

Institution: University of Sheffield		
Unit of Assessment: A-03 Allied Health Professions, Dentistry, Nursing and Pharmacy		
Title of case study: ZedScan™: A novel device for the improved detection of cervical cancer		
Period when the underpinning research was undertaken: 2000-2020		
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:
Brian Brown	Professor of Medical Physics and Clinical Engineering	1982-2006
John Tidy	Professor of Gynaecological Oncology	2005-present
Period when the claimed impact occurred: Aug 2013-2020		
Is this case study continued from a case study submitted in 2014? N		
<p>1. Summary of the impact (indicative maximum 100 words)</p> <p>Cervical cancer has traditionally been detected by an invasive procedure called a colposcopy, with the test results taking weeks. Research at Sheffield on the use of non-invasive imaging led to the creation of a new hand-held device marketed as ZedScan™. This device non-invasively detects cervical cancer, allowing patients to immediate diagnoses and, if necessary, treatment. It is quick, sensitive, specific, acceptable to women and inexpensive. ZedScan™ has increased the accuracy and speed with which pre-cancerous conditions are detected and has been adopted by hospitals throughout the UK and nine other countries. Since 2018, it has been recommended by the National Institute for Health and Care Excellence (NICE) as an adjunct technique, especially in cases of low-grade abnormalities. ZedScan™ has improved patient experience, reduced overtreatment seven-fold, and reduced colposcopy costs by 24%.</p>		
<p>2. Underpinning research (indicative maximum 500 words)</p> <p>When abnormal cells are detected in the cervix, women are usually referred for a colposcopy. This is an invasive medical diagnostic procedure in which the clinician examines an illuminated, magnified view of the cervix and applies a solution (such as dilute acetic acid) to the cervix to identify where biopsies are needed. However, colposcopy has several disadvantages, including a wait time of up to 4 weeks for definitive histological results and limited diagnostic accuracy, with an estimated sensitivity of 68.5% and specificity of 75.9%.</p> <p>International HP Schwan Award winner Professor Brian Brown pioneered electric impedance tomography (EIT) and worked with Professors Tidy and Sharp (Sheffield Teaching Hospitals) to develop this non-invasive imaging technology into a medical device [R1]. Research conducted by Brown's team, funded by the NHS Emerging Technologies Scheme, showed that pre-cancerous or cancer tissues in which the tissue structure is altered, especially cervical epithelium, conduct more electricity than normal tissues [R1]. This provided the basis for the development of a non-invasive medical device [R1].</p> <p>In 2003, Professor Brown and colleagues developed a next generation device that could measure the real-time electrical spectra of cervical tissue. The novel device was handheld (similar to an electric toothbrush), with electrodes at the tip of the unit (with a disposable sheath) to measure the flow of current into the cervical tissue. In 2005, Brown, Tidy and colleagues</p>		

successfully tested the device in a prospective study of 87 women [R2] and patented their technology.

A prospective comparative, multicentre clinical study conducted by Brown, Tidy, and colleagues showed that since coming to market in 2013 as ZedScan™, the device has performed well against standard measures and minimises colposcopic subjectivity [R3]. The research showed that both sensitivity and specificity were significantly improved using ZedScan™ [R3]. The device was able to identify cases where immediate treatment could be carried out with a specificity of greater than 90% [R3]. A prospective cohort study by Tidy and colleagues also found that in populations with high-risk human papilloma virus (HPV) genotypes, the device, when compared to colposcopy, recognized an additional 42 cases of cervical cancer, irrespective of the risk genotype [R4].

