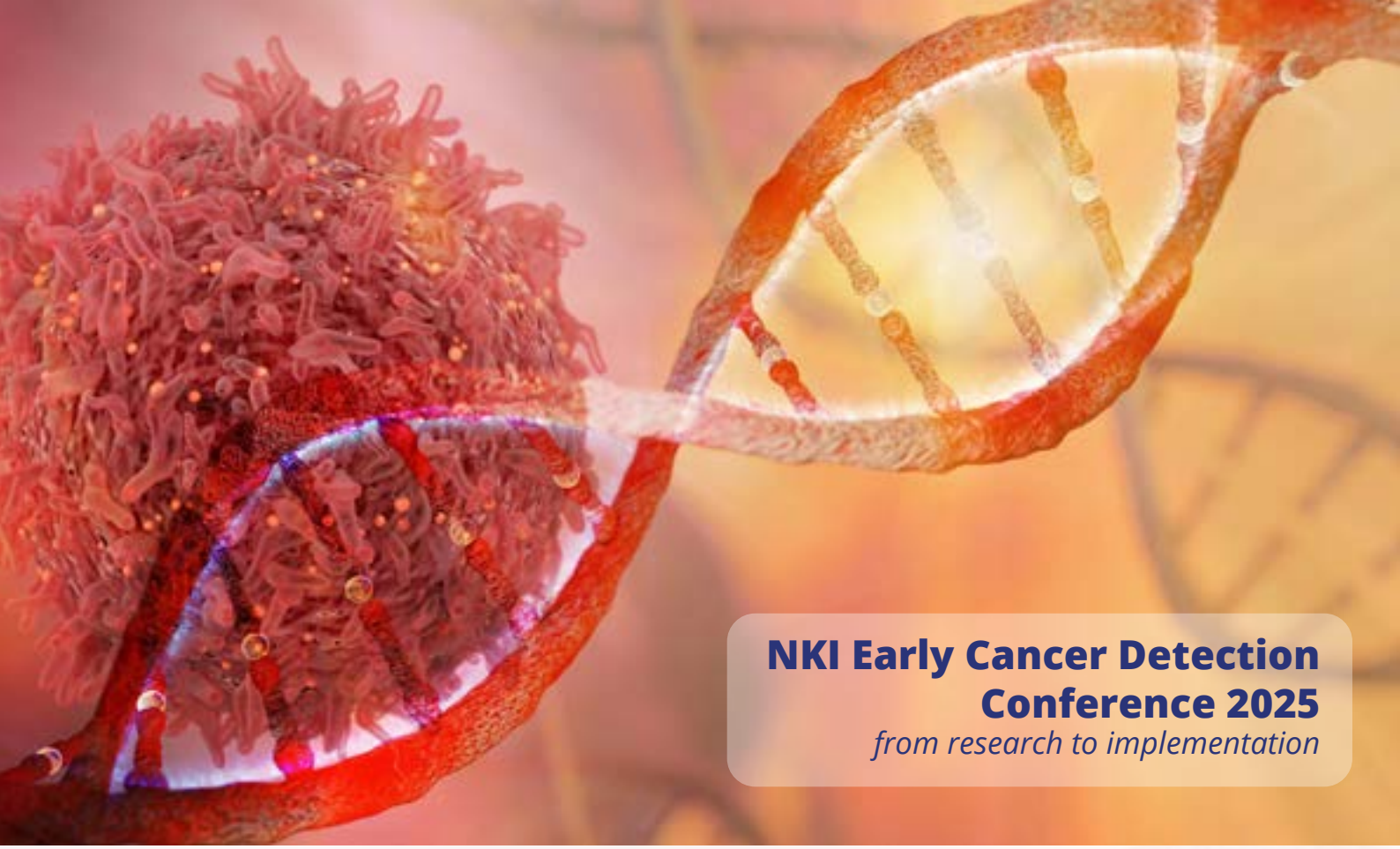


NKI Early Cancer Detection Conference 2025
from research to implementation

1ST EDITION

BOOK OF
ABSTRACTS 2025

MAY 14 AND 15, 2025
PIET BORST AUDITORIUM
Netherlands Cancer Institute, Amsterdam

center for early cancer detection
NETHERLANDS CANCER INSTITUTE

TABLE OF CONTENTS

WELCOME

The Netherlands Cancer Institute warmly welcomes you to the very first edition of the NKI Early Cancer Detection Conference 2025. We, the organizers, are extremely proud to share this special moment with you, and to be honest, a little bit nervous – after all, it's our first time!

This conference marks a milestone in a journey that began in January 2022 with the establishment of the Early Detection Center and the start of the NKI Early Detection research theme in 2023. The official launch of the NKI Center for Early Cancer Detection (CECD) in 2024 was a key moment when our ambition to elevate early cancer detection took a concrete form.

Early detection remains one of the most powerful tools to reduce the cancer burden. By identifying tumors at the earliest possible stage, we can deploy treatments more effectively and significantly reduce the disease burden. We also reduce disease and treatment burden to deescalate where possible. During this conference, we bring together researchers, clinicians, and innovators from various disciplines to share the latest insights, foster collaboration, and accelerate innovation.

We hope this conference leads to inspiring conversations, new collaborations, and most importantly, concrete steps toward faster, more accurate, and more accessible diagnostics.

We sincerely thank all authors, speakers, and attendees for their vital contributions. Your research, presentations, and active engagement have shaped the content and spirit of this conference. Together, you help create an inspiring environment for knowledge exchange, innovation, and progress.

Doreth Bhairosing

Research coordinator and manager biobank

Theo Ruers

Medical Head NKI Center for Early Cancer Detection

Marjanka Schmidt

Theme lead Early Detection NKI

Lisanne Verhoef

Project manager Early Detection

DETAILED PROGRAM

WEDNESDAY, MAY 14

08.30 - 09.00 Registration and welcome (Foyer)

09.00 - 09.15 Introducing the research theme Early Detection (PBA)
Marjanka Schmidt, Netherlands Cancer Institute

09.15 - 09.50 Keynote (PBA) - Cancer screening; what about prostate cancer
Monique Roobol, ErasmusMC

09.50 - 10.30 Biomarkers and risk stratification (part I) (PBA)
Chair: Daan van den Broek, Netherlands Cancer Institute
DCIS overdiagnosis: a call for precision
Jelle Wesseling, Netherlands Cancer Institute
Risk-based breast cancer screening: from equality to equity
Mireille Broeders, Radboud University Medical Center

10.30 - 11.00 Coffee break (Foyer)

11.00 - 12.00 Biomarkers and risk stratification (part II) (PBA)
Chair: Caroline Drukker, Antoni van Leeuwenhoek Hospital
Advancing detection and risk stratification of HPV-driven precancer lesions through DNA methylation biomarkers
Renske Steenbergen, AmsterdamUMC
A less-is-more strategy in surveillance of Barrett's esophagus in the Netherlands
Jacques Bergman, AmsterdamUMC
Separating pussycats and tigers: Risk stratification of prostate cancer using infrared imaging
Peter Gardner, University of Manchester

12.00 - 12.35 Lightning talks: Biomarkers and Risk stratification (PBA)
Chair: Mara Blonden, NKI Center for Early Cancer Detection
UroPanc Trial: Observational Study Update and Interim Analysis
Evelyn Kurotova, Queen Mary University of London
Enabling Molecular Subtyping and Grading for Ductal Carcinoma in Situ with Foundation Models
Marek Oerlemans, Netherlands Cancer Institute
Personalised Prostate Specific Antigen (PSA) Retesting Intervals in Primary Care
Kiana Collins, University of Oxford

DETAILED PROGRAM

Clinical performance of ASCL1/LHX8 DNA methylation on first-void urine: fully molecular cervical cancer screening for user-friendly samples
Severien van Keer, University of Antwerp
Prospective Evaluation of Biomarker Risk Stratification using Capsule Sponge in the Surveillance of Barrett's Esophagus: Results from UK Real-world Implementation Pilots
Caryn Ross-Innes, University of Cambridge

12.35 - 13.35 Lunch break (Foyer)

13.35 - 15.55 Population approaches (PBA)
Chair: Gerrit Meijer, Netherlands Cancer Institute
The future of cervical cancer screening: methodological perspectives
Hans Berkhof, AmsterdamUMC
The role of HTA analysis in early cancer detection
Esther Toes-Zoutendijk, Erasmus Medical Center
Prevention of CRC in Lynch syndrome
Joep IJspeert, Antoni van Leeuwenhoek Hospital
Population screening: present and future visions
Sandra van Dijk, National Institute for Public Health and the Environment

15.55 - 16.25 Coffee break (Foyer)

16.25 - 17.05 Artificial intelligence (PBA)
Chair: Hugo Horlings, Netherlands Cancer Institute
Early diagnosis of cancer; the power of routine care data from general practice
Kristel van Asselt, University Medical Center Utrecht
AI in healthcare: from innovation towards impact
Joost Huiskens, Microsoft

17.05 - 17.15 Closing remarks (PBA)

17.15 - 18.15 Poster session and networking drinks (Tiffany's bar)
18.15 onwards Dinner (optional) (Tiffany's bar)

DETAILED PROGRAM

THURSDAY, MAY 15

08.30 - 09.00 Registration and welcome (Foyer)

09.00 - 09.15 Introducing the Center for Early Cancer Detection (PBA)
Theo Ruers, NKI Center for Early Cancer Detection

09.15 - 09.50 Keynote (PBA) - The future of cancer early detection research; a UK perspective
David Crosby, Cancer Research UK

09.50 - 10.50 Innovations in diagnostic technologies (part I) (PBA)
Chair: Laura Mertens, Antoni van Leeuwenhoek Hospital
Developing early detection biomarkers for renal cancer: pitfalls & challenges
Kim Smits, Maastricht University
AI-Driven MRI for Early Detection of prostate cancer
Derya Yakar, University Medical Center Groningen
The Ultrasound Revolution: Ultra-Fast and Super-Simple
Chris de Korte, Radboud University Medical Center

10.50 - 11.20 Coffee break (Foyer)

11.20 - 12.40 Innovations in diagnostic technologies (part II) (PBA)
Chair: Theo Ruers, NKI Center for Early Cancer Detection
Lab-on-a-chip technologies for early cancer detection
Loes Segerink, University of Twente
Spectroscopic liquid biopsies for the earlier detection of cancer
David Palmer, Dxcover
A systems approach to cancer early detection
Gerrit Meijer, Netherlands Cancer Institute
What will be the role today of multi-cancer early detection tests?
David Weinberg, Fox Chase Cancer Center

12.40 - 13.15 Lightning talks: Innovations in diagnostic technologies (PBA)
Chair: Mara Blonden, NKI Center for Early Cancer Detection
Imaged-based Consensus Molecular Subtypes and colon cancer recurrence
Vera Wesselink, Wageningen University & Research
Deep plasma proteome profiling via phosphatidylcholine-nanoparticle technology for biomarker discovery
Amir Ata Saei, Karolinska Institute

DETAILED PROGRAM

Diagnostic accuracy of abbreviated magnetic resonance imaging for breast cancer screening among women with extremely dense breasts: a multi-reader study
Sophie van Grinsven, Julius Center for Health Sciences and Primary Care
AI-Guided Transabdominal Ultrasound for Early Prostate Cancer Risk Stratification
Liza Kurucz, NKI Center for Early Cancer Detection
AI Detection Performance on Pre-diagnostic Pancreatic Cancer CECT scans
Tijmen de Haas, Radboud University Medical Center

13.15 - 14.40 Lunch break and poster session (Foyer)
Invited focused session: Opportunities for Risk-Based Screening: *Where Can We Make an Impact?*
KWF (13.40 to 14.40) (Glazen Zaal)
Focused session: Implementing multi cancer early detection: transforming care or challenging the system?
Inspire2Live (13.40 to 14.40) (PBA)
Networking opportunities

14.45 - 15.45 Early detection: prevention and implementation (part I) (PBA)
Chair: Steven Linnebank, NKI Center for Early Cancer Detection
Evidence for lung cancer screening in Europe (including 4ITLR)
Harry de Koning, Erasmus Medical Center
The potential of reducing cancer patient referral time in primary care
Sjoerd Elias, University Medical Center Utrecht
The effect of opportunistic prostate cancer screening in the Netherlands
Pim van Leeuwen, Antoni van Leeuwenhoek Hospital

15.45 - 16.10 Coffee break (Foyer)

16.10 - 17.10 Early detection: prevention and implementation (part II) (PBA)
Chair: Marjanka Schmidt, Netherlands Cancer Institute
It's in the family
Caroline Willems, Stichting Erfelijke Kanker Nederland
Cancer screening: The earlier, the better? *Positive aspects and critical remarks*
Carin Louis, Dutch Federation of Cancer Patient Organizations
Cancer prevention: current evidence and guidance
Matty Weijenberg, Maastricht University

17.10 - 17.15 Poster award (PBA)
17.15 - 17.25 Closing remarks (PBA)

SPEAKER INFORMATION

WEDNESDAY, MAY 14

KEYNOTE: CANCER SCREENING; WHAT ABOUT PROSTATE CANCER

MONIQUE ROOBOL

Professor in Decision Making in Urology

Erasmus Medical Center

Department of Urology at Erasmus Medical Centre Rotterdam, The Netherlands since 1991. She is the PI of the European Randomized study of Screening for Prostate Cancer (ERSPC: www.erspc.org), she co-developed the "Rotterdam Prostate Cancer Risk calculator: www.prostatecancer-riskcalculator.com), and is co-PI of global studies on active surveillance: PRIAS (www.prias-project.org) and GAP3 (https://gap3.movemberprojects.com). Since 2018 she is part of the PIONEER European network for big data in prostate cancer (https://prostate-pioneer.eu), co-academic lead of another big data project for prostate, breast and lung cancer OPTIMA (https://www.optima-oncology.eu) and co-lead in the EAU led project on awareness and initiatives in prostate cancer screening in the EU (PRAISE-U; https://uroweb.org/praise-u). She is board member of the ERSPC Foundation, and the chairwoman of the Dutch Prostate Cancer Research Foundation (SWOP), (co)-authored over 450 scientific publications, book chapters and reviews. Her motto is: translate research into useful tools for use within clinical practice: "Bridging the gap between epidemiology and urology."

BIOMARKERS AND RISK STRATIFICATION

SESSION CHAIRS

DAAN VAN DEN BROEK

Clinical Chemist

Netherlands Cancer Institute

Since 2012, Daan has been working at the Antoni van Leeuwenhoek as a clinical chemist. He is responsible for the Clinical Chemistry Laboratory and Phlebotomy. The laboratory conducts a wide range of tests, including numerous tumor markers. Quality, reliability, and efficiency are central to his work. The daily support of patient care through reliable diagnostics, combined with Daan's drive to continuously search for better and more accurate diagnostic methods, is what makes the Antoni van Leeuwenhoek truly unique.

CAROLINE DRUKKER

Surgeon

Antoni van Leeuwenhoek Hospital

Since November 2021, Caroline has been working at the Antoni van Leeuwenhoek as a surgical oncologist. Her area of focus is the treatment of breast cancer. At the Antoni van Leeuwenhoek, the patient and personalized treatment are central. A dedicated team of both medical and nursing specialists surrounds each patient to make this tailored care possible. It is precisely this personal attention that makes working at the Antoni van Leeuwenhoek so special for Caroline. In addition to her clinical work, Caroline is involved in scientific research. Her research focuses on screening and prevention, as well as optimizing risk assessment in breast cancer.

SPEAKERS

JELLE WESSELING

Professor of Breast Pathology, LUMC and Pathologist, NKI

Netherlands Cancer Institute

Jelle Wesseling is a consultant breast pathologist and senior group leader at the Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital in Amsterdam and a professor at Leiden University Medical Center. Trained as both a basic scientist and clinical pathologist, he bridges the gap between research and patient care.

His work focuses on improving breast pathology, particularly moving from “fixed” to functional pathology to enhance prognostic and predictive accuracy. He specializes in Ductal Carcinoma In Situ (DCIS) and early invasive breast cancer, the most common cancers among women.

A major career milestone was receiving the Cancer Research UK Grand Challenge Award in 2017, in partnership with KWF Dutch Cancer Society. This $20-million award was based on his DCIS research and the formation of a global, multidisciplinary team for the PRECISION project, aimed at reducing overtreatment of DCIS. PRECISION addresses key questions on DCIS progression, risk stratification, and the safety of active surveillance. In 2023, he secured a €9 million grant from the Netherlands Science Organization to develop explainable dynamic risk modeling for DCIS using evolutionary AI, further advancing breast cancer diagnostics and treatment.

MIREILLE BROEDERS

Professor Personalized Cancer Screening

Radboud University Medical Center

Mireille Broeders, PhD, is a cancer screening epidemiologist and Professor of Personalized Cancer Screening at the IQ Health science department, Radboud university medical center, Nijmegen. She is principal investigator of the nation-wide PRISMA study (Personalised RISk-based MAmmography screening) and the recently started STREAM study (Screening Tomosynthesis trial with advanced REAding Methods). Her research focuses on the evaluation of long-term benefits and harms of screening, especially screening for breast cancer, and the added value of moving to risk-based screening approaches. Prof. Broeders is a member of the National Evaluation Team for Breast Cancer screening and the committee on Population Screening at the Dutch Health Council.

Prof. Broeders further holds a position as scientific supervisor at the Dutch Expert Centre for Screening in Nijmegen. Her research interests include the implementation and evaluation of technological developments in the breast screening programme, the effects of image processing, and pain experience during breast compression. At an international level, Prof. Broeders contributes to the European Commission Initiative on Breast Cancer and is the Past Chair of the Steering Committee of the International Cancer Screening Network.

RENSKE STEENBERGEN

Professor of Experimental Pathology

AmsterdamUMC

Renske Steenbergen is a Professor of Experimental Pathology at the Department of Pathology Amsterdam UMC, Cancer Center Amsterdam, the Netherlands. She has a MSc degree in Biomedical Sciences from the University of Leiden and gained her PhD degree cum laude from VU University Amsterdam, the Netherlands, in 1997. In 1999, she was awarded a fellowship from the Royal Netherlands Academy of Arts and Sciences (KNAW). She has a 30-year track record in basic and translational research focused on HPV-induced carcinogenesis (www.hpvstudies.nl).

Through the comprehensive molecular analysis of in vitro models and cross-sectional and prospectively collected clinical specimens, she developed and validated DNA methylation and microRNA biomarkers for cervical and anal cancer screening and risk stratification of HPV-induced precancerous disease. More recently, her research has expanded to explore early cancer detection in at-home collected samples, like urine.

JACQUES BERGMAN

Professor of Gastrointestinal Endoscopy and Deputy Chair of the department

AmsterdamUMC

Jacques Bergman, born in 1965, is a leading Dutch gastroenterologist who qualified from the University of Utrecht in 1991. He completed his PhD in Amsterdam, focusing on endoscopic management of gallstone disease, and trained in Gastroenterology in Den Bosch and Amsterdam. In 2001, he was appointed Consultant Gastroenterologist at the Academic Medical Center (AMC) in Amsterdam, becoming Associate Professor in 2005 and Professor of Gastrointestinal Endoscopy and Head of Endoscopy in 2011. Bergman leads the AMC Esophageal Research Team, which includes 3 interventional endoscopists, 17 clinical research fellows, 3 research nurses, and 2 physician assistants.

The team focuses on three main research areas:
1. Endoscopic Imaging – Enhancing early neoplasia detection in Barrett's esophagus, including AI-assisted detection, led by Dr. Jeroen de Groof (6 PhD fellows).
2. Barrett's Surveillance & Biomarkers – Improving surveillance efficiency and biomarker-based risk prediction, led by Dr. Lucas Duits (4 PhD fellows).
3. Endoscopic Treatment of Upper GI Neoplasia – Optimizing resection and ablation of early cancers, especially T1b, led by Dr. Roos Pouw (4 PhD fellows).
The team collaborates internationally with institutions like TU Eindhoven, UCSF, and the National Cancer Institute in the Netherlands.

PETER GARDNER

Professor of Analytical and Biomedical Spectroscopy

University of Manchester

Peter Gardner is a Professor of Analytical and Biomedical Spectroscopy and a fellow of the Royal Society of Chemistry. He obtained a Ph.D. in surface vibrational spectroscopy in 1988 from the University of East Anglia. This was followed by postdoctoral appointments at the Fritz Haber Institute (MPG) in Berlin and Chemistry Department at the University of Cambridge where he was involved in the development of surface infrared spectroscopic methods.

In 1994 he was appointed as a Lecturer in Chemistry Department at UMIST and he was promoted to a Senior Lecturer in 2000 and a Reader in 2010. In 2004, with the formation of the University of Manchester, he joined the School of Chemical Engineering and Analytical Science.

Since 2000 he has built a successful biomedical spectroscopy group that has focussed on using vibrational spectroscopy in the diagnosis of prostate and other cancers. His group also has a keen interest in understanding the fundamental causes of spectroscopic discrimination and separating biochemical and physical spectral influences.

LIGHTNING TALKS: BIOMARKERS AND RISK STRATIFICATION

SESSION CHAIR

MARA BLONDEN

Managing Director

NKI Center for Early Cancer Detection

Currently serving as Director of Business at the Netherlands Cancer Institute, Mara brings a strong track record in strategic leadership and innovation within the healthcare sector. With a deep commitment to societal impact, Mara has shaped transformative initiatives that bridge medical excellence with sustainable business growth.
Prior to joining the Netherlands Cancer Institute, Mara was Head of Strategy and Innovation at Spaarne Hospital, where she led the development of forward-thinking healthcare solutions and fostered partnerships that improved patient outcomes. Earlier in their career, Mara gained critical industry insight at a healthcare insurance company, further refining her expertise in the broader healthcare ecosystem.
Specializing in strategy and business development, Mara is passionate about aligning purpose-driven innovation with long-term value creation. Her work consistently reflects a dedication to improving systems, creating social value, and driving impactful change in healthcare.

SPEAKERS

EVELYN KUROTOVA

UroPanc Trial: Observational Study Update and Interim Analysis

Queen Mary University of London

Evelyn Kurotova studied Medical Biochemistry at the University of Leicester, where she first became interested in the field of Cancer Research, as she was eager to work in a field which has the potential to directly impact the lives of patients. At the moment, she works in early cancer detection, namely focusing on early detection of pancreatic cancer. She is a part of professor Tatjana Crnogorac-Jurcevic's group at Barts Cancer Institute, Queen Mary University of London. The team concentrates on discovering and validating early cancer biomarkers of pancreatic cancer. In particular, they are eager to find non-invasive methods for aiding early detection, which is the reason why they work primarily with urine. Evelyn is presently working as part of the UroPanc trial team, an observational study which is now entering its final phases.

MAREK OERLEMANS

Enabling Molecular Subtyping and Grading for Ductal Carcinoma in Situ with Foundation Models

Netherlands Cancer Institute

Marek Oerlemans is a PhD candidate in the research groups of Jelle Wesseling and Jonas Teuwen at the Netherlands Cancer Institute. He holds master's degrees in Econometrics and Applied Mathematics, specializing in statistical methods for finance and numerical techniques for physics. During his PhD, he became involved in a new challenge involving heterogeneous types of data. He is currently developing deep learning models for DCIS, focusing on high-resolution pathology imaging and RNA expression data. Over the years, Marek has built a strong foundation in mathematical and statistical modelling. He is particularly interested in leveraging this expertise to design and refine prediction models tailored to data-specific characteristics. In addition, Marek is passionate about bridging the gap between technical researchers and clinical practitioners.

KIANA COLLINS

Personalised Prostate Specific Antigen (PSA) Retesting Intervals in Primary Care

University of Oxford

Kiana K Collins is a Researcher and DPhil student in the Nuffield Department of Primary Care Health Sciences at the University of Oxford. Her research aims to improve the early detection of prostate cancer. She uses UK electronic health records data to determine personalised monitoring intervals with the prostate specific antigen (PSA) test to balance the benefits of the early diagnosis of prostate cancer with the harms of over testing.

SEVERIEN VAN KEER

Clinical performance of *ASCL1/LHX8* DNA methylation on first-void urine: fully molecular cervical cancer screening for user-friendly samples

University of Antwerp

With a master in Biomedical Sciences and PhD in Medicine and Health Sciences from the University of Antwerp, Severien is continuing her work as Assistant Professor at the Vaccin & Infectious Disease Institute. Her research focusses on clinical and translational research (e.g., www.ScreenUrSelf.be) to demonstrate the clinical performance and acceptability of HPV DNA testing in first-void urine with host cell methylation marker triage. This research is expanding to screening for other female gynaecological tumors, using self-sampling for cervical cancer screening as a model.

CARYN ROSS-INNES

Prospective Evaluation of Biomarker Risk Stratification using Capsule Sponge in the Surveillance of Barrett's Esophagus: Results from UK Real-world Implementation Pilots

University of Cambridge

Dr. Caryn Ross-Innes is a senior research associate in Professor Rebecca Fitzgerald's group at the Early Cancer Institute, University of Cambridge, UK. Caryn completed her PhD at the Cancer Research UK Cambridge Institute at the University of Cambridge where she focussed on further understanding oestrogen receptor biology using different genomics approaches. After completing her PhD she joined Professor Rebecca Fitzgerald's group and developed and tested a risk stratification biomarker panel for use on the non-endoscopic, capsule sponge device with the objective of identifying Barrett's oesophagus patients who have a higher risk of progressing to oesophageal adenocarcinoma in the simplest way possible. After working in a drug discovery spin out company, Caryn recently returned to work on the capsule sponge to assist with its clinical development and impact.

POPULATION APPROACHES

SESSION CHAIR

GERRIT MEIJER

Professor of Pathology

Netherlands Cancer Institute

As Head of Research and Innovation, Gerrit Meijer is responsible for driving innovation in patient care within the department through translational scientific research. At the research institute of the Antoni van Leeuwenhoek, he leads the Diagnostic Translational Oncology section and heads a research group focused on biomarker development for early detection, prognosis, and prediction of therapy response in colorectal cancer. In addition, he is actively involved in local and (inter)national research infrastructure programs, particularly in the field of biobanking and related areas.

