Institution: King's College London

Unit of Assessment: 12 Engineering

Title of case study: NHS' adoption of stereotactic ablative radiotherapy (SABR) technology for metastatic cancers

Period when the underpinning research was undertaken: 2004 – 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:
Anastasia Chalkidou	Senior Research Fellow	From 02/06/2014
Kate Goddard	Health Technology Assessor	From 19/01/2015
Jamie Erskine	Health Technology Assessor	From 03/07/2017
Thomas Macmillan	Information Specialist and Health Technology Assessor	26/07/2016 – 31/03/2020
Stephen Keevil	Honorary Professor of Medical Physics (Category C); Director of King's Technology Evaluation Centre (KiTEC)	15/09/1988 – 30/09/2005; From 01/08/2010
David Hawkes	Professor of Computational Imaging	01/02/1988 – 31/12/2004
Derek Hill	Professor of Medical Imaging Sciences	01/10/1989 – 31/12/2004; 04/07/2005 – 31/03/2007
Paul Marsden	Professor of PET Physics	From 15/07/1991
Andrew King	Reader in Medical Image Analysis	From 01/10/2006
Claudia Prieto Vasquez	Professor of Imaging Sciences	From 10/01/2008

Period when the claimed impact occurred: 2015 - 2020

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

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

The multi-disciplinary engineering research in imaging sciences at the School of Biomedical Engineering and Imaging Sciences at King's College London (King's) created the environment for the establishment of King's Technology Evaluation Centre (KiTEC).

KiTEC's research demonstrated significant improvements in overall survival, local control and cost-effectiveness of stereotactic ablative radiotherapy (SABR) technology in oligometastatic cancer (i.e. cancer that has spread beyond its primary site to a small number of other locations). Previously, SABR appeared promising in this condition, but there was insufficient evidence to justify adoption by the NHS. Our research led directly, and very rapidly, to NHS England changing its policy in 2020 to make SABR available for routine clinical use. This benefits at least 2,200 patients per year in England. It has been particularly useful during the COVID-19 pandemic as it has reduced the number of visits to hospitals by patients.

2. Underpinning research (indicative maximum 500 words)

Underpinning, pioneering engineering research in the School on respiratory motion correction can be traced back to work carried out at King's by David Hawkes, Derek Hill and colleagues in the 2000s [R1], with substantial follow-on work conducted at King's by Marsden, King, Prieto and colleagues on respiratory motion modelling and motion reconstruction with application to positron emission tomography (PET) and magnetic resonance (MR) imaging [R2,R3,R4,F1,F2]. These methods include MR-derived motion models for PET respiratory motion correction to improve the

accuracy of uptake values and increase lesion detectability and contrast to inform treatment planning [R2,R3], as well as patient-specific breathing motion models that can be used directly for more precise image-guided treatment delivery [R4].

Because of our unique position as an engineering School embedded within an NHS foundation Trust, we were able to establish the King's Technology Evaluation Centre (KiTEC) as a health technology assessment (HTA) research centre specialising in imaging technology and medical devices in 2011. It combines the School's strengths in these areas with multidisciplinary expertise in health economics, research methodology, medical statistics, information science and evidence synthesis. KiTEC is embedded in an engineering research environment, but also has ready access to expert collaborators in all clinical and scientific specialisms from across the King's Health Partners AHSC (Academic Health Sciences Centres). The aim is to perform impactful research that supports the introduction and diffusion of novel health technologies based on innovative engineering. As a result of the strong track records of the School and the wider multidisciplinary team, KiTEC obtained funding from The National Institute for Health and Care Excellence (NICE) for research into a number of medical technologies and interventions. This funding was secured in competition with other universities, healthcare organisations and consultancies.

SABR is an advanced form of radiotherapy technology in which high radiation doses are delivered very precisely (within 1-2mm) to cancerous tumours. It relies on advanced imaging technologies to maximise dose delivery to the target while minimising dose to surrounding healthy tissues. However, translation of this promising SABR technology into routine clinical practice for patients with extracranial oligometastatic cancer was impeded by a lack of sufficient evidence of safety, clinical effectiveness and cost-effectiveness.

In 2015, KiTEC was funded to investigate SABR as part of NHS England's Commissioning through Evaluation (CtE) programme [F3]**.** Within this programme, patients are able to access promising treatments that are not normally available through the NHS. Research using data from these patients is used to inform future decisions as to whether the new treatment should be provided routinely.