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

- R1. Brown, B. H., Tidy, J. A.,** Boston, K., Blackett, A. D., Smallwood, R. H., & Sharp, F. (2000). Relation between tissue structure and imposed electrical current flow in cervical neoplasia. *The Lancet*, 355(9207), 892–895. [https://doi.org/10.1016/s0140-6736\(99\)09095-9](https://doi.org/10.1016/s0140-6736(99)09095-9)
- R2. Brown, B. H.,** Milnes, P., Abdul, S., & **Tidy, J. A.** (2005). Detection of cervical intraepithelial neoplasia using impedance spectroscopy: a prospective study. *BJOG: An International Journal of Obstetrics and Gynaecology*, 112(6), 802–806. <https://doi.org/10.1111/j.1471-0528.2004.00530.x>
- R3. Tidy, J. A., Brown, B. H.,** Healey, T. J., Daayana, S., Martin, M., Prendiville, W., & Kitchener, H. C. (2013). Accuracy of detection of high-grade cervical intraepithelial neoplasia using electrical impedance spectroscopy with colposcopy. *BJOG: An International Journal of Obstetrics & Gynaecology*, 120(4), 400–411. <https://doi.org/10.1111/1471-0528.12096>
- R4. Tidy, J. A.,** Lyon, R., Ellis, K., Macdonald, M., & Palmer, J. E. (2020). The impact of age and high-risk human papillomavirus (hrHPV) status on the prevalence of high-grade cervical intraepithelial neoplasia (CIN2+) in women with persistent hrHPV-positive, cytology-negative screening samples: a prospective cohort study. *BJOG: An International Journal of Obstetrics & Gynaecology*, 127(10), 1260–1267. <https://doi.org/10.1111/1471-0528.16250>

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

In the UK, cervical cancer is the 14th most common cancer among women and the most common cancer in women under 35; it affects around 3,200 women every year, and incidence rates for cervical cancer are estimated to increase by 43% between 2014 and 2035. However, if diagnosed at its earliest stages, about 95% of women with cervical cancer will survive for five years or more.

Through their research, the Sheffield team developed a device that can be used as an adjunct to colposcopy to increase the chances of early detection of high-grade cervical intraepithelial neoplasia (CIN) or abnormal cell growth on the surface of the cervix. Brown founded a spin-out company, Zilico, that took the patented device to market under the name ZedScan™, which was released for worldwide distribution, ISO 13845, and CE marked in 2013. Since 2006, Zilico has grown to 12 employees and received £15m of investment, with ZedScan™ winning several

innovation awards such as an HSJ Partnership Award for Medical Device or Hardware Innovation (2019) and an Excellence in Supply Award for Clinical Innovation (2018) [S1] and resulting in multiple impacts.

Increased accuracy and speed in the detection of pre-cancerous conditions

ZedScan™ offers quicker and more accurate real-time detection of pre-cancerous cells than standard colposcopy. A clinical study showed that the detection rate for women with known HPV status was higher for ZedScan™ (96.2%) than for colposcopy alone (83.4%) [S2]. Another clinical investigation found that using Zedscan™ with colposcopy increased the detection of high-grade lesions by 47.3% [S3]. The reported sensitivity of ZedScan™ with colposcopy was higher (93.3%) than that of colposcopy alone (61.3%) [S3]. ZedScan™ takes around 2 to 3 minutes to scan the cervix and display an immediate result, while colposcopy procedure takes around 15-20 minutes with a wait of up to 2 weeks for results.

Adoption of Zedscan™ across hospitals in the UK and other countries

During the impact period, forty-nine UK hospitals used ZedScan™ as an adjunct to standard colposcopy [S4] in 29,000 tests. In 2015, NICE included ZedScan™ in its guidelines and cited it as the first device of its kind to use EIT for the detection of cancerous cells. The guidelines recommended that the device be used in “assessing suspected cervical abnormalities”, especially when “standard colposcopy is subjective” [S5].

Regarding HPV screening, a clinical lead at Birmingham Women’s Hospital [said](#), “*I think adjuncts, particularly ZedScan™, will be very useful in helping to streamline the services [...] we are going to be seeing a lot of women at the lower end of the spectrum and ZedScan™ will be able to help us be more confident in discharging women back to the community*” [S4].

The lead colposcopist at NHS Grampian [agreed, stating](#), “*Having this adjunctive technology with ZedScan™ means we can be more efficient [...] For the women who have disease, we will increase the number we detect at the first visit [and] we’ll be able to offer them treatment*” [S4].

The success of ZedScan™ has resulted in its adoption in nine other countries, including Australia, New Zealand, Finland, and Poland [S6]. In 2018, Zilico made a \$12m royalties deal with China’s Max Health group to sell Zedscan™ to the Chinese market [S7].