As a pathologist, Gerrit observes disease processes in intricate detail through the microscope. He analyzes and classifies his observations to determine their significance for diagnosis and treatment. With the rise of Personalized Medicine, the field of pathology is undergoing a major transformation—something that is clearly reflected in his department as well. Thanks to its unique bridging role between fundamental disease research and clinical application, pathology is at the core of translational research at the Antoni van Leeuwenhoek.

SPEAKERS

HANS BERKHOF

Professor of Biostatistical and Health Economic Modelling

AmsterdamUMC

Hans Berkhof is a biostatistician and Professor of Biostatistical and Health Economic Modelling at the Amsterdam UMC. He and his colleagues have developed statistical models to describe HPV transmission and progression to cancer, which have been used to inform policymakers on HPV vaccination and screening.

He is also the principal investigator of IMPROVE, the first HPV self-sampling trial in a regular screening population, and the general coordinator of the EU-funded RISCC consortium on risk-stratified cervical

cancer screening in various European settings. Furthermore, he is a member of the European Commission Initiative on Cervical Cancer and the Vaccination Committee of the National Health Council. In addition to his work in cancer prevention, Hans has been the lead statistician in oncology and neurology trials and has developed methods for the design and analysis of diagnostic and adaptive trials.

ESTHER TOES-ZOUTENDIJK

Epidemiologist and assistant professor of Public Health

Erasmus Medical Center

Esther, a trained epidemiologist and assistant professor at the Erasmus MC Department of Public Health in Rotterdam, focuses on evaluating and improving the national colorectal cancer screening programme. She is actively involved in several national studies aimed at improving organised cancer screening, including exploring the potential of risk-stratified screening and improving access for vulnerable populations.

JOEP IJSPEERT

Gastroenterologist

Antoni van Leeuwenhoek Hospital

I am a gastroenterologist and staff member at the department of gastrointestinal oncology at the Netherlands Cancer Institute (AVL). I have a special focus on the diagnosis and treatment of esophageal cancer, gastric cancer, and hereditary colorectal cancer.

Previously, I completed my training as a gastroenterologist at Amsterdam UMC (2023), followed by a gastrointestinal oncology fellowship at the AVL (2023/2024). I obtained my PhD cum laude (2017) at the AMC, focusing on serrated polyps of the colorectum, after completing my medical degree at VUmc (2013) and my clinical epidemiology training at AMC (2015).

SANDRA VAN DIJK

Head of the Cancer Screening Department

National Institute for Public Health and the Environment

Sandra van Dijk studied Biomedical Sciences in Utrecht and has worked in Public Health since 2008, including at a Municipal Health Service (GGD), the Ministry of Health, Welfare and Sport (VWS), and the National Institute for Public Health and the Environment (RIVM).

Following the introduction of HPV screening in 2017, she became the program manager for the cervical cancer screening program. During that time, she was responsible for improving the triage process, preparing for the inclusion of vaccinated women, and increasing the use of the self-sampling kit. In 2023, she became the head of department for all three cancer screening programs: cervical cancer, colorectal cancer, and breast cancer. She leads the teams in both the Netherlands and the Caribbean Netherlands. Her key priorities include ensuring accessibility of the screening programs for everyone, including people with lower health literacy, reducing barriers to participation, and increasing the pace of innovation.

ARTIFICIAL INTELLIGENCE

SESSION CHAIR

HUGO HORLINGS

Pathologist

Antoni van Leeuwenhoek Hospital

Hugo is a Dutch-certified anatomic pathologist at the Antoni van Leeuwenhoek (AVL) and clinical leader of the Computational Pathology group at the Netherlands Cancer Institute (NKI). He earned his PhD at NKI (2005–2011), focusing on breast cancer classification via genetic and gene expression analysis, and completed his pathology training at Amsterdam UMC (2009–2014).

Supported by a Dutch Cancer Society fellowship (2014–2018), Hugo researched molecular biomarkers in breast and ovarian cancer, collaborating internationally with experts at UBC (Canada) and Stanford University (USA). His expertise lies in molecular diagnostics and computational pathology, particularly using AI and deep learning to analyze tumor-immune interactions and improve personalized immunotherapy.

SPEAKERS

KRISTEL VAN ASSELT

General Practitioner and associate professor of General Practice and Nursing Science

University Medical Center Utrecht / Julius Center for Health Sciences and Primary Care

Kristel van Asselt is a general practitioner and associate professor at the Julius Center, Department of General Practice and Nursing Science, UMC Utrecht. Her research focuses on the pivotal role of primary care in cancer prevention, early detection, and survivorship. She has contributed to studies using routine care data to map the diagnostic pathways from initial symptoms to cancer diagnoses.

More recently, artificial intelligence and machine learning techniques have been explored into general practice notes to predict cancer at an earlier stage. AI-based algorithms have shown potential in supporting earlier detection of lung cancer using free text data, though prospective clinical evaluation remains essential to validate its value in real-world practice.

JOOST HUISKENS

Chief Medical Information Officer and Account Executive

Microsoft

Joost is the Chief Medical Information Officer (CMIO) and Account Executive for Dutch Academic Hospitals at Microsoft in the Netherlands. He collaborates with hospitals on the digital transformation of healthcare. Joost aims to connect all stakeholders in healthcare with the goal of turning innovation into impact. With clinical experience as a physician and a PhD in medical and surgical oncology, he seamlessly integrates his work at Microsoft with clinical research. This unique combination allows him to better understand the needs of his clients.

Joost actively collaborates with healthcare providers and industrial partners. He also conducts research on how advanced technologies can be deployed efficiently and safely at the patient's bedside. His vision for the future of healthcare revolves around realizing innovation.

THURSDAY, MAY 15

KEYNOTE: THE FUTURE OF CANCER EARLY DETECTION RESEARCH; A UK PERSPECTIVE

DAVID CROSBY

Head of prevention and Early Detection Research

Cancer Research UK

David Crosby is head of prevention and early detection research at Cancer Research UK (CRUK), a fundraising research charity and the world's second largest non-commercial funder of cancer research, after the US government. He also recently worked part-time for the UK government, advising the Office for Life Sciences on the UK's Cancer Mission.

David began life as a baby, before becoming a pharmacologist, completing a PhD studying cell signalling in platelets. He spent time in academia, lecturing in clinical pharmacology. He moved into industry, identifying and evaluating new clinical development opportunities for Linde Gas Therapeutics, the world's largest medical gases company.

He then moved into the public sector, joining the UK government research funding agency, the Medical Research Council, where he oversaw various science areas and research funding programmes (including inflammation, cardiovascular and respiratory research), leading the MRC-NIHR methodology research programme, and MRC's strategy and investments in experimental medicine.

He is now developing and implementing a new strategy and programme of research investments at CRUK which aims to accelerate progress towards earlier detection and prevention of cancer, through an integrated multidisciplinary approach, driven by equitable improvements in health outcomes.

INNOVATIONS IN DIAGNOSTIC TECHNOLOGIES

SESSION CHAIRS

LAURA MERTENS

Urologist

Antoni van Leeuwenhoek Hospital

Laura Mertens is a urologist at the Antoni van Leeuwenhoek, specializing in the diagnosis and treatment of bladder and prostate cancer. She began her career at the institute in 2011 with a PhD on bladder cancer diagnostics and imaging, later completing her urology training at Amsterdam UMC and a fellowship in oncological urology.

Since 2020, Laura has been part of a multidisciplinary team treating urological cancers, combining high-quality patient care with cutting-edge research. She is active in national and international consortia, with a focus on improving outcomes and quality of life for cancer patients through personalized, evidence-based treatment and translational research.

THEO RUERS

Medical and Innovation Director

NKI Center for Early Cancer Detection

As the Medical Director of the NKI Center for Early Cancer Detection (CECD) and the AVL Center for Early Diagnostics, Theo plays a pivotal role in steering medical strategies and initiatives aimed at advancing early detection technologies. His responsibilities include guiding clinical research, integrating innovative diagnostic methods, and fostering collaborations that drive the mission of both centres forward.

In addition to his leadership roles, Theo is an experienced surgeon in surgical oncology and a professor at the University of Twente in the Netherlands. At the AVL hospital, he leads a research group specialising in image-guided surgery. His combined academic and clinical expertise drives advancements in surgical innovation, with a particular focus on precision diagnostics.

SPEAKERS

KIM SMITS

Epidemiologist and associate professor of Pathology,

Maastricht University

Kim is a molecular epidemiologist working as an associate professor at Maastricht University Medical Center, specialized in cancer biomarkers and biomarker methodology. Next to her training at Maastricht University, she has been trained at the Ospedale Maggiore in Milan, the Sidney Kimmel Comprehensive Cancer Center, John Hopkins University, and the department of Therapeutic Radiology, Yale University.

Her research mainly focusses on biomarkers for melanoma, renal and colorectal cancer and she has developed and patented several multivariate prediction models including molecular biomarkers in tissue and liquid biopsies, for cancer detection and prognosis. Recently, she initiated a prospective urinary biobank for renal and bladder cancer biomarker research, that currently aims to cover the South-east region of the Netherlands. In addition, coming from her epidemiological background, part of her research concentrates on optimizing the methodology of (molecular) biomarker research and she is often invited as a methodological advisor for both academic as well as industrial partners.

DERYA YAKAR

Radiologist and Associate Professor of AI-Supported Radiology

University Medical Center Groningen

Dr. Derya Yakar, an Associate Professor of AI-Supported Radiology and a radiologist, specializes in developing advanced AI algorithms for oncological imaging. Holding positions at the University Medical Center Groningen and the Netherlands Cancer Institute, she focuses on enhancing CT and MRI diagnostic performance, particularly for abdominal diseases like liver disease, pancreatic cancer, and prostate cancer.

Dr. Yakar has secured research grants from prestigious organizations such as Health Holland, NWO, and the Hanarth Fund. She is committed to improving healthcare efficiency and accessibility by leveraging AI to streamline imaging protocols and automate radiologists' workflows, with the ultimate goal of enhancing healthcare accessibility and affordability.
An advocate for ethical AI, Dr. Yakar emphasizes transparency and fairness, integrating patient perspectives and social science insights to ensure equitable AI implementation. Her multidisciplinary approach addresses critical healthcare needs and sets new standards for the integration of AI into medical research and practice.

CHRIS DE KORTE

Professor on Medical Ultrasound Imaging

University of Twente

Chris L. de Korte is a Full Professor of Medical Ultrasound Imaging at both Radboudumc and the University of Twente. He holds an M.Sc. in Electrical Engineering from Eindhoven University of Technology and a Ph.D. in Medical Sciences from Erasmus University Rotterdam. Since joining Radboudumc in 2002, he became Head of the Clinical Physics Laboratory in 2004 and founded the Medical UltraSound Imaging Center (MUSIC) in 2012.

His research focuses on functional imaging and acoustical tissue characterization for cancer and vascular diagnostics, as well as AI-driven applications for Point of Care Ultrasound. He has authored over 200 peer-reviewed articles and holds four patents.

Dr. de Korte has received multiple prestigious Dutch Research Council (NWO) grants (VENI, VIDI, VICI) and the EUROSON Young Investigator Award. He is President of the Netherlands Society for Medical Imaging, leads the national ultra-X-treme program, and became an IEEE Fellow in 2023.

LOES SEGERINK

Professor Biomedical Microdevices

University of Twente

During her PhD project, Loes developed a point-of-care semen analyzer system that measured the concentration and motility of spermatozoa in human semen. After 4 years, she successfully defended this work and its impact has been recognized by the Simon Stevin Leerling award (2011), Simon Stevin Gezel award (2012), and enormous media exposure.

After a postdoc visit at KTH in Sweden, she obtained a Veni grant to develop new techniques to assess and select spermatozoa for assisted reproductive technologies. In 2014 she started as assistant professor, became full professor in 2021 and chair of the BIOS group in 2022. Currently her research focuses on biomedical microdevices. She can divide her current research into four themes (1) spermatozoa on chip; (2) organs on chip (3) biomarker detection on chip and (4) protoplast on chip.

Characteristic of her research are the translational component, multidisciplinary approach, and outreach activities.

DAVID PALMER

Chief Scientific Officer

DxCover

David Palmer obtained a Master's in Chemistry from the University of Sheffield in 2001, and a PhD in Chemistry at the University of Cambridge in 2008. Prior to beginning an independent academic career in 2014, he completed postdoctoral work at the Max Planck Institute for Mathematics in the Sciences in Leipzig and held a Marie Curie Intra-European Fellowship at the University of Strathclyde. He is currently co-founder and Chief Technical Officer at Dxcover Ltd, and a Reader in Chemistry at the University of Strathclyde. Dxcover develop spectroscopic liquid biopsies for the early detection of cancer.

GERRIT MEIJER

Professor of Pathology

Netherlands Cancer Institute

Gerrit Meijer is a professor of Pathology with a special interest in gastrointestinal oncology and translational research. Professor Meijer leads a translational research group that focuses on gastrointestinal cancer, especially biomarker development for early detection of colorectal cancer, as well as on definition of molecular intermediate endpoints for screening. This work is amongst other funded by a Stand Up To Cancer & Dutch Cancer Society "Dream Team" grant for early detection of colorectal cancer. Next to that he is involved in the development of (inter-)national research infrastructures for biobanking and research IT, including TraIT, Health-RI, BBMRI, EATRIS, tranSMART foundation as well as AACR GENIE.

Gerrit Meijer has been closely involved in the development, implementation and execution of the Dutch national colorectal cancer screening program, serving on several program committees.

DAVID WEINBERG

Professor and Chairman of Medicine

Fox Chase Cancer Center

David Weinberg MD, MSc is Professor and Chairman of Medicine at Fox Chase Cancer Center in Philadelphia where he holds the Audrey Weg Schaus and Geoffrey Alan Weg Chair in Medical Science. Fellowship trained in gastroenterology and cancer epidemiology, his research interests center on gastrointestinal cancer prevention and control with a particular focus on colorectal and pancreatic cancers. He has received continuous NIH funding to support his research efforts since completing his training. Since 2022, he has served as co-Editor-in-Chief of Gastroenterology.

LIGHTNING TALKS: INNOVATIONS IN DIAGNOSTIC TECHNOLOGIES

SESSION CHAIR

MARA BLONDEN

Managing Director

NKI Center for Early Cancer Detection

Currently serving as Director of Business at the Netherlands Cancer Institute, Mara brings a strong track record in strategic leadership and innovation within the healthcare sector. With a deep commitment to societal impact, Mara has shaped transformative initiatives that bridge medical excellence with sustainable business growth.

Prior to joining the Netherlands Cancer Institute, Mara was Head of Strategy and Innovation at Spaarne Hospital, where she led the development of forward-thinking healthcare solutions and fostered partnerships that improved patient outcomes. Earlier in their career, Mara gained critical industry insight at a healthcare insurance company, further refining her expertise in the broader healthcare ecosystem.

Specializing in strategy and business development, Mara is passionate about aligning purpose-driven innovation with long-term value creation. Her work consistently reflects a dedication to improving systems, creating social value, and driving impactful change in healthcare.

SPEAKERS

VERA WESSELINK

Imaged-based Consensus Molecular Subtypes and colon cancer recurrence

Wageningen University & Research

Vera's research focuses on how diet, lifestyle factors, genetics, and immune-related tumor characteristics influence cancer progression. She is particularly interested in how these factors interact with one another to affect disease outcomes.

She was trained as a nutritionist, specializing in nutritional physiology at Wageningen University in the Netherlands. After completing her studies, she began her PhD project at Wageningen University & Research, investigating the role of vitamin D and inflammation in relation to outcomes in colorectal cancer patients. During her PhD, she explored the association between vitamin D concentrations over time and colorectal cancer outcomes, and whether inflammation served as an underlying mechanism for the observed associations.

Currently, Vera is working as a postdoctoral researcher at the Netherlands Cancer Institute, where she continues to study the role of nutrition and lifestyle in cancer outcomes, and their interactions with genetics and immune-related tumor characteristics. In addition, she is a guest researcher at the Fred Cancer Research Center, where she investigates associations between diet, tumor immune-cell infiltration, and survival.

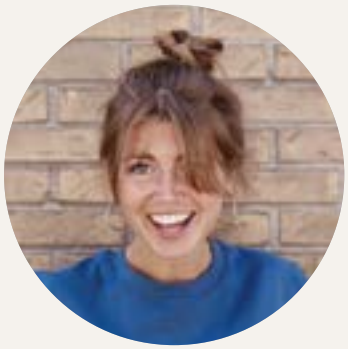
AMIR ATA SAEI

Deep plasma proteome profiling via phosphatidylcholine-nanoparticle technology for biomarker discovery

Karolinska Institute

Amir Ata Saei holds a doctorate in pharmaceutical sciences and received his PhD in proteomics and bioinformatics in Prof. Roman A. Zubarev's group at Karolinska Institutet in 2019. He pioneered several mass spectrometry-based chemical proteomics approaches for identification of drugs targets. He then worked as a Swedish Research Council postdoctoral fellow, with Prof. Steven P. Gygi's laboratory at Harvard Medical School, applying chemical proteomics to study cancer metabolism. In 2022, he joined Prof. Michael N. Hall's laboratory at Biozentrum, initially as a postdoc and later as a SNSF-funded Ambizione Fellow to identify and characterize the targets and functions of polyamines, in the context of mTOR-driven liver cancer. He received a faculty-funded assistant professorship position from Karolinska Institutet and is leading a group at the Department of Microbiology, Tumor and Cell Biology at Karolinska Institutet

since 2024. The Saei lab focuses on bridging proteomics, cancer and metabolic disease, aiming to identify biomarkers and druggable targets and develop novel therapeutics.



SOPHIE VAN GRINSVEN

Diagnostic accuracy of abbreviated magnetic resonance imaging for breast cancer screening among women with extremely dense breasts: a multi-reader study

Julius Center for Health Sciences and Primary Care

I hold a Master's degree in Epidemiology from Utrecht University, during which I joined the Cancer Epidemiology team at the Julius Center (UMC Utrecht) for my internship, focusing on the determinants of extremely dense breast tissue.
During this internship, I became interested in breast cancer screening and the challenges related to dense breasts. Therefore, I continued with a PhD in the same group on the same topic. I'm currently in the third year of my PhD, with my research focused on the DENSE(1) and DENSE-2 trials—both aimed at improving breast cancer screening for women with extremely dense breasts.

LIZA KURUCZ

AI-Guided Transabdominal Ultrasound for Early Prostate Cancer Risk Stratification

NKI Center for Early Cancer Detection

Liza Maria Kurucz holds a degree in Technical Medicine from Delft University of Technology. She is currently a PhD candidate at the NKI Center for Early Cancer Detection, where her research focuses on improving prostate cancer risk stratification by developing AI-driven tools for diagnostics with transabdominal ultrasound. Her work aims to increase the accessibility of prostate cancer diagnostics, with more accurate, simple and patient-friendly procedures for both clinicians and patients.

TIJMEN DE HAAS

AI Detection Performance on Pre-diagnostic Pancreatic Cancer CECT scans

Radboud University Medical Center

MSc Tijmen de Haas is a PhD candidate at the Diagnostic Image Analysis Group (DIAG) of Radboud

University Medical Center, where he focuses on the development of AI tools for medical image analysis. His PhD research investigates AI for opportunistic screening of pancreatic cancer using CT scans.
Tijmen obtained his BSc and MSc in Artificial Intelligence from Radboud University, graduating cum laude for his Master's. During his studies, he specialized in neurotechnology and healthcare, and completed his degree with a thesis regarding AI methods for lung cancer screening.
Currently, Tijmen is building upon the work initiated in the European PANCAIM project, particularly the research by N. Alves and M. Schuurmans. One outcome of this line of work is the PANORAMA challenge, which aims to benchmark AI models for pancreatic cancer detection.
At the Early Cancer Detection Conference, Tijmen will present the performance of the PANORAMA AI model on an external, pre-diagnostic, pancreatic cancer dataset.

EARLY DETECTION: PREVENTION AND IMPLEMENTATION

SESSION CHAIRS

STEVEN LINNEBANK
General Practitioner
NKI Center for Early Cancer Detection

Since becoming a registered General Practitioner in 2009, Steven has been working for Stichting Amsterdamse Gezondheidscentra (SAG), a network of healthcare centers in Amsterdam committed to accessible, high-quality primary care. He currently practices at Gezondheidscentrum Zeeburg, located in the eastern part of the city, where he provides comprehensive care to a diverse patient population.

In November 2023, Steven joined the Center for Early Diagnostics with the aim of improving early cancer detection in general practice. He believes that general practitioners play a vital role in recognizing early warning signs and enhancing patient outcomes through timely diagnosis. To support this mission, he has initiated and led focus groups with fellow GPs, exploring innovative and practical diagnostic approaches suitable for daily clinical practice.

At the Center for Early Diagnostics, Steven also offers prostate consultations through the 'Huisartsenpluspunt' initiative. These consultations include prostate ultrasound examinations, contributing to a structured risk stratification strategy for prostate cancer. By combining clinical experience with diagnostic innovation, he strives to bridge the gap between early detection and accessible care within the general practice setting.

MARJANKA SCHMIDT
Theme lead Early Detection
Netherlands Cancer Institute

Marjanka leads the "Early Detection" program at the NKI, which aims to develop, coordinate and support excellent research and strengthen the collective and interdisciplinary mission to improve early detection of cancer. Within this role, she also drives strategic initiatives to enhance the impact of early detection research within the institute and in (inter)national collaboration.

Marjanka is also the Head of the Division of Molecular Pathology at the NKI, where her research group is based, and a professor of Genetic Epidemiology of (breast)cancer at Leiden University. Her research group is dedicated to investigating the impact of genetic variants on the risk, prognosis, and long-term outcomes of breast cancer subtypes. Her work integrates epidemiological and molecular research to advance personalized medicine, aiming to develop preventive and therapeutic interventions tailored to an individual's genetic profile.

SPEAKERS

HARRY DE KONING
Professor of Public Health & Screening Evaluation
Erasmus Medical Center

Harry de Koning is Deputy Head and Professor of Public Health & Screening Evaluation at Erasmus MC in Rotterdam. His work focuses on designing, conducting, and evaluating population-based randomized controlled screening trials, assessing screening programs and clinical tests, and informing public health policies through advanced modeling techniques.

A pioneer in cancer screening research, Harry played a key role in the ERSPC prostate cancer screening trial and is Principal Investigator (PI) of the NELSON lung cancer screening trial, known for its innovative design. He also led the only RCT on screening for language disorders in toddlers and initiated the ROBINSCA trial on cardiovascular disease screening through an Advanced Researcher Grant. Currently, he leads the 4-in-the-lung-run lung cancer trial under Horizon2020.

Harry's expertise includes micro-simulation modeling of disease progression, risk prediction, and cost-effectiveness analysis. His team monitors and evaluates the Dutch national breast, cervical, and colorectal cancer screening programs, and he coordinates multiple European projects to enhance screening

effectiveness and implementation across Europe.

He is also involved in the evaluation of vision and hearing screening and is co-PI on seven U.S. NIH/NCI-funded CISNET projects that model the impact of interventions across various cancers. Harry's work significantly shapes screening strategies and public health policy both in the Netherlands and internationally.

SJOERD ELIAS

Associate Professor of Clinical Epidemiology

University Medical Center Utrecht / Julius Center for Health Sciences and Primary Care

Sjoerd Elias, MD PhD, obtained his MSc in Clinical Epidemiology at the Netherlands Institute for Health Sciences (2002), and graduated from Medical School in 2005, after which he worked as a resident in radiology (2006-2007).

A personal Dutch Cancer Society Research Fellowship to study biomarkers for molecular imaging for breast cancer screening (2009-2013) enabled him to work at the Molecular Imaging Program at Stanford (Sanjiv Gambhir), the Department of Radiology and Biomedical Imaging at the UCSF (Nola Hylton), and the Department of Molecular Pathology at the Netherlands Cancer Institute (Laura van 't Veer).

He is currently an Associate Professor of Clinical Epidemiology and heads the Research Program Cancer at the Julius Center for Health Sciences and Primary Care at the UMC Utrecht. Furthermore, he is a daily board member of the UMC Utrecht Strategic Program Cancer, and coordinator of the PhD program Clinical and Translational Oncology.

His main research focus is on the translation and clinical evaluation of cancer biomarkers to better inform medical decisions, including the diagnostic work-up of patients suspected of colorectal cancer in primary care and risk-stratification for improved cancer surveillance.

PIM VAN LEEUWEN

Urologist

Antoni van Leeuwenhoek Hospital

Pim van Leeuwen is a urologist at the Antoni van Leeuwenhoek, specializing in the treatment of prostate, kidney, bladder, penile, and testicular cancers. He values the institute's unique integration of high-quality oncological care with scientific research, enabling innovative, personalized treatment throughout the patient journey—from diagnosis to rehabilitation.

Pim is trained as a urologist at Erasmus Medical Centre in Rotterdam, with part of his training at St. Vincent's Prostate Cancer Centre in Sydney, Australia. He earned his PhD studying early prostate cancer diagnosis within the European Randomized Study for Prostate Cancer (ERSPC). His primary clinical and research focus is on prostate cancer.

He is part of the Prostate Cancer Network Netherlands, where he performs robotic prostate surgeries using the Da Vinci system, aiming to enhance treatment outcomes through shared expertise. At Antoni van Leeuwenhoek, he is actively involved in the Prostate Cancer Early Diagnosis Centre, which emphasizes innovation and quality improvement in early detection. The center runs a fast-track clinic and hosts twice-weekly multidisciplinary meetings to ensure personalized, evidence-based treatment plans.

Pim combines patient care with research to continually advance prostate cancer diagnosis and treatment. His approach centers on delivering individualized, high-quality care while maintaining a strong focus on post-treatment quality of life.

