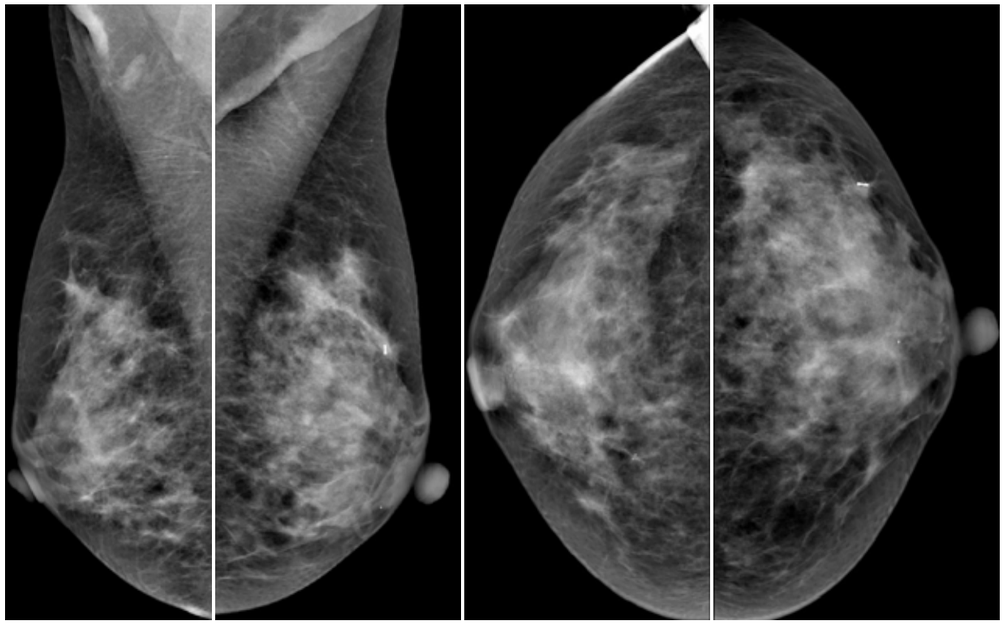
Why is the position to remain using vitamin E pills important?

"To perform a correct US/MRI fusion, it is key to overlap two different MRI and Ultrasound 'volume datasets'. For this purpose, we need to identify three corresponding points in the pertinent volumes to be sure that the volumes correspond to each other. Before performing MR imaging you must place these markers on the patient breast surface volume that will be recognized in live US. We decided to use three vitamin E pills during examination of the MR to have the reference during the live ultrasound examination. You can choose your own position but we choose to place the pills on the three o'clock, midday and nine o'clock positions for guidance according to the position of the lesion."

Case history

47 years old woman came during annual screening with mammography.
Previous QUART (quadrantectomy) at lower inner quadrant of the right breast for DCIS three years before.
Breast biopsy with mammography-guidance at the upper external quadrant of the left breast one year before.
No family history.
No genetic test.

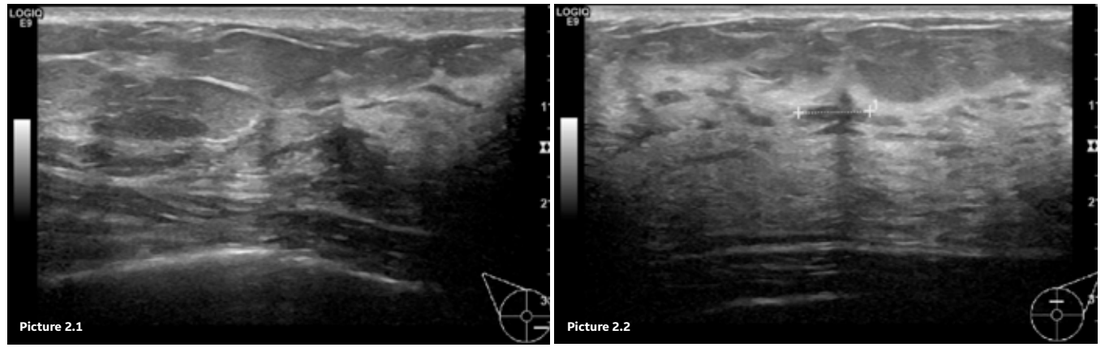
Mammography | BIRADS 1



Picture 1 In the Mammography exam, we could see the marker left after the XR-guided biopsy.

The overall image showed a pattern of the breast with some small calcifications. The exam was classified BI-RADS 1 being not suspicious. Due to the History of the patient, an ultrasound was performed.

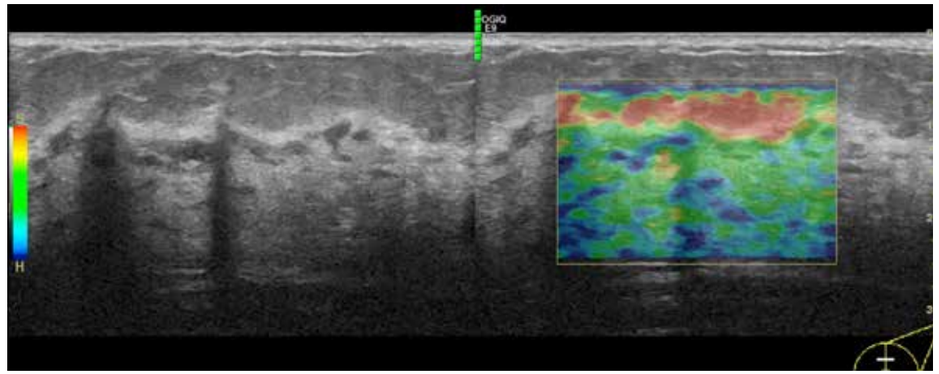
Breast us



Pictures 2 In Ultrasound we started from the right breast where we could see some details of the inner quadrant that underwent into previous quadrantectomy. Here we identified an enlarged duct (Picture 2.1), the axilla was negative. So diagnosis was a Segmental ductal ectasia at the lower internal quadrant of the right breast in the area of the previous QUART.

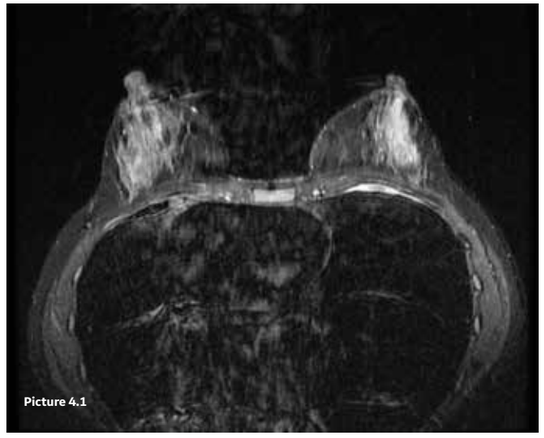
Left breast: in a homogeneous glandular pattern, at the confluence of the upper quadrants of the left breast, it was visible an irregular hypoechoic breast lesion of about 7 mm (Picture 2.2). The axilla was also negative.

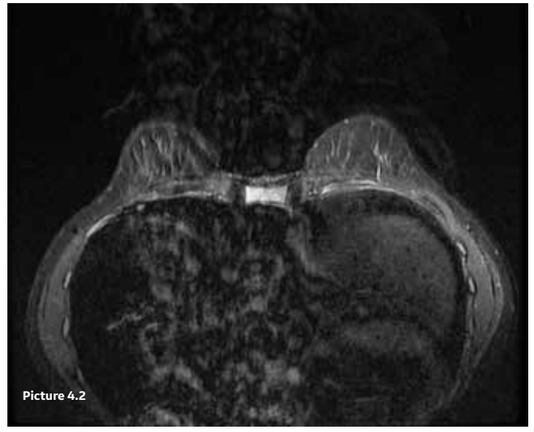
Breast us elastography | BIRADS 4a



Picture 3 A Strain elastography examination of the 7 mm lesion in the left breast was then performed. The exam was negative but the morphological classification of the lesion was BI-RAD 4a. Decision to perform a Breast MRI because of the history of previous quadrantectomy for DCIS.

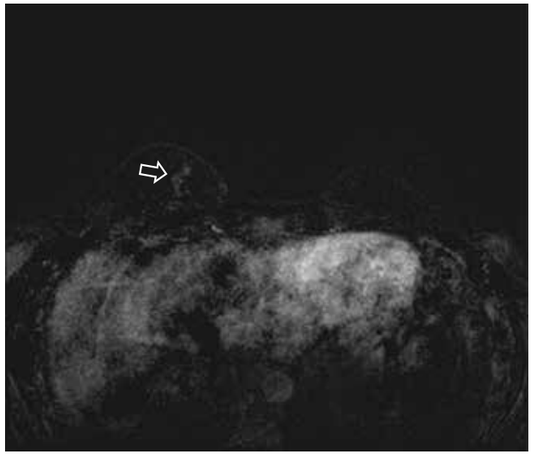
Breast MRI: STIR seq.





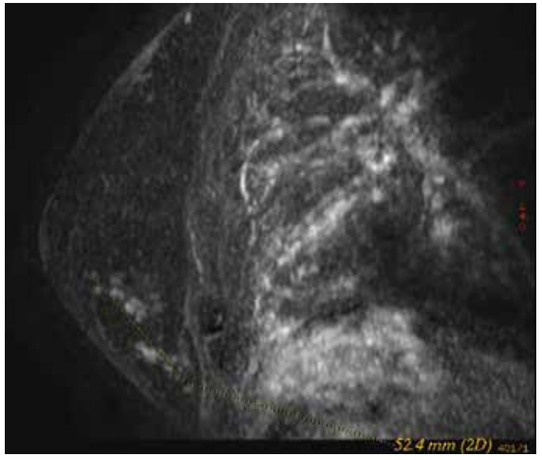
Picture 4 Breast MRI with a STIR sequence. The image acquisition was negative, not suspicious finding.

Breast MRI: DYN seq.



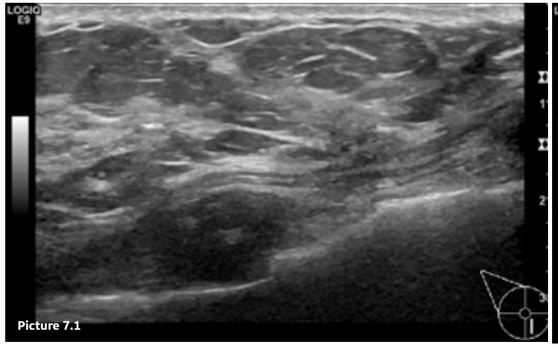
Picture 5 MRI with a Dynamic subtraction post contrast sequence. Findings: lesion in the inner quadrant of the right breast.

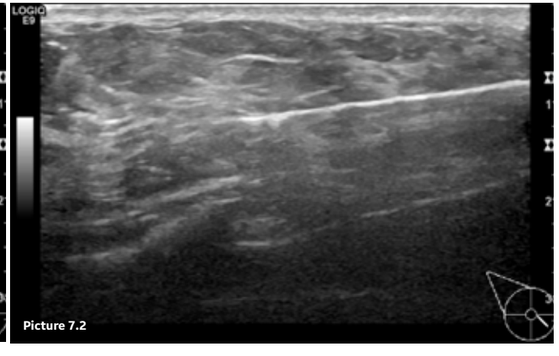
Breast MRI: MIP DYN seq.



Picture 6 The maximum density projection of the right breast showed a 52 mm lesion in the area of the ductal ectasia. This looked very suspicious within the history of a previous quadrantectomy for DCIS.

Breast us - Guided biopsy



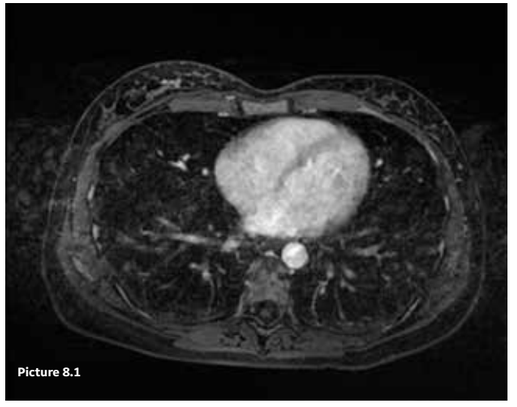


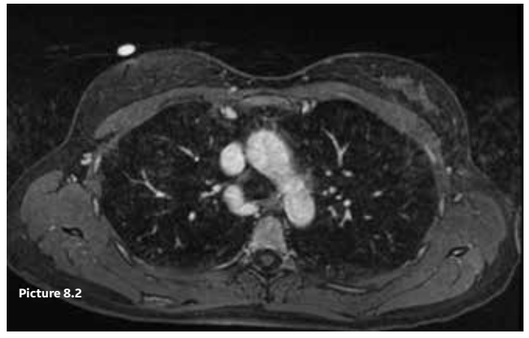
Pictures 7 US-guided breast biopsy of the ectasia. Can see the needle in its length (Picture 7.1, 7.2).

