Institution: Royal Holloway, University of London

Unit of Assessment: 9 Physics

Title of case study: Commercial exploitation of quantum technologies for functional brain imaging, driving international investment and serving global markets

Period when the underpinning research was undertaken: 2002-2015

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:
Professor Victor Petrashov	Professor in Physics	1996-present

Period when the claimed impact occurred: January 2015- December 2020

Is this case study continued from a case study submitted in 2014? N

1. Summary of the impact

Research in Royal Holloway's nanotechnology and nanophysics group led to innovative technologies for diagnosing brain diseases, driving global scientific and industrial markets. Early diagnosis of brain diseases is a crucial clinical need that is largely unmet. Magnetoencephalography, MEG, is a non-invasive functional brain imaging technique that can improve diagnosis. Uptake of MEG has been limited by difficulties in fabricating enough sensors for MEG scanners. Royal Holloway's research generated a new sensor, the HyQUID, which solves this global problem. York Instruments, a start-up company launched in 2015, exploited the commercial potential of the HyQUID by developing a new generation of MEG scanners. This led directly to GBP15,000,000 investment, enabling York Instruments to create 46 new jobs. This technology is licensed to Croton Healthcare, establishing the company as a world leader in MEG.

2. Underpinning research

Context: The nanotechnology and nanophysics group had a focus on the area of nanoscale quantum devices, in particular the study of superconducting circuits containing *Josephson junctions*. These circuit elements form the building blocks of *Quantum Technologies* critical to the development of quantum computers. One method to investigate the properties of these circuit elements is to use SQUIDs (Super conducting Quantum Interference Devices), these are devices that have been used to measure magnetic fields with un-paralleled sensitivity, and are the traditional sensor technology used in MEG scanners. However the use of SQUIDs to measure the properties of these circuit elements was problematic and led to an interaction between the SQUID and the circuit element called *back-action*. To overcome this problem, and in attempt to simplify the readout of these circuits, Petrashov invented a new type of a device called the **HyQUID [S3]**, (a Hybrid Quantum Interference Device).

Measurements of superconducting circuits, through a simple resistance measurement of the HyQUID demonstrated a negligible back-action on the quantum circuit [R1]. This has been exploited by the group resulting in a greater understanding of the properties of quantum circuits, in the PhD work of Dr Chris Checkley [R3]. This led to the patent GB2482008 [R4] for the HyQUID device. Further work on the operation of HyQUIDs developing a simple readout methodology of observing modulation of a resistance as a function of applied magnetic field was published in 2011 [R2].

Advantages of the HyQUID: The HyQUID is a novel development of the generic SQUID, it retains the sensitivity of the SQUID to magnetic field whilst having better overall performance characteristics and, critically, is simpler to fabricate. Fabrication of a state-of-the-art SQUID typically requires the deposition of seven layers, each step in the process needs to be optimised

and can result in failure of the device. By contrast, the HyQUID can be fabricated with only three layers, vastly reducing the complexity and increasing the yield of a production run.

Potential for MEG: After a presentation of the properties of HyQUIDs by Victor Petrashov at the York Neuroimaging centre in 2014 it was recognised that the advantages of HyQUIDs could be exploited in a new type of MEG scanner if HyQUIDs could be operated in a magnetometer mode (this makes it more sensitive to external fields coming from specific regions in space). MEG scanners require hundreds of sensors so the high yield is vital. Further research to fabricate and test this element was carried out by Dr Chris Checkley as a PDRA at Royal Holloway (2014-2015). York Instruments was founded in 2015 with the express purpose to develop a MEG scanner based upon the HyQUID. Dr Chris Checkley was recruited by York Instruments as their Senior Physicist to enable co-production of a commercial MEG scanner product. A further patent related to the manufacture of superconducting devices was co-produced between Checkley and Petrashov [R5]**.**

3. References to the research

The research was carried out from 2002 in the group led by *Prof Victor Petrashov* with *Dr Chris Checkley* (initially as a PhD student 2006-2010 and as a PDRA in 2015) with nanofabrication support from *Dr Rais Shaikhaidarov* (senior research scientist). The work has been published in leading peer reviewed journals, including *Physical Review Letters* (Impact Factor: 9.227) and the *Journal of Physics* (Impact Factor: 2,711), and has been the subject of presentations at international conferences. References R1 and R2 best indicate the quality of the research.