KiTEC's research on SABR involved working with 17 NHS Trusts recruiting 1,422 patients with oligometastatic cancer while building a bespoke database and data dictionary. KiTEC carried out assessment on the clinical effectiveness, toxicity, and cost-effectiveness of stereotactic ablative radiotherapy (SABR) as an emerging radiation technology in oligometastatic cancer. KiTEC's assessment demonstrated significant improvements in overall survival, local control and cost-effectiveness in patients treated by SABR [R5,R6]**.**

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

R1. Blackall J, Ahmad S, Miquel M, Landau D, Hawkes D (2004). Techniques for constructing breathing motion models for 4D radiotherapy planning in lung cancer. Radiotherapy and Oncology, 73:S361-S362. DOI: 10.1016/S0167-8140(04)82714-2

R2. Polycarpou I, Tsoumpas C, King AP, Marsden PK (2015). Quantitative Evaluation of PET Respiratory Motion Correction Using MR Derived Simulated Data. IEEE Transactions on Nuclear Science 62(6):3110-3116. DOI: 10.1186/2197-7364-1-S1-A62

R3. Munoz C, Kolbitsch C, Reader AJ, Marsden P, Schaeffter T, Prieto C (2016). MR-based cardiac and respiratory motion-compensation techniques for PET-MR imaging. PET clinics, 11(2):179-191. DOI: 10.1016/j.cpet.2015.09.004

R4. Baumgartner CF, Kolbitsch C, McLelland JR, Rueckert D, King AP (2017). Autoadaptive motion modelling for MR-based respiratory motion estimation. Medical Image Analysis 35 pp85-100. DOI: 10.1016/j.media.2016.06.005

R5. Bourmpaki E, Bunce C, Chalkidou A, Coker B, Eddy S, Elstad M, Goddard K, Jin H, Keevil S, Macmillan,T, Peacock J, Pennington M, Radhakrishnan, M, Reid F, Summers J (2019), Commissioning through Evaluation: Stereotactic ablative body radiotherapy (SABR) for patients with oligometastases report. KiTEC - King's Technology Evaluation Centre

R6. Chalkidou A, Macmillan T, Grzeda MT, Peacock J, Summers J. Eddy S, Coker B, Patrick H, Powell H, Berry L, Webster G, Ostler P, Dickinson PD, Hatton MQ, Henry A, Keevil S, Hawkins

MA, Slevin N, van As N (EPub December 2020), Stereotactic ablative body radiotherapy in patients with oligometastatic cancers: a national prospective, single-arm, evaluation study, Lancet Oncology, 22(1):98-106. DOI: 10.1016/S1470-2045(20)30537-4

Grants awarded to King's College London / KiTEC

F1. King, AP, Prieto,C, Marsden, PK, "PET-MR Motion Correction Based Purely on Routine Clinical Scans", EPSRC. GBP590,238, 31/03/2015-31/10/2018

F2. Hawkes, DJ, Penney, GP, Leach, MO, Alexander, D, Batchelor, P, Atkinson, D, Hajnal, JV, Smith, N, Schaeftter, Razavi, R, Rueckert, D, Prieto, C, Ourselin, S, Webb, "Intelligent Imaging: Motion, Form and Function Across Scale", EPSRC. GBP6,053,494, 01/06/2010-30/11/2015

F3. External Assessment Centre for NICE Sponsor: NICE, GBP3,310,736.00, 01/04/2014-31/03/2022

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

Background: Metastatic cancer is diagnosed in approximately 140,000 patients in England per year. Patients with a relatively small number of metastases (usually no more than 5 in a maximum of 3 separate locations) are considered to have oligometastatic cancer. Although there is scarce evidence from randomised controlled trials on the treatment of extracranial oligometastatic cancer (that is oligometastases outside the head), there is a growing body of evidence from multiple non-comparative studies to suggest that patients may be cured if all lesions are eradicated using SABR, an emerging treatment that uses external beam radiation therapy to deliver a high dose of radiation with high precision (within 1-2 mm) to a cancerous lesion. In addition, a course of SABR treatment involves fewer fractions of radiotherapy (and, consequently, requires fewer hospital visits) than standard radiotherapy – approximately 8 or fewer for SABR compared with 20 to 30 sessions for standard radiotherapy.

Pathway to Impact: KiTEC's research on SABR included the following components.

- Working with 17 NHS Trusts to recruit 1,422 patients with oligometastatic cancer, the largest cohort recruited internationally.
- Development of analysis protocols and target outcomes, requiring synthesis of input from NHS England, NICE and numerous clinical stakeholders.
- Development of a bespoke database and data dictionary, in collaboration with University Hospitals Birmingham.
- Analysis of patient-level data to determine overall survival, local control, and safety. To improve outcome detection, KiTEC linked this data to the Hospital Episode Statistics (HES) and Office for National Statistics (ONS) registries. Cost-effectiveness analysis compared SABR with alternative treatments such as surgery and radiofrequency ablation.
- Qualitative analysis of the experience of the 17 centres.
- Systematic review of the evidence base regarding clinical effectiveness, toxicity, and cost-effectiveness.

The research showed clinically and statistically significant improvement in overall survival (92.3% at 1 year and 79.2% at 2 years) and local control rates (86.9% at 1 year and 72.3% at 2 years) using SABR. It further showed that the **treatment is safe** (less than 5% of patients experienced severe toxicity). In health economics, the value of a medical intervention is often expressed in terms of the number of additional years of life gained weighted to reflect quality of life, producing a measure known as a QALY (Quality Adjusted Life Year). In our study, we found that in comparison with surgery, SABR results in both a gain in QALYs (0.0214 per person on average) and a cost saving (GBP2,912 per person on average) [R5].

