Institution: University College London

Unit of Assessment: 1 - Clinical Medicine

Title of case study: CT colonography for diagnosis of colorectal cancer in older symptomatic patients

1. Summary of the impact

Work led by researchers at UCL has had a national and international impact on the way that patients with symptoms suggestive of colorectal cancer are investigated. Specifically, investigation of the role of CT colonography (a relatively novel and non-invasive method of investigating the large bowel using an X-ray scanner) has led to this examination replacing the standard alternative of barium enema in the UK National Bowel Cancer Screening Programme and for symptomatic patients in the NHS. The research has also led to easing of pressure on over-subscribed endoscopy services in the NHS because patients can be safely diverted towards CT colonography as an alternative.

2. Underpinning research

The impacts reported here arise from a systematic review of CT colonography and two multicentre clinical trials led by researchers at UCL. Prior to this research, the usual approach to investigating patients with symptoms of bowel cancer was either barium enema examination or colonoscopy of the large bowel (amounting to over 700,000 patients per year in the UK). Both investigations had limitations whereas CT colonography offered theoretical advantages. However, CT was usually advocated to screen asymptomatic patients for pre-malignant polyps but no randomised controlled trials had been undertaken.

Professor Steve Halligan (Centre for Medical Imaging, UCL Division of Medicine) realised that most published trials of CT had actually recruited symptomatic patients and believed that existing data showed that CT colonography was likely to have high diagnostic accuracy for detecting established cancer in such patients. In order to confirm this he performed a systematic review with the primary aim of extracting data on cancer detection, from primary studies, with statistical collaborators at Oxford (Altman, Mallett) and cancer epidemiologists at Imperial (Atkin). The systematic review found a pooled sensitivity for cancer by CT colonography of the order of 96% - i.e. equivalent to colonoscopy, the current "gold-standard" **[1]**.

Aware of CT colonography as a potentially useful diagnostic test and seeing these data abstracted, the NHS's Health Technology Assessment programme commissioned research on the technology in the NHS. An application for funding was led by Professor Halligan as CI. Two multicentre pragmatic randomised controlled trials of CT colonography versus the existing NHS standards of barium enema and colonoscopy in symptomatic patients were proposed. Endpoints included cancer detection, economic modelling within and beyond the trial time-horizon, and health-psychology **[2]**. A specific focus was how detection of pathology outside the bowel influenced use of the test in the NHS. Key collaborators were Atkin (Imperial, cancer epidemiology), Lilford (Birmingham, health-economics and modelling), and Wardle (UCL, health psychology).

The application was successful and 8,484 patients in 21 NHS hospitals were registered and 5,384 randomised and ultimately analysed (BE trial: 2527 BE, 1277 CTC. Colonoscopy trial: 1047 colonoscopy, 533 CTC). Known as the "SIGGAR" (Special Interest Group in Gastrointestinal & Abdominal Radiology) trial, this was the first RCT of CT colonography worldwide and the largest RCT in gastrointestinal radiology. Procedure detection rates and subsequent tests/resources were collected and false-negative diagnoses of intra- and extra-colonic cancer identified via NHS Information Centre three years post-randomisation, and trial arms compared. Preliminary data were presented orally in 2009.

SIGGAR found that CT colonography was superior to barium enema for diagnosis of colorectal

cancer and large polyps **[3]**. There was no significant difference between CT colonography and colonoscopy **[4]**. CT colonography was significantly better perceived by patients, and was associated with fewer immediate and delayed adverse events **[5]**. CT colonography was significantly more cost-effective than barium enema (both within trial and extrapolated) and equally cost-effective as colonoscopy **[3]**. Extra-colonic tumours were detected by CT colonography in approximately 4% of recruited patients, of which around half were malignant.

