Institution: Loughborough University		
Unit of Assessment: UOA9 - Physics		
Title of case study: Improving brain activity imaging for better understanding of brain-functionality, diagnosis and treatment of brain diseases		
Period when the underpinning research was undertaken: Feb 2013 - Dec 2017		
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:**
Boris Chesca	Senior Lecturer in Physics and Quantum Computing	02/2006 to date
Daniel John	Research Associate	07/2014-07/2018
Period when the claimed impact occurred: Jan 2018- Dec 2020		
Is this case study continued from a case study submitted in 2014? No		

1. Summary of the impact (indicative maximum 100 words)

Magnetoencephalography (MEG) using single-SQUIDs (Superconducting-QUantum - Interference-Devices) is the most sensitive brain activity imaging technique used in the research, diagnosis, and treatment of brain diseases such as depression, schizophrenia, dementia, epilepsy, and strokes. SQUID-based MEG is currently used by more than 170 medical facilities/hospitals worldwide. Based on a technological breakthrough achieved in 2015, Loughborough researchers developed and patented a superior new SQUID-array MEG-imaging technology. The world leader in brain imaging devices, CTF-MEG (British-Columbia/Canada), **adopted this new technology** for their next generation devices in collaboration with the world-leader in superconducting-technology, Star-Cryoelectronics, (Santa-Fe/US) and Loughborough University.

2. Underpinning research (indicative maximum 500 words)

Dr Chesca led a team of researchers at Loughborough University – Dr Daniel John (Research Associate), Dr Marat Gaifullin (Lecturer), and Prof Sergey Saveliev – to investigate the operation of various types of SQUID-arrays connected in parallel in multiple applications such as transistors [R1], magnetically-tunable diodes [R2], or emitters/receivers of electromagnetic radiation [R3, R4]. Furthermore, Dr Chesca and Dr John demonstrated that magnetic sensors based on SQUID-arrays connected in series operating at 77 K and above showed 5 times superior sensitivity relative to optimized single-SQUIDs made of low-temperature superconductors and operating at 4.2 K. In addition, when compared to single-SQUIDS capable of operating at 77 K the SQUID-arrays showed up to 10 times improved sensitivity [R5]. This is particularly important in the application of SQUID sensors in MEG, where improved sensitivity could enable earlier diagnoses of brain diseases (and subsequent better chances of treatment and quicker recovery times) as well as better understanding of brain-functionality. In addition, whilst operating at 4.2 K requires liquid helium, operating at 77 K could be achieved with liquid nitrogen, which is much more readily available, cost effective, and environmentally friendly.

As the most sensitive magnetic sensors, single-SQUIDs are routinely used in many applications in medicine (MEG and magnetocardiography), as well as: SQUID-magnetometers for investigation of magnetic properties of materials; electronics (SQUID-amplifiers); geology (oil prospecting, mineral exploration); particle and X-ray detectors; astronomy; and military applications.

Between Feb-2013 and Dec-2017 the team developed a superior magnetic sensor technology based on these SQUID-arrays as summarized by the research milestones outlined below.

1. Multiple advanced designs were developed to produce highly integrated SQUID-arrays connected in series, parallel or in series-parallel configurations operating coherently for various applications.
2. For their practical implementation, [redacted].
3. High quality SrTiO bicrystal substrates were acquired [redacted].
4. The SrTiO substrates were sent to [redacted] to deposit high quality YBaCuO superconducting thin films.
5. The films were then subsequently patterned [redacted]. Thus, various advanced designs of multiple SQUID-array prototypes were fabricated.
6. The prototypes were subsequently tested in Dr Chesca's laboratory at Loughborough University for low-temperature, high performance electrical transport measurements. The SQUID-array prototypes showed an ultra-sensitive and coherent response to a small applied magnetic field. Large SQUID arrays connected in series and operated as new magnetic sensors showed a dramatic improvement in the magnetic sensitivity over the best-known magnetic sensors to date [R5].
7. Our understanding of the operation of SQUID-arrays has improved continuously between Feb 2013 and December 2020. Fundamental theoretical/experimental investigations were performed on various types of SQUID-arrays connected in parallel to understand their suitability for other applications [R1-R4].