CAROLINE WILLEMS
Board Member and Co-Founder
Stichting Erfelijke Kanker Nederland

Caroline Willems is a dedicated patient advocate in the field of hereditary cancer. As co-founder of the Hereditary Cancer Foundation Netherlands (www.kankerindefamilie.nl), she is committed to supporting the large group of individuals with a family history of cancer. This includes providing reliable information, facilitating peer support, and representing the interests of families affected by hereditary cancer.
With her experience in evaluating scientific research, Caroline contributes to shaping and organizing healthcare, ensuring that individuals with (a possible) hereditary or familial predisposition to cancer are fully supported in making informed decisions about genetic testing and risk-reducing strategies. Her dedication and expertise make her a valuable voice for those facing hereditary cancer.

CARIN LOUIS
Advocate for Innovative Treatments and Diagnostics
Dutch Federation of Cancer Patient Organizations

Carin Louis works as an advocate for the Dutch Federation of Cancer Patient Organizations (NFK), the umbrella organization of 21 cancer patient organizations. Her expertise lies in molecular diagnostics, early diagnosis, and access to innovative treatments in oncology.
In collaboration with various stakeholders, she is committed to optimizing the availability of molecular

diagnostics in the Netherlands, with the goal of ensuring that every patient has equal access to the best possible (molecular) diagnostics and subsequent treatment. Additionally, Carin works with field partners to improve the early detection of cancer in high-risk groups.

Before joining NFK, Carin held various roles within the pharmaceutical industry, including in marketing, medical affairs, and patient engagement.

Matty Weijenberg

Professor of Molecular Epidemiology of Cancer

Maastricht University

Matty Weijenberg is Professor of Molecular Epidemiology of Cancer and Chair of the Department of Epidemiology at Maastricht University. Her research is part of the GROW research institute's oncology and reproduction programme, with a focus on cancer prevention and survivorship.

She is the principal investigator of the EnCoRe study, a prospective cohort study examining how lifestyle factors—such as diet, physical activity, and body composition—impact prognosis and quality of life in colorectal cancer survivors, with specific interest in fatigue and chemotherapy-induced peripheral neuropathy (CIPN). EnCoRe is part of international consortia including FOCUS (on folate-related biomarkers and recurrence) and MetaboCCC (on metabolic profiles in colorectal cancer survivorship).

Matty also contributes to the Netherlands Cohort Study (NLCS), exploring how lifestyle influences colorectal cancer incidence and outcomes, considering genetic and epigenetic tumor heterogeneity.

Internationally, she serves as deputy chair of the World Cancer Research Fund (WCRF) International's Global Cancer Update Programme (CUP Global), which analyzes global evidence on diet, physical activity, and cancer in partnership with AICR, WCRF UK, and WKOF. Additionally, she is a member of the Lifestyle Working Group for the development of the 5th Edition of the European Code Against Cancer, part of the World Code Against Cancer initiative led by IARC and WHO.

ABSTRACTS

BIOMARKERS AND RISK STRATIFICATION

no.02	Line Hjøllund Pedersen	Danish Cancer Society
no.03	Nanette van Roermund	AmsterdamUMC
no.05	Sanne Westerhout	ErasmusMC
no.06	Sanne Westerhout	ErasmusMC
no.07	Dmitrey Sergeev	DKFZ
no.08	Jasleen Singh	ErasmusMC
no.09	Jos Poell	AmsterdamUMC
no.10	Beatriz Carvalho	NKI
no.11	Vincent Pappalardo	NKI
no.13	Mei-Chee Tai	Cancer Research Malaysia
no.15	Clara Frick	DKFZ
no.18	Severien van Keer	University of Antwerp
no.19	Pradeep Virdee	University of Oxford
no.20	Pradeep Virdee	University of Oxford
no.21	Leon Klimeck	DKFZ
no.22	Bea Wisman	UMCG
no.24	Evelyn Kurotova	Queen Mary University of London
no.25	Jayni Shah	Queen Mary University of London
no.26	Eltjo Heddema	OncoInv.
no.29	Stuart Wright	University of Manchester
no.31	Yuri van der Burgt	LUMC
no.32	Lindy Kregting	Radboud UMC
no.33	Marek Oerlemans	NKI
no.35	Agne Krilaviciute	Technical University of Munchen
no.36	Kiana Collins	University of Oxford
no.37	Caryn Ross-Innes	University of Cambridge
no.38	David Weller	University of Edinburgh
no.39	Kim Chu	Queen Mary University of London
no.40	Bram Pronk	Delft University
no.41	Eef van den Borst	University of Antwerp
no.45	Olly White	ErasmusMC
no.46	Lianlian Wu	Early Cancer Institute Cambridge
no.47	Bruno Achutti-Duso	Gustav Roussy
no.49	Jim Peters	RadboudUMC
no.51	Iris Glykofridis	NKI
no.52	Lot Mulder	NKI
no.53	Agustin Enciso-Martinez	LUMC

ABSTRACTS

INNOVATIONS IN DIAGNOSTIC TECHNOLOGIES

no.01	Jillian Bracht	AmsterdamUMC
no.04	Mark Witteveen	Center for Early Cancer Detection
no.12	Laura Meulenbroeks	AmsterdamUMC
no.14	Vera Wesselink	Wageningen University & Research
no.16	Liza Kurucz	Center for Early Cancer Detection
no.17	Amir Ata Saei	Karolinska Institute
no.23	Athurva Gore	Singlera Genomics Incorporated (USA)
no.27	Eltjo Heddema	OncoInv.
no.28	Phil Sanders	Flomics Biotech
no.30	Jasika Paramasamy	ErasmusMC
no.34	Paul van der Leest	NKI
no.42	Sophie van Grinsven	Julius Center for Health Sciences and Primary Care
no.43	Sophie van Grinsven	Julius Center for Health Sciences and Primary Care
no.48	Tijmen de Haas	RadboudUMC

ABSTRACT NO.01

PRE-ANALYTICAL CHALLENGES PREVENT CLINICAL TRANSLATION OF BLOOD-BASED BIOMARKERS

Jillian Bracht[1], Mendel Engelaer[2], Edwin van der Pol[1,2], Rienk Nieuwland[1]

[1]*Laboratory of Experimental Clinical Chemistry, Amsterdam UMC, location University of Amsterdam, Amsterdam, the Netherlands*
[2]*Department of Biomedical Engineering and Physics, Amsterdam UMC, location University of Amsterdam, Amsterdam, the Netherlands*

INTRODUCTION

Human blood plasma contains clinically relevant information that can be used to develop disease biomarkers. Despite intensive research, >99.9% of biomarkers never reach the clinic[1]. A possible explanation is the inconsistent composition of plasma samples. Although plasma is considered to be "cell-free", it still contains 1E5-1E8 erythrocyte ghosts (ery-ghosts) and platelets per mL after two centrifugation steps[2,3]. Moreover, the concentration of remaining cells varies per sample and depends on the operator and centrifugation protocol (>200 existing protocols).

Importantly, remaining cells can bias downstream extracellular vesicle (EV) and EV-miRNA measurements[2]. Because the concentration of remaining cells is too low for visual confirmation, and their downstream effects on other analytes (DNA, proteins) are unknown, this issue remains unrecognized and underestimated.

METHODS

We developed a procedure to specifically and simultaneously sort and concentrate ery-ghosts and platelets from double-centrifuged human plasma. Cell concentrations before and after sorting were measured by flow cytometry. The presence of ery-ghosts and platelets was evaluated by super-resolution microscopy (SRM), using specific capture- and detection antibodies. We also developed a filtration method to remove remaining ery-ghosts and platelets from plasma.

RESULTS

After the sorting procedure, the concentration of ery-ghosts and platelets increased 64-fold and 40-fold, respectively. Subsequently, SRM confirmed that the sorted particles were ery-ghosts and platelets. Ery-ghosts were both membrane dye and CD235a positive, whereas platelets showed characteristic pseudopods and were membrane dye and CD63 positive. Our filtration method removed >98% of the remaining cells from plasma, while the detectable concentration of EVs (100-1000 nm) remained unaffected.

CONCLUSIONS

We have developed methodologies to (1) remove remaining cells from plasma, and (2) isolate remaining cells, allowing us to characterize and quantify their effects on downstream analyses. By standardizing the quality and composition of plasma samples, a more uniform playing field is being prepared for enhanced biomarker development.

ABSTRACT NO.02

PRSONAL: RISK-STRATIFIED BREAST CANCER SCREENING - A RANDOMIZED CLINICAL TRIAL

Line Hjøllund Pedersen[1,2], Janne Bigaard[1], Pia Rørbæk Kamstrup[3,4], Berit Andersen[5,6], Ilse Vejborg[7,8], Antonis C Antoniou[9] and Stig Egil Bojesen[3,4]

[1]*Prevention and Information, Danish Cancer Society, Copenhagen, Denmark*
[2]*Cancer Survivorship, Danish Cancer Institute, Danish Cancer Society, Copenhagen, Denmark*
[3]*Department of Clinical Biochemistry, Copenhagen University Hospital – Herlev and Gentofte, Herlev, Denmark*
[4]*Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark*
[5]*UNICCA – University Research Clinic for Cancer Screening, Department of Public Health Programs, Randers Hospital, Denmark*
[6]*Department of Clinical Medicine, Faculty of Health and Medical Sciences, University of Aarhus, Denmark*
[7]*Capital Breast Cancer Screening Program, Denmark*
[8]*Department of Breast Examinations, Copenhagen University Hospital – Herlev and Gentofte, Herlev, Denmark*
[9]*Centre for Cancer Genetic Epidemiology, Department of Public Health and Primary Care, University of Cambridge, UK*

BACKGROUND

Breast cancer accounts for 14% of all cancer-related deaths among women. Danish women aged 50–69 years are offered biennial mammography, reducing breast cancer-specific mortality. However, this approach does not account for individual risk variation. Simulations suggest that risk-stratified screening detects more early-stage cancers while reducing unnecessary biopsies and false positives. This trial will investigate whether multifactorial risk-stratified screening is feasible, acceptable, cost-efficient, and safe.

METHODS

A minimum of 962 consenting women aged 50–67 years will be randomized 1:1 into either a control group receiving standard biennial screening or an intervention group undergoing risk-based screening. Women in the intervention group will receive a personalized breast cancer risk assessment, with screening schedules adjusted accordingly.

Risk factor data—including family history of breast cancer, lifestyle, reproductive history, mammographic density, height, and weight—will be collected. Intervention group participants will provide a blood sample for DNA analysis. Using the multifactorial risk prediction model BOADICEA, participants will be stratified into four risk groups: low, intermediate, elevated, and high risk. Screening intervals will be adjusted every four years for low-risk, every two years for intermediate-risk, and annually for elevated/high-risk women. Elevated-risk participants will receive supplemental tomosynthesis, while high-risk women will additionally undergo breast magnetic resonance imaging and be referred to a specialized Breast Center.

Data collection, communication, and follow-up will occur online via a digital tool co-designed with women from the target group. The primary outcome is the proportion of low-risk women who, within 800 days of their baseline mammogram, refrain from their legally ensured biennial screening. Secondary outcomes include quality of life, anxiety, and breast cancer worry, measured at baseline and three times during follow-up. Additionally, health economy analyses will be conducted.

CONCLUSION

The findings will inform the development of large-scale risk-stratified screening trials.
The trial is registered at ClinicalTrials.gov (Identifier: NCT06060938).

ABSTRACT NO.03

POST-COLONOSCOPY COLORECTAL CANCER RISK IN INDIVIDUALS WITH ≥10MM POLYPS WITHOUT OTHER HIGH-RISK FEATURES

Nanette S. van Roermund[1,2,3], Monique E. van Leerdam[4,5], Manon C. W. Spaander[6], Evelien Dekker[1,2,3], Joep E.G. IJspeert[5]

[1]Department of Gastroenterology and Hepatology, Amsterdam University Medical Center, Location VU Medical Center, University of Amsterdam, the Netherlands
[2]Amsterdam Gastroenterology, Endocrinology & Metabolism, Amsterdam, the Netherlands
[3]Cancer Center Amsterdam, Amsterdam University Medical Center, Amsterdam, the Netherlands
[4]Department of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, the Netherlands.
[5]Department of Gastrointestinal Oncology, Netherlands Cancer Institute-Antoni van Leeuwenhoek, Amsterdam, the Netherlands
[6]Department of Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, the Netherlands.

BACKGROUND AND STUDY AIMS

Post-polypectomy guidelines classify individuals with polyps, where a size of ≥10mm is the sole high-risk feature, as having advanced lesions, thereby warranting strict surveillance. This study compares post-colonoscopy colorectal cancer-risk (PCCRC) between individuals with ≥10mm polyps without other high-risk features and polyp-free individuals.

PATIENTS AND METHODS

Data of quality-assured baseline colonoscopies in the Dutch fecal immunochemical test-based CRC screening program (2014-2020) was used. For individuals with ≥10mm adenomas without high-grade dysplasia or ≥10mm serrated polyps without dysplasia which were advised a 5-year surveillance recommendation, PCCRC-risk within 5 years was assessed and compared to the risk of polyp-free individuals using multilevel cox regression analysis. Secondly, endoscopists adenoma detection rate (ADRs) was categorized in tertiles to assess their impact on PCCRC-risk.

RESULTS

In total 21.522 individuals with ≥10mm polyps and 68.688 individuals without polyps were included, having 21 and 108 PCCRCs within 5 years respectively. Individuals with ≥10mm polyps at baseline colonoscopy showed comparable risk of PCCRC as polyp-free individuals (HR 0.67; CI95% 0.42-1.07); PCCRC incidence was 3.07 (CI95% 1.76-4.38) and 5.02 (CI 95% 4.08-5.97) per 10.000 person-years of follow up (PYFU) respectively. Among individuals with ≥10mm polyps, incidence was 0.93 PYFU (CI95% 0.66-2.23) when scoped by endoscopists with high ADRs.

CONCLUSIONS

Individuals with polyps ≥10mm without other high-risk features showed a low PCCRC-risk within 5 years, comparable to polyp-free individuals. These findings challenge current strict surveillance advice for individuals with polyps ≥10mm without other high-risk features, particularly for those scoped by endoscopists with high ADRs.

ABSTRACT NO.04

AI-POWERED HYPERSPECTRAL IMAGING FOR EARLY DETECTION OF SKIN CANCER

Mark Witteveen[1], Nicole Kukutsch[1], Elsemieke Plasmeijer[1,2], Remco van Doorn[2], Theo Ruers[1], Behdad Dashtbozorg[1]

[1]Center for Early Cancer Detection, Netherlands Cancer Institute (NKI), Plesmanlaan 121, 1066CX Amsterdam
[2]Melanoma Center, Leiden University Medical Center (LUMC), Albinusdreef 2, 2333 ZA Leiden

In the Netherlands, 70,000 people are diagnosed with skin cancer each year, accounting for over half of all cancer cases, with numbers expected to rise due to an aging population and increased UV exposure[1]. Melanoma, the deadliest form, has a rising mortality rate of 2.35% per year (1990–2023)[2], and intensified screening would further strain the healthcare system, particularly well-trained dermatologists.

Early skin cancer can reduce unnecessary biopsies, wait times, stress, and healthcare costs while easing system pressure. A 2024 study[3] in the Netherlands found dermal therapists correctly diagnosed pigmented skin lesions 63% of the time and GPs 73%, highlighting the need for improved early detection tools at first line of contact.

Hyperspectral imaging (HSI) technology has the ability to differentiate between malignant and healthy tissue when combined with AI[4-6]. This method holds significant promise due to its rapid processing, non-contact nature, and the absence of required contrast agents. Hyperspectral images are captured using specialized cameras, which can capture light reflectance over a much broader spectral range beyond the three primary colors of the RGB spectrum and human vision range. However, the implementation of HSI in clinical practice faces several challenges, including the size, complexity, and costs of conventional HSI systems.

To address these challenges, within the NKI Centre for Early Cancer Detection, in collaboration with Melanoma Center at LUMC, we are developing a small, portable, and affordable HSI device. This device could function as a phone clip-on for the early detection of skin cancer. Within this study, we are working on collecting HSI data from a large patient population (over 1000 patients) to identify key wavelengths and radiomic features using AI. We will use these features in combination with a custom light source that captures small surface differences between healthy and malignant skin to build a smaller, more accessible AI-powered HSI device that can significantly enhance the reach and impact of skin cancer diagnostics.

[1]K Thoonen, A van Dijk, and W Hagens. "Advies aan VWS over de inhoud van een voorlichtingscampagne over huidkanker". In: RIVM rapport 2022- 0063 (2022).

[2]World Bank. Population, total - Netherlands, 1960 - 2023.

[3]Amber H.J. Barten et al. The effect of a dermoscopy training programme on diagnostic accuracy and management decisions regarding pigmented skin lesions: a comparison between dermal therapists and general practitioners.

[4]Guolan Lu and Baowei Fei. "Medical hyperspectral imaging: a review". In: Journal of Biomedical Optics 19.1 (Jan. 2014), p. 010901. issn: 1083-3668.

[5]Thomas Haugland Johansen et al. "Recent advances in hyperspectral imaging for melanoma detection". In: Wiley Interdisciplinary Reviews: Computational Statistics 12.1 (Jan. 2020), e1465. issn: 1939-0068.

[6]Hung Yi Huang et al. "A Review of Recent Advances in Computer-Aided Detection Methods Using Hyperspectral Imaging Engineering to Detect Skin Cancer". In: Cancers 15.23 (Dec. 2023), p. 5634. issn: 20726694.

ABSTRACT NO.05

VARIABILITY IN PI-RADS SCORING ON PROSTATE MRI: INTEROBSERVER AGREEMENT IN A PROSTATE CANCER NETWORK

Sanne Westerhout[1], Marias Hagens[2], Thierry Boellaard[3], Stijn Heijmink[3], Laura Mertens[2], Bart de Wit[4], Anne van Geel[4], Remy Geenen[4], Eveline Krul[5], Rinze Reinhard[5], Jan Peringa[5], Garmt van der Horn[6], Dennis de Putter[6], Gerwin Fransen[7], Steven Kerssemakers[7], François van Hoorn[7], Jeroen Tielbeek[8], Margot Henebiens[8], Merel Scheurkogel[9], Chris Bangma[1], Henk van der Poel[2,11], Monique Roobol[1], Pim van Leeuwen[2], Ivo Schoots[3,10]

[1]Department of Urology, Erasmus MC Cancer Institute, Erasmus University Medical Centre, Rotterdam, The Netherlands
[2]Department of Urology, Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands
[3]Department of Radiology, Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands
[4]Department of Radiology, Northwest Clinics, Alkmaar, The Netherlands
[5]Department of Radiology, OLVG, Amsterdam, The Netherlands
[6]Department of Radiology, St Jansdal, Harderwijk, The Netherlands
[7]Department of Radiology, Zaans Medisch Centrum, Zaandam, The Netherlands
[8]Department of Radiology, Spaarne Gasthuis, Hoofddorp, The Netherlands
[9]Department of Radiology, Dijklander Hospital, Hoorn, The Netherlands
[10]Department of Radiology, Erasmus MC Cancer Institute, Erasmus University Medical Centre, Rotterdam, The Netherlands
[11]Department of Urology, Amsterdam University Medical Centers, Amsterdam, The Netherlands

BACKGROUND

Interobserver variability in pre-biopsy PI-RADS assessment among radiologists could affect clinical biopsy decisions in men with suspected prostate cancer (PCa). As part of a quality assessment program within a prostate cancer network involving 11 participating medical centers, we evaluated the interobserver agreement between initial MRI assessments and centralized, secondary MRI readings in referred men.

METHODS

Retrospectively, 607 pre-biopsy prostate MRI scans (PI-RADS 3-5) were included from men who had been referred for second opinion, treatment, or biopsies (January 2018 to December 2020). Initially read by radiologists at one of the 11 centers, all scans were centrally read again by a urogenital radiologist using PI-RADS v2.1, unblinded to the original reports and biopsy results. The highest PI-RADS score per scan was compared to the initial highest score and categorized as concordant, upgraded (central review higher than initial score), or downgraded (lower than initial score). Interobserver agreement for each medical center was calculated using Cohen's weighted kappa (κ).

RESULTS

PI-RADS scores were concordant in 75% (457/607, 95% CI: 72-79%), downgraded in 8.4% (51/607, 95% CI: 6.4-11%), and upgraded in 16% (99/607, 95% CI 14-19%). Among the downgraded cases, 19 of 51 (37%) were reduced to a PI-RADS score of two or lower. The averaged interobserver agreement between central and original reading was moderate (κ = 0.56). Interobserver agreement was very good (range 0.81-0.90) in 1/11 centers, substantial (0.61-0.80) in 4/11, moderate (0.41-0.60) in 4/11, and minimal (0.21-0.40) in 2/11 (Figure 1).

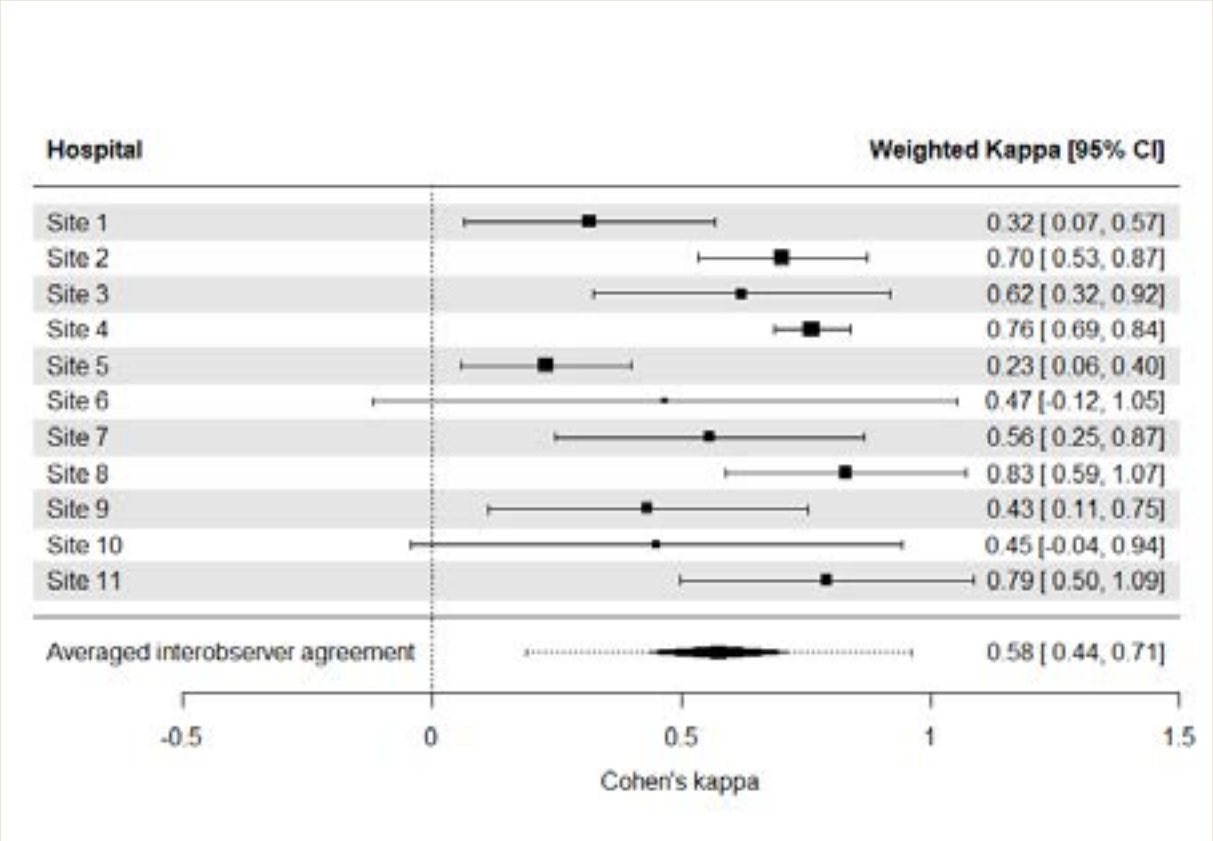


Figure 1. *Forest plot with Cohen's kappa estimates for PI-RADS interobserver agreement across 11 medical centers. CI: confidence interval.*

CONCLUSION

Compared to initial assessments, centralized secondary MRI assessment showed significant variability in PI-RADS scoring, which may influence biopsy decisions. To enhance equity in the PCa diagnostic pathway, a prospective multicenter study will begin in 2025 to investigate whether AI-assisted MRI assessment reduces interobserver variability.

ABSTRACT NO.06

IMPACT OF PSA VARIATION ON PROSTATE MRI OUTCOME IN MEN WITH CLINICALLY SUSPECTED PROSTATE CANCER

Sanne Westerhout[1], Marias Hagens[2], Sebastiaan Remmers[1], Nanne Aben[3], Laura Mertens[2], Chris Bangma[1], Thierry Boellaard[4], Ivo Schoots[1,5], Monique Roobol[1], Pim van Leeuwen[2]

[1]*Department of Urology, Erasmus MC Cancer Institute, University Medical Center Rotterdam, Rotterdam, The Netherlands*
[2]*Department of Urology, Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands*
[3]*Kaiko, Amsterdam, The Netherlands*
[4]*Department of Radiology, Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands*
[5]*Department of Radiology, Erasmus MC Cancer Institute, Erasmus University Medical Centre, Rotterdam, The Netherlands*

BACKGROUND
Risk-based patient selection for MRI and biopsy in prostate cancer (PCa) diagnostics has been adopted in daily practice; however, it is generally based on a solitary elevated prostate-specific antigen (PSA) level. We analyzed the impact of PSA variation after a repeat PSA test on prostate MRI outcomes.

METHODS
This prospective registry (May 2022 to July 2024) enrolled men undergoing prostate MRI with a clinical suspicion of PCa based on PSA levels (PSA1) between 3.0-20 ng/mL. A repeat PSA test (PSA2) was obtained within 6-8 weeks. All men underwent digital rectal examination (DRE), transrectal ultrasound and prostate MRI. Two radiologists evaluated the MRIs according to PI-RADS v2.1: PI-RADS 3 to 5 was considered positive. Men were classified into three PSA-variation groups: increased PSA (>10% rise in PSA2), decreased PSA (>10% decline in PSA2), and stable PSA (variation within 10%). Multivariable logistic regression was performed predicting a positive MRI using abnormal DRE, prostate volume, previous negative biopsies, PSA1, and PSA variation.

