

Institution: Swansea University		
Unit of Assessment: 9		
Title of case study: Raman Spectroscopy Application to the Diagnosis of Colorectal Cancer; Translation of Healthcare Technology via University Spin-out CanSense Ltd		
Period when the underpinning research was undertaken: 2014-2020		
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:
Peter Dunstan	Professor	1999-present
Cerys Jenkins	PDRA	2018 – 2020
Dean Harris	Honorary Chair, Medical School	2013 - present
Period when the claimed impact occurred: 2016-2020		
Is this case study continued from a case study submitted in 2014? No		
1. Summary of the impact Developing technology to enable the non-invasive early detection of cancers is one of today's global challenges. Bowel cancer is the third most common cancer globally and accounts for 900,000 deaths every year. Symptoms of bowel cancer are non-specific making it challenging for GPs to detect. Many patients are sent to hospital for an invasive colonoscopy which is usually negative. There is a desperate need to improve primary care triage methods to ensure the correct patients are prioritised for treatment and unnecessary referrals avoided. By the time many (~60%) patients present with symptoms, it is often at an advanced stage. Using a multi-disciplinary approach, a research team led by Professor Peter Dunstan (Physics Dept, Swansea University) and colorectal surgeon Professor Dean Harris (Swansea Bay University Health Board & Medical School, Swansea University) have used spectroscopy and AI technology to develop a rapid blood-based test effective in detecting early-stage bowel cancer. On the back of this success and the significant potential of our technology platform for the early detection of other cancers, we have established CanSense Ltd, an award-winning spin out company. The company has advanced development of the diagnostic, identified and commenced on a clear route to market, championed public awareness and charity research support, and put patients at the forefront of our plans to detect cancer early when it is most treatable.		
2. Underpinning research Professor Peter Dunstan co-leads a cutting edge Biospectroscopy research group together with clinician and consultant colorectal surgeon, Professor Dean Harris. The group represents a significant multidisciplinary initiative between Swansea University's (SU) Physics Department and Medical School and utilises SU's Centre for Nanohealth. Early research Dunstan's developments in Raman spectroscopy, soft matter and analytics can be demonstrated from earlier work based upon the development of nanoscale sensors for intercellular pH measurement using surface enhanced Raman Spectroscopy (SERS) [R1]. Using principal component analysis (PCA) a more reliable and robust methodology than peak ratiometrics was established to identify spectral changes. Subsequently Dunstan collaborated with clinician and consultant colorectal surgeon, Professor Dean Harris (honorary clinical professor at the Medical School, SU) on a funded pilot study of the analysis of serum from colorectal cancer (CRC) patients [G1]. Based on the pilot study showing the ability to produce distinctive spectra from blood serum, the opportunities offered by SERS and PCA analytics, and knowing patient CRC outcomes, the group were successful in winning a competitive Cancer Research Wales grant [G2]. The grant supported PhD researcher C. Jenkins and an initial evaluation article of Raman spectroscopy applied to cancer diagnostics, from surface enhanced Raman spectroscopy through to endoscopic approaches was published [R2]. Extending our studies to SERS labelling of specific proteins were found to be subject to inconsistencies, complex assay development and inadequate performance. A label-free approach with serum was investigated using PCA analytics and it was found that with		

technical adaptations to sampling approaches the spectra demonstrated sensitivities to patient clinical outcomes in relation to colorectal cancer [R3].

Identification of key spectral biomarkers for bowel cancer

In recent years, interest in the field of liquid biopsies has grown, given they can be less invasive for patients. Research by Dunstan et al. [R3] thus developed a high throughput (HT) platform for Raman spectroscopy based around biofluids (blood/serum samples). Laser molecule interactions produce a spectral output from a patient's serum sample. These are generated on a modified Raman spectrometer with innovations in biofluid handling and high-throughput capability for producing rapid and reproducible results. This was combined with machine learning (ML) analytics to develop a label-free platform for cancer diagnostics [R4, patent filed – at National Phase]. The algorithms interrogate Raman spectral features identified as cancer-specific amide, lipid and nucleic acid by-products which dynamically change with cancer activity.

