PACES – Participant Information Sheet

Pathology Artificial-Intelligence Clinical Evaluation Study

Welcome!

- We would like to invite you to take part in our research study. Joining the study is entirely voluntary. Before you decide, it is important that you understand why the research is being done and what it would involve.
- Please take time to read this information and discuss with others if you wish. If anything is not clear, or you would like more information, please ask us by emailing: paces@medsci.ox.ac.uk. You can take as much time as you need to think about joining the study. If you don't want to join, you don't have to, and this decision won't affect your healthcare.
- By conducting cancer research, doctors and scientists hope to learn more about how cancer can be detected, diagnosed, treated and prevented, with the ultimate aim of improving patient care and quality of life. Cancer research done today will help shape better medical practice in the future. We hope you will join us in this mission.
- **Being invited to join this study does not mean you have cancer, and the aim of this study is not to provide a cancer diagnosis**. You have been invited to join PACES as you have been referred for further investigation of certain symptoms. We are looking for participants across all stages of care in order to assess if the algorithms included in this study can potentially improve current NHS clinical pathways and procedures.

If you decide to join this study, the care you receive will not be changed in any way, you will also not have to attend any additional hospital appointments. We are simply asking permission to use anonymised images of samples collected as part of your standard treatment in our study analysis. Further details are outlined below.

Why are we doing this study?

- Nearly 43,000 people are diagnosed with bowel cancer every year in the UK, making it the fourth most common cancer among adults. Surgery is the most common treatment for bowel cancer, and often patients receive additional treatment before or after their surgery. However, there are many different types of additional treatments (such as radiotherapy, chemotherapy or immunotherapy) and doctors must consider lots of factors when deciding on the best pre- or post-surgery treatment for their patients.
- New computer-based technologies are being developed to help doctors make the best treatment decisions more quickly and accurately.

- Cancer researchers and medical professionals predict that a branch of artificial intelligence (AI), known as machine learning (ML) may revolutionise clinical care and cancer research in the coming years. For example, these new technologies could help doctors make more accurate and personalised decisions about how patients will benefit from their treatment.
- Using AI technology, algorithms (a type of mathematical computer programme) have been developed that analyse digital images of samples taken from bowel cancer patients during surgery, or from pre-surgery diagnostic tests (such as a colonoscopy). These algorithms have the ability to differentiate between different types of tumours, and can subsequently make a prediction on the best course of treatment for individual patients.
- These samples are already analysed manually by doctors and scientists. However, we think that computers can add to the information that doctors get from these digital sample images. Results from algorithms could, in theory, help patients and doctors make better decisions on the best course of treatment. We plan to test this theory in our study.

For more information on what artificial intelligence and machine learning algorithms are and how they might impact healthcare in the future, please visit:
https://transform.england.nhs.uk/information-governance/guidance/artificial-intelligence/

What is our aim?

- Our aim is to assess if, in theory, machine learning algorithms could be integrated into current NHS bowel cancer diagnostic and pathology practice, and investigate if they have the potential to predict, support, influence or change decisions made between patients and their doctors on bowel cancer treatments. We hope to learn how these technologies will be used to improve cancer care, and whether they can be integrated into current NHS practice.

Why have I been invited to take part?

- You have been invited to participate in our study as you have been diagnosed with, or are being investigated for, bowel cancer (also known as colorectal cancer or colorectal carcinoma) as some of your symptoms can be caused by bowel cancer.
- As a result, you may have been scheduled for, or already have had, an investigational biopsy (for example a colonoscopy), surgery or other anti-cancer treatments and investigations.

Being asked to participate in this study does not mean you have bowel cancer. You may be invited to participate before a diagnosis has been made. You will not be diagnosed as part of this study. Very few investigational colonoscopies detect cancer.

- Throughout the study, we aim to recruit up to 170 participants. Recruiting this many participants will help the study generate sufficient data to answer our main research aims.

Do I have to take part?