RESULTS
429 patients were included, in which PSA2 was stable in 48% (204/429), increased in 22% (94/429), and decreased in 30% (128/429). The median PSA1 was 7.1 (IQR 5.1-11) and PSA2 7.0 (IQR 4.7-10). Men with a decreased PSA had fewer positive MRIs compared to those with stable or increased PSA (Table 1). Multivariable logistic regression showed that a decreased PSA was associated with a statistically significantly lower risk of a positive MRI compared to a stable PSA (OR: 0.32, 95% CI 0.19-0.53).

Table 1. *Number of men with a negative (PIRADS 1-2 lesion) or a positive MRI (PIRADS 3-5 lesion), based on PSA variation*

	NEGATIVE MRI (PI-RADS 1-2)	POSITIVE MRI (PI-RADS 3-5)
PSA INCREASED >10% (N=94)	22 (23%)	72 (77%)
STABLE PSA (N=204)	41 (20%)	163 (80%)
PSA DECREASED >10% (N=131)	55 (42%)	76 (58%)

CONCLUSIONS
In more than 50% of men with an initially elevated PSA level, repeat PSA testing within 6-8 weeks shows a change greater than 10%. A decrease of >10% was associated with a lower risk of a positive MRI. A standard repeat PSA test is a low-invasive and inexpensive way to avoid unnecessary additional investigations.

ABSTRACT NO.07

MORE EFFECTIVE USE OF FIT-BASED SCREENING FOR PREVENTING EARLY-ONSET COLORECTAL CANCER: A SIMULATION STUDY FOR GERMANY

Dmitry Sergeev[1], Thomas Heisser[1], Michael Hoffmeister[1], Hermann Brenner[1]

[1]*Clinical Epidemiology and Aging Research DKFZ, Heidelberg, Germany*

BACKGROUND & AIMS

The optimal starting age and frequency for colorectal cancer (CRC) screening remain uncertain, in particular in times of increasing incidence of early-onset CRC. In Germany, screening by fecal immunochemical tests (FIT) has been offered annually between 50 and 54 years, followed by biennial FIT or colonoscopy (CS) every 10 years starting at age 55. We aimed to explore benefits of switching from annual FIT screening between 50 and 54 years to biennial screening between 45 and 53 years.

METHODS

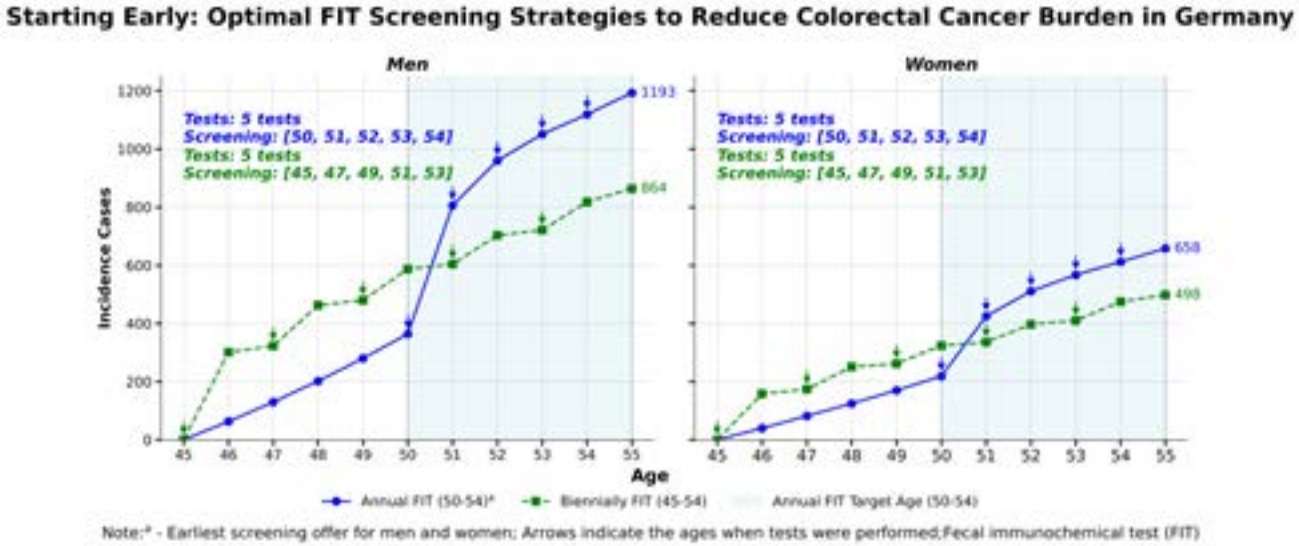
This study simulated hypothetical cohorts of 100,000 men and women followed from age 45 to 55 with respect to CRC incidence using COSIMO, a validated Markov-based multi-state simulation model.

RESULTS

Switching from annual FIT based screening between 50 and 54 years to biennial screening between 45 to 53 (5 FITs in total for each strategy) reduced cumulative incidence between 45 and 55 years of age by 28 % and mortality by 47% among men. For women, reductions were 24% and 48%, respectively.

DISCUSSION

Switching from annual FIT based screening between 50 and 54 years to biennial screening between 45 to 53 may substantially lower the burden of early-onset CRC in Germany without increasing the numbers of screening tests.



ABSTRACT NO.08

EXPLORING PATIENTS' VIEWS ON A POTENTIALLY MORE ACTIVE ROLE FOR ALLIED HEALTHCARE PROFESSIONALS IN THE IDENTIFICATION OF SUSPICIOUS SKIN LESIONS: AN IN- DEPTH QUALITATIVE STUDY

J Singh, PhD[1,2], JC Korevaar, PhD[2], K Houten, MSc[1], R Drie, MSc[2], MFR Vondenhoff, PhD[2], TEC Nijsten, MD PhD[1], R van den Bos, MD PhD[1], M Lugtenberg, PhD[1,3]

[1]*Department of Dermatology, Erasmus MC Cancer Institute, University Medical Centre Rotterdam, The Netherlands*
[2]*Oncological Care Research Group, The Hague University of Applied Sciences, The Hague, The Netherlands*
[3]*Department Tranzo, Tilburg School of Social and Behavioral Sciences, Tilburg University, Tilburg, The Netherlands*

BACKGROUND
The global incidence of skin cancer is alarmingly high and continues to rise, imposing a substantial burden on healthcare systems. Early detection of suspicious skin lesions is essential to alleviate healthcare burdens and improve patient outcomes. Allied Healthcare Professionals (AHPs), regularly exposed to patients' skin, offer an opportunity to enhance early detection efforts, although patient perceptions remain unclear.

AIM
This study aims to explore patients' views on a potential more active role for allied healthcare professionals (AHPs) in the identification of suspicious skin lesions.

METHODS
A qualitative study was conducted, comprising four focus groups with a total of 25 participants. Patients were eligible if they received consultation for a suspicious skin lesion within the past five years. Purposive sampling was used to ensure a diverse sample in gender, age, type of healthcare request sought, diagnostic outcomes, and proficiency in digital health. The focus groups were semi-structured, guided by a topic guide, and moderated by experienced researchers. All sessions were transcribed verbatim and analyzed using inductive thematic content analysis, incorporating principles of grounded theory.

RESULTS
Patients generally expressed support for a more active role of AHPs, emphasizing that it should remain advisory and depend on AHPs' educational background. Several key benefits, barriers, facilitators, and risks were identified. Benefits included increased patient awareness, encouragement of self-examinations, and reduced burden on skin cancer care services. Barriers included concerns about AHPs' skin cancer-related knowledge and capabilities, accessibility challenges, and uncertainty regarding their motivation to fulfill this role. Essential facilitators included adequate training, adherence to professional standards, increased collaboration with physicians, and performance monitoring, potentially through eHealth tools. Risks involved incorrect diagnoses and exclusion of certain subpopulations.

CONCLUSION
While patients are generally positive towards an advisory role for AHPs, significant barriers and potential risks must first be addressed. Successful implementation requires prioritizing training, supervision, and performance monitoring, possibly through eHealth tools.

ABSTRACT NO.09

SUPERSENSITIVE AND ROBUST DISEASE MONITORING IN OROPHARYNGEAL CANCER PATIENTS BY CIRCULATING TUMOR HPV-DNA SEQUENCING

A. S. Pierik[1,2], J. B. Poell[1,2], A. Brink[1,2], M. Stigter- van Walsum[1,2], F. Jansen[1,3], R. de Bree[4], J. Hardillo[5], J. A. Langendijk[6], R. P. Takes[7], F. Lamers[8,9], I. M. Verdonck-de Leeuw[1,8,9,10], J. J. Hendrickx[1,3], S.A. Koppes[11], C. R. Leemans[1,2,3], R. H. Brakenhoff[1,2]

[1]Amsterdam UMC location Vrije Universiteit Amsterdam, Otolaryngology/Head and Neck Surgery, De Boelelaan 1117, Amsterdam, The Netherlands
[2]Cancer Center Amsterdam, Imaging and Biomarkers, Amsterdam, The Netherlands
[3]Cancer Center Amsterdam, Treatment and Quality of Life, Amsterdam, The Netherlands
[4]Department of Head and Neck Surgical Oncology, University Medical Center Utrecht, Utrecht, The Netherlands
[5]Department of Otorhinolaryngology, Erasmus MC Cancer Institute, University Medical Center, Rotterdam, The Netherlands
[6]Department of Radiation Oncology, University Medical Center Groningen, Groningen, The Netherlands
[7]Department of Otorhinolaryngology-Head and Neck Surgery, Radboud University Medical Center, Nijmegen, The Netherlands
[8]Amsterdam UMC location Vrije Universiteit Amsterdam, Psychiatry, Amsterdam, The Netherlands
[9]Amsterdam Public Health, Mental Health, Amsterdam, The Netherlands
[10]Vrije Universiteit Amsterdam, Clinical, Neuro and Developmental Psychology, Van der Boechorststraat 7-9, Amsterdam, The Netherlands.
[11]Department of Pathology, Erasmus MC Cancer Institute, University Medical Center, Rotterdam, The Netherlands

BACKGROUND
In most Western countries oropharyngeal squamous cell carcinoma (OPSCC) is mainly caused by persistent human papillomavirus (HPV) infection. Patients are treated by chemoradiotherapy with good outcomes, but disease monitoring after treatment is a major issue, leading to unnecessary diagnostic and treatment procedures during follow-up. In this study we employed target-enrichment sequencing for detecting circulating tumor HPV DNA (ctHPV-DNA) in liquid biopsies for longitudinal monitoring of patients with HPV-positive OPSCC.

METHODS
The target-enrichment panel included HPV16 and all other high-risk HPV E7 sequences. The assay was tested on plasma from 30 non-cancer controls and 33 patients with HPV-positive tumors, 15 of whom had residual or recurrent disease, and 18 who remained disease-free. Samples were analyzed from baseline up to 24 months after treatment.

RESULTS
Statistical cut-off values to call samples positive or negative were determined at baseline, and ctHPV-DNA was detected in plasma of all patients with HPV-positive OPSCC at baseline and absent in plasma of all non-cancer controls. In OPSCC patients who remained disease-free, follow-up plasma samples stayed negative for ctHPV-DNA. In contrast, ctHPV-DNA was detected in plasma of all OPSCC patients with recurrent disease during follow-up up to a year before clinical diagnosis. Cases with residual disease in the neck that after dissection demonstrated a necrotic lymph node metastasis without vital tumor tested correctly negative for ctHPV-DNA in plasma.

CONCLUSIONS
A robust diagnostic assay was developed using target-enrichment sequencing of plasma, and it shows 100% accurate detection of ctHPV-DNA at baseline. Longitudinal monitoring of OPSCC patients with this diagnostic assay confirmed the excellent performance. At present a national study with 480 patients with HPV-positive OPSCC is performed to implement plasma ctHPV-DNA profiling by sequencing in clinical care and compare test characteristics with digital droplet PCR.

ABSTRACT NO.10

PRE-ANALYTICAL CHALLENGES PREVENT CLINICAL TRANSLATION OF BLOOD-BASED BIOMARKERS

Pieter H.A. Wisse[1,2], Carmen Rubio-Alarcón[1], Suzanna J. Schraa[3], Adria C. Mosquera[1], Mark Sausen[4], Remond J.A. Fijneman[1], Geraldine R. Vink[3,5], Meike de Wit[1], Jillian Phallen[6], Victor E. Velculescu[6], Beatriz Carvalho[1], Gerrit A. Meijer[1]

[1]*Department of Pathology, Netherlands Cancer Institute, Amsterdam, the Netherlands*
[2]*Department of Gastroenterology and Hepatology, Erasmus University Medical Center, Rotterdam, the Netherlands*
[3]*Department of Medical Oncology, University Medical Center Utrecht, Utrecht University Utrecht, the Netherlands*
[4]*Personal Genome Diagnostics (Labcorp), Baltimore, USA*
[5]*Department of research and development, Netherlands Comprehensive Cancer Organisation, Utrecht, the Netherlands*
[6]*The Sidney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, USA*

BACKGROUND
The fecal immunochemical test (FIT) is widely used in colorectal cancer (CRC) screening. Recently, circulating tumor DNA (ctDNA) detection through liquid biopsy has emerged as a new early detection method. Comparison of performance of these two types of test is largely unknown. This exploratory study compared pre-operative ctDNA results with FIT results in CRC patients who had participated in a population-based screening program.

METHODS
Participants from two ctDNA minimal residual disease (MRD) studies, PLCRC-MEDOCC and PLCRC-PROVENC3, were matched with the Dutch national CRC screening program database to retrieve their most recent FIT results. The study assessed concordance and complementarity between tumor-informed next-generation sequencing-based ctDNA tests and FIT results.

RESULTS
Among 120 CRC patients identified, 3 had stage I (2.5%), 57 had stage II (47.5%), and 60 had stage III (50.0%) CRC. At a 20 µg/g threshold, FIT was positive in 83.3% (100/120) of patients. The pre-surgery ctDNA test was positive in 75.8% (91/120) of cases. Concordance between the two tests was 60% (72/120), while nearly all patients (99.2%, 119/120) tested positive in at least one of the two modalities.

CONCLUSIONS
This study found that FIT and ctDNA testing were frequently positive in CRC patients, with both tests demonstrating concordance and complementarity. The findings suggest that combining FIT with ctDNA testing could improve CRC screening sensitivity. However, the study's ctDNA tests were tumor-informed, which is not feasible in real-world screening programs. It remains unclear how effective non-tumor-informed ctDNA testing would be. Additionally, the study only included CRC patients, limiting insights into false positivity rates for a broader screening population. Further research is needed to assess the real-world applicability of combining FIT and ctDNA testing for CRC screening.

ABSTRACT NO.11

GENOMIC MARKERS FOR RISK ASSESSMENT IN BARRETT'S ESOPHAGUS WITH LOW-GRADE DYSPLASIA

V.Y. Pappalardo[1], P. Stougie[3], N.F. Frei[3] , A.M. Khoshiwal[3], R. Menezes[1], L.C. Duits[3], J.J. Bergman[3], M.D. Stachler[2]

[1]Netherlands Cancer Institute, Antoni van Leeuwenhoek, Biostatistics Centre, Department of Psychosocial and Epidemiological Research,, Amsterdam, The Netherlands
[2]University of California, Department of Pathology, San Francisco, USA
[3]Amsterdam UMC location University of Amsterdam, dept. of Gastroenterology and Hepatology, Amsterdam, The Netherlands

INTRODUCTION
Risk assessment for Barrett's esophagus (BE) primarily relies on histological evaluation of dysplasia, but this approach is often inconsistent and lacks predictive accuracy, especially for low-grade dysplasia (LGD). This retrospective study investigates genomic markers to improve risk stratification in BE patients diagnosed with LGD in a community setting.

METHODS
This analysis included BE patients with a community-based diagnosis of LGD, categorized into progressors to early esophageal adenocarcinoma (EAC) and non-progressors. Genomic alterations, including mutations and copy number variations (CNVs), were identified using targeted sequencing. Likely pathogenic variants were filtered, xand statistical analyses such as logistic regression and mixed-effects models were applied. A joint survival-mixed-effects model was used for spatiotemporal data analysis.

RESULTS
A total of 220 samples were analyzed, consisting of 28 progressors with a median progression time of 1.2 years (IQR 0.4–2.2) and 95 non-progressors with a median progression-free follow-up of 7.9 years (IQR 5.9–10.6). Significant associations with progression included TP53 mutations ($p < 0.0001$, HR = 13.39), 17p chromosomal arm loss ($p < 0.0001$, HR = 10.24), mutational burden ($p < 0.001$, HR = 1.52), and CNV count ($p < 0.0001$, HR = 1.48). Any genetic alteration presence (mutation, amplification, deletion, or CNV) was predictive of progression ($p < 0.0001$, HR = 1.15). A model combining TP53-CNV model achieved 64% sensitivity, 96% specificity, and an AUC of 0.837.

CONCLUSION
This study highlights TP53 mutations and 17p loss as key markers for progression risk in BE patients with LGD, supporting the use of genomic profiling for improved risk stratification. The results were validated in a nested case-control study with an independent cohort.

ABSTRACT NO.12

EARLY DETECTION OF ORAL CANCER AND PREMALIGNANT LESIONS WITH A NON-INVASIVE GENETIC ASSAY

L. Meulenbroeks[1,2], A. Brink[1,2], L.A.N. Peferoen[3,4], E.R.E.A. Brouns[4], R.H. Brakenhoff[1,2], J.B. Poell[1,2]

[1]*Amsterdam UMC, location Vrije Universiteit Amsterdam, Otolaryngology - Head and Neck Surgery, Amsterdam, The Netherlands*
[2]*Cancer Center Amsterdam, Imaging and Biomarkers, Amsterdam, The Netherlands*
[3]*Amsterdam UMC, location Vrije Universiteit Amsterdam, Pathology, Amsterdam, The Netherlands*
[4]*Amsterdam UMC, location Vrije Universiteit Amsterdam, Oral and Maxillofacial Surgery and Oral Pathology, Amsterdam, The Netherlands*

BACKGROUND

Early diagnosis of oral squamous cell carcinoma (OSCC) will improve patient outcomes with less invasive treatment. OSCC is preceded by precancerous mucosal changes, which may remain invisible to the naked eye until malignant progression. However, some precancerous mucosal changes are macroscopically visible, such as oral leukoplakia (OL), a white patch that often harbors cancer-associated genetic alterations. Clinical management of OL encompasses a biopsy for histopathological examination, excision when possible, and regular follow-up visits for watchful surveillance. This study investigates the potential of non-invasive methods for improved detection and monitoring of oral (pre)cancer.

METHODS

Oral rinses and brush samples are prospectively collected from OL patients at baseline and longitudinally. Genetic alterations are identified by low coverage whole genome sequencing and capture-based DNA-sequencing of selected cancer genes.

RESULTS

Sequencing of 41 OL brushes and paired biopsies indicate that brush samples accurately reflect copy number changes and mutations in the tissue biopsies in 85%. We found a remarkably high number of mutations in some oral rinse samples, in reads that appeared to map to other species, indicative of non-human DNA and likely from ingested food. Therefore, we analyzed oral rinse samples from healthy volunteers collected before and after consuming animal products (chicken, pig, cow), and indeed found reads uniquely mapped to the respective genomes (0.26%, 0.21%, 0.17%) after food intake, but not before. Concerningly, non-uniquely mapping reads may appear as human sequences with mutations. False mutation calls were minimized by hybrid genome mapping.

CONCLUSIONS

We will further explore the promising potential of oral rinses and brush samples for early detection of oral (pre)cancer and comprehensive oral cavity mucosa surveillance. Food ingestion with animal products causes animal DNA contamination in oral rinse samples, which needs to be analyzed in an adjusted data-mining strategy.

ABSTRACT NO.13

POLYGENIC SCORE FOR BREAST CANCER RISK PREDICTION IN ASIAN BRCA1 AND BRCA2 PATHOGENIC VARIANTS CARRIERS

Mei-Chee Tai[1], Joe Dennis[2], Sue Kyung Park[3,4,5], Sung-Won Kim[6], Jong Won Lee[7], Nur Tiara Hassan[1], Ava Kwong[8,9,10], Mikael Hartman[11,12,13], Sook-Yee Yoon[1], Joanne Yuen Yie Ngeow[14,15], Yin-Ling Woo[16], Boyoung Park[17], Zhi-Lei Wong[1], Goska Leslie[2], Manjeet K. Bolla[2], Daniel R. Barnes[2], Michael T. Parsons[18], Penny Soucy[19], Jacques Simard[19], Nur Aishah Mohd Taib[20,21], Cheng-Har Yip[22], Douglas F. Easton[2,23], Georgia Chenevix-Trench[24], Antonis C. Antoniou[2], Soo-Hwang Teo[1,20,*], Weang-Kee Ho[1,25,*]

[1]*Cancer Research Malaysia, Selangor, Malaysia*
[2]*Centre for Cancer Genetic Epidemiology, Department of Public Health and Primary Care, University of Cambridge, Cambridge, UK*
[3]*Department of Preventive Medicine, Seoul National University College of Medicine, Seoul, Korea*
[4]*Cancer Research Institute, Seoul National University, Seoul, Korea*
[5]*Integrated Major in Innovative Medical Science, Seoul National University College of Medicine, Seoul, Korea*
[6]*Department of Surgery, Daerim St. Mary's Hospital, Seoul, Korea*
[7]*Department of Surgery, Ulsan College of Medicine and Asan Medical Center, Seoul, Korea*
[8]*Hong Kong Hereditary Breast Cancer Family Registry, Cancer Genetics Centre, Hong Kong*
[9]*Department of Surgery, The University of Hong Kong, Hong Kong*
[10]*Department of Surgery, Hong Kong Sanatorium and Hospital, Hong Kong*
[11]*Department of Surgery, National University Hospital and National University Health System, Singapore;*
[12]*Department of Surgery, Yong Loo Lin School of Medicine, National University of Singapore and National University Health System, Singapore*
[13]*Saw Swee Hock School of Public Health, National University of Singapore and National University Health System, Singapore*
[14]*Cancer Genetics Service, National Cancer Centre Singapore, Singapore*
[15]*Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore, Singapore*
[16]*Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia*
[17]*Department of Preventive Medicine, Hanyang University College of Medicine, Hanyang University Korea, Seoul, Korea*
[18]*Public Health Division, QIMR Berghofer Medical Research Institute, Brisbane, Queensland, Australia*
[19]*Genomics Center, CHU de Québec-Université Laval Research Center, Québec, Canada*
[20]*Department of Surgery, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia*
[21]*University Malaya Cancer Research Institute, University of Malaya, Kuala Lumpur, Malaysia*
[22]*Sime Darby Medical Centre, Selangor, Malaysia*
[23]*Centre for Cancer Genetic Epidemiology, Department of Oncology, University of Cambridge, Cambridge, UK*
[24]*Department of Haematology-Oncology, University of Adelaide, The Queen Elizabeth Hospital, Australia*
[25]*Faculty of Science and Engineering, University of Nottingham Malaysia, Selangor, Malaysia.*

BACKGROUND

Polygenic scores (PGS) have been shown to be predictive of breast cancer risk and to enable personalised clinical management in European BRCA1 and BRCA2 pathogenic variant (PV) carriers, but their utility in Asian populations has not been evaluated. In this study, we aimed to evaluate the utility of existing PGS in predicting breast cancer risk in BRCA1 and BRCA2 PV carriers of Asian ancestry.

METHODS

Using weighted Cox regression analyses adjusted for birth cohort and ancestry principal components, we evaluated the association of two breast cancer PGS developed for the East Asian general population (331 single-nucleotide polymorphisms (SNPs) and ~1million SNPs and three versions of a PGS developed for the European general population (313SNPs with different weight) on breast cancer risk in 604 BRCA1 (390 affected by breast cancer) and 785 BRCA2 (552 affected by breast cancer) PV carriers of self-reported Asian ancestry from Malaysia, Singapore, Hong Kong and Korea.

RESULTS

Only the Asian-based PGS, constructed using approximately one million SNPs, showed a significant association with breast cancer risk (Hazard Ratio (HR) per standard deviation (95% Confidence Interval (CI) is 1.47 (1.10-1.95) for BRCA1 and 1.43 (1.04-1.95) for BRCA2). Consistent with findings in the general population, this PGS exhibited a stronger association compared with the European ancestry derived PGS, albeit with lower HR estimates than those observed in the general population (1.43 - 1.47 vs 1.62).

CONCLUSIONS

A PGS optimised for the Asian population was associated with breast cancer risk among Asian BRCA1 and BRCA2 PV carriers. Incorporating this PGS into risk prediction models may improve cancer risk assessment among Asian ancestry PV carriers. study investigates the potential of non-invasive methods for improved detection and monitoring of oral (pre)cancer.

ABSTRACT NO.14

IMAGED-BASED CONSENSUS MOLECULAR SUBTYPES AND COLON CANCER RECURRENCE

Evertine Wesselink[1,2], Dieuwertje E. Kok[1], Maxime W. Lafarge[3,4], imCMS consortium, Anne-Sophie van Lanen[1], Iris D. Nagtegaal[5], Miriam Koopman[6], Ellen Kampman[1], Viktor H. Kölzer[3,4], Anne M. May[7,8] and Fränzel J.B. van Duijnhoven[1]

[1]Division of Human Nutrition and Health, Wageningen University & Research, Wageningen, the Netherlands
[2]Division of Molecular Pathology, The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands.
[3]Institute of Medical Genetics and Pathology, University Hospital Basel, Basel, Switzerland
[4]Computational and Translational Pathology Lab, Department of Biomedical Engineering, Faculty of Medicine, University of Basel, Allschwil, Switzerland
[5]Department of Pathology, Radboud University Medical Center, University of Nijmegen, Nijmegen, The Netherlands
[6]Department of Medical Oncology, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands
[7]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht University, Utrecht, The Netherlands
[8]Division of Psychosocial Research & Epidemiology, The Netherlands Cancer Institute – Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands.