Critical to identifying key cancer biomarkers in the blood was establishing reliable measurement criteria and sampling consistency - sample preparation and protocols formed a major part of this effort. In terms of analysis time, the HT platform takes only 10 minutes per sample and based on pilot dataset of serum from 30 patients with CRC and 30 matched controls, achieved a sensitivity of 83% and specificity of 83% for detecting colorectal cancer [R3]. The in-house development of propriety data analytics and chemometric methods utilising high performance computing methods and bespoke analytic packages (written in Mathematica, Matlab, Python and R-programming language) that incorporate patient outcome and machine learning has been a key factor in producing an early-stage diagnostic technique that can impact upon healthcare provision.

Based on the outcomes from R4, funding has been won from the Welsh government [G3] and Cancer Research Wales [G4] to help extend the number and type of patient samples, and also to compare Raman with FIT (faecal test) in 800 primary care patients [G5]. As part of the patent development [R4] the team were also funded [G6, G7] to explore commercialisation routes and evaluate the diagnostic market.

3. References to the research

All papers have been peer-reviewed. [R2, R3] were supported by Cancer Research Wales.

- [R1]. Williams, A., Flynn, K.J., Xia, Z., Dunstan, P.R. (2016) Multivariate spectral analysis of pH SERS probes for improved sensing capabilities. *Journal of Raman Spectroscopy* 47:819-827, <https://doi.org/10.1002/jrs.4910>
- [R2.] Jenkins, C., Lewis, P., Dunstan, P. & Harris, D. (2016) Role of Raman spectroscopy and surface enhanced Raman spectroscopy in colorectal cancer. *World Journal of Gastrointestinal Oncology* 8:427, <https://doi.org/10.4251/wjgo.v8.i5.427>
- [R3]. Jenkins, C. A., Jenkins, R. A., Pryse, M., Welsby, K. A., Jitsumura, M., Thornton, C. A., Dunstan, P. R. Harris, D. A. (2018) A high-throughput serum Raman spectroscopy platform and methodology for colorectal cancer diagnostics. *The Analyst* 143: 6014-6024, <https://doi.org/10.1039/c8an01323c>
- [R4]. Harris, D., Dunstan, P., Jenkins, C. (2017) Method and Apparatus for use in diagnosis and monitoring of colorectal cancer (PCT/GB2018/050627), <https://bit.ly/3eRAE5J>

Grants

- [G1]. Harris, D. (PI) [2013-2014]. Raman spectroscopy: towards early diagnosis in colorectal cancer. St. David's Medical Foundation Seed Corn Grant [JJR546], 3000GBP.
- [G2]. Harris, D., Dunstan, P. (PIs) [2014-2017] Raman spectroscopy and colorectal cancer: towards early diagnosis and personalised medicine. Cancer Research Wales [JJR553], GBP99,604.
- [G3]. Harris, D., Fegan, G., Dunstan, P. (PIs) [04/2017-03/2018]. Transforming the urgent suspected colorectal cancer pathway through Raman spectroscopy technology. Welsh Government Efficiency Through Technology (ETTF), [X.481.HTT], GBP130,327.

- [G4]. Harris, D., Dunstan, P. (PIs) [01/2018-01/2021] Raman Spectroscopy and Colorectal Cancer: Transforming the USC Referral Pathway. Cancer Research Wales [JHR1136], GBP 358,424.
- [G5]. Harris D. (PI) Dunstan, P. (CoI) [10/2018-09/2020] Patient Acceptability and Clinical effectiveness of combined Raman/FIT testing for colorectal cancer diagnosis in primary care. Health and Care Research Wales [RfPPB-17-1458], GBP228,129.
- [G6]. Harris, D. (PI), Dunstan, P. (PI) [2016-2017] Colorectal Cancer Diagnostic based on Raman Spectroscopy. Swansea Healthcare Innovation Partnership Programme (SHIP) grant, [SHIP-0004] GBP40,243.
- [G7]. Dunstan, P. (PI) [2017-2018] Next Generation Colorectal Cancer diagnostics - Raman Spectroscopy. AgorIP/Wales European Funding Office, [MSR1022-126], GBP89,828, (administrated by AgorIP).

4. Details of the impact

Introduction

We have founded an award-winning spin-out company, CanSense Ltd, that takes Raman spectroscopy as the base technology for application to rapid biomarker testing for early cancer detection via a blood test. Its primary product is based around colorectal cancer (CRC) detection and relies on award winning research [C1] by Harris and Dunstan in 2016.

