**Institution:** University of Bristol

**Unit of Assessment:** 9 - Physics

**Title of case study:** Innovative products for microscopy and analysis provide economic and healthcare benefits in a wide range of industries

## 1. Summary of the impact

Research at the Interface Analysis Centre (IAC) has made innovative analysis products available in a wide range of industries and research fields.

- The design of a novel SEM-Raman instrument has resulted in multi-million pound sales for Renishaw PLC.
- Rolls-Royce PLC has commissioned and used bespoke instruments and non destructive examinations to maintain its competitive advantage and is modifying its technical processes to incorporate these into its standard manufacturing and maintenance procedures.
- In healthcare, work on Raman probes for cancer detection has influenced support of innovation in the NHS.
- Two companies have been formed to develop and market computer control and data acquisition and analysis systems conceived in the course of this work.

## 2. Underpinning research

In 1998 Renishaw PLC, a leading manufacturer of Raman spectroscopy systems, commissioned Dr John Day at the IAC to design and develop a novel fibre optic coupled system to acquire Raman spectra from within a scanning electron microscope (SEM). This drew on Dr Day's PhD and post doctoral experience of developing optical spectrometers and spectroscopic imaging systems. The research brief was for an instrument to obtain spectra, with high spatial resolution, from the same sample position viewed by the SEM without impeding any other analytical functions such as Energy Dispersive X-Ray Spectroscopy or Electron Backscatter Diffraction (EBSD). Dr Day led a team including Dr Graham Meaden (PDRA 1998- 2003) and Dr Angus Bewick (PDRA 1998-2002) who worked together to design a novel kinematic mount and a double parabolic, aberration correcting focussing system. This fibre optic coupled system was capable of obtaining spectra from a 1μm spot with an efficiency equal to conventional laboratory Raman systems. This design was protected by patents taken out by Renishaw [4,5]. Dr Day wrote software to integrate the optical and SEM imaging and provide instrument control. A pre-production prototype was built and tested at Bristol and installed in Kochi University, Japan by Dr Day. This prototype formed the basis of a Renishaw product that has been commercially available since 2002.

This successful collaboration between Renishaw PLC and the IAC team of Day and Meaden developed further with a three year EPSRC funded project to design and construct a miniature fibre optic Raman probe for the endoscopic detection of cancer of the oesophagus [1]. This project started in September 1998, with Gloucestershire Royal Hospital and Keymed Olympus ltd also collaborating. This work demonstrated the possibility of cancer detection by Raman spectroscopy of the oesophagus and was further funded by a second award from the Health Technology Devices Program (Jan 05 to Oct 07). These miniature fibre optic probes continue to be developed for medical applications [2] and have been identified by NHS Innovations South West (NISW), the regional innovation hub, as the most exciting and promising medical device innovation from the region. Work continues at the University to bring these probes to clinical trials. In 2011 an EPSRC KTS award funded Dr Jo Hutchings of Gloucestershire Hospitals NHSFT to be seconded to the IAC. Within this collaboration 3D printing was investigated as a method of manufacturing optical devices and resulted in a new patent application. A £0.7M NIHR i4i grant is currently funding collaboration between Dr Day, the University of Exeter and Gloucester Hospital NHSFT for the development of a needle based Raman probe for the detection of lymphomas [3].

Miniature fibre optic Raman probes may be adapted to many diverse applications. In an EPSRC, ESR21 funded project in 2003, Dr Day demonstrated the use of such probes for the analysis of protective coatings on gas turbine blades in power stations. Raman spectroscopy was shown to be a valuable tool for investigating the effect of thermal cycling on the thermal barrier coatings of turbine blades. Following this work, Rolls-Royce PLC (R-R) has placed 15 commercial contracts

with the IAC to exploit and evaluate various aspects of this technology for aerospace applications and is currently sponsoring a PhD Case studentship. Work has included studies to analyse corrosion and contamination seen on and within ex-service components in the lab and the design and construction of bespoke miniature fibre optic probes, based on those designed for cancer detection [1,3], for analysis on wing. Uses of these probes have included the in situ identification of corrosion and contamination products and the measurement of thermal paints, which change colour depending on engine temperature. A spectroscopic imaging system for the rapid detection of Alumina coatings on components [6] has been developed and used at R-R plants in Derby, East Kilbride and Montreal. R-R continues to validate these systems to bring on line within their plants in the near future.

Within these projects Drs Day and Meaden developed computer programming and machine interfacing skills that they applied to the large array of surface science instrumentation at the IAC. Specifically Dr Day developed Windows based software and electronic interfaces to replace the diverse range of computer control systems then available on SEMs and SIMS, Auger and XPS spectrometers within the department. This provided a standardised software interface for the machines in the IAC, which became increasingly in demand by other laboratories.
Dr Meaden further developed his ideas on strain measurement using Raman and EBSD and helped supervise a PhD project on the technique. This work drew on the original research of Prof David Dingley in the Bristol Physics department. Dr Meaden left the IAC in 2003 and, in close collaboration with Prof. Dingley formed BLG Productions to further develop the skills and ideas conceived at the University of Bristol. Dr Meaden is currently a Visiting Fellow at the IAC and continues to collaborate with the IAC on testing his company's products.