Evidence synthesis of these results at King's with the published literature **led NHS England to conclude that there is sufficient evidence to support the routine use of SABR for patients with extracranial oligometastatic disease** [S1].

The NHS England Policy Working Group estimates that **approximately 2,200 patients per year**

with extracranial oligometastases would be suitable for SABR treatment, in line with the criteria established by KiTEC's research [S1]. Our qualitative research has helped to define the main priority areas for future commissioning of SABR and in particular has highlighted workforce implications and emphasised the benefits of providing SABR treatments at a larger number of NHS organisations so that they are more accessible to patients. In the words of the Medical Director of The Royal Marsden NHS Foundation Trust, *"The design of this programme and the data analysis has therefore been transformative for delivery of this novel radiation technology in the UK and will have a significant impact on both patient outcome and appropriate use of healthcare resources within the NHS"* [S2].

A new technology has been adopted in routine use as a result of KiTEC's work

The National Institute of Health and Care Excellence (NICE) updated the guidelines for radical radiotherapy (including SABR) for people with non-small-cell lung cancer in March 2019 [S4]. Quoting the guidance 1.4.27 *"For people with stage I–IIA (T1a–T2b, N0, M0) NSCLC who decline surgery or in whom any surgery is contraindicated, offer SABR".*

Impact on professional practice

Our work in collaboration with University Hospitals Birmingham NHS Foundation Trust (UHB) resulted in the **first registry in the UK,** developed to collect imaging and outcomes data from multi-centre radiotherapy studies in a single framework, implemented as the Platform for Radiotherapy Plan Evaluation and Learning (PROPEL) [S3]. KiTEC engineered PROPEL based on feedback from various stakeholders - clinical experts, NHS England, NICE and the Radiotherapy Trials Quality Assurance (RTTQA) group. PROPEL is now fit for purpose to host data from future national and international radiotherapy trials, including radiotherapy treatment planning images as well as textual data. This assures the quality of treatment planning as SABR is implemented at a wider range of centres in keeping with the results of our qualitative research. Professor Stuart Green, Director of Medical Physics at UHB, says, *"Analysis of the data stored in PROPEL from the Commission through Evaluation programme is continuing and focused on the derivation of guidance for treatment planners to ensure that future patients have a high quality treatment regardless of the experience of the clinical team and the treating centre. This is particularly important now that these treatments are being rolled-out nationally. Further impact comes from the wider and continuing use of PROPEL and its development as platform for plan quality analysis"* [S5].

Helped serve more patients during the COVID crisis

Because SABR treatment involves fewer visits to hospitals by patients, it is particularly valuable during the COVID-19 pandemic when there is a desire to minimise hospital visits and risk of infection. According to Dr Nicholas van As, a leading clinical oncologist and the Medical Director, The Royal Marsden NHS Foundation Trust, *"SABR is a technology that is delivered in a small number of fractions and then therefore extremely efficient treatment; this has been crucial as a method of getting more patients through treatment in the COVID crisis."* [S2]. This aspect is also commented on in a testimonial from NICE [S6]. The approach adopted by KiTEC to managing and delivering this complex project will readily translate to similar real-world data collection and analysis exercises in the context of NHS commissioning, bringing additional future impact. To quote from the testimonial received from NICE, *"The principles used to achieve high data quality are being used in subsequent CtE and are useful in planning 'Managed Access' projects undertaken by KiTEC on behalf of NICE"* [S6].

In summary, the impact of this work was a change in NHS policy leading to availability of a novel cancer treatment based on innovative engineering, resulting in improved health outcomes for many patients. This was achieved by combining underpinning engineering expertise with a multidisciplinary approach to medical device HTA to ensure that novel technology is not just translated into healthcare but is firmly embedded and diffused through effecting evidence-based changes to national policy.

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

S1. NHS England Clinical Commissioning Policy. Stereotactic ablative radiotherapy (SABR) for patients with metachronous extracranial oligometastatic cancer (all ages)

S2. Testimonial from: Nicholas van As, Medical Director, The Royal Marsden NHS Foundation Trust, 27th January 2021

S3. PROPEL database: University Hospital Birmingham and KiTEC application for BIR IEL team award, 25th February 2019

S4. NICE guidelines (NG 122) Lung Cancer Treatment and Management (section 1.4.27) and 3rd recommendation on the list from March 2019

S5. Testimonial from Stuart Green, Director of Medical Physics, University Hospitals Birmingham NHS Foundation Trust, 1st February 2021

S6. Testimonial from Hannah Patrick and Helen Powell, National Institute for Health and Care Excellence (NICE) Managed Access Team, 5th February 2021