BACKGROUND

Survival of patients with colon cancer differs by Consensus Molecular Subtypes (CMS). These findings highlight the prognostic value of CMS, but its association with recurrence remains largely unexplored.

METHODS

A nested case-control study was implemented in two prospective cohort studies of colon cancer patients. Participants who developed a recurrence were included as cases (n=167). Matched controls (n=668) were selected based on incidence density sampling. Whole Slide images (WSIs) of standard haematoxylin and eosin-stained sections of formalin-fixed paraffin-embedded tumour specimens were used to infer image-based CMS calls (imCMS). Tumour and microenvironment regions in each WSI were annotated by a team of trained annotators. All the annotated regions were sampled in overlapping image tiles. An externally trained and validated deep learning model (imCMSv1.5) was used to compute imCMS probability scores for each tile. For each slide, an overall imCMS call was assigned as the class with the highest probability score after averaging all its tile-level scores. Associations between imCMS and recurrence were investigated using multivariable conditional logistic regression analyses.

RESULTS

imCMS2 (37%) was most common, followed by imCMS4 (18%), imCMS1 (18%), imCMS3 (16%) and mixed (12%). Patients with an imCMS4 compared to those with an imCMS2 tumour had a higher risk of recurrence (IRR 2.02 95%CI 1.15; 3.55). Compared to imCMS2, no differences in recurrence risk were observed for imCMS1 (IRR 1.38 95%CI 0.76-2.52) and imCMS3 (IRR 1.61 95%CI 0.89-2.90). In a sensitivity analyses we selected tumours in which the imCMS could be predicted with a more than 50% certainty, retaining 416 of 655 observations. Slightly stronger associations were observed, for example IRR 2.27 95%CI 1.14-4.50 for imCMS4 compared to imCMS2.

CONCLUSIONS

Patients with an imCMS4 tumour had the highest risk of recurrence. This finding suggests that these patients may benefit from enhanced surveillance strategies to facilitate early detection of recurrent disease.

ABSTRACT NO.15

RISK-ADAPTED LUNG CANCER SCREENING STARTING AGES FOR FORMER SMOKERS

Clara Frick[1,2*] MSc, Megha Bhardwaj[1] PhD, Prof. Ben Schöttker[1] PhD, and Prof. Hermann Brennera,[3] MD

[1]Division of Clinical Epidemiology and Aging Research, German Cancer Research Center (DKFZ), Im Neuenheimer Feld 581, 69120 Heidelberg, Germany
[2]Heidelberg Medical Faculty, Heidelberg University, Im Neuenheimer Feld 672, 69120 Heidelberg, Germany
[3]German Cancer Consortium (DKTK), German Cancer Research Center (DKFZ), Im Neuenheimer Feld 280, 69120 Heidelberg, Germany

BACKGROUND

The US Preventive Services Task Force (USPSTF) recommends lung cancer screening for individuals aged 50–80 with ≥20 pack-years of smoking and ≤15 quit-years. This implies that former heavy smokers with ≥20 pack-years would either be offered screening from age 50 onwards or not at all, depending on a dichotomous classification by time since cessation. An alternative strategy that would better match individual risks could be to define risk-adapted starting ages of screening, according to time since cessation.

METHODS

Based on data from the UK Biobank cohort, we assessed the relationship between smoking cessation time, pack-years, age, and lung cancer risk among ever heavy smokers using multivariable Cox proportional hazards models. We estimated "risk postponement periods" (RPPs) from the regression coefficients for the time since cessation and age and used these RPP estimates to derive risk-adapted starting ages for lung cancer screening among former heavy smokers, using 50 years as the reference starting age for current heavy smokers.

RESULTS

The RPPs for smoking cessation ranged from 3.1 (95% CI 1.7, 4.5) years for former heavy smokers who quit 6-10 years ago to 14.6 (95% CI 13.0, 16.3) years for former heavy smokers who quit more than 15 years ago, which translate to risk-adapted starting ages of screening between 53 and 65 years.

CONCLUSIONS

Our analysis provides an empirical basis for risk-adapted starting ages of lung cancer screening among former heavy smokers.

ABSTRACT NO.16

AI-GUIDED TRANSABDOMINAL ULTRASOUND FOR EARLY PROSTATE CANCER RISK STRATIFICATION

Liza M. Kurucz, Tiziano Natali, Theo Ruers, Behdad Dashtbozorg, Pim van Leeuwen, Laura Mertens

Center for Early Cancer Detection, Netherlands Cancer Institute, Plesmanlaan 121, 1066CX Amsterdam

The prostate volume (PV) is essential for determining prostate-specific antigen (PSA) density, key for prostate cancer (PCa) risk stratification. Traditionally, transrectal ultrasound (TRUS) is used to estimate the PV manually by measuring the prostate diameters, utilizing the Ellipsoid Formula. However, TRUS involves an invasive rectal examination, causing patient discomfort.

Transabdominal ultrasound (TAUS) offers a patient-friendly alternative for PV estimation and is generally more accessible, potentially enhancing PCa risk stratification workflows by enabling PSA density measurement in primary care, reducing unnecessary referrals. Nevertheless, TAUS imaging can be challenging due to reduced prostate visibility, requiring proper training in TAUS examination and image interpretation.

To address these challenges, we developed a real-time prostate detection system[1] combined with a framework for automatic PV estimation[2]. This system employs deep learning models to detect, segment and extract the prostate area on plane-specific TAUS images, and an algorithm to extract the prostate diameters, enabling automatic PV calculation.

During this study, TAUS acquisitions from 118 participants with an average PV of 61.1 ± 33.7 mL were collected, with MRI-reference volume measurements. An expert annotated the prostate boundaries on TAUS, providing ground truth data. The dataset was divided into a training set and a test set to evaluate the performance of the system on unseen data.

When we compared the predicted PV estimations from the TAUS test set using the trained model to the MRI-reference measurements, we observed an average volume difference of 7.2 ± 15.9 mL, achieving a relative volume difference of ≤ 25% in 79% of the cases.

These results demonstrate the feasibility of using TAUS for automated PV measurements. The combination of live prostate guidance and automated PV prediction facilitates straightforward and robust PSA density measurements at the early diagnostic stage. This advancement in TAUS technology could significantly enhance patient comfort and streamline diagnostic workflows in primary care settings.

[1]Natali, Tiziano, Mark Wijkhuizen, Liza Kurucz, Matteo Fusaglia, Pim J. van Leeuwen, Theo JM Ruers, and Behdad Dashtbozorg. "Automatic real-time prostate detection in transabdominal ultrasound images." In Medical Imaging with Deep Learning. 2024.

[2]Natali, Tiziano, Liza M. Kurucz, Matteo Fusaglia, Laura S. Mertens, Theo JM Ruers, Pim J. van Leeuwen, and Behdad Dashtbozorg. "Automatic Prostate Volume Estimation in Transabdominal Ultrasound Images." arXiv preprint arXiv:2502.07859 (2025).

ABSTRACT NO.17

DEEP PLASMA PROTEOME PROFILING VIA PHOSPHATIDYLCHOLINE-NANOPARTICLE TECHNOLOGY FOR BIOMARKER DISCOVERY

Amir Ata Saei and Morteza Mahmoudi

Department of Microbiology, Tumor and Cell Biology, Karolinska Institute, Stockholm, Sweden

BACKGROUND

Plasma is a valuable source of biomarkers essential for monitoring health and disease progression. However, the identification of novel biomarkers remains challenging due to the dominance of high-abundance proteins, such as albumin, which overshadow low-abundance proteins in mass spectrometry-based proteomics analyses. Conventional methods for depleting such dominant proteins are often costly, and impractical for large-scale applications.

METHODS

We have invented a novel approach to enhance plasma proteome profiling using a natural small molecule, phosphatidylcholine, in combination with a single nanoparticle. We leverage the specific interaction of phosphatidylcholine with plasma albumin to efficiently and reproducibly deplete this high abundant protein from plasma and fish the low-abundance proteins using a single nanoparticle type.

RESULTS

This strategy allows for a more comprehensive analysis of the plasma proteome. Utilizing this patented technology, we successfully quantified 1,450 proteins from a single plasma sample, significantly increasing the depth of detection compared to traditional methods. We are currently applying this approach to identify biomarkers for early detection of various cancers and other diseases.

CONCLUSIONS

This advancement holds great potential for the early detection of cancer. The improved sensitivity and scalability of this method could facilitate breakthroughs in diagnostic research and precision medicine, offering new avenues for early intervention and treatment.

Ashkarran AA, Gharibi H, Sadeghi SA, Modaresi SM, Wang Q, Lin TJ, Yerima G, Tamadon A, Sayadi M, Jafari M, Lin Z, Ritz D, Khakhniashvili D, Guha A, Mofrad MRK, Sun L, Landry MP, Saei AA*, Mahmoudi AA*. 2024. Small molecule modulation of protein corona for deep plasma proteome profiling. Nature Communications [corresponding author].

Gharibi H, Ashkarran AA, Jafari M, Voke E, Landry MP, Saei AA*, Mahmoudi M*. 2024. A uniform data processing pipeline enables harmonized nanoparticle protein corona analysis across proteomics core facilities. Nature Communications [corresponding author].

Ashkarran AA, Gharibi H, Voke E, Landry MP, Saei AA*, Mahmoudi M*. 2022. Measurements of heterogeneity in proteomics analysis of the nanoparticle protein corona across core facilities. Nature Communications. 6610 [corresponding author].

ABSTRACT NO.18

CLINICAL PERFORMANCE OF *ASCL1/LHX8* DNA METHYLATION ON FIRST-VOID URINE: FULLY MOLECULAR CERVICAL CANCER SCREENING FOR USER-FRIENDLY SAMPLES

Severien Van Keer[1], Rianne van den Helder[2,3], Laura Téblick[1], Annemie De Smet[1], Gilbert Donders[4,5,6], Steven Weyers[7], Jean Doyen[8], Nienke van Trommel[3], Constantijne H Mom[9], Harold Verhoeve[10], Chris JLM Meijer[2], Maaike Bleeker[2], Ann Cornelis[11], Koen Van de Vijver[12], Katty Delbecque[13], Birgit Lissenberg-Witte[14], Alex Vorsters[1], Renske DM Steenbergen[2]

[1]Centre for the Evaluation of Vaccination (CEV), Vaccine & Infectious Disease Institute (VAXINFECTIO), Faculty of Medicine and Health Sciences, University of Antwerp, Edegem, Belgium
[2]Department of Pathology, location VUMC, and Cancer Center Amsterdam, Imaging and Biomarkers, Amsterdam University Medical Center, Amsterdam, The Netherlands
[3]Center for Gynecologic Oncology Amsterdam, location Het Nederlands Kanker Instituut, Antoni Van Leeuwenhoek, Amsterdam, The Netherlands
[4]Department of Obstetrics and Gynaecology, General Regional Hospital Heilig Hart, Tienen, Belgium
[5]Femicare vzw, Clinical Research for Women, Tienen, Belgium
[6]Department of Obstetrics and Gynaecology, Antwerp University Hospital (UZA), Edegem, Belgium
[7]Department of Obstetrics and Gynecology, Ghent University Hospital, Ghent, Belgium
[8]Department Gynaecology-Obstetrics, University Hospital Liège, Liège, Belgium
[9]Department of Gynaecological Oncology, Cancer Center Amsterdam, Center for Gynaecological Oncology Amsterdam, location VUMC, Amsterdam University Medical Center, Amsterdam, The Netherlands
[10]Gynaecology department, OLVG, Amsterdam, The Netherlands
[11]Department of Pathology, General Regional Hospital Heilig Hart, Tienen, Belgium
[12]Department of Pathology, Ghent University Hospital, Ghent, Belgium
[13]Department of Pathology, University Hospital Liège, Liège, Belgium
[14]Department of Epidemiology and Data Sciences, Amsterdam UMC, Amsterdam, The Netherlands

BACKGROUND/OBJECTIVES

DNA methylation analysis provides a promising triage strategy for cervical intraepithelial neoplasia (CIN) and cervical cancer detection following primary Human Papillomavirus (HPV) testing that could be directly applied on self-collected samples, including urine. This study aimed to develop an entirely molecular cervical screening approach based on HPV and DNA methylation analysis in at-home collected first-void urine.

METHODS

First-void urine samples were collected from healthy females (n=69; METc VUmc 2018.657) and a referral population (n=228/385 <CIN2, n=50/385 CIN2, n=66/385 CIN3, n=41/385 cancer; METc VUmc 2020.020 and NCT04530201). Samples were analyzed for high-risk (hr)HPV DNA and *ASCL1/LHX8* methylation following random allocation to a training (n=285) and validation cohort (n=160). CIN3+ detection was analyzed by multivariate logistic regression.

RESULTS

Methylation levels of *ASCL1* and *LHX8* in first-void urine increased significantly in relation to disease severity. The area under the curve-values for CIN3+ detection by *ASCL1/LHX8* methylation were 0.81 (95% CI: 0.74-0.88) and 0.83 (95% CI: 0.74-0.92) in the training and validation cohort, respectively. This corresponded to a validated CIN3+ sensitivity of 73.0% (95% CI: 57.0-84.6%) at 81.9% specificity (95% CI: 73.5-88.1%; <CIN2). Urinary hrHPV DNA testing was more sensitive (83.8%; 95% CI: 68.9-92.3%) although less specific (59.6%; 95% CI: 50.0-68.5%). For triage of hrHPV positives, *ASCL1/LHX8* methylation and HPV16/18 genotyping had

a similar CIN3+ sensitivity (75.0%; 95% CI: 62.8-84.2% vs 73.3%; 95% CI: 61.0-82.9%), with lower genotyping specificity. Combining *ASCL1/LHX8* methylation with HPV16/18 genotyping yielded a 85.0% sensitivity (95% CI: 73.9-91.9%) at 50.5% specificity (95% CI: 40.8-60.1%).

CONCLUSIONS

The *ASCL1/LHX8* methylation test detected nearly all cancers and a majority of CIN3 in first-void urine, supporting the potential of full molecular screening in urine by primary HPV testing and methylation triage.

ABSTRACT NO.19

EXTERNAL VALIDATION OF THE FULL BLOOD COUNT TRENDS FOR COLORECTAL CANCER DETECTION (BLOODTRACC) RISK PREDICTION MODELS IN ENGLISH PRIMARY CARE

Pradeep S. Virdee[1], Jacqueline Birks[2], Tim Holt[1], Kym Snell[3], Gary Abel[4], Brian D. Nicholson[1]

[1]*Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK*
[2]*Oxford University Hospitals NHS Trust, Oxford, UK*
[3]*Institute of Applied Health Research, University of Birmingham, Birmingham, UK*
[4]*Department of Health and Community Sciences, University of Exeter, Exeter, UK*

BACKGROUND

The majority of colorectal cancers are diagnosed late-stage in the UK. To support earlier diagnosis, we developed the BLOODTRACC model, utilising age, sex, and trends over repeat full blood count (FBC) tests for risk of colorectal cancer. We aimed to externally validate the BLOODTRACC model.

METHODS

We performed a cohort study using primary care patient data between 01/01/2000 and 31/12/2019 from the Clinical Practice Research Datalink AURUM, linked to the National Cancer Registration and Analysis Service. Eligible patients had at least one FBC test and no history of colorectal cancer before their current FBC (baseline). Using historical FBCs over five years prior to the current FBC, trends informed risk of cancer diagnosis in two years. Symptoms and faecal immunochemical test (FIT) results co-occurring with the baseline FBC were extracted. Model performance was assessed using the area under the curve (AUC), calibration statistics, and diagnostic accuracy measures.

RESULTS

We included 6,038,936 patients, with 0.5% (n=31,759) diagnosed with colorectal cancer in two years. Mean (SD) age at baseline FBC was 60.8 (13.5) years for men and 62.2 (15.0) years for women. The AUC (95% CI) of the model was comparable for both men and women (0.75 (0.74-0.75)) and between patients with and without colorectal cancer-related symptoms for both men (with 0.75 (0.73-0.78); without 0.74 (0.74-0.75)) and women (with 0.71 (0.69-0.74); without 0.74 (0.74-0.75)). Combining blood test trend with presence of co-occurring change in bowel habit gave the highest AUC (men 0.81 (0.75-0.87); women 0.76 (0.67-0.85)). The calibration slope (95% CI) was 0.97 (0.95-0.99) for men and 0.98 (0.96-0.99) for women. Performance by FIT results will be presented.

CONCLUSIONS

The BLOODTRACC model identifies patients with undiagnosed colorectal cancer with good discrimination. Further work is underway to enhance model performance and investigate the role of blood test trend for detection of other cancers.

ABSTRACT NO.20

ENHANCING CANCER RISK STRATIFICATION USING BLOOD TESTS IN PATIENTS PRESENTING TO ENGLISH PRIMARY CARE WITH NON-SPECIFIC SYMPTOMS

Pradeep S. Virdee[1], Clare Bankhead[1], Rafael Perera[1], FD Richard Hobbs[1], Brian D. Nicholson[1]

[1]*Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK*

BACKGROUND

Non-specific symptoms (e.g. constipation and nausea) result in diagnostic delays in primary care. Combining blood tests with non-specific symptoms may enhance cancer risk stratification. We conducted a diagnostic accuracy study of blood tests in patients presenting with non-specific symptoms in English primary care.

METHODS

We performed a cohort study using patient data between 01/01/2000 and 31/12/2019 from the Clinical Practice Research Datalink, linked to further databases. The first occurrence of each of 19 non-specific symptoms was selected for inclusion (19 cohorts). Commonly performed blood tests in primary care, such as liver function tests, co-occurring with the symptom (-3 to +1 month) were extracted. The positive predictive value (PPV) for cancer in six months following symptom presentation was derived by age, sex, co-occurring blood test abnormality and symptoms.

RESULTS

Among the 19 cohorts, the sample size ranged from 121,948 (bloating) to 3,432,338 (back pain). Six-month cancer incidence was highest for patients with unexplained weight loss (4.7%, n=15,888) and lowest for back pain (0.7%, n=24,156). Incidence increased with increasing age and was higher for men than women regardless of symptom type. The PPV (95% CI) was higher for patients with a co-occurring blood test abnormality than for patients without for every symptom. For example, appetite loss: without 2.1% (2.0, 2.2), with 6.6 (6.4, 6.8); vomiting: with 3.8% (3.7, 3.9), without 1.3 (1.2, 1.3); weight loss: with 6.2% (6.1, 6.3) without 2.6 (2.5, 2.7). Across cohorts, the PPV increased as the number of co-occurring abnormalities and symptoms increased. Low albumin gave the highest PPV for 13 of the 19 symptom cohorts (range 5.2-15.6%), followed by raised platelets and low mean cell volume. Results will also be presented by cancer site and stage.

CONCLUSIONS

Monitoring blood test abnormalities in primary care patients presenting with symptoms may offer improved risk stratification for cancer diagnosis.

ABSTRACT NO.21

FIT SCREENING IN ADULTS UNDER 50: A POPULATION-BASED ANALYSIS IN GERMANY

Leon Klimeck, Thomas Heisser, Michael Hoffmeister, Hermann Brenner

INTRODUCTION

Following the introduction of effective screening programs, the incidence and mortality of colorectal cancer (CRC) have declined in individuals aged 50 and older, whereas they continue to rise among younger adults in many countries, raising suggestions to lower the starting age of CRC screening. However, evidence on the expected results of screening below age 50 remains limited.

METHODS

Using anonymized data from the German insurance provider BARMER, which invited people aged 40 and older for FIT-based screening in 2023, we assessed the rate of diagnostic colonoscopy within at least five months following FIT use in routine care for the age groups 40–49 and 50–59. Additionally, we examined polypectomy rates among individuals who underwent colonoscopy.

RESULTS

The sample included 20,966 (40.9% men) and 7119 (38.9% men) individuals in age groups 40-49 and 50-59 who returned a FIT. The proportions of FIT followed by colonoscopy were similar in men and women and both age groups, ranging from 4.3 to 5.2%. However, the proportion of polypectomies among participants undergoing colonoscopies was much higher among men than among women and increased with age. The proportion of FIT participants who finally had a polypectomy was higher in 40-49 year old men (1.06%) than in 50-59 year old women (0.97%).

CONCLUSION

The observed patterns suggest that expanding FIT-based screening might be beneficial for men below age 50 and should be explored in cost-effectiveness analyses for which our results may provide relevant empirical background information.

	MEN		WOMEN		TOTAL	
	40-49	**50-59**	**40-49**	**50-59**	**40-49**	**50-59**
FITS	8572	2770	12394	4349	20,966	7119
COLONOSCOPIES (CS)	374	135	535	227	909	362
PROPORTION OF FITS	4.4%	4.9%	4.3%	5.2%	4.3%	5.1%
POLYPECTOMIES	91	41	94	42	185	83
PROPORTION OF CS	24.3%	30.4%	17.6%	18.5%	20.4%	22.9%
PROPORTION OF FITS	1.06%	1.48%	0.76%	0.97%	0.88%	1.17%

ABSTRACT NO.22

CLINICAL VALIDATION OF A THREE-MARKER METHYLATION PANEL TO DETECT CIN3+ IN THE DUTCH POPULATION-BASED SCREENING PROGRAMME

J. de Waard[1], A. Bhattacharya[2], M.T. de Boer[1], B.M. van Hemel[3], M.D. Esajas[4], K.M. Vermeulen[5], G.H. de Bock[5], E. Schuuring[3*], G.B.A. Wisman[1*]

[1]*Department of Gynaecologic Oncology, University Medical Center Groningen, Groningen, the Netherlands*
[2]*Department of Medical Oncology, University Medical Center Groningen, Groningen, the Netherlands*
[3]*Department of Pathology, University Medical Center Groningen, Groningen, the Netherlands*
[4]*Department of Obstetrics and Gynaecology, University Medical Center Groningen, Groningen, the Netherlands*
[5]*Department of Epidemiology, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands*

BACKGROUND

Self-sampling is a promising screening method for cervical cancer. However, cytology cannot be performed on self-sampling material after a high-risk human papilloma virus (hrHPV)-positive result. In our recent discovery study, we identified a three marker panel (*LHX8*, *EPB41L3* and *ANKRD18CP*) with high sensitivity and specificity for CIN3+. Here, we performed the clinical validation of this three-marker panel on a hrHPV-positive self-samples obtained through the Dutch population-based screening programme (PBS).

MATERIAL AND METHODS

LHX8, *EPB41L3* and *ANKRD18CP* were analyzed using quantitative methylation-specific PCR (QMSP) on DNA from a consecutive cohort of hrHPV-positive self-samples (n=2482: 408 women with CIN3 and cancer (CIN3+) and 2074 women with CIN2 or less (<CIN3)). Diagnostic performance was determined by area under the curve (AUC) of receiver operating characteristics (ROC) analysis. Scenario analysis was performed on a virtual population of 100,000 hrHPV-positive women who used the self-sampling device comparing our methylation triage test in versus cytology triage testing, considering that 10-20% will visit their general practitioner for cytology, regarding referral rate (for colposcopy), and number of detected CIN3 and cancer cases.

RESULTS

The three marker panel showed an AUC of 0.82 with a 75% sensitivity and 78% specificity to detect CIN3+, and 96% (22/23) cancers were detected. Scenario analysis revealed that referral rates (29.4% vs 31.2%) and detection of CIN3 (72% vs 68-77%) were similar between methylation analysis and cytology, but interestingly more cancer cases (864 vs 770) were detected with our methylation panel.

CONCLUSION

DNA methylation analysis using the three-marker panel *LHX8*, *EPB41L3* and *ANKRD18CP* shows good performance to detect CIN3+ and therefore is feasible to be implemented as triage test after a positive hrHPV-result on self-sampling material. The implementation of DNA methylation as molecular triage test on the same DNA used for hrHPV-testing, would not only make the GP visit unnecessary but also result in quicker decision-making regarding referrals and shorter uncertain waiting times.

ABSTRACT NO.23

NONINVASIVE DETECTION OF PANCREATIC DUCTAL ADENOCARCINOMA USING THE METHYLATION SIGNATURE OF CIRCULATING TUMOR DNA

Justin Dang[1], Qiye He[2], Zhixi Su[2], Athurva Gore[1], Rui Liu[2]

[1]Singlera Genomics Incorporated, 505 Coast Boulevard, Suite 309, La Jolla, CA 92122, USA
[2]Singlera Genomics (Shanghai) Ltd., No. 500, Furonghua Road, Shanghai 201203, China

BACKGROUND

Pancreatic ductal adenocarcinoma (PDAC) has the lowest overall survival rate of cancers primarily due to the late onset of symptoms and rapid progression. Reliable and accurate tests for early detection are lacking. We aimed to develop a non-invasive test for early PDAC detection in high-risk patients by capturing circulating tumor DNA (ctDNA) methylation signatures in blood.

METHODS

Genome-wide methylation profiles were generated from PDAC and nonmalignant tissues and plasma. Methylation haplotype blocks (MHBs) were examined to discover both PDAC-specific and overall cancer markers, and were screened for PDAC classification accuracy. The most accurate MHBs were used to develop PDACatch, a targeted methylation sequencing assay. PDACatch was applied to additional PDAC and healthy plasma cohorts to train, validate and independently test a PDAC-discriminating classifier. Finally, the classifier was compared with carbohydrate antigen 19-9 (CA19-9) to evaluate its accuracy and utility.

RESULTS

In total, 90 tissues and 721 plasma samples were collected from 324 PDAC patients, 25 chronic pancreatitis (CP) patients and 406 healthy controls as part of separate training, validation, and independent test cohorts. A total of 171 de novo PDAC-specific markers and 595 multicancer markers were screened for classification accuracy; 56 markers were included in PDACatch, from which a classifier was trained, validated and independently tested. In the independent test cohort, the classifier was able to detect PDAC at a sensitivity of 83% with a specificity of 94%. Importantly, the PDACatch classifier was able to detect PDAC even in CA19-9-negative plasma at a sensitivity of 100%.