## 3. References to the research

### Peer Reviewed publications


1. *J. C. C. Day, R. Bennett, B. Smith, C. Kendall, J. Hutchings, G. M. Meaden, C. Born, S. Yu, and N. Stone, "A miniature confocal Raman probe for endoscopic use.," *Physics in medicine and biology*, vol. 54, no. 23, pp. 7077–87, Dec. 2009, doi:10.1088/0031-9155/54/23/003
2. L. Almond, J. Hutchings, G. Lloyd, H. Barr, N. Shepherd, J. Day, O. Stevens, S. Sanders, M. Wadley, N. Stone, C. Kendall, Endoscopic Raman spectroscopy enables objective diagnosis of dysplasia in Barrett's esophagus, *Gastrointestinal Endoscopy*, 22 July 2013, ISSN 0016-5107, doi:10.1016/j.gie.2013.05.028
3. * J.C.C. Day and N. Stone, "A subcutaneous Raman needle probe." *Applied spectroscopy*, vol. 67, no. 3, pp. 349–54, Mar. 2013. doi: 10.1366/12-06651


### Patent Publications


4. * US 6885445 (B2) Electron microscope and spectroscopy system. April 26 2005 Applicant Renishaw PLC. Inventors Bennett, Wolfrey, Bewick and Day. Priority Date 9/5/98
5. JP5095587 (B2) — 2012-12-12 Adapter for performing optical analysis of sample. Applicant Renishaw PLC. Inventors Bennett, Wolfrey, Bewick and Day. Priority Date 3/8/01.
6. P2011158474 also published as US2011180727 , SG173282 EP2362181 and CA2727352 – Device and Method for checking presence of Alumina Layer on component surface. 18/08/2011 Applicant Rolls-Royce PLC. Inventors Kell and Day.


## 4. Details of the impact

**Renishaw PLC:** Our most established and commercially significant impact is the SEM Raman system originally designed by Dr Day's team and currently marketed by Renishaw PLC. The first instrument sold by Renishaw was built by Dr Day in 2002 and installed in Kochi University, Japan by Dr Day and Renishaw staff under his instruction. The patents [4,5] that resulted from the original work by the IAC helped Renishaw to protect this strategically important technology and it remains the only manufacturer of such an instrument. These instruments provide researchers with the means of combining two complimentary analytical techniques simultaneously at the same microscopic point on a sample. Conventional EDX analysis performed in an SEM gives the simple

elemental makeup of a sample however Raman spectra acquired at the same point can identify the chemical bonds present and allow the researcher to positively identify chemical compounds or distinguish between allotropes such as Graphite and Diamond. Uses include the identification of contaminants in semiconductor fabrication lines and the investigation of oxidation in reactor steel. Renishaw does not wish to disclose commercial sales figures but sales are of the order of £1,000,000 per year. Renishaw states* that "*Dr Day has made a significant contribution to our business that has enabled us to produce a novel combined technology. The interface remains a unique offering that is a capital item with complete systems selling for upwards of £200,000. In the period 2008 to present we have made and continue to make regular sales of these systems, the majority of which have gone for export. This product has assisted the Spectroscopy Division of Renishaw PLC commercially and in maintaining Renishaw's position as a world leading supplier of Raman spectrometers*" [A].

**Rolls-Royce PLC:** Rolls-Royce states* "*Our ability to understand and manage gas turbine products throughout the product lifecycle is a key capability which enables us to maintain our competitive advantage and exceed customer expectations. The work undertaken at the University of Bristol has been strategically supported to allow us to look at manufacturing and material processing. Furthermore, we are able to identify and analyse chemical species during component manufacture and in-service by deploying techniques in-situ. The ability to identify and analyse components using this technique allows feedback to enable operating lives, product integrity and through-life performance.*"[B]. Within the REF period, Rolls-Royce has placed contracts to the value of £350,000 with the IAC to research and develop the application of spectroscopic techniques. Miniature Raman probes designed and built at the IAC have been purchased and used to detect and analyse contaminates within engines in situ, reducing the need for dismantling of the engines, which can cost £300,000 per engine. In situ analyses have been performed at the trial stages of the Trent 900 and Trent 1000 engines. Rolls-Royce is now commissioning a Raman system to be included in its standard collection of inspection instruments for field use. The work at Bristol to analyse Thermal Paints in situ with Raman probes has resulted in Rolls-Royce investing in the development of paints with optimised Raman response to increase the reliability and sensitivity of the method. An imaging system developed at Bristol to replace the visual tests used to detect alumina coatings on turbine blades has resulted in a Rolls-Royce patent application [6].