Clinical impact

Our pilot work developing a CRC blood test has overcome previous limitations affecting Raman spectroscopy in clinical diagnostics using new sampling innovations on a modified research Raman microscope (currently at TRL4). The test has a clinical proof of concept with expanded patient training sets producing the **latest results**, showing **sensitivity of 84% and specificity of 91% for CRC** [C2]. The cancer AI model also detects pre-malignant polyps (adenomas) down to 2 mm size with 84.2% sensitivity and 89.5% specificity [C2, C3].

A high negative predictive value (**NPV**) **>98%** means that there is high confidence in the test ruling out cancer (c.f. colonoscopy NPV 99.5%). Additionally, good patient acceptability was found when the test was employed within an academic study of primary care patients (n=595). [C4, preprint]. The study introduced a mechanism for the introduction of the test directly into primary care as a triage tool for GP referrals and evidenced that it would be well received. The positive predictive value (**PPV**) (**> 11.8%**) offers GPs the opportunity to triage patients more effectively for referrals (c.f. only 3% under current NICE guidelines for suspected cancer pathway referrals), **potentially reducing colonoscopies by 49.8%** representing **significant NHS savings ~GBP418 per patient and ~GBP265,000,000 annually**.

Our test's clinical potential has been guided by the company's co-founder Dean Harris, a practicing colorectal cancer surgeon and researcher. Trial patient testimonials include *"It has changed my life, to know to have a blood test which can prove very very quickly if the cancer has come back. This is incredible."* [Patient testimonial, C5]

Our blood test has been endorsed by the National Cancer Clinical Director for Wales, Clinical Lead Transforming Cancer Services, Professor Tom Crosby OBE who said, *"Thousands of bowel cancer deaths could be prevented every year through earlier diagnosis of this disease. This is a potentially game changing innovation in terms of population-based access to a cheap, convenient and acceptable test. This innovative test will mean subjecting less patients to invasive endoscopic examinations. This is an important step in the development of precision medicine undertaking the right test for the right patient at the right time."* [C6, page 10].

CanSense Ltd now has access to more than 1300 patients which have been recruited through this network and current on-going trials will considerably increase this number. NHS services and trained personnel including GPs are also impacted as they help the trial recruit patients, and then process, store and record all samples prior to transfer into our laboratory.

“You can say to (the patient) there’s a 98% chance it’s not going to be cancer, how relieving is that. It would be a huge weight off his mind and reduce a lot of patient anxiety” [GP testimonial, C5] and “Being Timely, if the blood test is normal, you can get on with your rest of your life!” [GP testimonial, C5].

We have already witnessed greater patient acceptance of a blood test rather than the usual unpleasant, poor compliance screening techniques (faecal sample/ colonoscopy), as clearly identified in the first mixed methods clinical evaluation study which evaluated test performance and patient acceptability via focus group interviews [C4]. Further trials which continue to expand evidence on this are underway.

A new national clinical trial called Combined Raman and FIT (CRaFT) commenced in 2018 with the goal of recruiting 800 participants. The trial now has participating GPs from at least 4 Welsh health boards across South Wales and one English health board. This trial will inform on Raman performance compared to current faecal testing (FIT) and reports in the next 12 months.

Formation in 2018 of an Award-Winning spin-out company - CanSense Ltd

As a vehicle to achieve wider immediate translation of the diagnostic technology a spin-out company, CanSense Ltd [C5], was registered in 2018. CanSense is working in partnership with SU and Swansea Bay University Health Board to clinically develop the technique to detect cancer early. Along with the researchers (Dunstan, Harris, Jenkins), a share-holding CEO with over 20 years’ finance experience was appointed in 2018, along with 5 advisory board members (ranging from specialised healthcare consultants to a patient involvement consultant). CanSense leveraged ongoing clinical trials in 2020 (>35 primary care practices participating) and has recruited 4 secondary care champions to influence stakeholders in health boards and ensure wide scale clinical interest, adoption and procurement in various Welsh regions. Since 2019, 3 Pharmaceutical companies (under NDA) have expressed an interest for their trials of oncology therapeutics as a test for minimal residual disease detection. CanSense is a business-to-business service provider with a direct fee-for-service model through a centralised processing laboratory. Given the need for timely primary care decision-making in line with the Single Cancer Pathway we have modelled returning the result to the GP within 48 hours.