CONCLUSIONS

The PDACatch assay demonstrated high sensitivity for early PDAC plasma, providing potential utility for noninvasive detection of early PDAC and indicating the effectiveness of methylation haplotype analyses in discovering robust cancer markers.

ABSTRACT NO.24

UROPANC TRIAL: OBSERVATIONAL STUDY UPDATE AND INTERIM ANALYSIS

Evelyn Kurotova[1], Silvana Debernardi[1], Jayni Shah[1], Lucia Pueyo Valles[1], Nurshad Ali[1], Ismita Chhetri & team[2], Stephen P. Pereira & team[3], Patrick Wilson[4], William Greenhalf & team[5], Melody Ni[6], Oleg Blyuss[7], Tatjana Crnogorac-Jurcevic[1]

[1]*Centre for Biomarkers and Biotherapeutics*
[2]*Centre for Experimental Cancer Medicine, Barts Cancer Institute, Queen Mary University of London, London, UK*
[3]*University College London, Royal Free Hospital, London, UK*
[4]*Barts Health, Royal London Hospital, London, UK*
[5]*University of Liverpool, Liverpool, UK*
[6]*Imperial College London, London, UK*
[7]*Centre for Cancer Screening, Prevention and Early Diagnosis, Wolfson Institute of Population Health, Queen Mary University of London, London, UK*

BACKGROUND/OBJECTIVES

Pancreatic ductal adenocarcinoma (PDAC) is one of the deadliest malignancies. To improve patient outcomes, it is necessary to detect the disease early. We have identified three urinary biomarkers- LYVE1, REG1B and TFF1- for use as early indicators of PDAC[1] and are currently running an observational, prospective trial, UroPanc (ClinicalTrials.gov NCT04449406), as a means of validating their performance. The analysis from the panel is used in conjunction with CA19.9 and age, to create a risk score, PancRISK[2-4], which stratifies patients into those with normal and elevated risk of developing PDAC.

METHODS

We are recruiting symptomatic individuals across multiple sites (Royal Free Hospital, University College London Hospital, Royal London Hospital, UK and San Raffaele Hospital, Italy), as well as asymptomatic individuals from the European Registry of Familial Pancreatic Cancer and Hereditary Pancreatitis (EUROPAC, University of Liverpool). Urine and blood samples are being collected alongside relevant clinical data, including, where available, histopathological records. To date, we have collected 1,489 samples, of which 825 have been analysed. Interim analysis was completed using commercially available ELISAs to test the functionality of the PancRISK score. The risk score was subsequently compared with patient diagnoses; in instances where the diagnosis did not match the risk score, clinical information was revisited for updates. Specificity and Sensitivity (SP/SN) were determined to see the accuracy of the diagnostic test, as well as the positive predictive value/negative predictive value (PPV/NPV).

RESULTS AND CONCLUSION

The interim analysis showed a SP/SN of 91% and 86%, respectively, with 90% accuracy when comparing control samples vs PDAC. Seven samples, initially benign, were identified as having elevated risk and later found to have an updated diagnosis of PDAC. A clinical grade assay is currently under development, and we are hoping to introduce it into the patient diagnostic pathway, to accelerate and improve it, in the near future.

[1]Radon TP, et al. Identification of a three-biomarker panel in urine for early detection of pancreatic adenocarcinoma. Clinical Cancer Research. 2015
[2]Blyuss O, et al. Development of PancRISK, a urine biomarker-based risk score for stratified screening of pancreatic cancer patients. BJC. 2020
[3]Debernardi S, et al. A combination of urinary biomarker panel and PancRISK score for earlier detection of pancreatic cancer: A case–control study. PLoS Medicine. 2020
[4]Debernardi S, et al.Urine biomarkers enable pancreatic cancer detection up to 2 years before diagnosis. IJC. 2023

ABSTRACT NO.25

URINARY BIOMARKERS FOR EARLY DETECTION OF PDAC IN PANCREATIC CYSTIC LESIONS AND OTHER CANCERS

Jayni Shah[1], Élodie Bendriss-Otiko[1], Evelyn Kurotova[1], Nurshad Ali[1], Julia Giemza[1], Silvana Debernardi[1], Oleg Blyuss[2], Farzana Haque[3], Leonid Nikitenko[3], Anthony Maraveyas[3], Emma Crosbie[4], Vincent J. Gnanapragasam[5], Stephen P. Pereira[6], William Greenhalf[7], Tatjana Crnogorac-Jurcevic[1]

[1]*Centre for Cancer Biomarkers and Biotherapeutics, Barts Cancer Institute, Queen Mary University of London, London, United Kingdom*
[2]*Centre for Cancer Screening, Prevention and Early Diagnosis, Wolfson Institute of Population Health, Queen Mary University of London, London, UK*
[3]*Centre for Clinical Sciences, The Hull York Medical School, York, UK*
[4]*Gynaecological Oncology Research Group, Division of Cancer Sciences, Faculty of Biology, Medicine and Health, University of Manchester, St Mary's Hospital, Manchester, United Kingdom*
[5]*Division of Urology, Department of Surgery, University of Cambridge, UK*
[6]*Institute for Liver and Digestive Health, University College London, London, United Kingdom*
[7]*Department of Molecular and Clinical Cancer Medicine, Institute of Translational Medicine, University of Liverpool, Liverpool, United Kingdom*

BACKGROUND

Pancreatic ductal adenocarcinoma (PDAC) is a lethal malignancy with an exceedingly low 5-year survival rate of between 9-11%. This is primarily due to late-stage diagnosis, when the disease has already spread locally or metastasised to other organs. The asymptomatic nature of PDAC complicates its early detection, and no biomarkers are currently in practice for early-stage identification. Our group has discovered and validated a panel of three urinary biomarkers (LYVE1, TFF1 and REG1B) that showed promise for the early detection of PDAC[1-3].

PDAC can originate from pancreatic intraepithelial neoplasm (PanINs), and cystic lesions: intraductal papillary neoplasm (IPMNs) and mucinous cystic neoplasms (MCNs). While PanINs are microscopic lesions that are not detectable by imaging, cystic lesions are a common finding and are detected on 2.4% to 19.6% of imaging scans4. In this study, we wanted to test if our three urinary biomarkers can differentiate PDAC from cystic lesions. In addition, by assessing biomarker expression levels across different cancers, we sought to assess whether our panel is uniquely indicative of PDAC or could also be elevated in other malignancies.

METHODS

ELISA assays were performed on 730 retrospectively collected urine samples from patients with pancreatic cystic lesions (n = 45), PDAC and other cancers (n = 425), as well as relevant benign and healthy controls (n = 260). Statistical analysis was performed in GraphPad Prism.

RESULTS AND CONCLUSION

Our results further validated the potential of LYVE1, TFF1 and REG1B as valuable biomarkers for the early detection of PDAC. They effectively distinguished IPMNs from PDAC, a significant finding given the high progression risk of IPMNs and their importance in guiding clinical management. The biomarkers also demonstrated strong potential in detecting cholangiocarcinoma but showed no utility in detecting reproductive or hormone-associated cancers, reinforcing their high specificity for PDAC.

[1]Radon TP et al. Identification of a three-biomarker panel in urine for early detection of pancreatic adenocarcinoma. Clinical Cancer Research. 2015
[2]Debernardi S, et al. A combination of urinary biomarker panel and PancRISK score for earlier detection of pancreatic cancer: A case–control study. PLoS Medicine. 2020
[3]Debernardi S, et al. Urine biomarkers enable pancreatic cancer detection up to 2 years before diagnosis. International journal of cancer. 2023
[4]Morana G, et al. Cystic pancreatic lesions: MR imaging findings and management. Insights into Imaging. 2021 Aug 10;12(1):115.)

ABSTRACT NO.26

A PANEL OF FOUR PROTEIN TUMOR MARKERS FOR EFFECTIVE AND AFFORDABLE LUNG CANCER EARLY DETECTION BY ARTIFICIAL INTELLIGENCE

Eltjo Heddema[1], Bing Wei[2], Wenjian Wang[3], Shuaipeng Geng[4], Wei Wu[5], Chenyu Ding[4], Dandan Zhu[4], Shuoyao Cheng[4], Qiurong Zhao[4], Yi Luan[6], Shiyong Li[5], Mao Mao[7,]

[1]*OncoInv B.V., Duwboot 20, 3991 CD Houten, The Netherlands*
[2]*The Affiliated Cancer Hospital of Zhengzhou University and Henan Cancer Hospital, Zhengzhou 450003, China*
[3]*Department of Thoracic Surgery, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou 510000, Guangdong Province, China*
[4]*Clinical Laboratories, Shenyou Bio, Zhengzhou 450000, China*
[5]*Research & Development, SeekIn Inc, Shenzhen 518000, China*
[6]*Clinical Laboratory, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou 510000, Guangdong Province, China*
[7]*Research & Development, SeekIn Inc, San Diego, CA 92121, USA*
[8]*Yonsei Song-Dang Institute for Cancer Research, Yonsei University, Seoul 03722, Korea*

INTRODUCTION

Lung cancer is the most common and deadly malignancy worldwide. While low-dose computed tomography (LDCT) reduces mortality in high-risk populations, its high false-positive rate and the required specialized infrastructure and radiologists limit its application. This study assesses LungCanSeek, a novel blood-based protein test for lung cancer early detection.

METHODS

This study enrolled 1,814 participants (1,095 lung cancer, 719 non-cancer) from three independent cohorts. Blood samples were analyzed for four protein tumor markers (PTMs) using Roche cobas. Artificial intelligence (AI) algorithms were developed for lung cancer detection and subtype classification (lung adenocarcinoma (LUAD), lung squamous cell carcinoma (LUSC), and small cell lung cancer (SCLC)). A two-step lung cancer screening approach was modeled, using LungCanSeek for initial screening, followed by LDCT for LungCanSeek's positive cases.

RESULTS

LungCanSeek showed 83.5% sensitivity and 90.3% specificity overall. Sensitivities of LUAD, LUSC, and SCLC were 83.3%, 81.4%, and 91.9%. Sensitivity increased with clinical stage in non-small cell lung cancer (NSCLC): 59.5% (I), 69.8% (II), 86.5% (III), and 91.3% (IV). Sensitivities of limited- and extensive-stage SCLC were 91.3% and 93.0%. The subtype classification accuracy was 77.4%. Compared with the other blood-based lung cancer early detection tests like OncImmune's EarlyCDT-Lung (41.0% sensitivity, 91.0% specificity) and DELFI's FirstLook-Lung (84.1% sensitivity, 50.9% specificity), LungCanSeek's performance was superior. A screening was modeled for 9 million high-risk adults, based on the number of 15 million eligible individuals in the USA in 2024 at a 60% rate, with a 1.2% lung cancer incidence. LungCanSeek reduced false positives to 862,524, and two-step further lowered them to 202,693, compared to LDCT's 2,089,620. LDCT's total cost was $2,493 million, exceeding LungCanSeek's $720 million and two-step's $978.5 million.

CONCLUSION

LungCanSeek is a non-invasive, easy to perform, cost-effective (reagent cost $15) and robust test for lung cancer early detection. The two-step approach offers a cost-effective strategy for population-wide lung cancer screening.

ABSTRACT NO.27

A COST-EFFECTIVE TWO-STEP APPROACH FOR MULTI-CANCER EARLY DETECTION IN RISK-ELEVATED POPULATIONS

Eltjo Heddema[1], Mao Mao[2,3], Shuaipeng Geng[4], Shiyong Li[5], Wei Wu[5], Yinyin Chang[4]

[1]*OncoInv B.V., Duwboot 20, 3991 CD Houten, The Netherlands*
[2]*Research & Development, SeekIn Inc, San Diego 92121, USA*
[3]*Yonsei Song-Dang Institute for Cancer Research, Yonsei University, Seoul 03722, Republic of Korea*
[4]*Clinical Laboratories, Shenyou Bio, Zhengzhou 450000, China*
[5]*Research & Development, SeekIn Inc, Shenzhen 518000, China*

Population-wide cancer screening must address three key aspects: number of cancer cases identified, number of false positives, and screening cost. A high false positive rate wastes healthcare resources, and large-scale screening inevitably leads to significant financial burdens on the healthcare system, limiting nationwide screening efforts.

A two-step multi-cancer early detection (MCED) screening approach was employed, using OncoSeek, a MCED test using a panel of seven plasma protein tumor markers (PTMs) and artificial intelligence (AI), for initial screening, followed by SeekInCare, integrating the same seven PTMs and four cancer genomic features (aneuploidy, fragment size, end motifs, and oncogenic viruses) from cell-free DNA (cfDNA) by shallow whole-genome sequencing, for OncoSeek's positive cases based on the threshold at 80.0% specificity.

In a case-control study (617 cancer, 580 non-cancer), OncoSeek showed 49.9% sensitivity at 91.0% specificity, while SeekInCare demonstrated 60.0% sensitivity at 98.3% specificity. The two-step yielded 46.2% sensitivity and 99.0% specificity. We simulated a screening in 5 million adults aged ≥ 50 years with 1.9% cancer incidence (i.e. the eligible population in the Netherlands). The assumed real-world sensitivities of OncoSeek and two-step were adjusted to 28.0% and 25.9% based on the sensitivity differences between GRAIL's CCGA and PATHFINDER study. While at 91.0% specificity OncoSeek had 441,450 cases of false positives, the two-step significantly reduced them to 49,050 (1.0%). Although Galleri identified more cancer cases (27,455) than two-step's 24,605, its total cost reached $4,745 million. The positive predictive value (PPV) of two-step (33.4%) was close to Galleri (38.3%), but it reduced cost 4.4-fold, with a total cost of $1,080 million and $216 per individual screened. The cost of per cancer case detected using Galleri was $172,828 compared to $43,883 using the two-step, a 3.9-fold difference.

The two-step approach significantly reduces false positives and screening cost, offering a cost-effective strategy for population-wide cancer screening.
*The Galleri's real-world sensitivity and specificity were from the PATHFINDER study2 (prospective).
**Number needed to screen (NNS) is defined as the number needed to be screened for the detection of one cancer case.

[1]Klein EA, Richards D, Cohn A, Tummala M, Lapham R, Cosgrove D, et al. Clinical validation of a targeted methylation-based multi-cancer early detection test using an independent validation set. Ann Oncol 2021;32(9):1167-77 doi 10.1016/j.annonc.2021.05.806.

[2]Schrag D, Beer TM, McDonnell CH, 3rd, Nadauld L, Dilaveri CA, Reid R, et al. Blood-based tests for multicancer early detection (PATHFINDER): a prospective cohort study. Lancet 2023;402(10409):1251-60 doi 10.1016/s0140-6736(23)01700-2.

Table 1. *Performance and cost of OncoSeek, two versions of two-step MCED, and GRAIL's Galleri*

	ONCOSEEK	2-STEP MCED V1 (ONCOSEEK'S SPECIFICITY = 91.0%)	2-STEP MCED V2 (ONCOSEEK'S SPECIFICITY = 90.0%)	GALLERI
CASE-CONTROL STUDY (CANCER:NON-CANCER = 617:580)				**CCGA STUDY[1] (CANCER:NON-CANCER = 2823:1254)**
SENSITIVITY	49.9%	39.9%	46.2%	51.5%
SPECIFICITY	91.0%	99.3%	99.0%	99.5%
PERFORMANCE AND EFFICIENCY				
SENSITIVITY	28.0%	22.4%	25.9%	28.9%*
SPECIFICITY	91.0%	99.3%	99.0%	99.1%
NUMBER OF TRUE POSITIVES	*26,600*	*21,280*	*24,605*	*27,455*
NUMBER OF FALSE POSITIVES	*441,450*	*34,335*	*49,050*	*44,145*
NUMBER OF TRUE NEGATIVES	4,463,550	4,870,665	4,855,950	4,860,855
NUMBER OF FALSE NEGATIVES	68,400	73,720	70,395	67,545
POSITIVE PREDICTIVE VALUE	5.7%	38.3%	33.4%	38.3%
NEGATIVE PREDICTIVE VALUE	98.5%	98.5%	98.6%	98.6%
*NNS***	*188*	*235*	*203*	*182*
COST				
TOTAL	*$400 MILLION*	*$713.6 MILLION*	*$1,080 MILLION*	*$4,745 MILLION*
PER CANCER PATIENT IDENTIFIED	*$15,038*	*$33,534*	*$43,883*	*$172,828*
PER INDIVIDUAL SCREENED	$80	$143	$216	$949

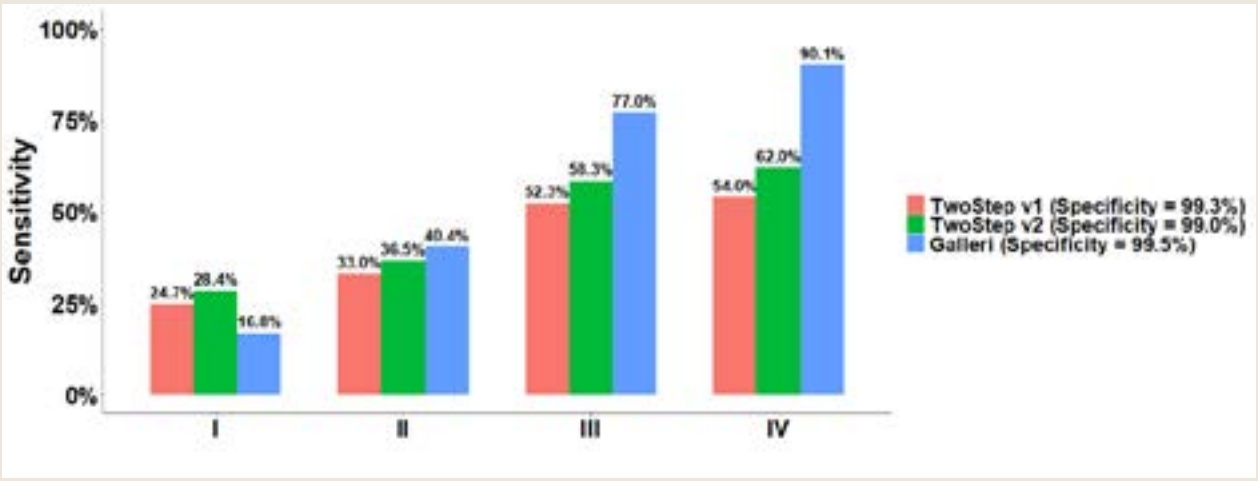


Figure 1. *Sensitivities of two versions of two-step MCED and GRAIL's Galleri at stages I-IV*

ABSTRACT NO.28

ADVANCING MULTI-CANCER EARLY DETECTION: HIGH-PERFORMANCE CELL-FREE RNA PROFILING WITH THE FLOMICS LIQUID BIOPSY PLATFORM

Phil Sanders[1], Lucila Gonzalez[1], Laura Sanchez[1], Beatriz Neto[1], Julien Lagarde[1], Marc Weber[1], Pablo Monteagudo[1], Cristina Tuñi[1], Giovanni Asole[1], Elena Rusu[1], Sol Garcia[2], Pilar Simón-Extremera[2], Sonia Panadero[3], Maria Concepcion Romero[3], Purificación Catalina[3], João Curado[1]

[1]Flomics Biotech, Barcelona, Spain
[2]Health and Biomedicine, Leitat Technological Center, Barcelona, Spain
[3]Andalusian Public Health System Biobank, Coordinating Node, Granada, Spain

Liquid biopsies are increasingly important diagnostic tools for cancer early detection, with cell-free RNA (cfRNA) emerging as a promising biomarker source. At Flomics Biotech we developed a high-quality cfRNA-Seq platform that robustly and reproducibly profiles human plasma cfRNA. Our platform combines state-of-the-art laboratory and bioinformatic methods for Next-generation Sequencing of plasma RNA with machine learning (ML) classification methods to identify cancer-related biomarker signatures.

Here we apply our cfRNA-Seq platform in the LiquiDx pre-clinical study with the aim of developing a multi-cancer early detection (MCED) test.

We profiled plasma cfRNA from over 1,000 individuals using our cfRNA-Seq platform. The cohort contains patients with colorectal, lung, breast, pancreatic or prostate cancer, or non-cancer diseases of the same organs, and healthy individuals. Early and late stage patients were recruited for each cancer type, with 22% of patients having stage I cancer. We identified differentially expressed genes (DEGs), performed gene set enrichment analysis (GSEA), and trained an ML classifier to predict patient status and cancer tissue of origin.

We identified 114 DEGs with GSEA revealing enrichment of metastasis, inflammation, and proliferation-associated genes in cancer patient cfRNA profiles. For cancer vs healthy classification, our ML classifier achieves a mean area under the ROC curve of 0.92 ± 0.01, and a sensitivity of 83% at 90% specificity. For classification of different cancer types, at 90% specificity our ML classifier achieves a sensitivity ranging from 69% for breast cancer to 99% for prostate cancer. In contrast to other liquid biopsy-based technologies, our platform maintains high performance in detecting stage I cancer patients (80% sensitivity).
The Flomics cfRNA-Seq platform delivers high-quality cfRNA biomarker identification and demonstrates transformative potential in MCED, particularly in stage I where detection is more challenging. The platform's high performance positions it as a revolutionary tool to improve global cancer diagnostics.

ABSTRACT NO.29

UNDERSTANDING THE PREFERENCES OF YOUNGER WOMEN FOR A BREAST CANCER RISK PREDICTION SERVICE IN THE UNITED KINGDOM

Stuart J Wright[1], Katherine Payne[1], Shabnam Thapa[1,2], Sarah Hindmarch[3], David French[3], Sacha J Howell[4,5]

[1]Manchester Centre for Health Economics, The University of Manchester, Oxford Road, Manchester, United Kingdom
[2]The National Institute for Health and Care Excellence, 3rd Floor, Picadilly Place, Manchester, United Kingdom
[3]Manchester Centre for Health Psychology, The University of Manchester, Oxford Road, Manchester, United Kingdom
[4]The Christie Hospital, Wilmslow Road, Manchester, United Kingdom
[5]Division of Cancer Sciences, The University of Manchester, Oxford Road, Manchester, United Kingdom

INTRODUCTION
Breast cancer (BC) is the biggest killer of women aged 35 to 50-years in the UK. Around 20% of breast cancers are diagnosed in women under age 50. Population-level breast screening is only available from the age of 50-years. A service to predict a women's risk of developing BC may be valuable to identify young women (30-39 years old) at increased-risk to enable early detection and prevention of BC. This study aimed to understand the preferences of younger women for a BC risk-prediction service in the UK.

METHODS
A discrete choice experiment (DCE), embed in an online survey, was sent to a representative sample of women (aged 30 to 39-years) recruited using an online panel provider. The DCE included six attributes identified using focus groups and interviews with 37 women: mode of risk-prediction; number of appointments needed; times when appointments are available; ability to book an appointment yourself; location of screening; proportion of women identified to be high-risk. The survey also contained questions to collect demographic information. Quality control measures were added to exclude fraudulent responses. The choice data were analysed using random parameter logit and latent class models.

RESULTS
The analysis was based on responses from 936 women. Women wanted a risk-prediction service. The preferred service: was available at evenings and weekends; needed one appointment; was bookable directly; identified women at high-risk of cancer. Women valued a risk-prediction tool including a genetic component but disliked needing to visit a hospital. Latent class analysis revealed the preferences could be used to group women into four distinct classes.

CONCLUSION
A breast cancer risk-prediction service was shown to be desirable in younger women. The potential uptake of the service was sensitive to its design and consideration should be given to meet the needs of different groups in the UK population.

ABSTRACT NO.30

REAL-WORLD INTEGRATION OF A COMBINED ARTIFICIAL INTELLIGENCE-BASED COMPUTER-AIDED DETECTION AND NATURAL LANGUAGE PROCESSING TOOL FOR PULMONARY NODULE DETECTION IN CHEST RADIOGRAPHS

Jasika Paramasamy[1], Asabi Leliveld[2], Mrunmayee Nasery[3], Sahil Chachad[3], Aayushi Kuchroo[3], Joachim G.J.V. Aerts[2], Aad van der Lugt[1], Arlette Odink[1], Jacob J. Visser[1]

[1] *Department of Radiology and Nuclear Medicine, Erasmus MC, University Medical Center Rotterdam, P.O. Box 2040, 3000 CA, Rotterdam, The Netherlands*
[2] *Department of Respiratory Medicine, Erasmus MC, University Medical Center Rotterdam, P.O. Box 2040, 3000 CA, Rotterdam, The Netherlands*
[3] *Qure.ai, Level 7, Oberoi Commerz II, Goregaon East, Mumbai 400063, India*

OBJECTIVES

This study aims to evaluate the effectiveness of Artificial Intelligence (AI)-based Computer-Aided Detection (CADe) combined with Natural Language Processing (NLP) as a safety net to improve the detection of lung nodules on chest radiographs.

METHODS

This retrospective study analyzed consecutive chest radiographs from a Dutch Academic hospital (September 2024 - February 2025) using the CADe component of the AI software for lung nodule detection. Simultaneously, finalized radiology reports were processed with the NLP component. The software was deployed in a research setting to avoid disrupting radiologists' workflow. Discordant cases—CADe-positive but NLP-negative—were reviewed by a senior radiologist with access to both CADe output and reports. The radiologist determined whether to accept or reject the findings, issuing an addendum if accepted, and providing an explanation if rejected.

RESULTS

Out of the 7,848 chest radiographs analyzed by AI, 279 were CAD-positive, of which 238/279 were concordantly positive for both NLP and CAD. Among these, 59/238 were classified as NLP-errors, while 168/238 were identified as known or previously reported nodules. 11/238 cases were excluded from further analysis (<18y). Of the remaining 41/279 cases that were CAD-positive but NLP-negative, a reassessment was required. In 35/41, the senior radiologist rejected the nodule as a false positive. However, 6/41 cases were accepted by the senior radiologist, of which 2/6 were found to be normal after CT evaluation. Notably, 4/6 cases were true missed findings, with 1/4 case revealing lung metastasis (patient deceased) and 3/4 others now under ongoing imaging surveillance.