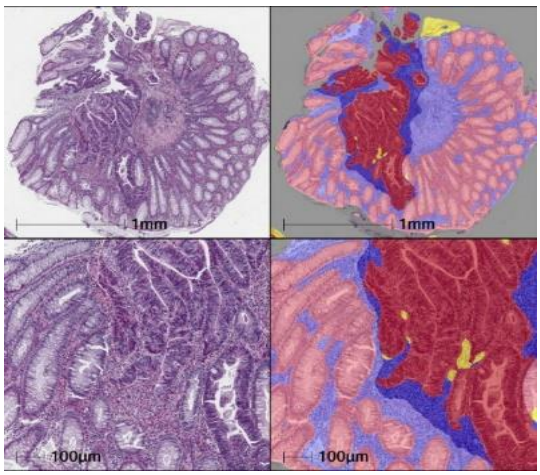
- No, taking part is entirely voluntary.
- The clinical care you receive won't be affected in any way if you decide not to take part.
- If you do decide to take part, you can withdraw from the study at any time if you change your mind, you won't have to give a reason why you've decided to withdraw.
- If you withdraw from the study, unless you state otherwise, any digital images of your samples collected up to that point will still be used for research as detailed in this participant information sheet. You are free to request that your digitised images are deleted.

What will happen to me if I decide to take part?

- It is important to understand that if you decide to take part in the study, the treatment you will receive will not change in any way and you will at all times follow the treatment you and your medical team decide upon.
- You will not need to attend any additional hospital appointments if you decide to take part.
- No additional samples will be taken above what is required as part of your standard care.
- Your participation in the study is finished 24 months after the date your registration to the study is confirmed.
- After your study registration is confirmed, we will email you a questionnaire to complete online. This questionnaire focuses on your opinions on the use of artificial intelligence in cancer care.
- It is normal practice that during your scheduled surgery, pre-surgery biopsy or investigational biopsy (for those only suspected of having cancer) standard-of-care samples are taken to help doctors further understand your individual cancer. These samples are usually made up of tissue taken from your tumour, or areas where a tumour is suspected to be near. These samples are processed onto microscope slides, scanned into a computer (or digitised) and reviewed by doctors and scientists to help inform decisions on your treatment.
- If you decide to join the study, this process will still happen and the decision on your treatment will be made between you and your care team in the usual way.

The below images are examples of cancer tissue that doctors routinely use to make a cancer diagnosis. On the left, is an example image of what is normally viewed under a microscope. The right image is an example of when a machine learning algorithm (similar to those used in this study) has

been designed to identify the cancer. As you can see, it is much easier to see the tumour (the dark red section). The patient from whom this tissue has been taken from cannot be identified by looking at these images. The images are taken from www.cancer.ox.ac.uk.



- If you decide to join the study, digitised images of your samples will be analysed by up to three different machine learning algorithms.
- Two of these algorithms have been developed by research groups at the University of Oxford. The third has been developed by Oxford Cancer Biomarkers Ltd, a private company.
- The machine learning algorithms will provide an outcome score based on certain scientific characteristics, such as biological markers associated with good or bad responses to different treatments. These scores will point to a recommended treatment pathway.

As the machine learning algorithms included in this study are still in the "test-phase," outcome scores generated from your digital sample images will not be used to help inform decisions on your treatment. You will not be able to find out algorithm scores based on your digitised sample images at any time during this study. Your doctors will not be able to inform you of algorithm outcome scores.

- As part of the study, we want to investigate if the machine learning algorithms supported or contradicted the treatment recommendation made to you by your doctor. We also want to test if the AI algorithms can correctly predict your cancer outcome. To do this, as part of the consent process, we ask your permission for our research team to have access to your NHS medical records for up to 24-months after you register to the study.
- Over the course of your treatment, you may have further medical procedures which result in standard of care samples being taken again. Digitised images of your samples may be generated again for these new samples. As part of this study, we will ask your permission to collect and use these new sample images in our study analysis.

- Similarly, we will ask for your permission to use your anonymised sample images to test and validate any future algorithms developed by the University of Oxford and our commercial collaborators. You do not have to agree to this to take part in the study.
- As part of your routine care, you may undergo procedures which result in samples being taken (for example biopsies and surgeries). During the PACES consent process, we will ask your permission to obtain a portion of these routinely collected samples to potentially use them in future research projects. You do not need to agree to this to participate in PACES. As your samples will always be stored anonymously, we will not be able to inform you if or when your samples have been used in research, or what that research entails.
- All samples of these nature will be requested through the Oxford Centre for Histopathology Research (OCHRe). If you would like further information, please go to their website: www.nds.ox.ac.uk/ochre.

How do I join the study?