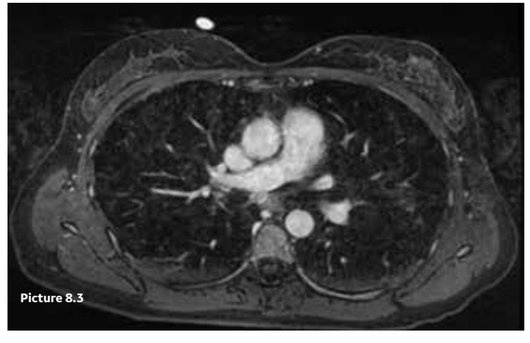
Pathology: Atypical Ductal Hyperplasia.

Literature shows a low concordance of Atypia from pathologists then decision was for additional investigations. Went for a US/MRI Fusion guided biopsy, because in a small breast and in this anatomical area would have given higher confidence and accuracy.

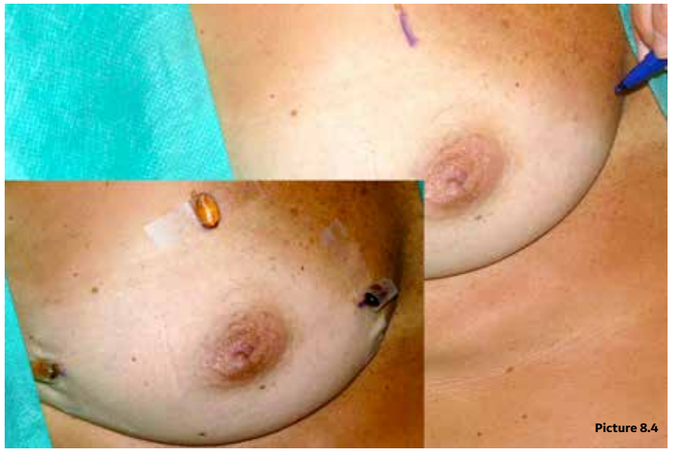
Dynamic Breast MRI in supine position



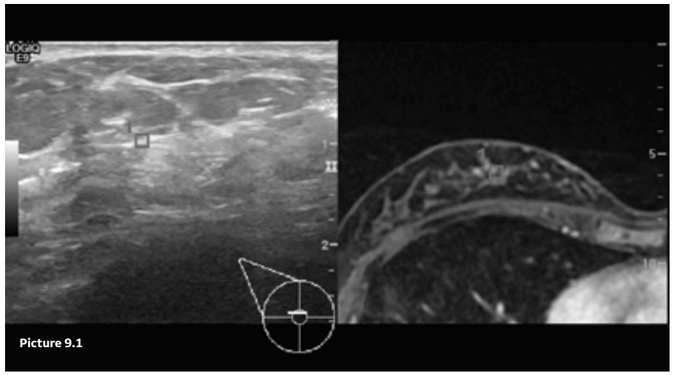


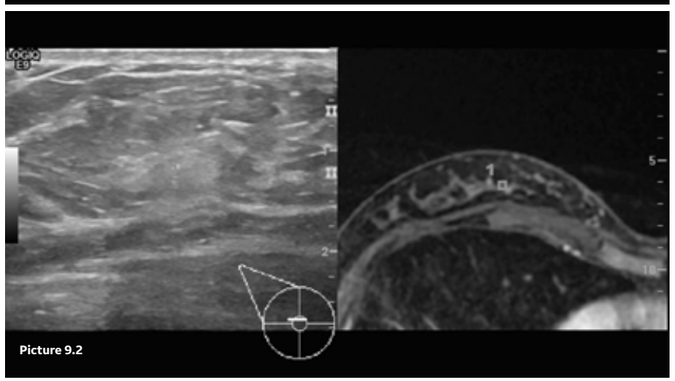


Pictures 8 To perform Fusion Imaging we had to acquire a MRI exam of the breast in supine position, placing some capsules of Vitamin E on the surface of the right breast (Picture 8.4), close to the lesion as reference points (Picture 8.1, 8.2, 8.3). We also did perform then an acquisition with the subtraction DYN sequence to have a volume where the lesion could be very well visible.


Picture 8.4

US/MRI Fusion guided biopsy


Picture 9.1

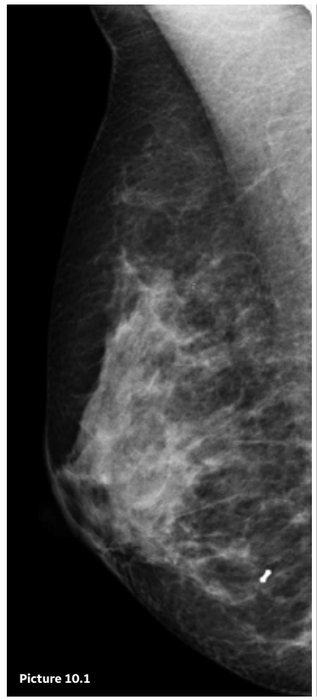

Picture 9.2

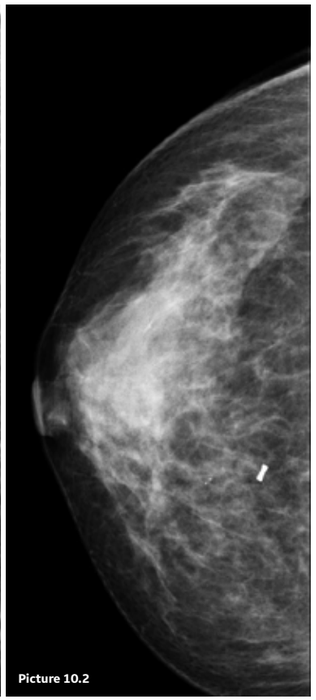
Picture 9 US/MRI Fusion Imaging performed using external vitamin E markers and internal anatomical structures as references to execute the Fusion registration (Picture 9.1)

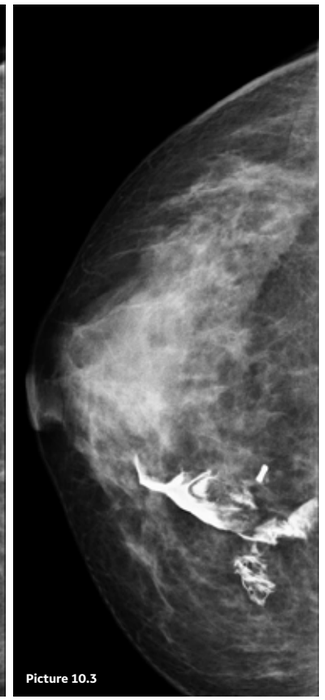
Once the registration in place, had perfect correspondence in between the two modalities, allowing to be accurate in biopsy targeting. The MRI image, showed very well the position of the lesion while ultrasound allowed a live guidance of the procedure

In Ultrasound could see the needle placing a tissue marker (bar-bell shaped pyrolytic carbon coated ceramic - BiomarC) for surgical intervention if needed (Picture 9.2)

MX correlation


Picture 10.1


Picture 10.2


Picture 10.3

Picture 10 It is important to find a correlation between the findings in MRI and Mammography.
We did perform a Mammography examination after the tissue marker was in place (Picture 10.1 - 10.2)
We then injected a mixture of vegetal charcoal and iodinated contrast media
(iopamidol) during the correlation to see the extension of the lesion in the area of the tissue marker positioning (Picture 10.3)
This allowed the surgeon to detect the area for pre-surgical assessment even when not detectable in the prior mammographic exam.

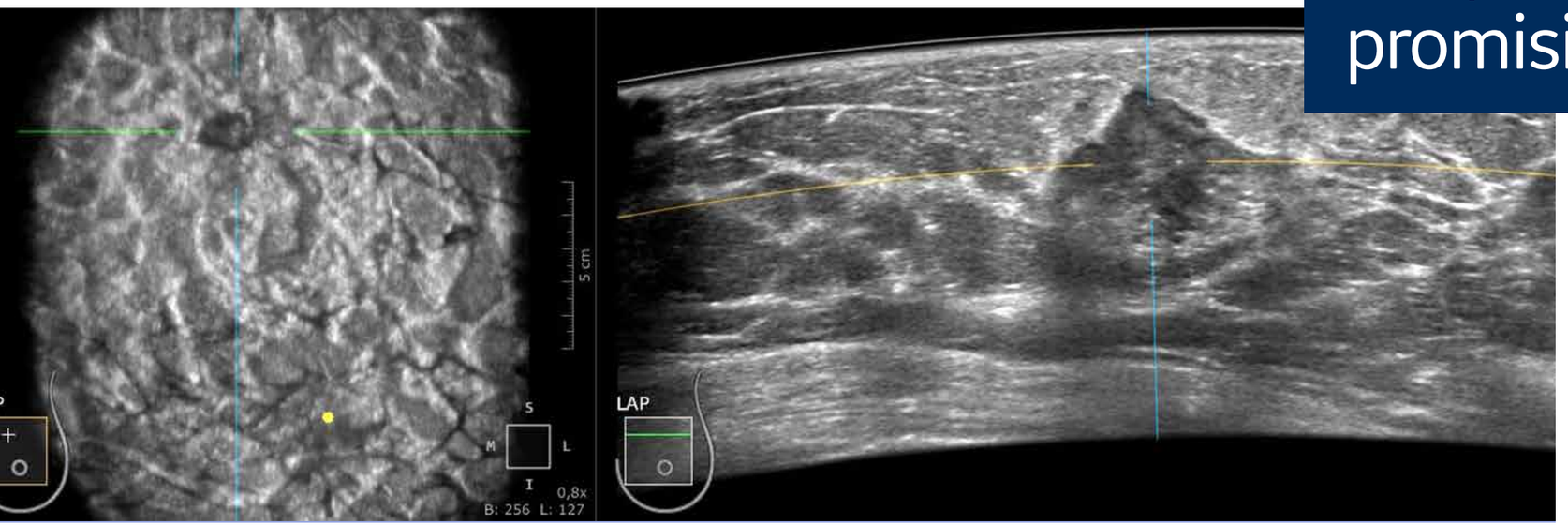
Final diagnosis

Pathology
Final diagnosis was a recurrent DCIS G2 of 43 mm

The statements reported here are based on results that were achieved in the customer's unique setting. Since there is no "typical" hospital and many variables exist, i.e., hospital size, case mix, etc., there can be no guarantee that other customers will achieve the same results.

Automated Breast Ultrasound (ABUS)

Imaging Women with Dense Breast Tissue: Description of the problem and ABUS as a promising solution

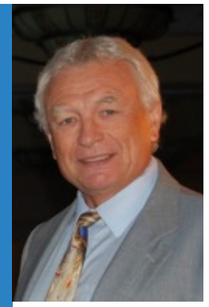


Personalizing Breast Care with Invenia™ ABUS 2.0 is transforming Breast Care from reactive to proactive enabling clinical and operational benefits along the Breast Care Pathway.
Invenia ABUS is the only FDA-approved ultrasound supplemental screening technology that is specifically designed for detecting cancer in dense breast tissue. The 3D coronal plane access is providing a comprehensive and standardized view of the breast to look differently at dense breast tissue. Clinical research studies demonstrate that when used as an adjunct to mammography, small cancers visible only through ABUS were predominantly invasive and node negative[1] [2]. Detecting them at this earlier stage has important prognostic implications and can reduce the total cost of care[3]. New clinical Indications like staging, prae-operative planning and monitoring under neoadjuvant chemotherapy are looking very promising, as ABUS is showing next to the great clinical advantages as well cost efficiency, especially comparing to other imaging modalities.
From a Patient Experience ABUS is very well tolerated as it's a non-invasive technology providing high patient comfort due to selectable compression levels and the Reverse Curve™ Transducer with its gentle shape perfectly fitting the women's anatomy.

