Institution: University of Bristol		
Unit of Assessment: 12) Engineering		
Title of case study: Non-Invasive, Safe and Comfortable Breast Cancer Imaging for Early Diagnosis		
Period when the underpinning research was undertaken: 2001 - 2015		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting HEI:**
Ian Craddock	Professor in Data-Driven Health	08/1997 - present
Alan Preece	Professor in Medical Physics Emeritus Professor	06/1996 – 04/2004 06/2004 - present
Maciej Klemm	Lecturer	01/2006 - 09/2018
Period when the claimed impact occurred: 1st August 2013 – 2020		
Is this case study continued from a case study submitted in 2014? No		

1. Summary of the impact

The University of Bristol developed world-first radar-based cancer detection system has been commercialised by spin-out Micrima and is now being sold and being used in hospitals. Current screening technology for breast cancer involves exposure to ionising X-ray radiation (itself a potential cause of cancer) and uncomfortable compression of the breast - many women choose not to attend their 3 yearly screenings and this very treatable disease tragically remains one of the most common causes of death in women. The University of Bristol approach avoids both ionising radiation and discomfort.

Since 2014, Micrima Ltd has received over GBP14 million of investment to commercialise the technology and now employs 25 staff. Having received CE product approval and signed a distribution agreement with multinational Hologic Ltd, its first commercial imaging systems were ordered and shipped to hospitals in mainland Europe in the summer of 2020, where they are now in routine use with patients.

2. Underpinning research

Breast cancer is the most common cause of death in women between the ages of 35 and 49 in the UK[1]. National breast screening programmes, using X-ray mammography, are the front-line weapon in the fight to improve breast cancer survival statistics.

X-ray equipment is bulky, expensive, and involves potentially harmful ionising X-ray exposure as well as discomfort for the patient due to the need for compression of the breast. Discomfort is the main reason that only around 70% of women attend their screening appointments. Furthermore, X-ray also performs poorly in the denser breasts of women under age 40 and hence women under age 50 are not offered routine screening in most countries, including the UK. However, women under 50 accounted for 18% of breast cancer incidences in the UK from 2015 - 2017 (the average number of new cases per year was just under 10,000 for this age range).

Bristol's work on landmine detection, led by Craddock and funded by the Ministry of Defence prompted the team to propose a novel radar-based breast cancer imaging system as an alternative to X-ray imaging. With funding from charitable sources and from EPSRC [i, ii] the Bristol team, led by Craddock as PI and including Preece, Leendertz, Klemm, Gibbins and Sarafianou, took the technology from theoretical simulation, through lab studies (Figure 1)

[1] https://www.gov.uk/government/publications/health-profile-for-england/chapter-2-major-causes-of-death-and-how-they-have-changed

and on to the implementation of a clinical system (Figure 2) at the University over the period 2001 to 2010. The team's expertise in radar signal processing, electromagnetic modelling of complex structures and wideband antenna design led to key breakthroughs included the design of suitable antenna and array structures [1, 2] along with focussing algorithms [3]. Such radar systems are clutter-limited rather than signal to noise (SNR) limited. The research challenges included obtaining sufficient bandwidth from an antenna small enough [1] to form into an array around the human body, reducing the large skin reflection and other clutter signals through multistatic signal processing [3] and being able to perform the necessary signal acquisition within the time period that a patient can lie still for.

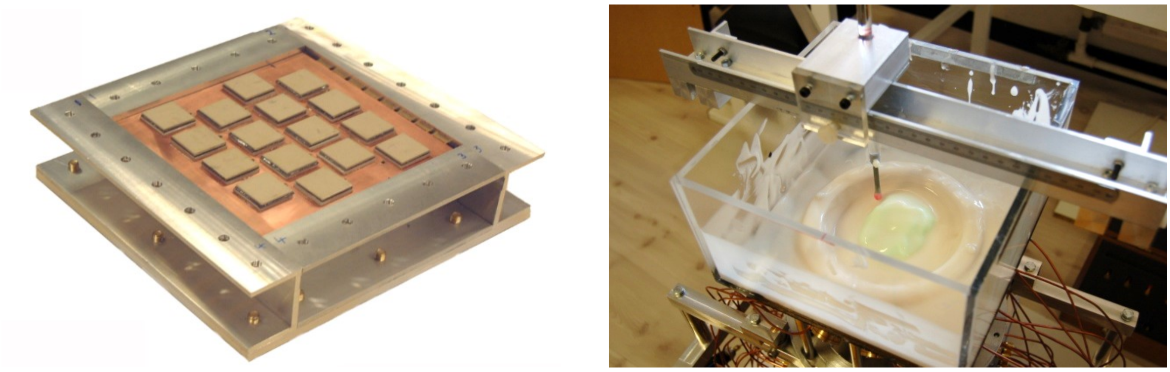

Figure 1: (left) original Bristol stacked patch antenna array, and (right) array performance being evaluated with a liquid "phantom" to replicate human tissue