- If you're interested in taking part in the study, you must first give your informed consent to do so, and only after you have read and fully understood the information in this Participant Information Sheet by ticking the box at the bottom of this page and pressing "Continue."
- The study team will be happy to answer any questions you may have about your participation. You can contact them by emailing paces@medsci.ox.ac.uk. Make sure you have received answers to your satisfaction before providing your consent to join the study.
- If you'd like assistance with completing the online consent form, just let your care team know. They will help you during your next appointment.
- As part of the consent process, we will ask you for some personal data including your email address, biological sex, date of birth and NHS number.
- You will also be asked if you would be happy to be approached by the University of Oxford regarding participation in future research studies. You do not need to consent to this in order to participate in PACES.
- Once you have provided your informed consent online you and the PACES study team will be emailed a copy of the completed consent form. Your care team will then need to confirm you meet the inclusion criteria. Therefore, there may be a small delay between providing consent and registration confirmation. Once your care team have confirmed you are eligible, your registration and participation in the study will be confirmed.

Once the consent and registration process are complete, you will be sent an automated confirmation email and link the "Participant Questionnaire". The confirmation email will contain a unique participant code. This code will be used to identify you throughout the study.

The questionnaires and automated email are securely monitored by a database called "REDCap", so you may see this name on the questionnaire or on the confirmation email you receive.

What should I consider?

- As your participation in the study follows normal standard-of-care procedures, you do not need to change anything regarding your normal medical care to take part.
- For example, you can continue taking your regular medication, any over-the-counter medication (with your doctor's guidance) and, if applicable to you, continue using contraception as you normally would (unless stated otherwise by your doctor).

Are there any risks of taking part?

- Overall, participation in this study is considered very low risk, as all procedures follow well established standard NHS processes.

What are the possible benefits of taking part?

- You will not directly benefit from taking part in this study. However, the information we gather from participants in this study might benefit other people with a similar condition to yours in the future.
- Data from this study will help us learn how new technologies could be used in real-world clinical settings to help doctors and their patients make better, personalised decisions on cancer treatment in the future.

Will my taking part in the study be confidential?

- Yes. When you register to the study and agree to participate, our database will generate a study code that is unique to you. All of your study records and digitised sample images will only be identifiable by this study code.
- We will only use your name, date of birth, biological sex and NHS number when this is necessary to link your NHS records with this study, for example checking to see the status of your cancer and accessing your medical records to look for historical evidence of certain biomarkers (a biomarker is a biological "clue" in your body that may be indicative of possible cancer). We ask for this identifiable data as more than one data-type is required to ensure the correct medical records are accessed.
- Information that could identify you will only be held securely on trusted research servers monitored directly by the study team. Identifiable information relating to you will only ever be used for the purposes of this study and will never be shared.
- Responsible members of the University of Oxford, regulatory bodies or NHS Trusts involved in the study may be given access to personal data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations.

What will happen to the samples I give?

You will not be asked to provide any additional samples to what is required as part of your standard NHS care. The information below relates to samples taken, and the digital images generated from those samples, as part of routine care:

- Conducting analysis on your digital images of your samples is essential to the success of this study. Samples of your tumour and tissue will be taken as per standard-of-care to help doctors and scientists learn more about your particular cancer, and help inform decisions on your future treatments.
- As part of this study, we will not be asking doctors or surgeons to take any more samples compared to what they would normally take. We are simply using digital images of the standard-of-care samples to help answer our research questions.
- Once your samples have been taken, a pathologist (a medically trained person who examines body tissues) will split your samples into smaller pieces and place these on microscope slides. The samples will then be scanned into a computer (or digitised) so that the algorithms can analyse them.
- As your physical samples taken are all for standard-of-care analysis, they will be stored and managed by the NHS.
- If you care team are unable to send a digital image of your samples for use in PACES, the study team may request access to your physical sample, which will be stored by the NHS are per normal practice, to generate the digital image themselves. Once the digital image has been created, the sample will be returned to NHS storage.
- After the algorithms have analysed the digital images of your samples, the images will be stored securely and anonymously on computer servers managed by the University of Oxford.
- We hope that digitised sample images collected as part of this study will help inspire and inform further cancer research studies. Therefore, your digitised images may be accessed by cancer researchers outside of the study team in the future, this may include commercial companies. We will only allow researchers to access your digitised samples if you have provided consent for us to do.
- Your digitised sample images will always be used in a form that does not identify you, mainly by local researchers, but ethically approved future research projects may take place in hospitals, universities, non-profit institutions, or commercial laboratories. Because they will be shared in a form that does not link back to you, it will not be possible to withdraw them after they are shared.
- Your digitised sample images will be stored by the University of Oxford for up to 15 years. After this time, they will be deleted (unless a significant reason has arisen for them to deleted earlier).