CONCLUSIONS

The integration of AI-based CADe and NLP enhances the detection of lung nodules on chest radiographs in a real-world clinical setting. This approach has the potential to improve patient outcomes by enabling earlier detection of malignant nodules, reducing diagnostic errors, and facilitating more timely interventions.

ABSTRACT NO.31

PROTEIN N-GLYCOSYLATION TRAITS ACCURATELY DISTINGUISH PANCREATIC CANCER CASES FROM HEALTHY CONTROLS AND BENIGN PANCREATIC DISEASES

Aleksander M. Bogdanski[1,2], Derk C.F. Klatte[1,2], Jeanin E. van Hooft[1], Kristin E. Clift[2], Manfred Wuhrer[3], Monique E. van Leerdam[1,4], Wilma E. Mesker[5], Yan Bi[2], Michael B. Wallace[2], Yuri E.M. van der Burgt[3]

[1]*Department of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, The Netherlands*
[2]*Department of Gastroenterology and Hepatology, Mayo Clinic, Jacksonville, FL, United States*
[3]*Center for Proteomics and Metabolomics, Leiden University Medical Center, Leiden, The Netherlands*
[4]*Department of Gastrointestinal Oncology, Netherlands Cancer Institute, Amsterdam, The Netherlands*
[5]*Department of Surgery, Leiden University Medical Center, Leiden, The Netherlands*

New methods are needed to detect pancreatic ductal adenocarcinoma (PDAC) earlier to improve outcomes.

We previously reported a panel of PDAC-specific protein N-glycosylation traits (NGTs). In this study the performance of the NGTs was further evaluated in a diverse cohort that better reflects clinical practice, including controls with benign pancreatic disorders. Our standardized glycomics workflow consists of an enzymatic release of N-glycans from plasma proteins, linkage-specific sialic acid derivatization, purification, mass spectrometry (MS)-based identification and quantification, and largely automated data analysis. Logistic regression on relatively quantified glycans as well as on glycosylation traits was performed to calculate odds ratios, AUC, sensitivity and specificity. The panel was furthermore compared with corresponding CA19-9 readouts, the only biomarker test that has been FDA-approved for use in the clinic, albeit with limited clinical utility.

The cohort included 45 PDAC cases and 176 control samples (53 healthy and 123 with benign pancreatic disease). In PDAC cases diantennary glycans were decreased and tri- and tetra-antennary glycans increased. Moreover, α2,6-sialylation compared to α2,3-linked sialylation was increased in cases. The AUC for differentiating PDAC from the total control cohort based on the combination of three biologically distinct NGTs was 0.79 (95%CI), with a sensitivity of 0.84 (95%CI) and specificity of 0.70 (95%CI). It was concluded that plasma NGTs accurately distinguish PDAC from a diverse control cohort, thereby providing insight into its disease-specificity.

Furthermore, the reported NGTs replicate the previously established N-glycomic PDAC signatures. This validated panel of NGTs holds promise for future use as a blood-based clinical biomarker in surveillance programs. For further development collaborations are needed in large multi-institutional consortia to obtain larger longitudinal collections of clinical data and biospecimens. It is foreseen that a glycomics profile can complement high-end imaging technologies which are in themselves insufficient as surveillance modality in high risk families.

[1]Klatte et al. Surveillance for Pancreatic Cancer in High-Risk Individuals Leads to Improved Outcomes: A Propensity Score-Matched Analysis. Gastroenterology. 2023;164(7):1223-1231.

[2]Vreeker et al. Serum N-Glycome analysis reveals pancreatic cancer disease signatures. Cancer Med. 2020;9(22):8519-29.

[3]Levink et al. Longitudinal changes of serum protein N-Glycan levels for earlier detection of pancreatic cancer in high-risk individuals. Pancreatology. 2022;22(4):497-506.

ABSTRACT NO.32

USING ADDITIONAL RISK FACTORS IN THE CREATION OF CERVICAL (PRE)MALIGNANCY RISK PROFILES FOR THE TRIAGE OF HIGH RISK HUMAN PAPILLOMAVIRUS POSITIVE WOMEN IN SCREENING

Lindy M. Kregting[1], Marleen S. Boonstra[1], Mireille J.M. Broeders[1,2], Daniëlle van der Waal[1,2], for the PREFER study-team

[1]*Radboud University Medical Center, IQ Health science department, Nijmegen, The Netherlands*
[2]*Dutch Expert Centre for Screening (LRCB), Nijmegen, The Netherlands*

BACKGROUND
The implementation of high risk Human PapillomaVirus (hrHPV) testing in cervical cancer screening led to an increase in women needing follow-up testing. Using additional risk factors in the triage of hrHPV+ women in cervical cancer screening can potentially limit the burden of unnecessary follow-up. However, there is no established prediction model yet to determine risk profiles.

METHODS
Women who tested hrHPV+ in screening were approached to complete an online questionnaire on possible predictors for cervical lesions. This data was linked to the national pathology database and multiple imputation was applied. A model was developed to predict the risk of cervical intraepithelial neoplasia (CIN) 2 lesions or higher using logistic regression analyses and backward selection ($p<0.2$). Predictor variables included were based on lifestyle factors and screening history. Area under the receiver-operating curve (AUC-ROC) and Nagelkerke's R2 were calculated and calibration curves were drawn to evaluate model performance.

RESULTS
In total, 3,375 online questionnaires were completed. Among them, 1,674 hrHPV+ women were eligible for included in the analysis. CIN2 was present in 229 women, CIN3 in 336 women and 49 women had cervical cancer. Risk factors that showed significant predictive properties included smoking in packyears, age at menarche, age at first sexual intercourse, recent use and duration of hormonal contraceptives, number of lifetime sex partners, previous participation in screening, age, and relationship status. The model showed an AUC-ROC of 0.64 and an R2 of 0.085. Calibration curves showed a strong calibration.

CONCLUSION
The developed model shows good calibration and moderate discrimination. This indicates that lifestyle factors and screening history have predictive value in addition to hrHPV status in prediction the risk of cervical malignancies and pre-cancerous lesions. This suggests that they may be useful for development of more risk-stratified triage strategies in hrHPV+ women in the cervical cancer screening program.

ABSTRACT NO.33

ENABLING MOLECULAR SUBTYPING AND GRADING FOR DUCTAL CARCINOMA IN SITU WITH FOUNDATION MODELS

S. Doyle MS[†1,2], M.A. Oerlemans MS[†1,3], E. Marcus PhD[1,2], J. Brunekreef PhD[1,2], L. Mulder[3] BS, Y . Liu[3] MS, I.Bouybayoune PhD, EJ. Sawyer PhD[7], AM Thompson MD[8], SE. Pinder PhD[7], Grand Challenge PRECISION Consortium[3], Prof Clara I. Sánchez PhD[2], J. Teuwen PhD[*1,4], Prof J. Wesseling PhD[*3,5,6], E. H. Lips PhD[*3]

[†]Shared first authors [*]Shared senior authors
[1] Division of Radiation Oncology, Netherlands Cancer Institute, Antoni van Leeuwenhoek, Amsterdam, the Netherlands.
[2]Informatics Institute, University of Amsterdam, Amsterdam, the Netherlands
[3]Division of Molecular Pathology, Netherlands Cancer Institute, Antoni van Leeuwenhoek, Amsterdam, the Netherlands.
[4]Department of Medical Imaging, Radboud University Nijmegen, Nijmegen, the Netherlands.
[5]Department of Pathology, Netherlands Cancer Institute – Antoni van Leeuwenhoek, Amsterdam, the Netherlands
[6]Department of Pathology, Leiden University Medical Center, Leiden, the Netherlands.
[7]School of Cancer & Pharmaceutical Sciences, King's College London, UK
[8]Department of Surgery, Baylor College of Medicine, Houston Texas, USA

INTRODUCTION

Ductal carcinoma in situ (DCIS) is a non-obligate precursor of invasive breast cancer. The inability to accurately predict progression has led to nearly all DCIS patients undergoing breast-conserving surgery and radiotherapy. To combat overtreatment, there is an urgent need for reliable biomarkers. Automated analysis of H&E whole slide images with AI allows robust and reliable biomarker detection and has the potential for DCIS risk stratification. As active surveillance for DCIS is now becoming an alternative for surgery, reliable risk prediction is even more needed.

MATERIAL AND METHODS

We developed a deep learning pipeline to predict ER status, HER2 status, and grade 1 and 2 vs grade 3. A foundation model trained on thousands of WSIs is used to extract features from WSIs and a classifier is trained for our specific use-case. Classifiers were trained and evaluated on H&E-stained WSIs from a Dutch multicenter dataset (n=761) split over 5 folds and externally validated on the UK-based Sloane dataset (n=225).

RESULTS

ER, HER2, and grade were predicted with mean AUROCs of 0.90, 0.84, and 0.86, respectively, on the Dutch dataset, and 0.80, 0.73, and 0.75 on the external dataset. Risk group stratification based on active surveillance trial criteria (ER positive, HER2 negative, grade 1/2), showed a balanced accuracy of 0.81 and 0.64 and an NPV of 0.86 and 0.79 on the Dutch dataset and external dataset, respectively.

CONCLUSION

Deep learning models using routine WSIs demonstrated consistent biomarker characterization in DCIS. These models effectively stratified patients into risk groups for active surveillance. Their performance was validated on an external dataset, showing the robustness of foundation models and the potential for DCIS risk prediction.

ABSTRACT NO.34

DIGITAL PCR ASSAY FOR THE SIMULTANEOUS DETECTION OF MUTATIONS AND DNA METHYLATION MARKERS IN MELANOMA

Paul van der Leest[1], Dorothé Linders[1], Mirthe Lanfermeijer[1], Kalpana Ramkisoensing[1], Jet Zielhuis[1], Vera Horneman[1], Joanna Kaplon[1], Roderick Slieker[2,3], Anke Kuijpers[4], Remco van Doorn[5,6], Daan van den Broek[1]

[1]*Department of Laboratory Medicine, Netherlands Cancer Institute, Amsterdam, Netherlands.*
[2]*Department of Molecular Cell Biology, Leiden University Medical Center, Leiden, Netherlands*
[3]*Department of Epidemiology and Biostatistics, Amsterdam Public Health Research Institute, VU University Medical Center, Amsterdam, the Netherlands*
[4]*Department of Surgery, Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands*
[5]*Department of Dermatology, Leiden University Medical Center, Leiden, Netherlands*
[6]*Department of Dermatology, Antoni van Leeuwenhoek Hospital, Amsterdam, Netherlands*

BACKGROUND
After treatment with curative intent of melanoma, patients enter long-term follow-up using imaging (CT/PET-CT/ultrasound) to allow early detection of recurrences. This one-size-fits-all approach results in an ever-increasing burden on radiology, patients, and the healthcare system. Circulating tumor DNA (ctDNA) is a minimally invasive, established routine biomarker with significant lead times over imaging, enabling ctDNA-based personalization of the imaging regimen. Introducing ctDNA analysis during surveillance of melanoma patients would preferably rely on a single method covering the majority of patients. Here, we designed and validated a combined mutation and methylation detection droplet digital PCR (ddPCR) assay for the early detection of ctDNA in patients with melanoma.

METHODS
Through extensive evaluation of available DNA methylation databases, CpG dinucleotides that were hypermethylated in melanoma and unmethylated in healthy controls were identified. Two differentially methylated targets were combined with screening assays for mutations in BRAFV600, NRASG12/13, and NRASQ61 in a multiplex ddPCR assay. The multiplex ddPCR assay was validated on melanoma cell lines and leukocytes from healthy individuals. The locked assay was used to analyze 78 circulating cell-free DNA (ccfDNA) samples from plasma of melanoma patients (stage 3-4; n=59) and non-cancer controls (n=29). The evaluation of early-stage melanoma patients (stage 1-2) and longitudinal samples is currently ongoing.

RESULTS
Overall, ctDNA was detectable in 92% of the plasma samples from melanoma patients. Virtually all tumor tissue mutations in BRAF (22/24, 92%) and NRAS (13/13, 100%) were retrieved in plasma. For the two novel targets, the highest percentage of methylation in healthy individuals was 2.5%, which was used as the cut-off to determine methylation positivity. Applying this cut-off, 52 out of the 59 melanoma patients (88%) were determined to be ctDNA positive based on methylation, including 19 of the 22 patients (86%) whose tumors did not harbor a mutation in BRAF or NRAS. ctDNA negativity seemed mostly related to ccfDNA input and not attributable to disease stage or tumor variant allele frequency.

CONCLUSION
Combining the detection of melanoma-specific mutations in combination with selected differentially methylated markers allows detection of ctDNA in 92% of the melanoma patients, even when mutations in BRAF and NRAS were absent (32%). Next steps involve longitudinal monitoring in relation to the current imaging strategies in a real-world cohort to determine the impact of this approach on the follow-up of patients with melanoma after treatment with curative intent.

ABSTRACT NO.35

THE NEED OF MORE PERSONALIZED RISK-ADAPTED SCREENING ALGORITHMS FOR PROSTATE CANCER – EXAMPLES FROM THE PROBASE TRIAL

Agne Krilaviciute[1], Kathleen Herkommer[2], Jürgen E Gschwend[2], Markus A Kuczyk[3], Nina N Harke[3], Jürgen Debus[4], Christoph A Grott[4], Glen Kristiansen[5], Lars Schimmöller[6], Gerald Antoch[7], Frederik L Giesel[8], Christian Arsov[9], Boris Hadaschik[10], Axel Benner[11], Petra Seibold[12], Rudolf Kaaks[13], Nikolaus Becker[14], Peter Albers[14,15], the PROBASE group

[1]*Division of Personalized Early Detection of Prostate Cancer, DKFZ, Heidelberg, Germany*
[2]*Technical University of Munich, Department of Urology, München, Germany*
[3]*Hannover Medical School, Department of Urology, Hannover, Germany*
[4]*Heidelberg University Hospital, Department of Radiation Oncology, Heidelberg, Germany*
[5]*Glen Kristiansen, University Hospital Bonn, Institute of Pathology, Bonn, Germany*
[6]*University Hospital of the Ruhr-University Bochum, Department of Diagnostic, Interventional Radiology and Nuclear Medicine, Herne, Germany*
[7]*University Dusseldorf, Department of Diagnostic and Interventional Radiology, Düsseldorf, Germany*
[8]*University Dusseldorf, Department of Nuclear Medicine, Düsseldorf, Germany*
[9]*Städtische Kliniken Mönchengladbach GmbH, Department of Urology and Paediatric Urology, Mönchengladbach, Germany*
[10]*University Hospital Essen, Department of Urology, Essen, Germany*
[11]*Division of Biostatistics, DKFZ, Heidelberg, Germany*
[12]*Division of Personalized Early Detection of Prostate Cancer, DKFZ, Heidelberg, Germany*
[13]*Division of Cancer Epidemiology, DKFZ, Heidelberg, Germany*
[14]*Division of Personalized Early Detection of Prostate Cancer, DKFZ, Heidelberg, Germany*
[15]*University Dusseldorf, Department of Urology, Düsseldorf, Germany*

BACKGROUND/OBJECTIVES

Prostate cancer (PCa) is the most common cancer among men; however, organized screening has yet to be implemented in most countries. The most established screening tests for identifying men at risk are prostate-specific antigen (PSA) testing in blood and magnetic resonance imaging (MRI). However, when used for general population screening, as proposed by the European Association of Urology (EAU), this strategy could lead to high rates of repeated testing and significant variability in PCa detection rates among different groups.

METHODS

The ongoing German PROBASE trial (>46,000 men recruited at the age of 45 years) provides an opportunity to report on outcomes of PSA-based screening in young men. The PROBASE protocol categorizes men into three groups: 1) PSA <1.5 ng/ml, classified as “low risk,” with retesting after 5 years (EAU suggests a cutoff of <1 ng/ml), 2) PSA 1.5-<3 ng/ml, classified as “intermediate risk,” with retesting after 2 years, and 3) confirmed PSA ≥3 ng/ml, classified as “high risk,” followed by MRI and biopsy.

RESULTS/CONCLUSIONS

PSA and MRI alone cannot differentiate between slow-growing and aggressive PCa. Additional markers and tools, for instance, AI-based methods, have yet to be implemented to better define groups that require more frequent testing. The following findings have been reported by the PROBASE trial so far: 1) MRI readings are challenging in young men, highlighting the need for expert centers; 2) digital rectal examination (DRE) in 45-51-year-olds with already elevated PSA misses almost all (86%) cancers; 3) the PCa rate within 5 years is only 0.06% for men with a baseline PSA <1.5 ng/ml at age 45; and 4) confirmatory PSA can exclude close to half of men from immediate diagnostics (ongoing work). These findings support the need to revise guidelines for more personalized risk-adapted screening protocols.

ABSTRACT NO.36

PERSONALISED PROSTATE SPECIFIC ANTIGEN (PSA) RETESTING INTERVALS IN PRIMARY CARE

Kiana K Collins, Jason L Oke, Pradeep S Vidree, Rafael Perera, Brian D Nicholson

Nuffield Department of Primary Care Health Sciences, University of Oxford

BACKGROUND

The prostate specific antigen (PSA) test is a diagnostic test for prostate cancer. Optimal PSA retesting intervals are unknown[1]. We aim to develop evidence for risk-stratified PSA retesting intervals by age and PSA to be used in primary care, that will maximise the benefit of early prostate cancer diagnosis while balancing the harms of over-testing.

METHODS

We analysed English primary care electronic health record data using the Clinical Practice Research Datalink Aurum between 2000 and 2018. Eligible patients were male, did not have a prostate cancer diagnosis prior to entering the study, and aged ≥ 40 years at their first PSA test. We compared two different methods for deriving retesting intervals: (1) Kaplan-Meier curves[2] estimated prostate cancer-free survival by PSA range and age. The retesting interval was set to the year when less than 99% of patients remained cancer-free; (2) an adapted Kirch and Klein model[3] set retesting intervals to be proportional to the square root of age and PSA-specific cancer incidence probability. For both methods, retesting intervals were calculated for five-year age bands and PSA ranges (<1, 1–1.9,2-2.9, 3–3.9, 4–4.9 ng/ml).

RESULTS

1,349,250 male patients were included from 1441 general practices in England. Median follow-up time in years was 5.4(IQR 2.1 to 6.4). During follow-up, 92,919(6.9%) patients were diagnosed with prostate cancer. An example of a recommended PSA retesting interval for patients aged between 50-54, was found to be eight-to-ten years for patients with a PSA <1ng/ml, four-to-six years for patients with a PSA 1-1.9ng/ml, and one-to-two years for patients with a PSA 2-2.9ng/ml.

CONCLUSION

PSA retesting intervals could be derived based on prostate cancer incidence and survival rates, conditional on PSA value and age. Further research is needed to externally validate our results and develop models incorporating multiple PSA tests over time.

[1]Harding, T.A., et al., Optimising the use of the prostate-specific antigen blood test in asymptomatic men for early prostate cancer detection in primary care: report from a UK clinical consensus. British Journal of General Practice, 2024. 74(745): p. e534.

[2]Randazzo, M., et al., A "PSA pyramid" for men with initial prostate-specific antigen <=3 ng/ml: a plea for individualized prostate cancer screening. European Urology, 2015. 68(4): p. 591-7.

[3]Kirch, R.L. and M. Klein, Examination schedules for breast cancer. Cancer, 1974. 33(5): p. 1444-50.

ABSTRACT NO.37

PROSPECTIVE EVALUATION OF BIOMARKER RISK STRATIFICATION USING CAPSULE SPONGE IN THE SURVEILLANCE OF BARRETT'S ESOPHAGUS: RESULTS FROM UK REAL-WORLD IMPLEMENTATION PILOTS

W. Keith Tan[1,2], Caryn Ross-Innes[1], Timothy Somerset[1], Greta Markert[3], Maria O'Donovan[4,5], Rebecca C. Fitzgerald[1] on behalf of the DELTA consortium

[1]*Early Cancer Institute, Department of Oncology, University of Cambridge, Cambridge, UK*
[2]*Department of Gastroenterology, Addenbrookes Hospital, Cambridge University NHS Foundation Trust, Cambridge, UK*
[3]*Cancer Research UK Cambridge Institute, University of Cambridge, Cambridge, UK*
[4]*Department of Histopathology, Cambridge University NHS Foundation Trust, Cambridge, UK*
[5]*Cyted Health, Cambridge, UK*

BACKGROUND
Endoscopic surveillance is the standard of care for Barrett's esophagus (BE), but its effectiveness is inconsistent and operator dependent. Pan-oesophageal cell collection devices with biomarkers provide patients with a less operator-dependent, cost-effective alternative. We previously developed a risk stratification score for capsule-sponge surveillance1.

OBJECTIVES
We prospectively evaluated the capsule sponge risk stratification tool to determine whether it can a) identify those at highest risk of having BE with dysplasia and thereby prioritise the timing of endoscopy and b) whether it is safe to follow up the low-risk group with the capsule sponge risk stratification biomarker panel and spare these patients from unwarranted endoscopies.

METHODS
Patients with a history of BE who had capsule sponge and endoscopy follow-up were recruited from thirteen hospitals (DELTA study ISRCTN91655550, 2020-2023, and NHS England implementation study 2022–2024). All capsule sponge samples were processed in an accredited laboratory (Cyted Health), with positive biomarker results (p53, atypia) independently reviewed by two pathologists. Patients were assigned into one of three risk groups: low (clinical and capsule sponge biomarkers negative), moderate (positive clinical biomarkers - age, sex, BE segment length), and high risk (positive capsule sponge biomarkers- p53 protein levels, glandular atypia).

RESULTS
The cohort consisted of 906 patients of which 138 (15.2%) were classified as high risk, 275 (30.4%) moderate risk and 493 (54.4%) low risk. The positive predictive value for predicting dysplasia in the high-risk group was 36.2%. Patients with both glandular atypia and significant p53 staining were more likely to have dysplasia or adenocarcinoma (Hazard ratio = 113.6). The prevalence of high-grade dysplasia or worse in the low-risk group was 0.4% (95% CI: 0.1-1.6%).

CONCLUSION
The biomarker panel substantially enriches for patients with dysplasia. The data are encouraging for use of the capsule sponge in clinically low-risk BO.

[1]Pilonis ND et al. Use of a Cytosponge biomarker panel to prioritise endoscopic Barrett's oesophagus surveillanceThe Lancet Oncology 2022.

ABSTRACT NO.38

STRATIFIED COLORECTAL (BOWEL) CANCER SCREENING IN THE UK: LATEST EVIDENCE AND A NEW CRUK-FUNDED STUDY TO EXPLORE FEASIBILITY AND OUTCOMES IN UK BOWEL SCREENING PROGRAMMES

David Weller[1], Susanne Maxwell[1], Juliet Usher-Smith[2], Joanne Cairns[3], Christian Von Wagner[4]

[1]*Usher Institute, University of Edinburgh 5 Little France Rd, Edinburgh EH16 4UX UK*
[2]*Department of Public Health and Primary Care, University of Cambridge. Robinson Way, Cambridge CB2 0SR UK*
[3]*Hull York Medical School, University of Hull, Cottingham Road, Hull, HU6 7HR, UK*
[4]*University College London, Department of Behavioural Science and Health, 1-19 Torrington Place, WC1E 6BT, London, UK*

BACKGROUND
Colorectal cancer is a leading cause of cancer-related deaths, ranking second only to lung cancer. Screening programmes for colorectal cancer are well established within the UK, but risk-based screening could target those most likely to benefit while reducing screening for low-risk individuals. Trials are currently underway to test the feasibility of stratified approaches.

OBJECTIVES
• To synthesise the current literature of stratified colorectal cancer screening, exploring risk prediction models and their potential for integration throughout the screening pathway, while examining their clinical, economic and ethical impacts.
• To describe a major new UK trial of stratified colorectal cancer screening, funded by Cancer Research UK

METHODS
A targeted literature search was conducted to identify relevant peer-reviewed articles, reviews and guidelines published up to November 2024 using electronic databases including PubMed, Embase & Google Scholar.

RESULTS
The literature explores various approaches for calculating an individual's colorectal cancer risk. There are two primary strategies: (1) using the full spectrum of quantitative FIT results to inform screening frequency, and (2) incorporating personal risk factors—such as age, sex, genetics, family history, and lifestyle—to determine screening eligibility and intervals. While stratified screening shows promise, it may exacerbate health inequalities due to disparities in genetic risk profiling and health literacy. The cost-effectiveness of stratified screening remains inconclusive, emphasising the need for robust real-world data to guide policy decisions. We also describe a 5 year programme of work, undertaken within bowel screening programmes in England and Scotland, which will provide the NHS with the evidence it needs to transition to stratified approaches, funded by Cancer Research UK. Comparisons will be drawn with similar trials in the Netherlands & Italy.

CONCLUSIONS
Stratified bowel cancer screening has the potential to improve outcomes without significant extra costs. Further research is needed to fully explore the implications of stratified screening in real world settings.

ABSTRACT NO.39

EFFECT OF BASELINE OESTRADIOL SERUM CONCENTRATION ON SIDE-EFFECT PROFILE OF ANASTROZOLE FOR PREVENTING BREAST CANCER IN POSTMENOPAUSAL WOMEN AT HIGH RISK: A STUDY FROM THE IBIS-II PREVENTON TRIAL

Kim Chu[1], Dr Adam Brentnall[1], Prof Jack Cuzick[2]

[1]*Centre of Evaluation and Methods, Wolfson Institute of Population Health, Queen Mary University of London, London, UK*
[2]*Centre for Cancer Screening, Prevention and Early Diagnosis, Wolfson Institute of Population Health, Queen Mary University of London, London, UK*

BACKGROUND/OBJECTIVES

The IBIS-II breast cancer prevention trial showed that anastrozole approximately halves breast cancer risk in post-menopausal women at increased risk, and most side-effects associated with oestrogen deprivation were not attributable to anastrozole. However, arthralgia, vasomotor and gynaecological symptoms were commonly reported, and had a slightly higher frequency in the intervention arm (1). We aimed to evaluate the extent to which these side effects are associated with baseline oestradiol serum concentration.