Improved patient experience, increased treatment efficiency and reduced costs

As a result of the increased accuracy and speed with which pre-cancerous conditions are detected following the adoption of ZedScan™ in hospitals, women have reported a more physically comfortable procedure and reduced anxiety [S4]. One patient commented that being called back for a colposcopy left her not knowing what to expect, as she did not know what a colposcopy was and ‘googling’ colposcopy was very frightening; however, her clinician used ZedScan™: “*I was quite scared before the appointment, but I was pleasantly surprised....it was really quick actually, much better than I was expecting, I didn’t experience any pain at all*” [S4]. She also reported feeling reassured that a device such as ZedScan™ could allow clinicians to obtain results with high accuracy and immediately determine where to take a biopsy if needed [S4]. The immediate results also allow patients with no evidence of disease to be quickly reassured.

In addition, ZedScan™ has had economic and clinical impacts by allowing clinicians to immediately offer the appropriate treatment to women identified as having severe abnormalities and while avoiding over-treatment. [Text removed for publication]. The use of ZedScan™ for women with CIN 2 or 3 (on a cervical cancer grading scale, where 1 is low and 4 is high) has reduced rates of over-treatment by seven-fold and reduced the number of follow-up appointments needed by 50% [S8].

Increased public awareness

The studies on the use of ZedScan™ to differentiate between normal, precancerous and cancerous cervical tissue have received considerable media coverage, e.g. in short informational videos [S9], as well as in *The Guardian* and *The Scotsman* newspapers, contributing to increased public awareness of cervical cancer. Information on the design and use of the ZedScan™ has also been reported in the *Express & Star*, *Mail on Sunday*, and *The Daily Mail* [S10].

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

- S1.** Zilico wins the Medical Device/Hardware Innovation Award. HSJ Partnership Awards 2019 (<https://www.hsj.co.uk/partnership-awards/winners-of-the-2019-hsj-partnership-awards-announced/7024698.article>).
- S2.** Macdonald, M. C., Brown, B. H., Lyon, R. E., Healey, T. J., Palmer, J. E., & Tidy, J. A. (2017). Influence of high risk HPV genotype on colposcopic performance: A large prospective study demonstrates improved detection of disease with ZedScan I , particularly in non-HPV 16 patients. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, 211, 194–198. <https://doi.org/10.1016/j.ejogrb.2017.02.020>
- S3.** Muszynski, C., Dupont, E., Vaysse, B., Lanta, S., Tidy, J., Sergent, F., & Gondry, J. (2017). The impact of using electrical impedance spectroscopy (ZedScan) on the performance of colposcopy in diagnosing high grade squamous lesions of the cervix. *Journal of Gynecology Obstetrics and Human Reproduction*, 46(9), 669–673. <https://doi.org/10.1016/j.jogoh.2017.08.007>
- S4.** Evidence of the benefits of ZedScan™ for hospitals and patients - Clinician and patient videos regarding ZedScan™ and its use hospital/Trust settings:
- Birmingham Women’s Hospital, Consultant Obstetrician & Gynaecologist and Colposcopy Lead, (June 25, 2018) (<https://vimeo.com/276834269/>)
 - NHS Grampian, Lead Colposcopist, (13 November 2018) (<https://vimeo.com/300517362>)
 - Patient testimonial (10 July 2017) (<https://www.youtube.com/watch?v=JIZrpNtIsS8> or <https://vimeo.com/224927214>)
- S5.** NICE. “Adjunctive colposcopy technologies for assessing suspected cervical abnormalities: The DYSIS colposcope with DYSISmap and the ZedScan™ I”, (25 April 2018) <https://www.nice.org.uk/guidance/dg32/chapter/3-The-diagnostic-tests>
- S6.** [Text removed for publication].
- S7.** PDF Webpage. Evidence of Zilico's diagnostic device moving towards Chinese and global markets and gaining registration with the Chinese Food and Drug Administration (CFDA).

Impact case study (REF3)

- S8.** Peron, M., Llewellyn, A., Moe-Byrne, T., Walker, S., Walton, M., Harden, M., Palmer, S., & Simmonds, M. (2018). Adjunctive colposcopy technologies for assessing suspected cervical abnormalities: systematic reviews and economic evaluation. *Health Technology Assessment*, 22(54), 1–260. <https://doi.org/10.3310/hta22540>
- S9.** A programme made by the Association of Health Tech Industries in 2019 on the ZedScan™ device (<https://vimeo.com/369843559>).
- S10.** “Breakthrough test could slash the cervical cancer death toll and DOUBLE the rate of early diagnosis”, *The Daily Mail* (13 January 2018), <https://www.dailymail.co.uk/health/article-5266759/Test-slash-cervical-cancer-death-toll.html>