



The Evelyn Trust Research Endoscopy Suite Cambridge Clinical Research Centre



UNIVERSITY OF
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A report prepared for The Evelyn Trust (REf 13/37)

NOVEMBER 2021

The Evelyn Trust generously pledged £1,000,000 in 2014 to support the Cambridge Clinical Research Centre (CCRC) Research Endoscopy Suite.

The Cambridge Clinical Research Centre is a dedicated clinical research facility that provides facilities and staff for the conduct of approved experimental studies in both patients and healthy volunteers. Part of the Centre is the Interventional Procedure Unit containing The Evelyn Trust Research Endoscopy Suite, which houses state of the art endoscopy facilities.

The University of Cambridge would like to express its sincere thanks to The Evelyn Trust for its generous support of our facility. This has allowed us to provide world-class care and research to our local community, nationally and internationally, leading to new understanding of conditions and the development of treatments.



Professor Krishna Chatterjee

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Director, Cambridge Clinical Research Centre
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Overview

During the COVID-19 pandemic, The Evelyn Trust Research Endoscopy Suite remained operational, continuing to see participants on designated priority experimental studies (i.e. a study providing a diagnosis and/or a treatment/intervention offering a significant benefit). Alongside this, we worked in collaboration with Cambridge University Hospitals NHS Foundation Trust (CUH) to offer NHS procedures while the main endoscopy suite was re-purposed for ITU surge beds. This assisted in reducing urgent cancer waiting lists and offering palliative procedures, such as stricture dilatations, to NHS patients – in addition the Cytosponge was fast-tracked as the standard of care for diagnosis during the pandemic again enabling patients on a two-week wait pathway to get a rapid diagnosis. The Evelyn Trust Research Endoscopy Suite was essential to CUH in helping maintain a functional Endoscopy service, as we undertook approximately 200 NHS endoscopies.

The past year has seen the first bronchoscopy study take place in The Evelyn Trust Research Endoscopy Suite, looking at the use of an inhaled drug for the treatment of rhinitis and, we have expanded staff skills to perform Lumbar punctures on participants on ‘never stop’ trials.

The COVID-19 pandemic led to new ways of working to ensure all staff and participants/patients were kept safe – in addition to COVID-19 testing of participants/patients, appropriate PPE and specific cleaning regimes between procedures, we have installed

mobile air filtration units. Utilising these COVID-19 precautions and specialist cleaning regimes we have also commenced a study investigating the effects of long COVID on swallowing and voice.

The last financial year (April 1st 2020 – March 31st 2021) has been unique due to the pandemic with studies being put on hold and additional studies moved to the Interventional Procedures unit to allow us to accommodate COVID-19 research on other floors in the CCRC. Despite this, The Evelyn Trust Research Endoscopy Suite undertook **467 endoscopic procedures** during this period, with an average of **29 active studies** continuing in the Interventional Procedures Unit. Approximately 11 studies are dormant or on hold due to COVID-19.



The Evelyn Trust Research Endoscopy Suite in use

Detection of cancer of the upper gastrointestinal tract

Dr Massimiliano di Pietro

Cancer of the upper gastrointestinal tract (oesophagus and stomach) has extremely poor prognosis, with less than a quarter of patients alive at five years after diagnosis. Despite refinement of oncological and surgical treatments, the survival rate has not dramatically improved in the last two decades. Early diagnosis is the key to reducing mortality rates, as the five-year survival can be as high as 80% when this type of cancer is detected early.

Luckily, the oesophagus and stomach are readily accessible with endoscopy, which allows direct inspection of the mucosal lining. Some patients have medical conditions that predispose to cancer of the oesophagus and stomach, also known as Barrett's oesophagus and gastric intestinal metaplasia, respectively. These patients are offered endoscopic monitoring with the aim of diagnosing cancer at an early stage. Unfortunately, early gastric and oesophageal cancers are difficult to 'see' with standard endoscopy, therefore multiple biopsies are required to diagnose these 'invisible' cancers. Not surprisingly, there is evidence that up to 10–25% of upper gastrointestinal cancers are missed at a previous endoscopy.