3. References to the research

[1] Halligan S, Altman DG, Taylor SA, Mallett S, Deeks JJ, Bartram CI, Atkin W. CT colonography in the detection of colorectal polyps and cancer: systematic review, meta-analysis, and proposed minimum data set for study level reporting. Radiology. 2005 Dec;237(3):893-904. http://dx.doi.org/10.1148/radiol.2373050176

[2] Halligan S, Lilford RJ, Wardle J, Morton D, Rogers P, Wooldrage K, Edwards R, Kanani R, Shah U, Atkin W. Design of a multicentre randomized trial to evaluate CT colonography versus colonoscopy or barium enema for diagnosis of colonic cancer in older symptomatic patients: the SIGGAR study. Trials. 2007 Oct 27;8:32. http://dx.doi.org/doi:10.1186/1745-6215-8-32

[3] Halligan S, Wooldrage K, Dadswell E, Kralj-Hans I, von Wagner C, Edwards R, Yao G, Kay C, Burling D, Faiz O, Teare J, Lilford RJ, Morton D, Wardle J, Atkin W; SIGGAR investigators. Computed tomographic colonography versus barium enema for diagnosis of colorectal cancer or large polyps in symptomatic patients (SIGGAR): a multicentre randomised trial. Lancet. 2013 Apr 6;381(9873):1185-93. http://dx.doi.org/10.1016/S0140-6736(12)62124-2

[4] Atkin W, Dadswell E, Wooldrage K, Kralj-Hans I, von Wagner C, Edwards R, Yao G, Kay C, Burling D, Faiz O, Teare J, Lilford RJ, Morton D, Wardle J, Halligan S; SIGGAR investigators. Computed tomographic colonography versus colonoscopy for investigation of patients with symptoms suggestive of colorectal cancer (SIGGAR): a multicentre randomised trial. Lancet. 2013 Apr 6;381(9873):1194-202. http://dx.doi.org/10.1016/S0140-6736(12)62186-2

[5] von Wagner C, Ghanouni A, Halligan S, Smith S, Dadswell E, Lilford RJ, Morton D, Atkin W, Wardle J; SIGGAR Investigators. Patient acceptability and psychologic consequences of CT colonography compared with those of colonoscopy: results from a multicenter randomized controlled trial of symptomatic patients. Radiology. 2012 Jun;263(3):723-31. http://dx.doi.org/10.1148/radiol.12111523

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NIHR HTA programme. CT colonography versus colonoscopy or barium enema for diagnosis of colorectal cancer in older symptomatic patients; Multicentre randomised controlled trials (HTA 02/02/01). 2004-11. CI: S Halligan, UCL. £1,858,578

NIHR. Programme Grant for Applied Research: Imaging diagnosis of colorectal cancer - Interventions for efficient & acceptable diagnosis in asymptomatic & symptomatic populations (RP-PG-0407-10338). 2008-13. CI: S Halligan, UCL. £1,516,044

4. Details of the impact

After learning of the results of our preliminary analysis of 2009, the Director of the NHS Cancer Screening Programmes asked Halligan to present the data to the next meeting of the National Bowel Cancer Screening Advisory Group. The data were orally presented in April 2010 when Halligan concluded that barium enema should be withdrawn from the NHS immediately (where circumstances allowed) and that CT colonography was a safe, sensitive, and acceptable alternative to colonoscopy for diagnosis of colorectal cancer. Within one month this led to an Interim Guidance Update being issued by the Bowel Cancer Screening Programme (BCSP IGU 007 Apr 1010), which was sent to the Director, Lead Nurse, and Lead manager of every NHS bowel screening centre, and to Quality Assurance Reference Centre (QARC) coordinators. This

stated that the SIGGAR trials "*show that double contrast barium enema is significantly inferior to CT colonography for detection of colorectal cancer and large polyps. It also shows that the false-negative rate for colorectal cancer is significantly higher for barium enema*." The screening centres were asked to use "*CTC rather than barium enema wherever local expertise and circumstances permit*" **[a]**.

The subsequent "Guidelines for the use of imaging in the NHS Bowel Cancer Screening Programme" (NHSBCSP Publication no. 5, July 2010) stated that, "*Where imaging is indicated, CTC is the preferred method. Double contrast barium enema is reported to have a fourfold false negative rate; it is therefore not appropriate for screening patients…Where high-quality CTC is not available locally, the patient should be referred elsewhere for examination*" **[b]**.