- **R1:** V. T. Petrashov, K. G. Chua, K. M. Marshall, R. Sh. Shaikhaidarov, J. T. Nicholls, *Andreev probe of persistent current states in superconducting quantum circuits*. Phys. Rev Lett. 95, 147001 (2005), DOI: https://doi.org/10.1103/PhysRevLett.95.147001.
- **R2:** C Checkley, A Iagallo, R Shaikhaidarov, J T Nicholls and V T Petrashov, *Andreev interferometers in a strong radio-frequency field,* Journal of Physics: Condensed Matter, Volume 23, Number 13 (2011) DOI: arXiv:1003.2176v1.

Accepted PhD Thesis:

- **R3:** C Checkley**,** *Andreev Interferometry of Flux Qubits Driven By Radio Frequency Field, PhD. Thesis (2009)* Available from HEI on Request. (Checkley was employed by Royal Holloway, University of London between 2005 and 2012)

External Funding and Patents:

- **R4:** Patent GB2482008: Quantum Interference Device. (2010) https://patentscope.wipo.int/search/en/detail.jsf?docId=GB137481080&recNum=141&docAn=201011855&queryString=EN_ALLTXT:(quantum)&maxRec=257319
- **R5:** Patent WO 2017/037436 Al: Superconducting device and method of manufacturing a superconductive device (2016) https://patentscope.wipo.int/search/en/detail.jsf?docId=WO2017037436
- **R5:** Nanoliquid BBSRC funded Tools development project 1/06/14 → 30/11/15, £147,294 Gateway Seed fund for demonstration measurements

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

Magnetoencephalography, MEG, analysis describes in vivo function of whole brain networks in real time, and has the potential to detect the very earliest changes in neurodegenerative disorders (such as epilepsy, Parkinson's disease and Alzheimer's disease) and assess preventative therapies of the future. Traumatic brain injuries are responsible for worldwide death and disability more than any other traumatic insult, MEG provides new quantitative and objective methods for detecting and assessing the severity of concussion.

However, unlike MRI systems which are present in most major hospitals and number in the tens of thousands, there are only hundreds of MEG systems clinically available globally. One reason for the low availability lies in the difficulties of fabricating the sensors contained within the MEG scanner. The impact described here is a technology driven stimulus to the MEG market. This impact is currently an economic impact but in the longer term will have societal and healthcare benefits following a proliferation of MEG scanners.

Discussions between Petrashov and researchers at the York Neuroimaging centre identified that the HyQUID could act as the magnetic field sensing element of a new generation of MEG scanners. This attracted capital investment of GBP15,000,000 into the UK from an American healthcare company, now called Croton Healthcare. Croton Healthcare, is a Florida based company with a mission to address an urgent need for a functional brain imaging device that can diagnose, analyse and monitor brain injuries. The Croton investment seeded a new UK based start-up, York Instruments Ltd. (a UK subsidiary of Croton Healthcare). The company was created to develop and bring to market a new design of MEG brain scanner based upon the use of HyQUID sensors.

Following a licensing agreement with Royal Holloway [S1], York instruments designed a MEG scanner based on the use of HyQUIDs operated at low temperatures using cryogen-free cooling technology. Petrashov and Checkley consulted on the co-design of the magnetometer configuration of the HyQUID needed for this application. Each MEG scanner requires 300 HyQUID devices, for which Royal Holloway received a fee (minimum GBP50,000 per year but scaling with the number of devices incorporated into commercial systems). Royal Holloway consulted on the manufacturability of the HyQUID, and York instruments established a process in which silicon wafers each containing 500 HyQUIDs were successfully fabricated in two commercial superconducting device foundries (one in the USA and the other in Sweden). This demonstrated the ease of fabrication of the HyQUIDs (versus the SQUIDs used in other MEG systems), removing one of the barriers for MEG uptake.