The magnetic sensors developed by the team based on SQUID arrays have shown a superior sensitivity relative to optimized single-SQUID sensors made of low-temperature superconductors [R5]. This remarkable achievement has opened up exciting opportunities to replace single-SQUIDs with SQUID-arrays in order to improve sensitivity/performance in many applications, including medical applications (SQUID-based MEG).

3. References to the research (indicative maximum of six references)

R1: B. Chesca, D. John, M. Kemp, J. Brown, and C.J. Mellor, *Applied Physics Letters* **103**, 092601 (2013), Parallel array of YBCO superconducting vortex flow-transistors with high current gains, https://doi.org/10.1063/1.4819461

R2: B. Chesca, D. John, R. Pollett, M. Gaifullin, J. Cox, C. Mellor, S. Savel'ev, *Applied Physics Letters* **111**, 062602 (2017), Magnetic field tunable vortex diode made of $YBa_2Cu_3O_7$ Josephson junction asymmetrical arrays, https://doi.org/10.1063/1.4997741

R3: B. Chesca, D. John and C.J. Mellor, *Supercond. Sci. Tech.* **27**, 085015 (2014), Amplification of electromagnetic waves excited by a chain of propagating magnetic vortices in YBCO Josephson-junction arrays at 77K and above, https://doi.org/10.1088/0953-2048/27/8/085015

R4: B. Chesca, D. John, M. Gaifullin, J. Cox, A. Murphy, S. Savel'ev, C. J. Mellor, *Applied Physics Letters* **117**, 142601 (2020), Magnetic flux quantum periodicity of the frequency of the on-chip detectable electromagnetic radiation from superconducting flux-flow-oscillators, https://doi.org/10.1063/5.0021970

R5: B. Chesca, D. John and C.J. Mellor, *Applied Physics Letters* **107**, 162602 (2015), Flux-coherent series SQUID array magnetometers operating above 77K with superior white flux noise than single-SQUIDs at 4.2 K, https://doi.org/10.1063/1.4932969

The research was peer reviewed and published in *Applied Physics Letters* [R1], [R2], [R4], [R5], which presents significant new findings and is the leading applied physics journal in the world.

4. Details of the impact (indicative maximum 750 words)

The superiority and novelty of our SQUID-array technology has been recognized worldwide: It has since been validated via several **patents** in countries with leading research/expertise in this area (in the UK-2017, the EU-2019, and the US-2020 [S1]). The technological breakthrough we achieved in [R5], was highlighted in *Nature* [S2], which presents the most significant advances in research worldwide, demonstrating the wider interest and far-reaching implications. It was the subject of numerous press releases and coverage [S3] in areas of application including medicine, physics (particle, X-ray detectors and astronomy), electronics, geology (oil prospecting, mineral exploration) and military. Further **pathways** to the impact of our research include multiple invited talks at prestigious international industry conferences such as the 30th International Symposium on Superconductivity (ISS2017) that was held in Tokyo, Japan, December 2017. The publicity around our SQUID-array technology drew the attention of the **world leader in brain imaging CTF-MEG** (British-Columbia/Canada, www.ctf.com) and the **world-leader in superconducting-technology, Star-Cryoelectronics** (Santa-Fe/US, starcryo.com) and we began a collaboration in January 2018 [S4, S5].

For context, for more than 25 years CTF-MEG have produced and installed the world's best MEG-systems (see Fig. 1 below). For example, CTF-MEG have installed their imaging system in the most prestigious medical institutions in the US, Canada, China, UK and Italy [S3] such as Cincinnati Children's Hospital, US; Children's Hospital of Philadelphia, US; Chinese Academy of Science; University College of London, Cardiff and Nottingham Universities; Surrey Memorial Hospital; Hospital for Sick Children, in Toronto, Canada; Institute for Mental Health, in Bethesda, MD, US; Ospedale San Camillo, in Venice, Italy; and Montreal Neurological Institute.