We investigate ways to improve detection of cancer of the upper gastrointestinal tract. Over the last 15 years we have been studying methods to allow early diagnosis of cancer of the oesophagus and stomach. Thanks to the facilities supported by The Evelyn Trust,



Dr Massimiliano di Pietro
MRC Senior Clinician Scientist and
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we have recently completed a randomised trial (ACE-B study) which looked at the combination of fluorescence endoscopy and a miniaturised endoscopic microscope to spot pre-cancerous and early cancerous changes before they can be seen at conventional endoscopy. As part of this study over 100 patients have been recruited in Cambridge. Each patient received two endoscopies at

different time points, one following the standard clinical protocol (white light endoscopy and multiple biopsies) and one with the experimental protocol (endoscopic microscopy and molecular biomarkers). We were able to demonstrate that the conventional protocol missed half of the patients with invisible cancer and that the experimental enhanced endoscopy can improve the sensitivity by 30%.

In collaboration with the Department of Physics, we have also developed an innovative type of endoscope using nine different wavelengths in the visible spectrum, compared with the standard endoscopy, which uses conventionally only three wavelengths. This novel endoscope, called multispectral, was tested in-vivo in the Clinical Research Facility (CRF) in a first in-human study in 20 patients (MuSE trial). We were able to show for the first time that the multispectral endoscope offers a reliable read-out of the vascular net and the blood volume present in early cancerous tissue, which are among the first detectable changes in early cancer. The first-generation multispectral endoscope had an accuracy of 85% in diagnosing early cancer. This is an exciting area of research and we are currently working on a second generation multispectral endoscope.

Finally, we are also looking at how we can improve the daily endoscopy practice and reduce the rate of missed cancer at endoscopy. In order to do this, we need to understand how often doctors and nurses performing endoscopies should diagnose pre-cancerous and early cancerous conditions of the oesophagus and stomach. This will allow us to develop diagnostic quality indicators to improve the performance of endoscopists in routine practice.

We are excited to have just received ethics approval to start the PROSPERO study, which will recruit over 1,000 patients referred for an upper GI endoscopy on any diagnostic pathways. The Cambridge CRF will be the central hub of this large study. Since COVID-19 struck, the endoscopy departments have been under



Full PPE in use in The Evelyn Trust Research Endoscopy Suite

massive pressure to deliver diagnostic tests within a completely different working strategy, made more and more complex by space restrictions and COVID-19 testing. We hope the PROSPERO study will provide fundamental evidence to inform development of key performance indicators to improve the quality of endoscopy and reduce the rate of missed cancer.



Step 2
Put on PPE (goggles, undergarments, fit check with hoods)

Step 3
Put on eye protection

The minor procedures room

Research highlights

In the past year, many other endoscopy studies have reached important milestones, contributing to our understanding of, and developing treatment options for, life-threatening and debilitating conditions. A few highlights are listed below, with links to associated publications for further details:

- **Research endoscopy has benchmarked development of the Cytosponge-TFF3 diagnostic device in Cambridge**, detecting 10-fold more cases of oesophageal cancer than standard care (L2-03, BEST- 3; [Lancet 2020](#)). It is now licensed to Medtronic, is US FDA and CE approved, and is being implemented in routine NHS practice.
- **Advanced technologies for imaging the gastrointestinal tract** including multispectral and hyperspectral endoscopy (L2-18, Ex-VISION; L2-17, MuSE; [Cancer Res. 2021](#)), and performing breath biopsy (Owlstone Medical collaboration) to detect cancer or liver disease (L2-20, PAN-study [Clin Transl Gastroenterol. 2020](#)), are being evaluated.
- **Early-phase trials of anti-IL23 antibody in Crohn's disease (L3/L2)** ([Lancet 2017](#); [Lancet Gastroenterol Hepatol 2018](#)) have recorded endoscopic remission endpoints, providing further evidence that anti-IL23 antibody has potential as an effective treatment option.
- **The genetic architecture of inflammatory bowel disease (IBD) biopsy tissue** has been defined, pointing to the role mutations play in causing IBD ([Cell 2020](#)). Prognostic blood biomarkers for IBD are also in development ([Gut 2019](#)), representing a step towards personalised therapy.



Staff member using scopes in The Evelyn Trust Research Endoscopy Suite

Future plans

The Evelyn Trust Research Endoscopy Suite continued to receive research participants throughout the pandemic, and as usual we have exciting and ground breaking new studies planned, such as the PROSPERO study which Dr di Pietro has highlighted above.

It would be extremely difficult to undertake these studies successfully within the NHS setting and the use of The Evelyn Trust Research Endoscopy Suite will be pivotal to their success.



Recovery bay pictured from the nurse station



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