York Instruments developed the software and electronics necessary to perform MEG measurements using this system and after successfully constructing a system prototype marketed a product, the MEGSCAN$_{TM}$ internationally [S4]. York Instruments generated orders for 6 systems, with installation costs in the range GBP2-6,000,000 depending on the size of the facility being created.

In 2018 York Instruments acquired MEGIN from Swedish medical equipment maker Elekta. MEGIN, based in Finland, is a market leader in SQUID based MEG systems with net sales of around GBP9,000,000 in 2017/18. During the period between 2015 and 2019 York Instruments employed 46 people in this new advanced manufacturing industry.

In 2020, Croton Healthcare took over MEGIN and established a new licencing agreement [S2] to continue to exploit the HyQUID for MEG scanners, combing the technology for a new generation of MEG scanners with the established market leaders in MEG. [text removed for publication] of Croton Healthcare writes in his testimonial [S5] that "*[text removed for publication]*."

The income generated for Royal Holloway through the York Instruments and Croton Healthcare licensing agreements, patent cost contributions and consultancy totals GBP327,236.[S9]

According to *Coherent Market Insights*, in 2018 the global magnetoencephalography devices market was valued at USD253,300,000 (08-2019), and is projected to exhibit a compound annual growth rate of 4.5% over the forecast period (2019 – 2026), they attribute the growth projection to increasing research and development of new MEG devices and explicitly cite the HyQUID and York Instruments as a new disruptive technology in the market-place [S7]. This projection was exceeded in 2019 with a market valuation of USD279,550,000 (10-2020) showing a 10% increase in a year [S8].

Speaking at the N20 Summit (a neuroscience conference in Buenos Aires) in November 2018, Dr Babak Kateb, head of the Society for Brain Mapping & Therapeutics, said about MEG that "*Our patients have been deprived access to this technology for decades. It is refreshing to see* MEGIN *has a convincing strategic plan to make this technology as prevalent and accessible as* MRI." [S6]

5. Sources to corroborate the impact

S1: Royal Holloway – York Instruments, Licence Agreement 2015

S2: Royal Holloway – Croton Healthcare, Licence Agreement 2020

S3: HyQuid$_{TM}$ trademark, https://trademarks.ipo.gov.uk/ipo-tmcase/page/Results/1/UK00914395164

S4: MEGASCAN$_{TM}$ marketing brochure

S5: Testimonial from Croton Healthcare

S6: Dr Babak Kateb (Head of the Society for Brain Mapping & Therapeutic) public statement about MEG at N20 Summit in 2018 https://megin.fi/2018/12/megin-ceo-speaks-at-neuroscience-20-world-brain-mapping-summit-in-argentina/

S7: Bloomberg Business News Article, '*Global Magnetoencephalography Devices Market to surpass US$ 359.5 million by 2026 - Coherent Market Insights*', 2019 https://www.bloomberg.com/press-releases/2019-09-10/global-magnetoencephalography-devices-market-to-surpass-us-359-5-million-by-2026-coherent-market-insights

S8: Global Magnetoencephalography Market 2020 By Indication, Global Forecast Report, 2020 https://transiliencemarketresearch.com/shop/healthcare/global-magnetoencephalography-market-2020-by-indication-dementia-autism-schizophrenia-multiple-sclerosisstroke-epilepsy-traumatic-brain-injury-and-othersby-end-user-hospitals-imaging-centers/

S9: The income generated for Royal Holloway through the York Instruments and Croton Healthcare licensing agreements, patent cost contributions and consultancy totals