What will happen to my data?

- Data protection regulation requires that we state the legal basis for processing information about you. In the case of research, this is 'a task in the public interest.' The University of Oxford is the sponsor for this study. It is the data controller, and is responsible for looking after your information and using it properly.

- We will be using information from you, your hospital, NHS England and any other NHS registries in order to undertake this study and will use the minimum personally-identifiable information possible.

- In the future, your anonymised digital sample images may be shared with academic, NHS and commercial researchers who may use them to help develop new algorithms. It will not be possible to identify you from your anonymised sample images and no identifiable data will ever be shared with researchers. We will only share your sample images with researchers if you have provided your consent for us to do so.

- We will store any research documents with personal information, such as electronic consent forms, securely at the University of Oxford for a maximum of 5 years after the end of the study, as part of the research record. We will keep any other identifiable information about you for 5 years after the study has finished.

- Data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at https://compliance.web.ox.ac.uk/individual-rights

- You can find out more about how we use your information by contacting paces@medsci.ox.ac.uk.

How have patients and the public been involved in the study?

- Patients who have had bowel cancer, and other volunteers with relevant lived experience of cancer, were consulted on the design of the study and were asked if the patient population felt there was a need for the research we are undertaking.

- Additionally, patients were asked to advise on certain practical aspects of taking part (for example, if using an online consent is a good idea). These individuals were also asked to review the consent form, this patient information sheet and any other "patient-facing documents."

- Members of the public with relevant lived experience of bowel cancer will continue to be informed on study progress, and be provided the opportunity to give feedback, throughout

the study, including on how best to present study results to study participants and the wider public.

- Any changes to patient facing documents will be reviewed and approved by patient and members of the public with relevant lived experience of bowel cancer before they are finalised and used in the study.

Who is organising and funding the study?

- The Chief Investigator responsible for leading the study is Dr. Alistair Easton, senior clinical researcher and consultant pathologist at the John Radcliffe Hospital, Oxford.
- The study is managed by the University of Oxford CRUK Centre and the University of Oxford also act as the research sponsor. This means they are legally responsible for the study organisation and for overseeing the work of the researchers.
- The study is funded by the University of Oxford CRUK Centre. and Oxford Cancer Biomarkers Ltd.

What will happen to the results of this study?

- The results of this study may be presented in meetings and conferences or published in peer-review medical journals.
- You will not be identifiable in any reports or publications that arise from this research study.
- Once the study is finished and results have been published, all participants will be invited to an online presentation of the results hosted by the Chief Investigator and key study team members (your email address will be retained by the study team for this purpose). Additionally, a written summary of the results will be made available to the public, and sent to all participants.

What if there's a problem?

- If you have a concern about any aspect of this study, please speak with the study team via email paces@medsci.ox.ac.uk. They will do their best to answer your questions.
- The University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study. NHS indemnity operates in respect of the clinical treatment provided.
- If you wish to complain about any aspect of the way in which you have been approached or treated, or how your information is handled during the course of this study, contact the study team at [study email] or you may contact University of Oxford Research Governance, Ethics & Assurance (RGEA) at rega.complaints@admin.ox.ac.uk or on 01865 616480.

- The Patient Advisory Liaison Service (PALS) is a confidential NHS service that can provide you with support for any complaints or queries you may have regarding the care you receive as an NHS patient. PALS is unable to provide information about this research study. If you wish to contact the PALS team, please email complaints@ouh.nhs.uk or call 01865 221473.

Who has reviewed the study?

- All research in the NHS is looked at by an independent group of people, called a Research Ethics Committee, to protect participants' interests. This study has been reviewed and given a favourable opinion by Oxford C Research Ethics Committee.

Participation in future research:

- During the consent process for this study, we will ask your permission to contact you about opportunities to participate in future research being conducted by the University of Oxford. Your decision about this will not affect your ability to participate in this study.
- All contact regarding future research opportunities will come from the research team of this study in the first instance. Agreeing to be contacted does not oblige you to take part in future research, and you can ask to be removed from the register at any time without providing a reason.
- Your contact details will be held securely, separately from this study on a password protected computer in the Department of Oncology accessible only by authorised individuals.

Further Information and Contact Details

If you should have any questions about the study, please contact a member of the study team on paces@medsci.ox.ac.uk.

Thank you for reading this information.

I confirm I have read and understood all of the information in this patient information sheet and are happy to begin the consent stage. [TICK BOX]