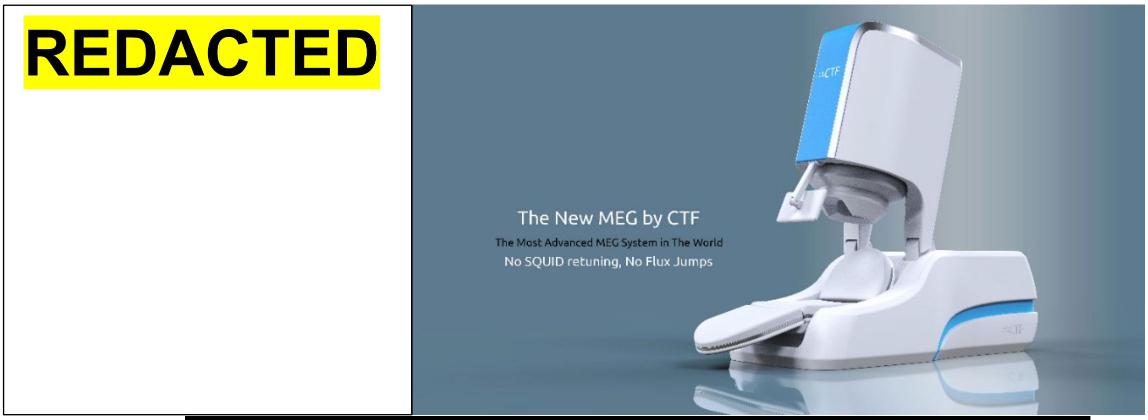

Fig.1. Left: [redacted] Right: the most advanced SQUID-based MEG system in the world currently produced by CTF-MEG. The price of a MEG system is about £3 million each.

[redacted]

The **impact** we have had on brain imaging technology product development is explained and evidenced below.

Impact: New technology adopted by the world leader in brain imaging

Since January 2018 we have collaborated with CTF-MEG, and their SQUID supplier Star-Cryoelectronics to replace the existing single-SQUID-technology currently used in their CTF-MEG systems with our superior patented SQUID-array technology for improved performance (see [S4, S5]).

> *"In 2015…your team showed the superior sensitivity of SQUID-arrays relative to that of single-SQUID-based magnetic sensors that we adopt in our MEG brain imaging devices. The upgrade of technology is timely, given the need felt for many years of improved accuracy of brain images, demanded by detailed medical assessments."*
> Mark Tillotson – Director of Engineering, CTF-MEG [S4]

[redacted]

[redacted]

> *"Following your technological breakthrough in magnetic sensing and the initiative of CTF-MEG, in January 2018, a strong collaboration was established between your group at Loughborough University, CTF-MEG and STAR Cryoelectronics to develop the world's most sensitive superconducting magnetic sensors for brain imaging (MEG). Our collaboration focuses on improving sensitivity that would enable earlier diagnoses of brain diseases (and subsequent better chances of treatment and quicker recovery times) as well as better understanding of brain-functionality." Dr.* Robin Cantor – Director of Star Cryoelectronics [S5]

To date, the full process of modifying/adapting the world's most sensitive CTF-MEG imaging system to incorporate our SQUID-array technology has led to:

[redacted]

The Director of Engineering at CTF-MEG, Mark Tillotson, confirmed that

> *"testing performed at the Star Cryoelectronics laboratories of the purpose-build SQUID-arrays prototypes for the CTF-MEG systems showed encouraging results confirming their superiority and justifying our interest in technology policy change to SQUID-arrays."* [S4]

5. Sources to corroborate the impact (indicative maximum of 10 references)

S1: SQUID array patents: European Patent EP3320357B1 granted on 07.08.2019; US Patent Nr. 10732234 granted on 04.08.2020; UK Patent GB2540146, granted on 11.01.2017.

S2: *Nature* 526, 613 (2015), Superconducting sensors warm up, https://doi.org/10.1038/526613c
S3: Press coverage of our SQUID array technology by multiple scientific communities: physics (American Institute of Physics), medicine (http://medicalphysicsweb.org), and electronics (http://spectrum.ieee.org).
S4: Support letter dated 23.11.2020, from Mark Tillotson – Director of Engineering, CTF-MEG.
S5: Support letter dated 18.11.2020 from Dr Robin Cantor – Director of Star Cryoelectronics.