The company collaborates with the University and the charity funders Cancer Research Wales (CRW). CRW’s strong endorsement of the activities of CanSense are provided in a letter of support [C7], which includes the following quote:

‘Importantly, the greatest accolades have come from the end-users themselves, patients, GPs and the Wales Cancer Network. Those patients who were involved in the trials for the Raman blood test are unanimous in their agreement that this blood test, even at the early pre-clinical stage is a welcomed and a much-needed novel intervention that can transform how, and the speed at which, bowel cancers are diagnosed’.

The company and its founders support bowel cancer awareness and the CRW charity champions to promote fund raising and awareness of the impact of the charity’s funding of research [C8]. This has led to a one-hour BBC Radio Wales programme which featured the blood test [C9] and wider dissemination through public talks and workshops.

Innovation Funding

At present the company has had innovation funding in excess of GBP250,000 since 2019. A proportion of this funding came from winning competitive catalyst/accelerator programs including:

- BioCity Oxford *Launch program 2020*, GBP50,000 in-kind funding and Venture Capital potential, GBP50,000 convertible note [C10]
- ICURE Midlands participant funding, GBP32,114 [C10]
- BioCity/Oxford AHSN *Accelerator program*, 2019, in-kind funding GBP25,000 [C10]
- University of Southampton Science park *Catalyst and Catalyst + programs 2019/2020*, in-kind funding GBP15,000 [C10]

Awards

CanSense has won a number of key awards since its inception, namely:

South Coast tech awards, best start up and best innovative tech company, winner 2020 [C11]

Empact Ventures-Super Connect for Good: Regional winner, 3rd place nationally, 2020 [C11]

MediWales: Best Innovation winner 2020 & Best Start-up winner 2019 [C11]

MediLink – Start-up award - CanSense Highly Commended 2020 [C11]

CanSense has interviewed over 200 customers (clinical commissioning groups, GPs, pharmaceuticals, diagnostic companies) thereby validating our business plan and identifying our early adopters as pharmaceutical clinical trials and private/public primary healthcare providers. CanSense is focussed on the product's clinical development for CE/UKCA marking and NICE approval.

The Coronavirus pandemic has undoubtedly affected our company journey in the past 12 months, as trial recruitment was suspended, and diagnostic clinical development impacted. This period has however highlighted the urgent need for rapid and early cancer diagnostics based around non-invasive procedures, and how diagnostic triage tools can reduce unnecessary referrals into secondary care. Due diligence is being conducted by several investors at time of writing (December 2020) and we await the outcomes of two impactful NIHR awards (AI: GBP1,400,000 and i4i PDA: GBP1,100,000).

5. Sources to corroborate the impact

[C1]. Research Excellence in the NHS Award – MediWales 2016. <https://bit.ly/3qwaasn>

[C2]. Letter from CanSense CEO verifying current status

[C3]. Embargoed thesis (C. Jenkins) detailing Cancer AI model results

[C4]. Jenkins, C., et al (2020). A new method to triage colorectal cancer referrals using serum Raman spectroscopy and machine learning. medRxiv 2020.05.20.20108209, <https://doi.org/10.1101/2020.05.20.20108209>

[C5]. Website testimonials from patients: <https://cansenseltd.com/>

[C6]. Quote from National Cancer Clinical Director, Wales, pg.10 in Advances Wales, 91, <https://bit.ly/30qnVhA>

[C7]. Letter of Support from Cancer Research Wales

[C8]. Examples of CRC awareness generation through Cansense <https://bit.ly/3vbmC9R> and <https://bit.ly/3cvko7F>

[C9]. BBC Radio Wales - A Healthy Future, Bowel cancer research in Wales <https://bbc.in/3kXbPpU>

[C10]. Business funding awards won by Cansense (i) Biocity/Oxford AHSN Launch programme: <https://bit.ly/3blwvit> (ii) Oxford AHSN Accelerator <https://bit.ly/3vkm0w> (iii) University of Southampton Science park Catalyst program: <https://bit.ly/3t2lJcp>, <https://bit.ly/3vIG6TS> and page 21 <https://bit.ly/2OudDe1>, (iv) ICURE award letter available on request

[C11]. Awards won by Cansense: (i) South Coast Tech Awards <https://bit.ly/3qy4GgR>, (ii) Empact Ventures-Super Connect For Good Regional Winners <https://bit.ly/3tbjeVg>, (iii) MediWales Innovation Awards -Innovation Winner 2020 <https://bit.ly/3eoxrtO> - Start-up Winner 2019 <https://bit.ly/3tbiP5q> (iv) Medilink award <https://bit.ly/38rkdcd>