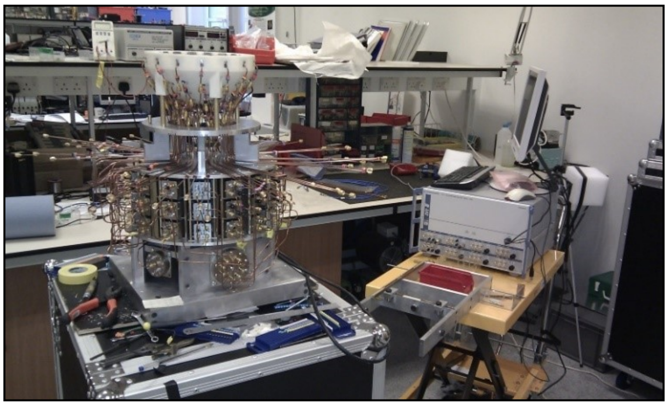

Figure 2: The University's original clinical prototype under construction in its laboratories

The prototype system was comprised of the University's antenna array and custom-built switching matrix to connect the antenna elements to a multi-port vector network analyser (VNA) and the baseband signal was processed using the University's multistatic focussing algorithms [3].

The resulting experimental system (Figure 2) was initially evaluated using human body "phantoms" [4] in which it proved capable of imaging phantom tumours down to 4 mm diameter (which would be classed as "early stage" cancer). It then progressed to world-first clinical trials of such an imaging system [5].

In recognition of these achievements, Craddock was awarded the 2005 IEE J. A. Lodge prize for outstanding work in Medical Electronics. The team was subsequently awarded the 1st prize and Gold Medal in the "SET for Britain" Competition at the House of Commons in 2006 and the Royal Colleges Medal in 2012.

In 2005, the University set up spin-out company, Micrima Ltd, to bring a workable device to market. In addition, subsequent inventive features based on the University's research have strongly influenced the signal processing algorithms employed in the company's prototypes [3]. In the period 2005 - 2015 further enhancements in signal processing techniques were pioneered by the University [6, F, G] and licensed to Micrima [A].

3. References to the research

[1] D Gibbins, **M Klemm, IJ Craddock**, J Leendertz, **AW Preece,** R Benjamin, "A Comparison of a Wide-slot and a Stacked Patch Antenna for the purpose of Breast Cancer Detection," IEEE Transactions on Antennas and Propagation, 58(3), 665 – 674, 2010. **DOI:**10.1109/TAP.2009.2039296

[2] **M Klemm, IJ Craddock**, JA Leendertz, **AW Preece**, R Benjamin, "Radar-Based Breast Cancer Detection Using a Hemispherical Antenna Array—Experimental Results," IEEE Transactions on Antennas and Propagation, 57(6), 1692 – 1704, 2009. **DOI:**10.1109/TAP.2009.2019856

[3] D Byrne, **IJ Craddock**, "Time-domain Wideband Adaptive Beamforming for Radar Breast Imaging", IEEE Transactions in Antennas and Propagation, 64, 1725 -1734, 2015. **DOI:**10.1109/TAP.2015.2398125

[4] **M Klemm**, J Leendertz, D Gibbins, **IJ Craddock, AW Preece**, R Benjamin, "Microwave Radar-based Breast Cancer Detection: Imaging in Inhomogeneous Breast Phantoms," IEEE Antennas and Wireless Propagation Letters, 8, 1349 – 1352, 2009. **DOI:**10.1109/LAWP.2009.2036748

[5] **AW Preece, IJ Craddock**, M Shere, L Jones, HL Winton, "MARIA M4: Clinical evaluation of a prototype ultra-wideband radar scanner for breast cancer detection", Journal of Medical Imaging, 3(3), 033502, 2016. DOI:10.1117/1.JMI.3.3.033502

[6] **Craddock IJ, Preece AW**, Nilavalan R, Leendertz JA. (2012). Granted Patent: "Methods and Apparatus for Measuring the Internal Structure of an Object" (European Patent EP1850743, Japanese Patent JP5312802).