Automated Breast Ultrasound (ABUS)

Prof. Dr. László Tabár, MD, Radiologist

Prof. Dr. László Tabár is Professor Emeritus of Radiology from Uppsala University and Medical Director Emeritus of the Department of Mammography in Falun Central Hospital, Sweden. He is Consultant Radiologist for numerous Comprehensive Breast Centers in the United States and since 1986 President of Mammography Education, Inc.
He is the Project Leader for Randomized Controlled Breast Cancer Screening Projects in Kopparberg County, Sweden, starting 1977 until present.
Prof. Tabar is Honorary member of various Medical Societies, like the American College of Radiology and many others. For his impactful scientific work, he received more than 10 Awards from Medical Associations and Societies. He published around 20 Books about Breast Care and is the author of more than 230 scientific publications.



Can you please make a short introduction of yourself?

"I have spent my entire professional life in fighting breast cancer that has a negative impact on half of the population in the world directly and influences the other half indirectly. Our generation of physicians is the first in the history of medicine that has given the opportunity of finding non-palpable breast cancers at asymptomatic women. I was fortunate to be one of the leaders of the largest randomized controlled population-based scientific trials that proved that early detection of breast cancer and treatment in early phase decreases mortality from the disease significantly."

What is the importance and the impact of a mammography screening program in general?

"The above-described scientific trials have become the foundation for population-based screening with mammography in many countries. Our most recent publications, evaluating the impact of nationwide service screening on mortality from breast cancer showed a 50% decrease in breast cancer death in women who participated in mammography screening regularly. These results can be considered one of the most important accomplishments in clinical cancer research during the past 50 years."

Could you please dive a bit more into the clinical challenge of breast density?

"High quality mammograms demonstrate three out of the four structural elements of the normal breast tissue, but, unfortunately, the fourth basic building block, the fibrous connective tissue can hide the other three components entirely. While reading mammograms of a fatty replaced breast results in high accuracy, the presence of the fibrous connective tissue causes considerable limitation and decreased accuracy; even palpable benign or malignant lesions can be occult on the mammograms of women with very dense breasts. In order to provide "equal care" for all women, everyone needs to use the multimodality approach in screening women with dense breast tissue."

Why do you believe in supplemental screening with ABUS, especially in all women with dense breast?

"The potential solution to the problem of imaging dense breast tissue is to add ultrasound examination to FFDM since the ultrasound beam penetrates the dense tissue (it serves as a "radar" going through the fibrous tissue), it does not use ionizing radiation and there is scientific evidence showing that 26-36% more invasive breast cancers can be detected when adding automated breast ultrasound to FFDM. The combination will result in detecting more breast cancers at an early phase, there will be fewer interval cancers, less radical treatment, less patient suffering and further decreasing mortality from the disease."

What's your recommendation towards all stakeholders responsible for Breast Cancer screening programs?

"Introduce the multimodality approach to screen women with dense breast tissue, i.e. add automated breast ultrasound (ABUS) to FFDM in order to provide equal care for all women regardless of their breast tissue density. When concerning the economic considerations of using ABUS as an adjunctive screening tool I recommend reading the following recently published article: https://www.dropbox.com/s/gc1kw7gxky78rfc/Dr.%20Scaperrotta%20et.%20al.%20095148481987096 3.pdf?dl=0

Introduction

This 51 year old woman felt a lump high up in the axillary tail of her left breast. Clinical breast examination confirmed the presence of a freely movable, firm but not very hard superficial lesion without overlying skin changes.

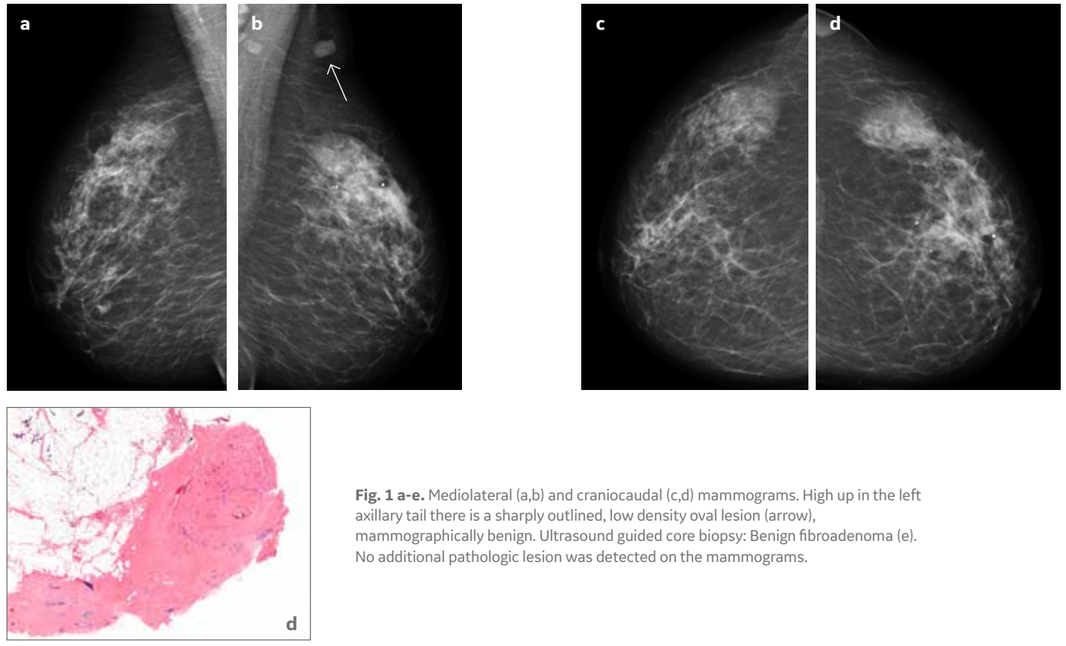


Fig. 1 a-e. Mediolateral (a,b) and craniocaudal (c,d) mammograms. High up in the left axillary tail there is a sharply outlined, low density oval lesion (arrow), mammographically benign. Ultrasound guided core biopsy: Benign fibroadenoma (e). No additional pathologic lesion was detected on the mammograms.

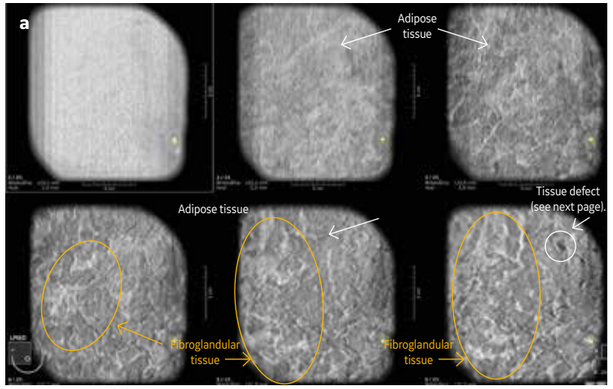


Fig. 2.a. Automated breast ultrasound (ABUS) of the left breast was performed to evaluate the mammographic finding. ABUS, medial compression, showing a series of images of 2 mm thick, consecutive coronal tissue slices. The yellow dot marks the nipple position. Image 1/23: skin level. Images of slices 2-3/23 show only adipose tissue; the fibroglandular tissue gradually evolves in the forthcoming images. There is a tissue defect on 6/23 image (see continuation on Fig. 2.b.)

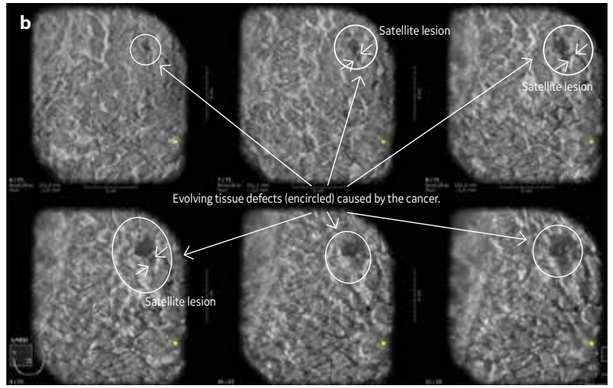
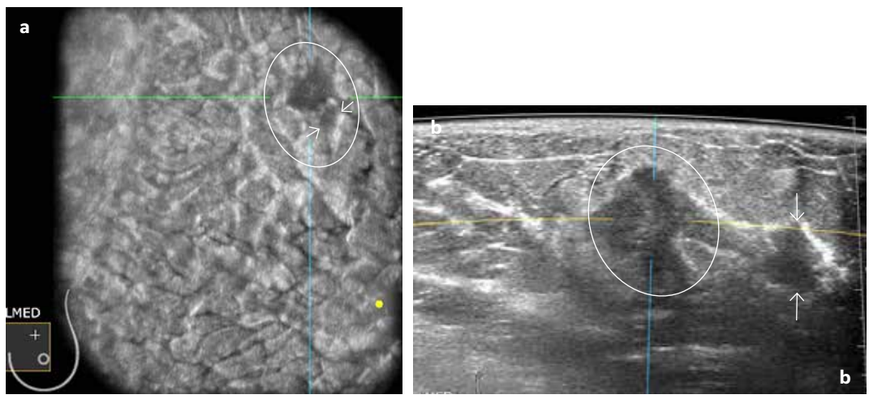


Fig. 2.b. Automated breast ultrasound (ABUS) of the left breast, medial compression, continuation of the series shown on Fig. 2.a. Images 6-11/23: there are two tissue defects in the upper half of the breast; the larger, more superficial, increases in size on images closer to the chest wall (6-11/23), while the smaller tissue defect is seen only on slices 7-9/23.



Figs. 3.a,b. Placing the cursor over the tissue defect on slice 9/23 produces a reconstructed 2D ultrasound image, showing two malignant tumors: the larger one is encircled, the smaller one is marked with arrows.

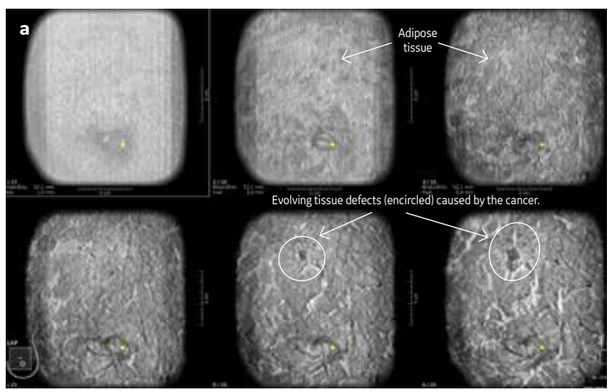
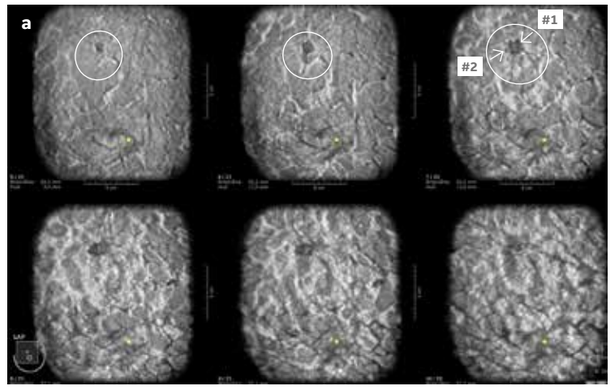
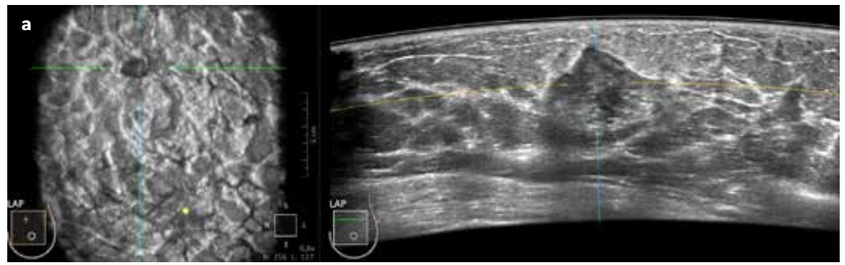


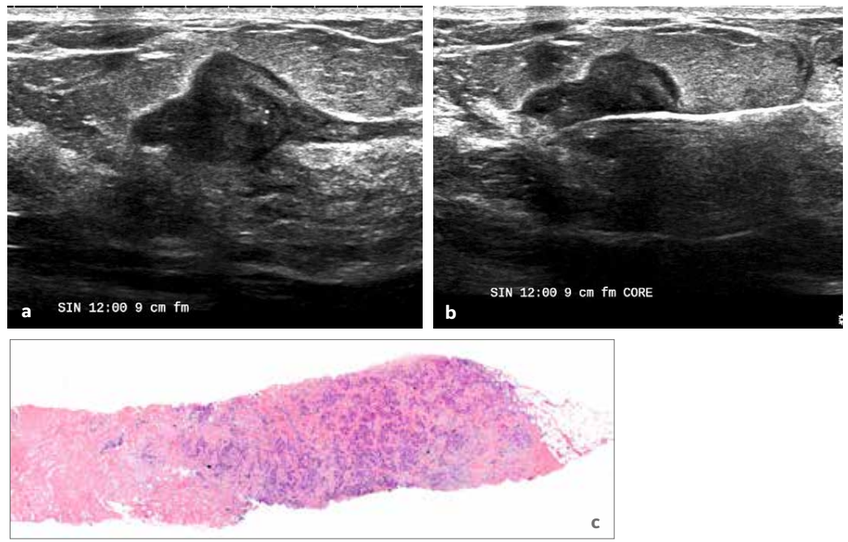
Fig. 4.a. ABUS, 2 mm thick multislice series. Coronal sections, anteroposterior compression. The tissue defect, caused by the larger cancer is seen on images 5-6/23.