**Healthcare:** NISW, the NHS regional innovation hub, have identified our miniature Raman probes as the most promising medical device innovations from the region. NISW states* "*These projects form part of a small portfolio that is managed by NISW and that were brought to the attention of senior figures within the NHS and the MP John Glen as being flagship examples of projects that could yield great benefit, but were being delayed through lack of investment and support from within the NHS. This led to a mention in a parliamentary debate on innovation within the NHS (Hansard 12th October 2011: Column 98WH) and subsequently resulted in a unique Innovation Development Fund being provided to NISW to support the key projects (a first within the NHS). Subsequently, the recognition of the need to improve the support for innovation and adoption processes within the NHS to realise the benefits from projects such as the Raman Probe helped to inform the review conducted by Sir Ian Carruthers whose outcome was enshrined in the Report ' Innovation, Health and Wealth' produced by Sir David Nicholson in December 2011. This led to far-reaching change and improved support at a local level within the NHS for innovation projects. Sir Ian Carruthers, as Chief Executive of NHS South, was the key decision-maker in the creation of the Innovation Development Fund and undoubtedly his awareness and understanding of the Raman projects helped to inform and shape some of the thinking that has changed the approach towards support of innovation in the NHS.*"[C]. The EPSRC KTS award resulted in a patent application jointly submitted by the University and NHS and provided Dr Hutchings with the expertise to apply for and win the 2012 industrial design fellowship from the Royal Commission for the Exhibition of 1851, mentored by Dr Day.

**New Companies:** Dr Meaden's company **BLG Productions ltd** develop and sell "CrossCourt 3" software that uniquely allows the determination of strain and rotation tensors to 1 part in $10^4$ precision. It is used for the analysis of metals, semiconductor, strained silicon devices, solar power, 3D chip design and mineralogical samples as well as academic research. Typical users include

power generation companies and semiconductor manufacturers. Dr Meaden states* "*Much of our expertise in EBSD and instrumentation originates from the original research done by Prof David Dingley in the Department of Physics at Bristol and my own experience of working in the Interface Analysis Centre. Between 1998 and 2003 I worked with Dr John Day at the IAC on optical interfaces to Auger spectrometers, the design of miniature Raman probes for cancer detection and applications of EBSD. The impact of that research inspired the formation of BLG Productions in 2004; which would not have happened without the experience and expertise acquired working for John Day. We continue to collaborate closely with Dr Day and the IAC. BLG Productions Ltd. is now expanding from its original core members. We have recently taken on our first new directly funded staff member and now have 10 associates across the world involved in marketing and technical support. We have achieved sales of over 30 units to a value exceeding £400,000 in the last 5 years, almost entirely exports.*"[D].

The demand for the software and control systems developed for analytical instruments led Dr Day to form **Dayta Systems ltd** in 1999, which he has run while working part time at the University. These systems have been supplied to approximately 50 companies and universities with total sales exceeding £500,000, predominantly exports [E]. In the REF period 2008-2013, sales included exports to the Universities of: Princeton, California Irvine, New Mexico, and Connecticut. Domestic customers included Renishaw, BAE Systems and the Universities of Loughborough and York.

*All statements quoted above are taken from letters provided by those named in section 5.

**5. Sources to corroborate the impact**

**[A] Renishaw PLC,** Dr Ken Williams, Sales Director, Provided letter of support and quoted statements are taken directly from this letter. Renishaw will not release sales figures, which they consider commercially confidential.
Product details available at http://www.renishaw.com/en/sem-raman-system--6639

**[B] Rolls-Royce PLC**, Dr Justin Burrows, Project Manager-Universities, can confirm all of the claims made relating to Rolls-Royce PLC. Burrows has seen the submitted document and consented to the sections relating to Rolls-Royce. Quoted statements are taken directly from a letter of support sent to us by Rolls-Royce.

**[C] NHS Innovations South West**, Mr Angus Donald, Business development manager, can confirm the claims made relating to NISW and NHS funding. Mr Donald has seen, and consented to the relevant sections of the submitted document. Quoted statements are taken directly from a letter of support sent to us by NISW.

**[D] BLG Productions Ltd**, Dr Graham Meaden, Director and Lead Scientist, may be contacted to confirm the claims made relating to his company. Dr Meaden has seen the submitted document and consented to the relevant sections. Quoted statements are taken directly from a letter of support sent to us by Dr Meaden.
Product details available at http://www.blgproductions.co.uk

**[E] Dayta Systems Ltd,** Dr S. Organ, Company Secretary, may be contacted to confirm the claims made relating to DaytaSystems. Dr Organ has seen the submitted document and consented to the section relevant to Dayta Systems.
Product details available at http://www.daytasystems.co.uk