Grants

[i] **Craddock IJ**. Enhanced UWB Radar Imaging of Breast Tumours, EPSRC (EP/G003084/1), 2008 – 2011, GBP561,887

[ii] **Craddock IJ**. Hybrid UWB Radar/Inverse Scattering for Breast Cancer Imaging, EPSRC (EP/J00717X/1), 2012 - 2015, GBP478,000

4. Details of the impact

Following the success of early research, the University of Bristol set up a spin-out company, Micrima Ltd in 2005, which licensed the relevant University IP [F, G] and took ownership of the experimental hardware and associated software. Within the current REF period the company has brought the concept to market both in the UK and overseas, with the aim of reducing nearly one million deaths each year.

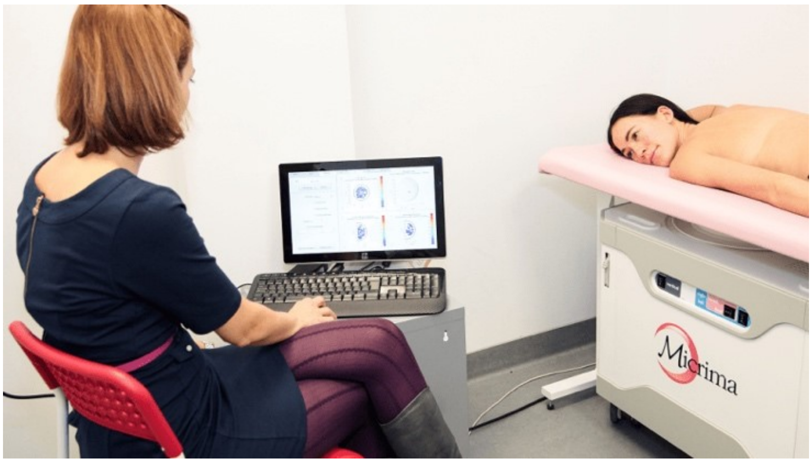

Figure 3: Micrima's MARIA system in use (with photographic model)

Micrima initially focussed on continuing the existing clinical trials process in order to evidence system performance in a spectrum of patients, to develop its IP portfolio, recruit an engineering team and understand, in collaboration with its suppliers Keysight, how to reduce the production costs of the University's original experimental system.

Commercialisation of novel technology

Regulatory compliance for medical devices is always a major hurdle en route to market and after refinement of the system hardware and software, Micrima commenced the regulatory approval process for its first commercial system MARIA^{TM} in 2014 (shown in Figure 3), leading to the milestone of European regulatory approval in 2015 [B]. As described in [B] the system was the first to market worldwide.

Improved cancer detection

In 2016, the company published its first trial data [5] to evidence system performance in a patient population. 86 imaged breasts yielded a detection rate of 74% which compares well to the 78% score reported in the digital mammographic imaging screening trial (DMIST) study [5]. In the dense breasts of younger women, MARIA detected 86% of the cancers - a notable improvement on the DMIST dense breast group performance of 78%. While the sample size is as yet insufficient to draw definitive conclusions, the MARIA results in dense breasts are especially important since women with dense breast tissue have a significantly higher risk of breast cancer.

Professor Iain Lyburn, consultant radiologist at Cheltenham General Hospital, stated: *"In the younger patients, who've got dense breasts […] the dense breast isn't a problem, as it were, for the MARIA scan; it treats the breast the same as if it's a very fatty breast, so potentially we'll be able to use this in the younger patient for whom we can't see things with mammograms at all. So in terms of diagnosis, and screening, and family risk patients […] this is one of the areas that's very exciting."* [C]. The approved MARIA device went into full commercial trials at the Royal Marsden in London, which are ongoing at the time of writing (the trials were suspended due to Covid-19), with 400 women screened to date.