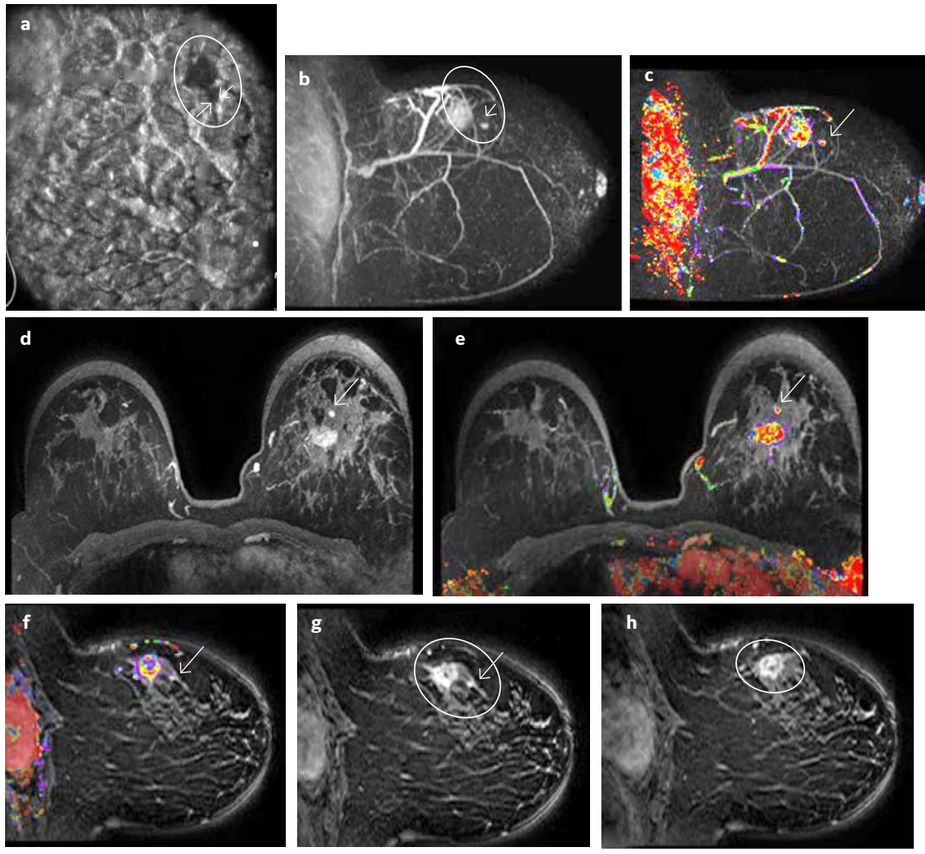
Figs. 5.a. Continuation of the ABUS images of 2 mm thick coronal tissue slices, anteroposterior compression, showing the larger tissue defect on images 7-10/23 (dashed arrow). There is another, smaller tissue defect (solid arrow).as well on image 9/23, suggesting the presence of another tumor.



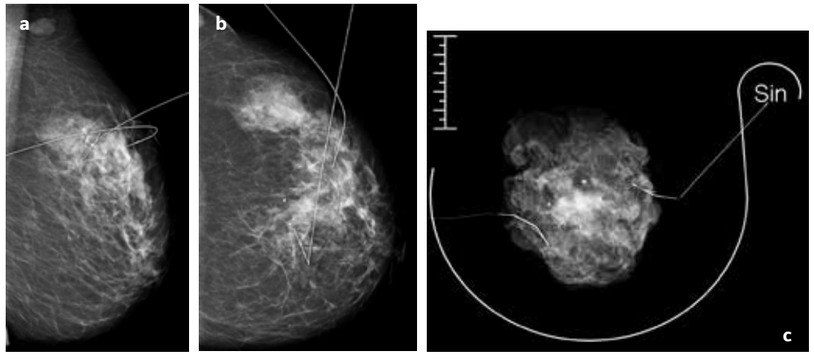
Figs. 6.a,b. Placing the cursor over the tissue defect (a) produces a reconstructed 2D ultrasound image, showing the larger malignant tumor (b).



Figs. 7.a-c. Hand-held ultrasound of the larger lesion (a). Image of the ultrasound guided 14G core biopsy (b). Histopathology of the core specimen (c): Invasive breast cancer.



Figs. 8.a-h. Comparison of an ABUS image of a 2 mm thick tissue slice with breast MRI images. Both tumors can be well seen on both modalities: the larger tumor is encircled on MRI, and an arrow points to the smaller, satellite tumor. Description of the MRI findings: a round-shaped 17x23x20 mm irregular tumor mass is seen in the left breast, nine cm deep to the nipple, in the upper-outer quadrant. Rapid, heterogeneous contrast uptake with delayed phase washout. Both morphology and kinetics are characteristic for a malignant tumor. Eight mm anterior to the index tumor there is a 5x5x3 mm satellite tumor. The relative position of the two tumors will not be exactly the same for the different imaging methods because of different positioning (ABUS: compressed breasts in supine position; MRI: prone position with the breasts hanging in the coil). Right breast with no MRI abnormality.



Figs. 9.a-c. Preoperative localization using the bracketing technique (a,b). Surgical specimen radiograph (c).

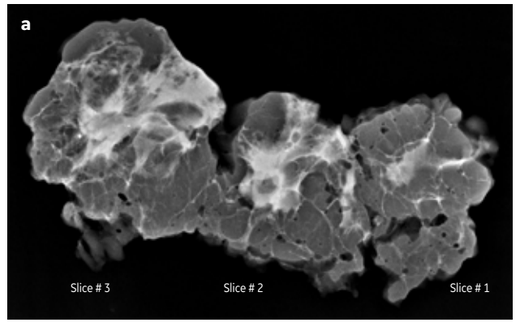
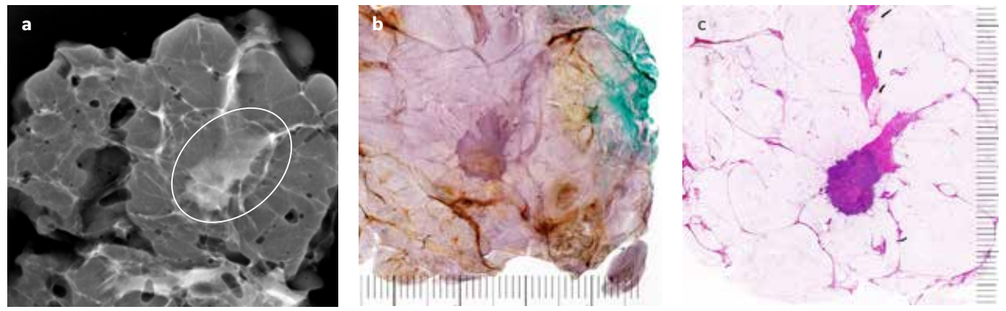
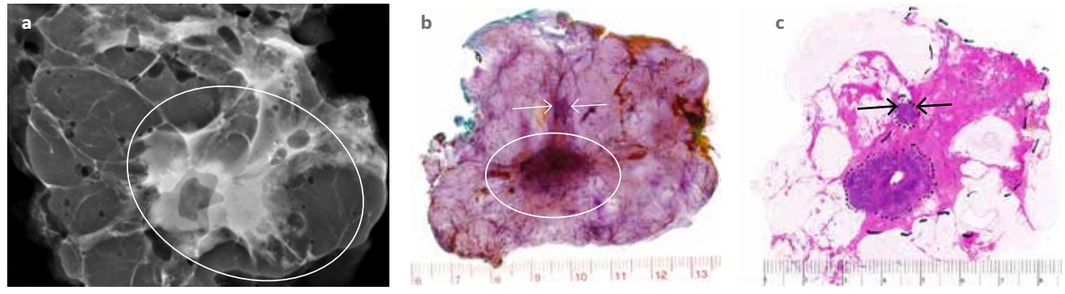


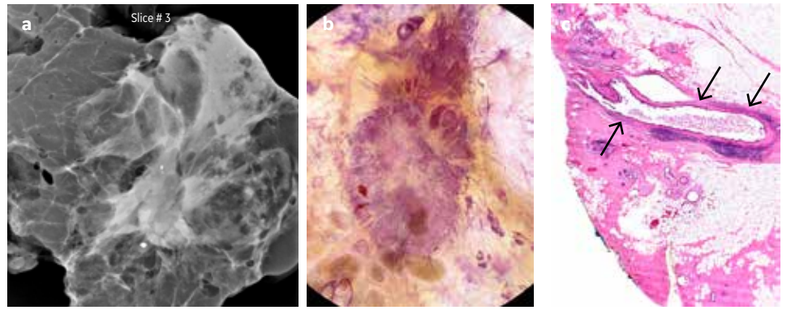
Fig. 10.a. Specimen slice radiographs.



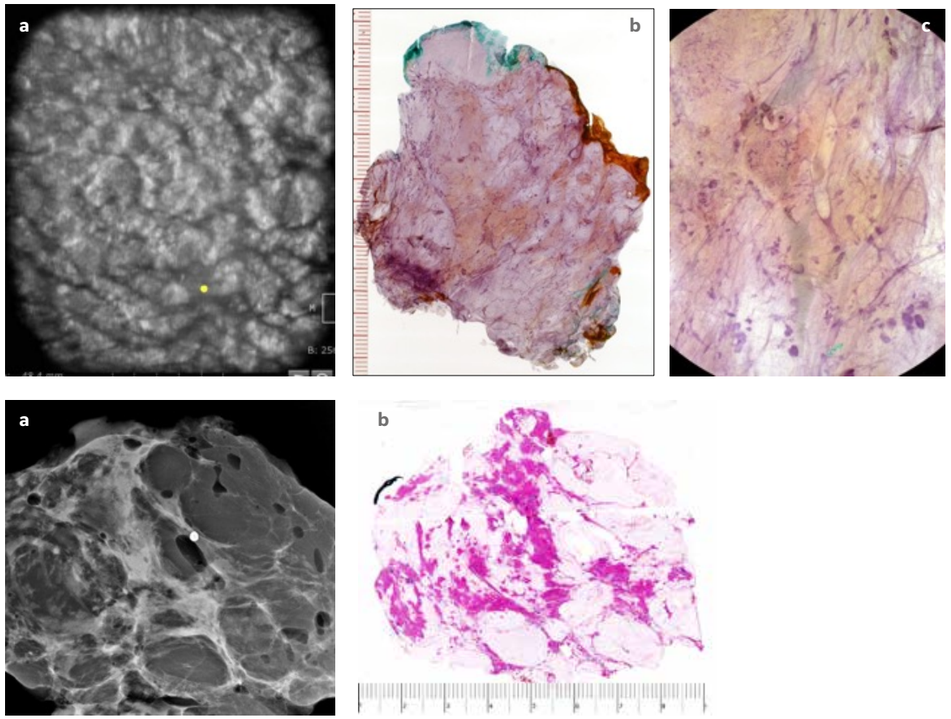
Figs. 11.a-c. Specimen radiograph, slice # 1 (a). The density with the convex contour is the image of the larger invasive cancer. Large format subgross (3D) (b) and thin section histopathology images (c) of the carcinoma.