In the light of the trials' findings, Halligan was asked to join the Bowel Cancer Screening Advisory Panel in 2010 to advise on the national implementation of CT colonography in the screening programme. Subsequently, the Programme Director asked that a committee be established with the specific remit to oversee the implementation of CT colonography in the Bowel Cancer Screening programme, and its subsequent quality control. The Bowel Cancer Screening Programme CT Colonography Steering Group was formed in February 2012 and Halligan was asked to sit as advisor. The group updated the Guidelines for the use of imaging in the National Bowel Cancer Screening Programme, published November 2012 **[c]**. The Guidance repeats the statement that barium enema should be discontinued immediately in favour of CT colonography and references the HTA monograph from the SIGGAR trials **[d]**. The trials are also cited on the "key research in bowel cancer and bowel cancer screening" page of the NHS Bowel Cancer Screening Programme website **[e]**.

Impact can be proven by analysis of imaging procedure rates within the Bowel Cancer Screening Programme. In 2007 and 2008 the numbers of barium enema and CT colonography studies performed in the Programme were approximately similar (71 vs 99 for 2007 and 210 vs 284 for 2008). In 2010, the year the guidelines for imaging were published, the figures were 265 barium enema vs 1,291 CT colonography. Figures for 2011 were 128 vs 1,833 and for 2012 were 76 vs 1,928 **[f]**.

The SIGGAR trials' findings that CTC was more accurate than barium enema and not significantly different to colonoscopy have also impacted on the provision of diagnostic services to symptomatic NHS patients. Firstly, barium enema services are being reduced in the light of the trials' findings and secondly, CT colonography provision is helping alleviate pressure on endoscopy services generated by both the symptomatic service and the screening programme **[g]**. The British Society of Gastrointestinal and Abdominal Radiology have convened a committee in parallel to the screening programme to oversee the implementation of CT colonography in the symptomatic NHS setting; Halligan also sits on this committee. In May 2013, a meeting of the Royal College of Radiologists Professional Support & Standards Board made the decision to revise its guidelines on the imaging of colorectal cancer in the light of the findings of the SIGGAR trials. Halligan joined the Working Party responsible for revising these guidelines (due December 2013) **[h]**.

The impact of the trials reaches beyond the UK: the trial data were used by a US radiologists Working Group on CT colonography in 2010 to justify a higher rating for CT colonography for screening in the American College of Radiology Appropriateness Criteria; they are also currently using the data to evaluate national reimbursement for CT colonography **[i]**. The trial data were also presented to the National Board of Health & Welfare in Sweden in 2012 during the development of new and updated National Guidelines on colorectal cancer to make the case that barium enema should be withdrawn in Sweden and replaced by CT colonography **[j]**. Reviewing the trials in March 2013, the most-prominent colonoscopist in the USA, Douglas Rex MD, stated, "these study findings justify widespread incorporation of CTC into U.S. hospitals, with subsequent abandonment of DCBE" **[k]**.

5. Sources to corroborate the impact

[a] Bowel Cancer Screening Programme. Interim Guidance Update number 007. April 2010. Copy available on request.

[b] Guidelines for the use of imaging in the NHS Bowel Cancer Screening Programme, First Edition. NHSBCS Publication no. 5, July 2010. Copy available on request.

[c] Guidelines for the use of imaging in the NHS Bowel Cancer Screening Programme, Second Edition. NHSBCS Publication no. 5, November 2012 (http://www.cancerscreening.nhs.uk/bowel/publications/index.html).

[d] HTA Programme; Project website: http://www.hta.ac.uk/project/1366.asp

[e] Key research in bowel cancer and bowel cancer screening. NHS Bowel Cancer Screening Programme. http://www.cancerscreening.nhs.uk/bowel/research.html

[f] Rates for barium enema vs CTC were obtained from the National Bowel Cancer Screening Programme. Contact details provided.

[g] The drop in barium enema can be seen from the national diagnostics statistics: https://www.gov.uk/government/news/nhs-diagnostics-waiting-times-and-activity-data-november-2012 Barium enema is down 12.1% in November 2012 compared to 2011.

[h] Working Party Terms of Reference and email from the Chair. Copies available on request.

[i] Statement from Chair, Colorectal Cancer Committee, American College of Radiology. Available on request.

[j] Statement from Professor working on guideline development, Department of Radiology, Sahlgrenska University Hospital. Available on request.

[k] http://www.jwatch.org/jg201303080000002/2013/03/08/ctc-vs-barium-enema-ctc-wins