Improved patient wellbeing

All feedback from the trials indicate that the scan is much more comfortable for women. In addition, Prof. Lyburn stated that *"Also, as I understand it, people find it quite comfortable. One of the problems with mammography is up to 20% of ladies find it quite uncomfortable. The patients that we've had through so far expressed how surprised they are about how comfortable it is, so of course that would increase compliance and tolerance and make it much easier for ladies to have the scan done. …having the patients on board is really helpful."* [C]. One trials patient, who had previously refused X-ray screening and was interviewed on BBC Breakfast, commented: "Brilliant, painless, safe. It's like a good meal in a restaurant. I'd go back." [A].

The MARIA device uses low power radio waves at a similar frequency to those commonly used by millions of mobile phones – it is harmless and non-ionising. Unlike X-ray therefore, there is no limit to how many times a woman can be imaged. Professor Lyburn emphasizes this *"The thing that's excellent about it is that potentially it could be used several times on people without any radiation burden."* [C].

Current status of company

Micrima is now an established company with 25 staff in its offices and laboratories in central Bristol, as well as supporting employment within its supply chain (for example, Keysight [C]). Since 2014, the company has raised GBP10.4 million in equity funding, GBP2 million from a corporate partner and GBP2.6 million in competitively awarded R&D grants. [A].

The company has received several awards, including the Frost and Sullivan New Product Innovation award (December 2018), Made in the South-West award (November 2018), the Disrupt SW Index award (September 2018) and the Medilink SW innovation award (February 2017). It was chosen as one of the Top Ten Best Healthcare Start-ups to watch in 2019 (July 2019) [D].

Following a marketing and distribution deal with Hologic Ltd, the first orders were received, and imaging systems shipped to hospitals in the summer of 2020 [A]. Following staff training with the team of Professor Uwe Fischer at the Diagnostic Breast Centre in Göttingen (Figure 4), the first system is being used with patients there. Delayed slightly by the pandemic, a second system is now in use at the University Medical Center Mainz, with Professor Andrea Teifke [E].

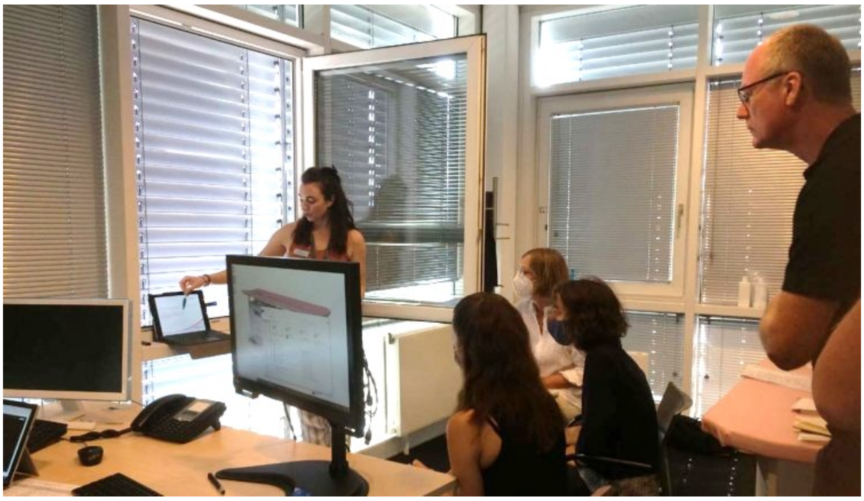

Figure 4: Staff training on the new MARIA breast imaging system in Germany, 2020 (courtesy of RAD Magazine, Sept 2020 [E]).

5. Sources to corroborate the impact

[A] Micrima Ltd. (2020). Corroborating statement - Non-Executive Chairman

[B] Keysight (2020). First-to-Market Radio Wave Breast Imaging System Achieved with Network Analyzer

[C] Micrima Ltd. (2018). Interview with Professor Iain Lyburn, [Accessed 25th June 2020].

[D] Micrima Ltd. (2020). Industry Awards, [Accessed 25th June 2020].

[E] RadMagazine (2020). Breast centre’s MRI protocol offers interesting data for imaging system [Accessed 8th Jan 2021].

Patents:

[F] **Craddock IJ, Klemm MB, Benjamin R**. (2014). Granted Patent, “Methods and apparatus for measuring the contents of a search volume”, (US Patent US8862409, Japanese Patent JP5417337).

[G] **Craddock IJ.** (2016). Granted Patent, “Antenna for Investigating Structure of Human or Animal” (European Patent EP2227140B1 and Japanese Patent JP5535926).