Figs. 12.a-c. Specimen radiograph, slice # 2 (a). Large format thick (3D) (b) and thin section (c) histopathology images of both cancers surrounded by dense fibrous tissue.



Figs. 13.a-c. Specimen radiograph, slice # 3 (a). Large format thick (3D) (b) and thin section (c) histopathology images of the rest of the invasive cancer. Dense fibrous tissue (yellow) and Grade 3 in situ carcinoma surrounds the invasive tumor (b). The in situ process, localized within a major lactiferous duct (arrows), can be found on the surgical margin (c).



Figs. 14.a-e. The deeper breast tissue slices, between the tumors and the chest wall, have a mixture of adipose and fibroglandular tissue. The ABUS slice (a) is compared with the subgross histopathology specimen (b,c), the specimen radiograph (d) and a large format thin section histopathology slice (e).

Final histopathology:

Poorly differentiated bifocal invasive breast cancer (23x17 mm and 6x5 mm) associated with poorly differentiated in situ carcinoma over a region measuring 60x40 mm. pN 0/1. Biomarkers: ER+ve, PR-ve, HER2-ve, Ki67 32%. EGFR-ve, E-cadh +ve.

Comment

This multifocal tumor was detected by automated breast ultrasound (ABUS) and was not detectable by mammography, magnification mammography or specimen radiography. Multifocality is an important, independent negative prognostic factor. The current TNM classification system, which predates the screening era, uses the size of the largest invasive focus as a major descriptive factor, and fails to take multifocality into account. However, treatment planning, including the surgical approach, should be determined by the overall extent of the malignancy, although this essential information is not included in the TNM classification. The preoperative imaging workup using the multimodality approach has the capability of describing the full extent of the disease. The best way of assessing tumor burden is to describe the overall tumor volume and also estimate the tumor surface area. Application of this information during the treatment planning process of each individual case will help to ensure complete removal of the malignant tissue. The use of dogmatic treatment guidelines, such as “lumpectomy and postoperative irradiation” for most breast cancer cases, has led to overtreatment of unifocal cases and undertreatment of multifocal cancers. Also, the failure to take multifocality into account places the unifocal tumor with excellent long-term prognosis and the multifocal tumors with the same maximum individual tumor size, but with poor prognosis, into the same TNM category. To offset this deficiency we propose that a quantitative evaluation of the tumor burden, in terms of total tumor volume and tumor surface area, be integrated into Cancer Registry databases. The resulting information will provide a more reliable outcome measure and will also serve as a solid database for therapeutic guidelines.

1. Brem RF, Tabár L, et.al. Radiology. 2015 Mar; 274(3): 663-73. | 2. Wilczek, et.al. European Journal of Radiology 85 (2016) 1554–1563 | 3. Foglia, Scaperrotta et.al. Health Services Management Research DOI: 10.1177/0951484819870963

The statements reported here are based on results that were achieved in the customer’s unique setting. Since there is no “typical” hospital and many variables exist, i.e., hospital size, case mix, etc., there can be no guarantee that other customers will achieve the same results.

Breast MRI - AI Impact on Diagnostic Confidence

Vicente Martinez de Vega, MD, Quirónsalud Madrid University Hospital, Madrid, Spain

Introduction

Dynamic contrast-enhanced MR (DCE MR) is commonly used for detection and characterization of malignancies in the breast. However, suboptimal compromises are often made between temporal and spatial resolution in conventional breast DCE MR1[1]. A high spatial resolution is required to characterize lesion morphology, whereas a high temporal resolution is required to accurately characterize contrast uptake both for semi-quantitative and quantitative analysis of contrast enhancement kinetics.

Since 2015, we were able to use a new variable spatiotemporal resolution dynamic contrast-enhanced (DCE) MR method, termed DIfferential Subsampling with Cartesian Ordering (DISCO), for imaging of breast cancer[2]. This sequence combines a SPGR sequence with SPECIAL fat saturation, a pseudorandom variable density, and a k-space segmentation. This sequence provides high resolution combined with high temporal resolution.

Recently, the ability to combine DISCO and Compressed Sensing technique named as HyperSense allowed us to reach a faster temporal resolution to study first pass perfusion.

DISCO with HyperSense ultrafast MRI sequence utilizes kinetic information of the very early phase within 90s after contrast injection with an achieved temporal resolution of 6s per phase. A previous study reported that these ultrafast protocols were useful for distinguishing the benign from the malignant lesions[3].

Moreover, artificial intelligence, particularly deep-learning (DL) techniques, have recently been introduced to improve image quality (SNR and sharpness) as well as enable scan time reductions. The recent introduction of the AIR™ Recon DL algorithm allows to remove noise and Gibbs ringing artifacts prior to final image formation[4].

The AIR™ Recon DL algorithm is embedded in the MR image reconstruction pipeline, requiring access to raw data. The neural network employs a cascade of over 100,000 unique pattern recognitions for noise and low resolution to reconstruct only the ideal object image. Users have the freedom to select their own level of SNR improvement through a user interface that provides a low, medium or high setting. The result is an image with higher SNR and spatial resolution.

The combination of both techniques drastically improves our clinical diagnostic confidence in our daily practice because in some cases, especially in pre-menopausal women, the fibro glandular tissue enhancement (background parenchymal enhancement –BPE) can be very intense even in the first minute and it is difficult to differentiate breast cancer from the overall enhancement of adjacent tissue.

Material and Method

The patient was positioned in the prone position with arms up.

The coil used is a 16 channels Breast coil from RAPID Biomedical GmbH.

MR acquisition is as follows:

Morphological and Parametric sequences:

1. Ax T2w FSE Fat Saturation with aspir pulse and AIR™ Recon DL with medium strength (3min)
2. Sag T2w FSE and AIR™ Recon DL with medium strength (1min37sec)
3. Ax STIR DWI b values 50/700 (3min53sec)

Dynamic Contrast-Enhanced (DCE) sequences:

1. Sag VIBRANT with HyperSense mask phase (1min)
2. Ax DISCO Ultra-Fast with HyperSense post injection, 6 sec/phase, 13 phases (total 1min43sec)
3. Sag VIBRANT with HyperSense, 1 min/phase, 4 phases (total 6min)
4. Ax VIBRANT with HyperSense High Spatial Resolution (2min)

Patient history

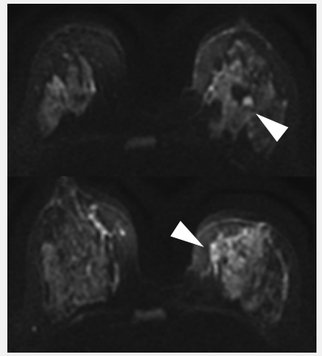
40 years old woman. Underwent initial mammographic screening and additional ultrasound (dense breast). The mammography and US showed two adjacent lesions located in the central region of the left breast and were considered BI-RADS® 5.

Case Report
Breast MRI

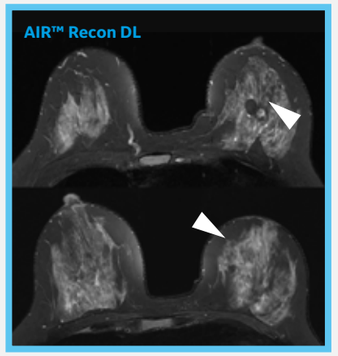
MRI was indicated for staging the two suspicious lesions in the central region (16 mm and 15 mm) and two other uptake areas were appreciated: one in the inner quadrant junction (6 mm nodule with slightly irregular margins), another in the inferior-internal quadrant (12 mm non-mass uptake). (figures 1 & 2)

A total of 4 lesions were found with MRI.

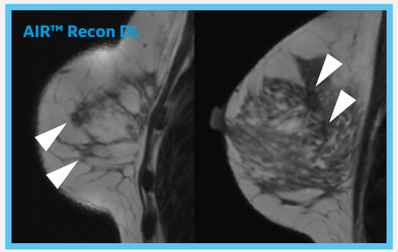
The combination of standard and ultra-fast DCE sequences allows us to get multi-parametric information of the lesion enhancement pattern. The ultra-fast sequence provides information on early enhancement characteristics, while the standard DCE sequence provides information on the entire perfusion. The



Ax STIR DWI b700
FOV 32x32cm Matrix 140x160
2.28 x 2 x 3.3mm3
3:53 min

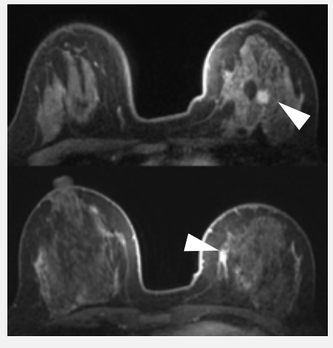


Ax FSE T2 FS AIR™ Recon DL
FOV 35x35cm Matrix 416x3521.05 x
1.25 x 3mm3
3 min

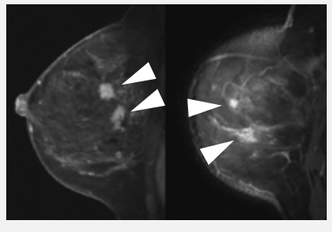


Sag FSE T2w AIR™ Recon DL
FOV 22x22cm
Matrix 352x2560.62x 1.25 x 4mm3
1:37 min

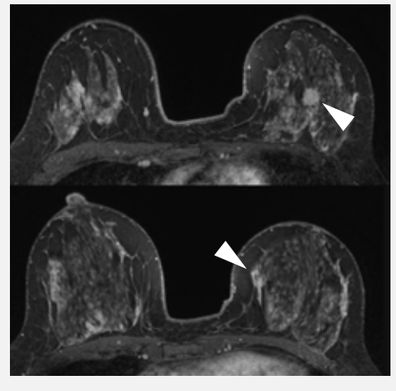
Fig. 1 MR Morphological and Parametric sequences, including AIR™ Recon DL images.



Ax DISCO LAVA aspir HS DCE
FOV 30x30cm Matrix 288x288
1 x 1 x 2.8mm3
6sec/phase 13 phases



Sag VIBRANT aspir HS DCE
FOV 22x22cm Matrix 338x338
0.65 x 0.65 x 2.8mm3
1 min/phase 5 phases



Ax VIBRANT aspir HS late
FOV 35x35cm Matrix 512x512
0.68 x 0.68 x 1mm3
2 min

Fig. 2 Post-contrast images from Dynamic Contrast Enhanced sequences (DISCO Ultra-Fast and VIBRANT). The use of HyperSense allows a gain both in spatial and temporal resolution.

phase of the initial enhancement was defined as the first appearance of tumour enhancement on the ultra-fast post-contrast images[5] and were around 12 sec for the 2 central suspicious lesions and > 25 sec for the 2 inner quadrant lesions.

Tumour enhancement was identified when the signal intensity within the region of interest (ROI) in the tumour became more than 1.5 times the average signal intensity of the three unenhanced images within the same ROI [5]. The 2 central lesions showed a fast uptake on the DISCO Ultra-Fast sequence of less than 30 sec compared to the aorta, while the 2 inner quadrant lesions were markedly slower at more than 90 sec. (figure 3 & 4)

Patient was referred for US-guided biopsy of the two central region lesions previously visualized in the initial ultrasound screening and were classified as infiltrating ductal carcinomas (Estrogen and Progesterone +, Her 2 negative, Ki 67 10%).

The patient then was referred for MR-guided biopsy for the two lesions in the inner quadrants, only detected through MRI. The 6mm nodule was a sclerosing adenosis. The 12mm focal lesion was a fibrocystic disease with fibrosis and ductal dilatations.

A conservative surgery and sentinel node were performed.

The malignant nodules were marked with ultrasound with Radio-guided Occult Lesion Localization technique (ROLL) and the specimen confirmed the presence of two tumor foci of 15.4 mm and 12.9 mm.

The sentinel lymph node was negative.

Conclusion

1. Using very fast sequences we are now able to get new information with high temporal resolution without loss of spatial resolution.

   Initial enhancement was significantly earlier in breast cancer than in benign tumors, which means that the contrast agent reaches breast cancer faster than it reaches benign tumors, as previously described by Sung Ui Shin in 2020 [5].

   New parameters which have to be evaluated that increases specificity are: Initial enhancement phase (BAT) and Slope and Slope max, while taking the initial enhancement of the aorta as a reference point of increase.

   The Correlation with prognostic factors indicates that:

   - The median TTE of invasive cancers was shorter than that of in situ cancers
   - High histologic/nuclear grade cancers had shorter TTE than low to intermediate grade cancers
   - HER2-positive cancers showed shorter TTE than HER2-negative cancers
   - he median TTE of cancers with high Ki-67 was shorter than that of cancers with low Ki-67

2. AIR™ Recon DL for morphological sequences provides:
   - Shorter exam times, increased patient throughput
   - Tolerance of protocol and patient variations to increase confidence in acquisition and diagnostic read
   - Intelligent ringing suppression (sharper)
   - User-selectable noise reduction (increased SNR) with AIR™ Recon DL strength levels.

To summarize, the use of hybrid protocols (Ultra-Fast DCE plus Standard DCE MRI) as well as AIR™ Recon DL in the clinical routine, can increase the specificity of the Breast MR technique, avoiding possible unnecessary biopsies.

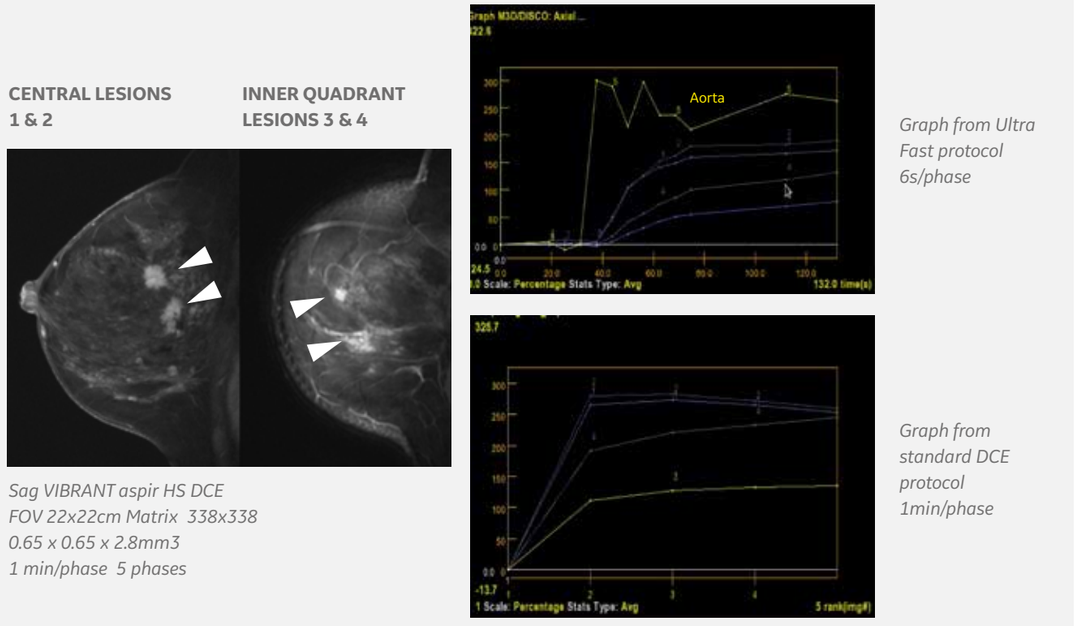


Fig. 3 Graphs of intensity time related curves of the Dynamic Contrast Enhanced sequences (DISCO Ultra-Fast and VIBRANT). The TTE relative to the aorta showed very fast enhancement of the 2 central lesions (yellow arrows) with a wash-out type III curve, while the 2 inner quadrant lesions (green arrows) showed slower enhancement and a continuous enhancement type I curve.

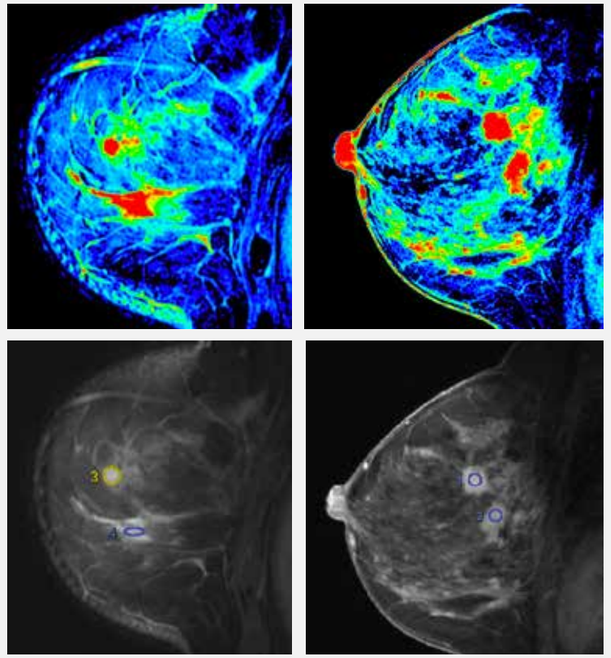


Fig. 4 Positive Enhancement Integral color maps of the 4 lesions (top row), ROIs positions of the central lesions (1 & 2) and inner quadrant lesions (3 & 4) of Fig.3 graphs (bottom row).

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PET/MR

PET/MR in the evaluation of breast cancer

By Maria Picchio, MD, Associate Professor of Nuclear Medicine at Vita-Salute San Raffaele University and Head of Molecular Imaging Unit, Clinical Research Unit of the Experimental Imaging Centre, Department of Nuclear Medicine, IRCCS San Raffaele Scientific Institute, Milan, Italy.
By Paola Scifo, PhD, Senior Researcher, Department of Nuclear Medicine, IRCCS San Raffaele Scientific Institute, Milan, Italy.

Both PET and MR imaging have an important role in the management of breast cancer, particularly in advanced disease on initial presentation and in therapy monitoring of metastatic disease. MR provides excellent soft tissue characterization for initial diagnosis and to rule out additional malignancies. PET delivers initial staging/restaging and treatment response of patients. When PET is added to MR, it may help improve specificity and reduce false positives. An integrated PET/MR delivers an advantage by providing an evaluation of primary cancer, lymph node involvement and distant metastatic disease in one clinical setting.

There are several advantages to using PET/MR for diagnosing cancer in soft tissue, as well as to define the local extent of the disease. PET and MR are often used to provide information on prognosis and treatment response. Therefore, a single integrated PET/MR study with information acquired simultaneously may be particularly beneficial[1].

IRCCS San Raffaele Scientific Institute is a university and research hospital established in 1971 to provide specialized care for the most complex and difficult health conditions, with 50,000 inpatients, 1.5 million outpatients and 30,000 surgical interventions per year. San Raffaele is recognized for the excellence of its teaching and research activities. In 2020, researchers from the campus (University and Scientific Institute) published 2,081 papers, with a mean impact factor of 5.6 and a total impact factor of 11,733. San Raffaele is ranked as one of the leading biomedical research institutes in Italy and Europe.

In early 2018, thanks to a funded grant from the Italian Ministry of Health, our institution installed the first hybrid, fully integrated PET/MR system with Time-of-Flight (TOF) imaging in Italy – the SIGNA™ PET/ MR. This new system is in addition to three PET/CT, one SPECT/CT and three SPECT systems in the Nuclear Medicine Unit, headed by Luigi Gianolli, MD. We also have cyclotron, radiochemistry and radiopharmacy labs working under GMP requirements to ensure the quality and safety of radiopharmaceutical production. A pre-clinical facility for small animals is also available. The clinical activity in oncology, neurology and cardiology is complemented by research and methodological programs in our institution.

The first clinical study on the SIGNA™ PET/MR was performed in March 2018. Until June 2021 we have conducted 1870 exams: 1,678 in oncology, 16 in neurology and 103 in patients with large vessel vasculitis. Our oncology exams by type of radiopharmaceutical tracer are: 1,200 with ^{18}F-FDG, 255 with ^{68}Ga- DOTATOC, 113 with ^{11}C-choline and 19 with ^{11}C-methionine‡.

The methodological development, set-up, functioning and maintenance of the PET/MR system requires a team that includes PET physicists Valentino Bettinardi, PhD, and Annarita Savi, PhD, and MR expert Paola Scifo, PhD, who together guarantee the optimal functioning, as well as the clinical and research implementation of the PET/MR system. A group of nuclear medicine physicians, Federico Fallanca, MD, Ana Maria Samanes Gajate, MD, Patrizia Magnani, MD, and Carla Canevari, MD, are specifically trained in working with PET/MR and work closely with the radiologists and neuroradiologists.
Moreover, Paola Mapelli, MD, a nuclear medicine physician, is currently working toward a PhD with a project focused on the use of PET/MR in prostate cancer and neuroendocrine tumors.

Breast cancer is an area where the combined PET/MR modality delivers an advantage in one clinical setting. In our institution, it is a clinical and clinical research focus with Dr. Canevari as the referring physician for breast cancer studies. PET has an important role in the management of breast cancer, particularly in initial staging, treatment response in metastatic disease and restaging of patients with equivocal findings[2-3-4]. MR delivers excellent soft tissue characterization and may be useful to rule out additional malignancy sites. While MR provides high sensitivity but low specificity in the detection of breast cancer, the addition of PET can help improve specificity and reduce false positives. Furthermore, MR is often used to rule out additional malignant sites in Stage 1 cancers that might be mammographically occult[5].

It is also known that MR is better than CT for the detection of metastases in the bone and liver. Catalano, et al, evaluated the staging performance of whole-body DWI, PET/CT and PET/MR in invasive ductal carcinoma of the breast. The authors concluded that when available, PET/MR should be considered for staging these patients because it may also detect bone metastases and very small liver metastases[6].

Of the 1,678 PET/MR oncology exams performed in our facility, 338 were breast cancer studies. 206 of these patients had both diagnostic PET and breast MR with contrast. Of these, 140 were for staging and 109 were for evaluation of treatment response or for follow-up of suspected recurrent disease.

Studies have also shown the advantage of imaging breast cancer patients in the prone position[7]. In our institution, our protocol consists of a whole-body PET/MR acquisition with seven bed positions in the supine position, followed by a high count statistics PET and MR in the prone position using GE's dedicated 8-channel breast coil.

"In less than one hour, we have a complete diagnostic PET and diagnostic MR breast study (Fig. 1)."

Whole-body PET acquisition (20 min./28 min.), supine position						
Bed 1 4 min.	**Bed 2 4 min.**	**Bed 3 4 min.**	**Bed 4 4 min.**	**Bed 5 4 min.**	**Bed 6 4 min.**	**Bed 7 4 min.**
MRAC LAVA Flex DWI b800	MRAC LAVA Flex DWI b800	MRAC LAVA Flex DWI b800	MRAC LAVA Flex DWI b800	MRAC LAVA Flex DWI b800	MRAC LAVA Flex DWI b800	MRAC LAVA Flex DWI b800
High count statistics PET acquisition (20 min.), prone position						
1 Bed on the breast						
MRAC	Axial T2 PROPELLER	DWI b50/800 1500	VIBRANT Multiphase (5 phases) with Gd injection			

Fig. 1 PET/MR breast protocol at IRCCS San Raffaele Scientific Institute.

11C-methionine is not approved by the US FDA and not be available for clinical use in all markets.

The statements reported here are based on results that were achieved in the customer's unique setting. Since there is no "typical" hospital and many variables exist, i.e., hospital size, case mix, etc., there can be no guarantee that other customers will achieve the same results.

Clinical cases

In the first case, we can visualize the lesion in the left breast (Figure 2A-2D). With the prone breast acquisition, the lesion is well defined and we can also detect a small satellite ipsilateral lesion that was not apparent in the supine position images (Figure 2E-2I).

In another patient with a lesion in the right breast, we can determine the involvement of the axillary lymph node in the supine position (Figure 3). With the acquisition in the prone position, we can more precisely define the anatomical localization of the right lesion (Figure 4A-4B). Furthermore, we could detect another small contralateral lesion that was not seen in the supine whole-body acquisition (Figure 4C-4G).

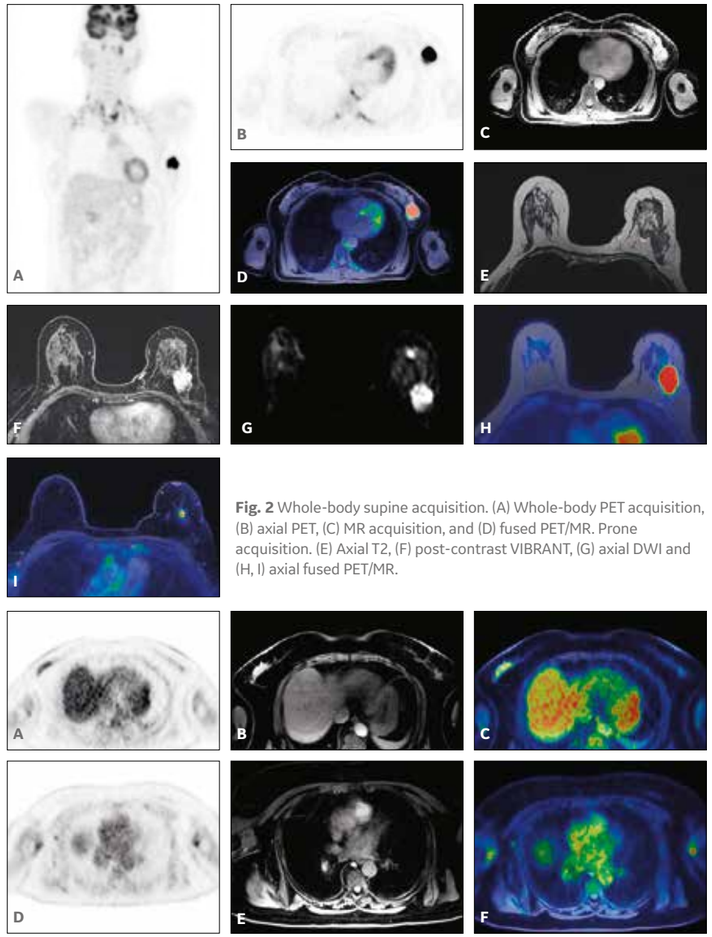

Fig. 2 Whole-body supine acquisition. (A) Whole-body PET acquisition, (B) axial PET, (C) MR acquisition, and (D) fused PET/MR. Prone acquisition. (E) Axial T2, (F) post-contrast VIBRANT, (G) axial DWI and (H, I) axial fused PET/MR.

Fig. 3 Whole-body supine PET/MR acquisition. (A, D) PET, (B, E) MR and (C, F) fused PET/MR.

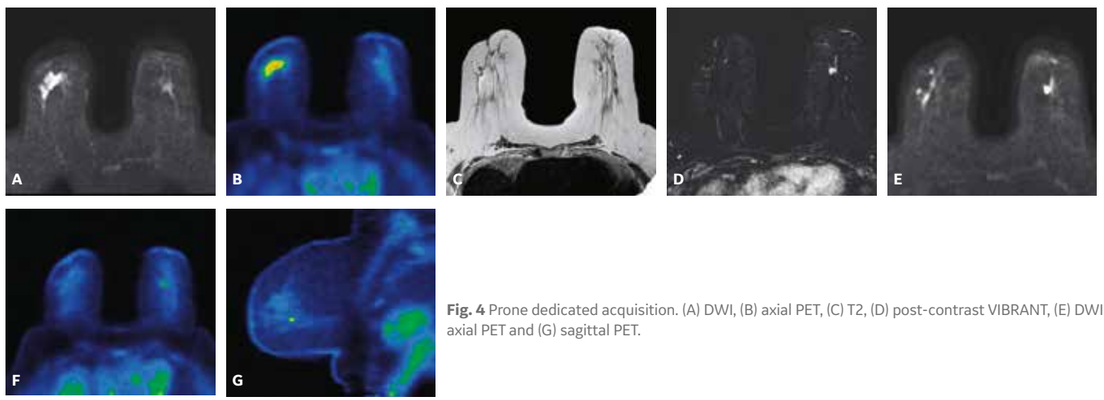

Fig. 4 Prone dedicated acquisition. (A) DWI, (B) axial PET, (C) T2, (D) post-contrast VIBRANT, (E) DWI, (F) axial PET and (G) sagittal PET.

With the third patient, referred for staging in the right breast (Figure 5), cancer was found to have metastatic involvement. With the high sensitivity PET images obtained during diagnostic MR study in the prone position, we could depict several small bone lesions and axillary lymph node involvement (Figure 6).

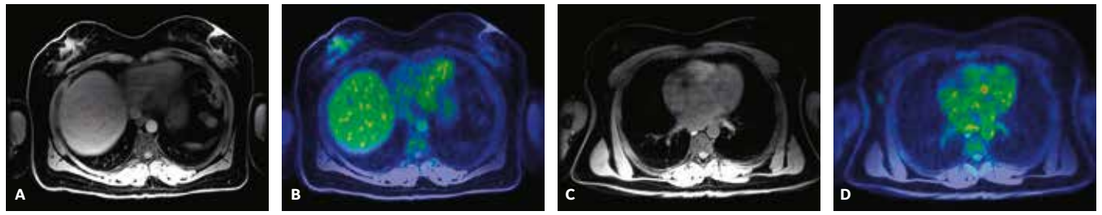

Fig. 5 (A) MR acquisition, (B) fused PET/MR, (C) MR acquisition and (D) fused PET/MR.

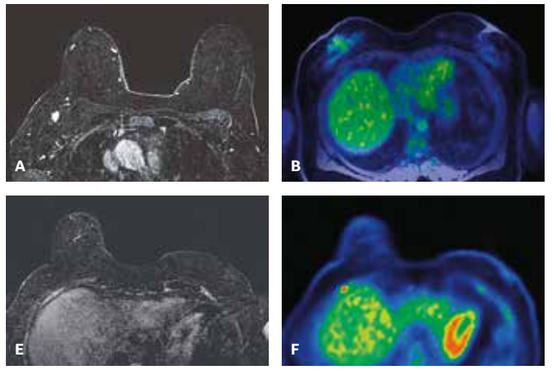

Fig. 6
Prone post-contrast VIBRANT MR acquisition (A, E)
Fused supine PET/MR (B, D)
Supine Lava-flex MR (C)
Prone PET (F)

The fourth patient was biopsied for infiltrating locular carcinoma (G1) and foci of lobular carcinoma in situ. Lobular carcinoma is a type of breast cancer that has the potential for a false negative in PET. In fact, in this case the PET results were negative. The MR acquisition helped to detect a small lesion not seen in the PET images (Figure 7).

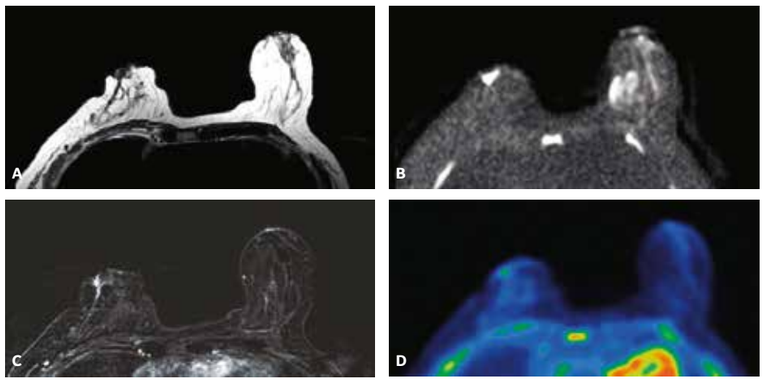

Fig. 7 Prone dedicated acquisition. (A) T2, (B) DWI, (C) post-contrast VIBRANT and (D) PET.

In another patient following surgical treatment of lobular carcinoma, PET/MR was performed to restage the disease. With PET/MR, we could detect bilateral uptake at the ovaries that resulted as metastases from lobular carcinoma after surgical treatment of bilateral salpingo- oophorectomy and omentectomy (Figure 8).

The patient began chemotherapy and underwent a second PET/MR during treatment. The follow-up PET/ MR demonstrated the presence of a pathological uptake and a morphological finding in the right breast, which was histologically confirmed to be intraductal carcinoma (Figure 9). Also depicted were multiple metastases in lobular histotype in the liver and the lymph nodes, and another infiltrating lobular carcinoma in the contralateral breast (Figure 10).

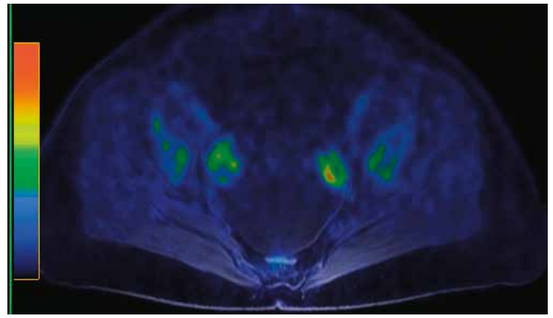

Fig. 8 Patient follow-up after surgical treatment for breast cancer. Fused PET/MR depicts metastases in the ovaries.

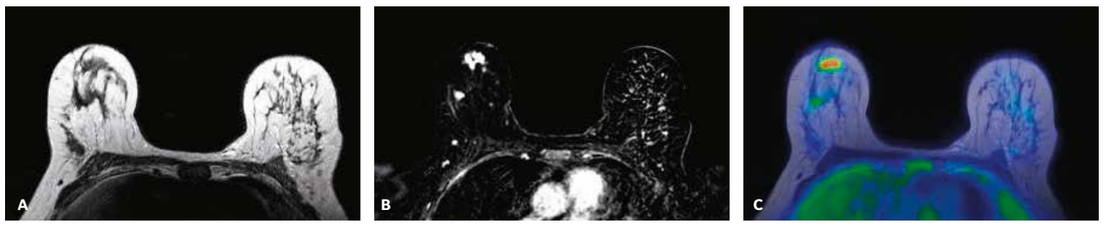

Fig. 9 Second PET/MR during chemotherapy for restaging. (A) T2, (B) post-contrast VIBRANT and (C) fused PET/MR.

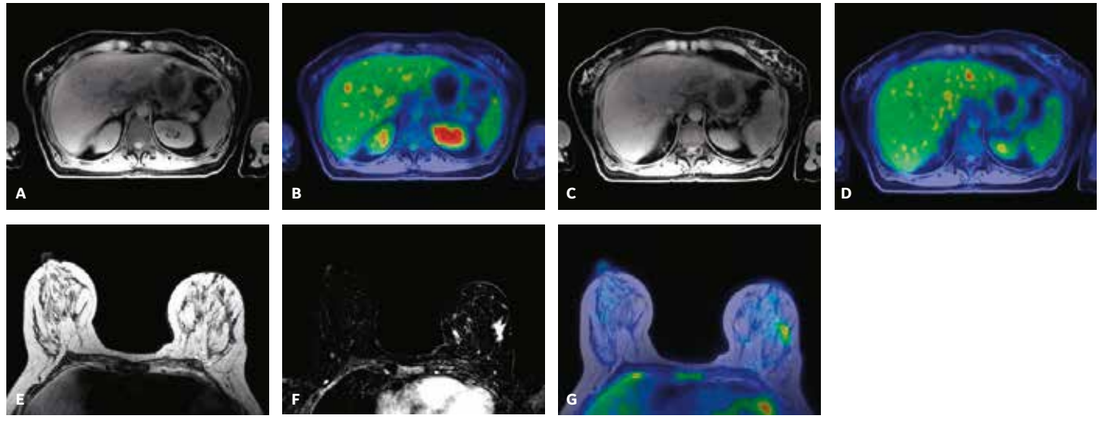

Fig. 10 Second PET/MR during chemotherapy demonstrates multiple metastases and infiltrating lobular carcinoma. (A, C) MR acquisition and (B, D) fused PET/MR depicting metastases in the liver. (E) T2, (F) post-contrast VIBRANT and (G) fused PET/MR showing the lesion in the contralateral breast.

This last case underscores a key point that PET/MR can detect very small lesions that may be important for primary cancer and also for the detection of multiple metastatic lesions. This is particularly important in the staging of the disease.

We are currently engaged in several research activities to evaluate the value of PET/MR in breast cancer patients. In particular, one is focused on patients with locally advanced cancer undergoing adjuvant chemotherapy and performing a PET/MR scan before and after treatment. Another clinical trial is using PET/MR for the evaluation of axillary staging in early breast cancer patients who undergo sentinel node biopsy. In addition, our group is working to improve attenuation correction maps with optimized MR-based attenuation sequences and examining the effect on PET quantification.

To conclude, breast cancer is an area that we believe PET/MR is useful for evaluating primary cancer, lymph node involvement and distant metastatic disease.

While there are situations where, based on the current knowledge, PET/MR may not provide an advantage compared to PET/CT, such as for local lymph node lesion detection, it

”In fact, one specific advantage of a fully integrated PET/MR is the whole-body acquisition where PET, together with MR, may improve the detection of distant metastases.”

appears that PET/MR is overall more sensitive for detecting bone and liver metastases[8].

Moreover, the use of the prone position with dedicated breast MR coils may improve local cancer staging and contrast-enhanced MR may also depict small cancer deposits.

Larger prospective trials are needed to finally understand the breast cancer patient subgroups that will benefit from PET/MR. However, based on our experience, PET/MR may be a one-stop solution for patients with advanced breast cancer and, in particular, in those with a poor prognosis.

In addition, the high performance of the fully integrated PET/MR, specifically with a very high sensitive PET system, an optimal SNR due to the TOF technology and an accurate quantitative reconstruction algorithm makes it a powerful diagnostic tool for clinical and research applications in breast cancer.

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Every Image Tells a Story

Taking medical technology on the road to you, across Europe and beyond

With the motto ”Every Image Tells a story”, a specially designed trailer has been making its way from Madrid, Spain since May 10. Equipped with GE Healthcare’s leading-edge imaging technologies in Women’s Health, X-ray, Bone & Metabolic Health and Oncology, along with knowledgeable staff and safety personnel, this exciting roadshow has been bringing medical technology closer to clinicians.

In Europe, this ambitious tour has been making its way for more than 29 weeks across 16 countries including Spain, Portugal, France, Belgium, Luxembourg, Czech Republic, Bulgaria, Hungary, Serbia, Greece, Croatia, Germany, Austria, Italy, Russia and the UK.

Against this backdrop, customer experience has taken on new meaning. Clinicians can share their own experiences and stay up-to date with the latest imaging technologies. While witnessing first-hand cutting-edge applications developed by GE Healthcare for the early detection of breast cancer, pneumothorax and pneumonia in the context of Covid -19, among other pathologies, they are anticipating a brighter post-pandemic era.

Connecting with customers where they are

Whatever happens, GE Healthcare continues to partner with and support our customers and the communities they serve. Since the outbreak of Covid-19, we have reinvented our customer experience efforts by ramping up remote accessibility, virtual meetings, digital engagement and online education.

When small groups of gatherings were permitted in some areas, GE Healthcare was ready to hit the road, taking innovation directly to customers. We have also brought fresh air and a warm personal touch to our thousands of customers and partners who had dealt with social isolation for over a year.

Indeed, after more than one year of long calls, e-mails, online events and meetings, Healthcare professionals were excited to be asked to discover applications relating to artificial intelligence in medical diagnosis, watch demos of innovations, and chat with peers.

While some bigger cities and countries may be lucky to have easier access to modern healthcare facilities, others have more urgent needs for medical equipment and investment. Our roadshow and live events have been the ideal vehicle to make inroads into these places to showcase advanced technology, while creating enthusiasm among medical professionals.

By directly engaging consumers to see and 'experience' our array of products, we have forged a deeper connection with customers in the evolution of our technologies.

Right time to prepare the post-Covid world

"With this pandemic, we need to adapt to this kind of new normal. At home, we are talking about mental health and metabolic health. By 2030, over 58% of the global adult population could be overweight[1]. The pandemic is contributing to this phenomenon. Also, millions of women didn't have the opportunity to have their mammogram screening whereas currently female breast cancer is the most commonly diagnosed cancer[2]. We understand the need and hear the call, we will adapt ourselves and find solutions," said Laura Hernandez, General Manager of Women's Health and X-Ray in Europe at GE Healthcare.

Hopefully, the Covid-19 pandemic will slowly but surely be behind us. Nonetheless, it has presented the greatest threat to European healthcare systems in generations. The hidden acute and chronic implications of the outbreak could also have a deep impact across populations, such as long-term damage to lungs and other organs, hesitation to seek treatment for safety reasons, and delayed cancer diagnoses.

Some evidence already exists of major, indirect, and undermanaged health impacts. For example, many health systems across Europe have cancelled or postponed tens of thousands of elective procedures and outpatient appointments[3].

Women's health was severely disrupted due to the Covid pandemic, with mammography screening

dropping by up to 90% in most countries[4]. Many women with breast cancer have no symptoms. This is why regular breast cancer screening is so important.

An estimated 100 million cancer screening tests were not performed in Europe during the pandemic, leading to later stage diagnoses and decreased overall survival rates[5]. It is estimated that one in two people with potential cancer symptoms were not urgently referred for diagnosis.

Cancer does not wait. Attending cancer screening appointments is critical to increasing the chance of early diagnosis when cancer can be more effectively treated. We need urgent measures to address this backlog and restore confidence in cancer care services.

While EU member states may differ in strategies to rebuild their economies including healthcare infrastructure, the European Commission has been taking center stage in supporting nations. Not only has it secured historic budgets of €5.3 bn for EU4Health[6] and €4 bn for the EU Cancer Plan[7], but it has also achieved an important place for health in the €672.5 bn EU Recovery and Resilience Facility (RRF)[8].

Measures that could by funded by the EU include innovative medical devices and technology, nationwide cancer screening, regular follow-up of chronic and health conditions, as well as green transition initiatives, digital transformation, supporting resilience in healthcare systems and their workforce, and more.

Our roadshow has been the best way to further reaffirm GE Healthcare's mission to support healthcare professionals in our commitment to deliver optimal care and support reforms and investments undertaken in healthcare by Member States.

Technology brought right to your doorstep

This amazing journey demonstrates the GE Healthcare team's creativity to evolve from virtual connections with customers to an exciting in-person roadshow, coming to a town near the customers. We have carefully designed our wide-ranging response to address the challenges that they face to make the tour worth their while!

The solutions that we brought on the road include intelligent and efficient imaging equipment and digital system in Women's Health, Bone & Metabolic Health and X-Ray that help customers improve rapid diagnosis while providing exceptional care with confidence. The following are just some examples of the diagnostic imaging advances, many empowered through artificial intelligence technologies.

- Our breast care solutions designed to provide the most precise, personalized care in a safe, efficient, patient-centric manner
- Algorithms for rapid detection of pneumothorax, which could lead to Covid-19 complications
- Tomosynthesis as an intermediate technique for diagnosing pneumonia in the Covid-19 context
- Powerful and smart enCORE v18 Software Platform for measuring bone mineral density
- Product demonstrations, thought leadership and networking

These advanced technologies, many driven by AI, are just a few of examples of how GE Healthcare can contribute to face the challenges faced in Europe, such as helping with early breast cancer detection when patients need it the most.

"The best defense against breast cancer is early detection. If women are diagnosed early, their risk of dying from the disease can be reduced by at least 25% to 30%. This is exactly why we have innovated to engage more women in breast cancer screening," said Agnes Berzsenyi, President and CEO of the Women's Health and X-Ray in Europe of GE Healthcare.

One great example that we took on the road is Serena Bright™, the industry's first contrast-enhanced guided biopsy solution and will help empower clinicians and patients in their fight against breast cancer. The contrast spectral mammography (CESM) helps clarify the images obtained in the procedure that may be inconclusive especially in patients with dense breast tissue.

This technology received U.S. Food and Drug Administration clearance one year ago and allows clinicians to conduct breast biopsy exams with contrast guidance using the same mammography equipment, in the same room and with the same staff as with a screening or diagnostic mammogram.

Along with the feature of easy positioning for the comfort of patients,

agility in detection also reduces anxiety in patients, and receiving results, diagnosis and treatment is quicker as the CESM biopsy can be done within 15 minutes[9], while an MRI biopsy can take between 60-90 minutes.[10]

"This approach has the potential to be a more affordable and faster alternative to MRI-guided biopsy for suspicious findings observed at CESM," explains Dr. Rodrigo Alcántara, head of Breast Radiology at the Hospital del Mar, the second center in the world and the first in Spain to perform breast biopsies guided by contrast mammography. He has been demonstrating the benefits this technology has brought to patients since its inception in 2019.

Together for Patient Experience

As opposed to the VISIBLE that matters to doctors, meaning early

detecting and rapid diagnosis by viewing tumors to save lives, we are introducing the INVISIBLE that matters during the WHXR Roadshow. We want to partner with healthcare professionals to promote women's self-awareness, self-efficiency and a healing wide-ranging journey, leading to increased survival rates. What you do every day may not be enough. Women have homework to do too! And too many women do not know that. They are not equally armed and informed. We want to support doctors by filling in known gaps in proactive education and woman-to-woman support and guidance that we know can be life-changing and life-saving!

Customers heard Cecilia Olsson, a Product Life Cycle Manager for GE Healthcare and also a Breast Cancer survivor. Cecilia and the team explained to customers how, by understanding and adapting to women's and patient's personal constraints, culture and known fears, the One Stop Clinic deploys a care path that is the shortest possible, reducing steps, and appointment and waiting times. They also highlighted how the human-centered design of our products Senographe Pristina™ and SenoBright™ CESM, the key solutions at the heart of mammography solutions play an important role in addressing ergonomic issues by placing women's well-being at the forefront.

Having a great time

At GE Healthcare, we understand that the human touch is always important in building trust and confidence. Finally moving past the phone calls, emails and virtual meetings, both customers and GE Healthcare teams have been thrilled to meet face-to-face. Conversations flow naturally, customers have their questions answered, are happy to experience the technologies in a real setting, while exchanging with peers.

Customers have taken the time to visit us, and our goal is to see them leave the tour safely and with a smile.

We have tried our best to make the tour pleasurable, with live and personalized demos, and a cozy, lively and safe environment to make the roadshow fun, interactive, inspirational, memorable, and safe. We help them "experience" the products, give hot topic presentations, and create a warm atmosphere of networking.

In order to facilitate and engage customers, we used digital tools such as MyWaitingRoom applications, Patient Experience Podcasts, and MyTour for trainings. We brought an unforgettable experience to visitors, so that their memories of the tour will be positive ones.

Many customers were fascinated by this in-person and interactive format. It allowed them to see and experience so many innovative products and applications at once that they wouldn't have been able to otherwise. They also spent a great time exchanging ideas and chatting with peers.

In partnership with BD

WHAT OUR CUSTOMERS SAY?

"We have just left the GE Healthcare Roadshow in Madrid, and we are delighted with the importance of new technologies, innovation, artifical intelligence applied to radiodiagnostic and it is a pride to be able to say that progress is being made in this sector to be at the service of the patient, in this case for the detection of #breastpathology and how with research we will arrive earlier and earlier to the early detection of breastcancer Thanks for the invitation and congratulations GE Healthcare."

"I liked a lot the format (of the Roadshow). Very innovative! By the way would it be possible to find a slot? I would like to bring one of the radiologists of the unit".

"Thanks for bringing awareness on how we can better support cancer, this is of great value. Patient experience is on top of every cancer journey".

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GE Healthcare

GE Healthcare provides medical technologies and services to help solve the challenges facing healthcare providers around the world. From medical imaging, software, patient monitoring and diagnostics, to biopharmaceutical manufacturing technologies, GE Healthcare solutions are designed to help healthcare professionals deliver better, more efficient and more effective outcomes for more patients.
GE Healthcare is betting big on digital; not just connecting hospital departments and physicians more effectively, but utilizing the masses of data from its equipment and the collaboration between hardware and software –"digital industrial" – to help clinicians make better care decisions. Sensors, software and smart data analytics are converging to enhance GE Healthcare's offerings not just in diagnostics, but also pathology, gene sequencing and even hospital asset tracking.

geheleathcare.com

The statements by GE's customers reported here are based on results that were achieved in the customer's unique setting. Since there is no "typical" hospital and many variables exist, i.e., hospital size, case mix, etc., there can be no guarantee that other customers will achieve the same results.