METHODS

An earlier case-control study was run to evaluate the effect of baseline oestradiol serum concentration on the efficacy of anastrozole (2). We report here results from a secondary analysis of this study, evaluating side effect profile in this study in cases and controls combined. The controls were used to determine quartiles of baseline oestradiol to sex hormone binding globulin (SHBG) ratio (oestradiol–SHBG ratio). Side effect frequency was evaluated by arm and quartile of baseline oestradiol–SHBG ratio, with Cochran-Armitage test for trend.

RESULTS

n=212 women randomised to anastrozole and n=416 placebo were included. Side effects were more common in the anastrozole group, as in the wider trial cohort. There was some evidence that higher oestradiol–SHBG ratios were associated with more vasomotor side effects in both arms (p(trend)=0.0048; Q4 vs Q1 oestradiol–SHBG: placebo 68/116 (59%) vs 44/94 (47%); anastrozole 38/50 (76%) vs 28/49 (57%)). There was little evidence for a trend for gynaecological or arthralgia symptoms by oestradiol–SHBG ratio.

CONCLUSIONS

There was little evidence to suggest a differential risk of these side effects by oestradiol–SHBG ratio; but oestradiol–SHBG ratio might be helpful to help personalise estimation of the absolute risk of vasomotor side effects.

[1]Cuzick J, Sestak I, Forbes JF, et al. Anastrozole for prevention of breast cancer in high-risk postmenopausal women (IBIS-II): an international, double-blind, randomised placebo-controlled trial. Lancet. 2014;383(9922):1041-1048. doi:10.1016/S0140-6736(13)62292-8

[2]Cuzick J, Chu K, Keevil B, et al. Effect of baseline oestradiol serum concentration on the efficacy of anastrozole for preventing breast cancer in postmenopausal women at high risk: a case-control study of the IBIS-II prevention trial. Lancet Oncol. 2024;25(1):108-116. doi:10.1016/S1470-2045(23)00578-8

ABSTRACT NO.40

A MULTI-OMIC MODEL FOR NON-INVASIVE TUMOUR LOAD QUANTIFICATION FROM BLOOD PLASMA

Pronk B[1, 2], van de Wiel M[3], Değer T[2], Wullaert L[4], Jansen M[2], Kraan J[2], Beaufort C[2], Grünhagen D[4], Boers R[5], Gribnau J[5], Sleijfer S[2], Verhoef C[4], Martens J[2], Wilting S[2] and Makrodimitris S[2,1]

[1]*Delft Bioinformatics Lab, Delft University of Technology*
[2]*Medical Oncology, Erasmus MC Cancer Institute*
[3]*Epidemiology and Biostatistics, VU Medical Center*
[4]*Oncologic Surgery, Erasmus MC Cancer Institute*
[5]*Developmental Biology, University Medical Center Rotterdam*

INTRODUCTION

Accurate quantification of circulating tumour DNA (ctDNA) load from liquid biopsies has several potential applications in cancer diagnosis and monitoring, but remains challenging. Variant Allele Frequency (VAF) of tumour-derived mutations determined by targeted sequencing of cell-free DNA (cfDNA) is a common proxy for ctDNA load, but requires prior knowledge of patient-specific mutations or large, costly sequencing panels. Alternative methodologies, such as enumeration of circulating tumour cells (CTCs) and genome-wide DNA methylation profiling of cfDNA, have been proposed as alternative, prior knowledge-independent strategies. This study compares and integrates these methods to quantify ctDNA load in patients with metastatic colorectal cancer (mCRC).

METHODS

In 102 mCRC patients we performed the following measurements: a) cfDNA quantification b) mutation profiling of 242 hotspot mutations in 14 genes commonly mutated in CRC c) genome-wide methylation profiling of plasma cfDNA, d) CTC quantification using immunofluorescence, and e) expression profiling of 94 mCRC-specific genes in CTCs using quantitative PCR. 70 out of 102 patients had a detectable hotspot mutation, the VAFs of which were used as ground truth for the tumour load in plasma. We then used machine learning to predict the VAF using a) a methylation-based tumour fraction estimate, b) the gene expression features, and c) all features.

RESULTS

The Spearman correlation coefficient to the observed VAF was the highest for methylation (ρ=0.80), followed by CTC count (ρ=0.35). Leave-one-out cross-validation determined that the multi-omic model using all five measurements was the best at predicting the VAF, while all models outperformed a baseline with only age and gender. Applying our best model to 32 pre-operative samples of resectable colorectal liver metastases without detectable mutations yielded non-zero tumour fraction estimates in all. Patients with recurrent disease within a year after resection had significantly higher predicted tumour load than those without (median 7.98% vs 1.61%, $p = 0.009$).

CONCLUSION

Methylation is the most reliable single predictor of ctDNA as determined by the VAF. Even more accurate predictions were obtained by combining different tumour-agnostic measurements in a multivariate model. Our model was validated on unseen patients by demonstrating its prognostic value, but further validation in larger cohorts is warranted.

ABSTRACT NO.41

DNA METHYLATION MARKERS FOR FEMALE GYNAECOLOGICAL CANCERS AND HPV-RELATED CANCERS: TYPE-SPECIFIC AND COMMON PATTERNS

Eef van den Borst[1,2], Joe Ibrahim[2], Yann Heylen[2], Tine Pinxteren[1,2], Severien Van Keer[1], Ken Op de Beeck[2], Guy Van Camp[2], Alex Vorsters[1]

[1]Centre for the Evaluation of Vaccination (CEV), Vaccine & Infectious Disease Institute (VAXINFECTIO), University of Antwerp, Edegem (Antwerp), Belgium
[2]Centre of Medical Genetics (CMG), University of Antwerp and Antwerp University Hospital (UZA), Edegem (Antwerp), Belgium

BACKGROUND

DNA methylation is a promising biomarker for early cancer detection and applicable in vaginal and urine self-samples, sparking interest for cervical cancer screening and detection of other gynaecological cancers. Yet, marker specificity is crucial as material from multiple sites may be present.

METHODS

We analysed Illumina 450K and EPIC methylation data from the Gene Expression Omnibus (GEO) and The Cancer Genome Atlas (TCGA) from cervical cancer (CC), endometrial cancer (EC), ovarian cancer (OC), and vulvar cancer (VC). Furthermore, we were interested in a DNA methylation signature induced by the human papillomavirus (HPV). To this end, we also collected data regarding head and neck cancer (HNC) and anal cancer (AC). In total, data (IDATs) was extracted from 466 CC, 120 normal cervix, 620 EC, 80 normal endometrium, 508 OC, 34 normal ovary or fallopian tube, 14 VC (3 HPV+), 6 normal vulva, 120 AC, 9 normal anus, 44 HPV+ HNC and 19 normal head and neck. Cancer vs. normal and cancer vs. cancer methylation patterns were compared to identify differentially methylated probes (DMPs, FDR<0.01) using an in-house developed bio-informatic pipeline starting from the ChAMP package.

RESULTS

Cancer vs. normal DMPs were 253.198 for CC, 220.239 for EC, 58.040 for VC and 170.546 for OC. The overlap was 27.680 DMPs and after filtering on delta-beta of >0.15, 8749 DMPs remained. Specific DMPs (FDR<0.01, delta-beta>0.15) determined based on overlap between cancer vs. normal and cancer vs. cancer comparisons, were 966 for CC, 2076 for EC, 3080 for VC and 741 for OC. The HPV-associated signature consisted of 4841 DMPs (FDR<0.01, delta-beta>0.15).

CONCLUSION

In conclusion, we identified methylation markers specific for CC, EC, OC, and VC as well as overlapping markers for female gynaecological cancers and HPV-induced cancers. Based on this, clinically relevant biomarkers can be discovered, aiding in correct clinical management.

ABSTRACT NO.42

DIAGNOSTIC ACCURACY OF ABBREVIATED MAGNETIC RESONANCE IMAGING FOR BREAST CANCER SCREENING AMONG WOMEN WITH EXTREMELY DENSE BREASTS: A MULTI-READER STUDY

Sophie E.L. van Grinsven, Ritse M. Mann, Evelyn M. Monninkhof, Katya Duvivier, Mathijn D.F. de Jong, Petra K. de Koekkoek- Doll, Claudette E. Loo, Ruud M. Pijnappel, Rogier van der Sluijs, Jeroen Veltman, Carla H. van Gils, Wouter B. Veldhuis, for the DENSE Trial Study Group

PURPOSE

Costs and time of a full multi-parametric MRI protocol may be reduced by using an abbreviated MRI (AB-MRI) protocol. The DENSE trial's multiparametric protocol provided the unique opportunity to study the accuracy of various abbreviated MRI protocols, focusing on identifying the minimal protocol necessary to maintain high diagnostic accuracy.

METHODS

Seven radiologists performed incremental reads of a subset of 518 MRI examinations from the DENSE trial (women with extremely dense breasts and negative mammography). Different sequences were added in four incremental steps, starting with: 1) both high resolution (hi-res) and ultra-fast T1-weighted images (T1WI), up to 120 seconds after contrast-injection only, 2) complemented by diffusion-weighted images (DWI), 3) T2-weighted images (T2WI), and 4) finally adding all remaining full protocol sequences: non-fatsat-T1-weighted pre-contrast images, all remaining dynamic phases, and curve-kinetics. Each radiologist assessed the same 518 MRI examinations and provided BI-RADS scores for all four incremental steps. We calculated the pooled sensitivity and specificity per incremental step by using a generalized estimating equation model.

RESULTS

The sensitivity of the most abbreviated MRI protocol (step 1) was not significantly different from that of the full multiparametric MRI protocol (step 4) ($p=0.68$). Similarly, specificity was not significantly different ($p=0.39$). The pooled reading time of step 1 was almost 50% shorter than that of the full multiparametric MRI protocol ($p<0.01$), and the MR acquisition time was 70-80% shorter, depending on the hospital and scanner vendor.

CONCLUSION

In a screening setting, a full multiparametric MRI protocol, including pre-contrast DWI and T2WI, and delayed post-contrast T1WI, did not provide significant additional diagnostic information for making a recall/no-recall decision compared to an ultrafast bi-dynamic T1WI-only protocol.

ABSTRACT NO.43

DENSE-2: SUPPLEMENTAL CONTRAST-ENHANCED MAMMOGRAPHY AND ABBREVIATED MRI SCREENING FOR WOMEN WITH EXTREMELY DENSE BREASTS

Sophie E.L. van Grinsven, Wouter B. Veldhuis, Marc B.I. Lobbes, Ritse M. Mann, Mireille J.M. Broeders, Nicolien T. van Ravesteyn, Evelyn M. Monninkhof, Carla H. van Gils
On behalf of the DENSE-2 consortium

PURPOSE
The results of the DENSE trial showed that supplemental MRI screening in women with extremely dense breasts significantly lowers the rate of interval cancers. Based on these and other results, the European Society of Breast Imaging now recommends supplemental screening with MRI for women with extremely dense breasts. However, although cost-effective MRI screening scenarios have been identified, the related costs and required capacity are a barrier for implementation. Therefore, the DENSE-2 trial will study contrast-enhanced mammography (CEM) and abbreviated MRI (AB-MRI) as supplemental screening techniques because we expect these techniques to be more efficient.

METHODS
The DENSE-2 trial is a randomized controlled trial (RCT), within the Dutch population-based biennial screening program (age 50-75). Women with extremely dense breasts (assessed with Quantra 2.2 software, category D) and negative mammography results (BI-RADS 1 or 2) will be randomized in a 1:1:4 ratio into three groups: CEM (n=6000), AB-MRI (n=6000), and a control group continuing with standard mammography-only screening (n=24,000). The trial consists of two consecutive screening rounds.

RESULTS
The primary outcome is the interval cancer rate in the intervention groups (CEM and AB-MRI) versus the control group. Other important outcomes are the cancer detection rates, the false positive rates, the participant and health professional user experience, the estimated extent of overdiagnosis and the cost-effectiveness.

CONCLUSION
DENSE-2 will provide solid evidence on whether supplemental screening with CEM or AB-MRI leads to earlier detection of clinically relevant breast cancers, reduces the incidence of interval cancers, and whether these techniques are affordable.

ABSTRACT NO.44

A PROSPECTIVE EVALUATION OF TUMOR-ASSOCIATED AUTO-ANTIBODIES AS EARLY DETECTION MARKERS FOR OVARIAN CANCER

Victoria Cooley[1,2], Rudolf Kaaks[1], Karen Anderson[3], and Renée Turzanski Fortner[1,4] for the PREDICT consortium

[1]*Division of Cancer Epidemiology, German Cancer Research Center (DKFZ), Heidelberg, Germany*
[2]*Medical Faculty Heidelberg, Heidelberg University, Germany*
[3]*Virginia G. Piper Center for Personal Diagnostics, Biodesign Institute, Arizona State University, Tempe, AZ, United States*
[4]*Department of Research, Cancer Registry of Norway, Norwegian Institute of Public Health, Oslo, Norway*

BACKGROUND

Epithelial ovarian cancer (EOC) is a lethal gynecologic malignancy that is typically diagnosed as disseminated disease and survival outcomes are poor. CA125 remains the best available EOC biomarker, however its discrimination in the prospective setting between cases and cancer-free individuals is limited, and could be potentially improved with the addition of tumor-associated autoantibodies (AAbs), such as AAbs to P53 proteins and cancer-testis antigens (CTAGs).

METHODS

We evaluated the discrimination capacity of circulating levels of 11 AAbs (CTAG1A, CTAG2, NUDT11, TP53, RIPK2, BMPR2, PVRB, SLC27A5, SPSB1, TRIM39, and ZNF626) identified in prior discovery studies, alongside CA125 as potential earlier detection biomarkers in the Prospective Early Detection Consortium for Ovarian Cancer (PREDICT). Blood samples taken ≤18 months prior to diagnosis in EOC cases were evaluated in comparison to matched controls. AAbs were measured using RAPID-ELISA. Areas under the ROC curves (AUCs) were calculated using logistic regression.

RESULTS (PRELIMINARY)

Overall, AAbs to TP53 and CTAG1A had the highest discrimination between cases and controls in the 0-<6 month lag-time interval (i.e. AUC (95%CI): TP53: 0.65 (0.58, 0.71) and CTAG1A: 0.63 (0.56, 0.70)) and generally decreased as the time between blood draw and cancer diagnosis increased (i.e. 12-≤18 month interval: TP53: 0.58 (0.52, 0.63) and CTAG1A: 0.53 (0.47, 0.58)). Patterns across the other AAbs were similar. The discrimination of CA125 followed a similar decline, but substantially higher values were observed across all lag-time intervals (i.e. 0-<6 months: 0.92 (0.88, 0.96) and 12-≤18 months 0.69 (0.64, 0.75)). Upon the separate additions of CTAG1A and TP53 to a model with CA125, no meaningful improvements in discrimination were observed (i.e. 12-≤18 month interval CA125 + TP53 : 0.70 (0.65, 0.76)).

CONCLUSIONS

Building on this important initial work, further work involving the development of multimarker models with CA125 and different combinations with the selected AAbs will be explored.

ABSTRACT NO.45

THE POTENTIAL OF PANCREATIC JUICE BASED BIOMARKERS: A MICROSIMULATION ANALYSIS

Olly White, Djuna Cahen, Iris Lansdorp-Vogelaar, Marloes Sprij, Gwenny Fuhler, Maikel Peppelenbosch, Inge de Kok

BACKGROUND/OBJECTIVES

Pancreatic cancer (PC) remains one of the most lethal cancers, with early detection being crucial for improving survival rates. Screening methods such as Magnetic Resonance Imaging (MRI) and/or Endoscopic Ultrasound (EUS) are used for high-risk individuals but have limited effectiveness in reducing mortality. Newly developed blood and pancreatic juice-based biomarker tests show promise for detecting PC at treatable stages, but it is unclear how well these tests need to perform to significantly reduce mortality. Serum carbohydrate antigen 19.9 (CA19.9) is currently the only biomarker used during PC surveillance. This study aims to determine the optimal test characteristics of potential new PC biomarkers.

METHODS

We utilized the MISCAN microsimulation model to evaluate the impact of different test sensitivities and specificities on PC surveillance outcomes. The model simulated a cohort of high-risk individuals (i.e. lifetime risk of 18%) undergoing regular screening using different testing types. Sensitivity and specificity values were increased from the reported values of CA19-9, which serves as a base case. Key outcomes measured included number needed to screen to prevent one PC death (NNS) and mortality reduction, compared to current surveillance programs using MRI/EUS. Optimal sensitivity and specificity values were determined by using the NNS of established cancer screening programs as a benchmark (breast cancer (111), lung cancer (320) and colorectal cancer screening (515).

RESULTS

A biomarker test that detects high-grade dysplasia or early-stage cancer with a sensitivity of 80% would increase the mortality reduction of current surveillance programs by 21%. An increase in test specificity from 79% to 95% resulted in 34% fewer unnecessary surgeries and reduced the NNS from 321 to 188.

CONCLUSIONS

Our findings suggest that pancreatic juice-based biomarkers could offer substantial improvements over CA19-9 in pancreatic cancer surveillance Future research should focus on finding PC biomarkers that fit these test characteristics to achieve the potential benefits outlined in this study.

ABSTRACT NO.46

DECONVOLVING THE PATTERNS OF COPY NUMBER ALTERATIONS IN BARRETT'S ESOPHAGUS PROGRESSION FROM MULTI-REGIONAL SEQUENCING

Lianlian Wu, Timothy Somerset, Zhidong Zhang, Ginny Devonshire, Massimiliano Di Pietro, Alexander Frankell, Rebecca Fitzgerald

Early Cancer Institute, University of Cambridge, Cambridge Biomedical Campus, Cambridge, UK

INTRODUCTION

The progression of Barrett's Esophagus (BE) to malignancy is accompanied by increasing copy number alterations (CNAs). However, the timing of CNAs events during evolution remains unclear. This study leverages multi-regional, longitudinal sequencing of BE to map CAN temporal dynamics, identify key drivers of BE progression, and improve risk stratification.

METHODS

Two BE cohorts were analyzed. The discovery cohort included shallow whole-genome sequencing (sWGS, 0.4X) from 777 BE samples across 88 patients, while the validation cohort included 256 BE samples from 95 patients. We refined the bioinformatics tool RASCAL[1] to improve absolute CNA analysis by automatically selecting high-quality samples. Phylogenetic trees were generated by MEDICC2[2] to classify CNAs along an evolutionary timeline (Figure 1). Risk scores were computed based on the probability of CNA occurrence in non-progressing vs. dysplastic BE samples. A random forest model was trained to predict dysplasia based on risk score and validated in an independent cohort.

RESULTS

In the discovery cohort, 52.3% (260/497) of NDBE and 75.2% (124/165) of dysplastic samples were high-quality, with 16.9% (21/124) of dysplastic samples exhibiting whole genome doubling (WGD). In the validation cohort, 79.4% (181/228) of NDBE and 86.2% (25/29) of dysplasia/cancer samples were high-quality, with WGD in 24.0% (6/25) of dysplastic cases. Early-stage CNAs in non-progressing BE showed specific chromosomal gains and losses, whereas later-stage CNAs in dysplasia were more widespread and less commonly shared. Risk scoring of known drivers revealed that SMAD4 losses and CCND3/GATA4 gains were linked to dysplasia. Our model with divergent evolutionary patterns predicted dysplasia with an AUC of 0.89 (Sensitivity: 80.6%, Specificity: 95.7%) in the discovery set and AUC of 0.84 in the validation set (Sensitivity: 73.1%, Specificity: 93.9%).

CONCLUSION

This study maps CNA evolutionary trajectories in BE, demonstrating selective constraints in early evolution and stochastic processes in dysplastic progression. CNA-based risk scores offer a promising tool for lesion risk stratification.

[1]Sauer C M, Eldridge M D, Vias M, et al. Absolute copy number fitting from shallow whole genome sequencing data. Biorxiv, 2021: 2021.07. 19.452658

[2]Kaufmann T L, Petkovic M, Watkins T B K, et al. MEDICC2: whole-genome doubling aware copy-number phylogenies for cancer evolution. Genome biology, 2022, 23(1): 241

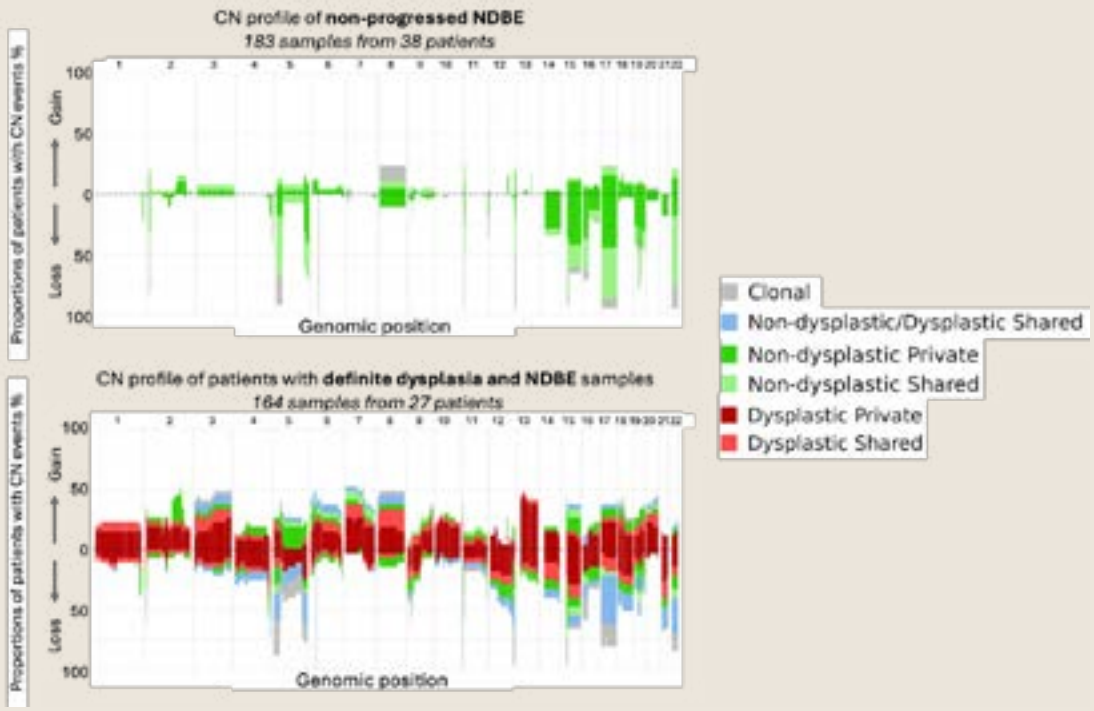


Figure 1. *The copy number profiles of early and later events across different stages of Barrett's Esophagus (BE). This figure illustrates the copy number alteration (CNA) profiles associated with dysplastic progression in BE. For low-risk CN events, the profile of patients were not progressed were shown. For high-risk CN events, the patients who have both dysplastic and NDBE samples were displayed, from which the early CN events can be distinguished from those associated with dysplasia. CNAs are classified based on phylogenetic analysis, progressing from early to later stages: clonal CNAs (earliest, shared across all samples from a patient), followed by non-dysplastic shared, dysplastic shared, non-dysplastic private, and dysplastic private CNAs, each visualized using distinct colors. Low-risk evolutionary trajectories—observed in patients who never progressed to cancer or in cases where alterations were inferred to have occurred before histological signs of progression—exhibited a distinct pattern of specific chromosomal gains and losses, typically occurring early in the evolutionary timeline, while later-stage CNAs appeared widely across the genome.*

ABSTRACT NO.47

MULTICENTER DIGITAL-BASED EARLY DETECTION AND RISK REDUCTION INTERVENTION FOR INDIVIDUALS AT HIGH RISK OF CANCERS

Lucie Veron[1], Claudia Lefeuvre-Plesse[2], Mélanie Besnier[2], Jade Gelinier[2], Marc Alfonsi[3], Pierre Schillinger[3], Béatrice Fervers[4], Pauline Vidican[4], Tiphaine Renaud[5], Anika Bensen[5], Youssef Tazi[6], Isabelle Guillot[6], Thomas Pudlarz[1], Pamela Abdayem[1], Tarek Ben Ahmed[1], Marion Aupomerol[1], Hélène Caron[1], Muriel Wartelle[7], Clara Bechet[8], Stéphane Chaillou[7], Claire Bladier[1], Suzette Delaloge[1], Olivier Caron[1]

* Bruno Achutti-Duso

[1]*Interception program, department of medical oncology, Gustave Roussy Cancer Center, France*
[2]*Eugène Marquis Cancer Center, Rennes, France*
[3]*Sainte Catherine Cancer Center, Avignon, France*
[4]*Léon Bérard Cancer Center, Lyon, France*
[5]*Bergonié Cancer Center, Bordeaux, France*
[6]*Strasbourg Oncologie Libérale, Strasbourg, France*
[7]*Informatic department, Gustave Roussy Cancer Center, France*
[8]*Data protection office, Gustave Roussy Cancer Center, France*

OBJECTIVES
Large-scale deployment of precision prevention aiming to intercept cancer among individuals identified at high risk is a major unmet medical need.

METHODS
In 2021, we launched the Interception program that includes 1. Identification of individuals at high risk of several cancers in the general population by primary care providers (PCP); 2. A One Stop prevention clinic aiming at informing, educating, motivating and empowering the participants through individual visits and examinations, group workshops or training sessions (lifestyle), and producing a shared personalized prevention plan (PPP); 3. A digital-based long-term follow-up. Insurance coverage is provided for the full pathway, with no cost for participants. A dedicated App is provided to the participants that includes all questionnaires, allows them to retrieve their data, get additional information, have access to their PPP and scheduled examinations + reminders.

RESULTS
Among 2300 participants so far, only around 20% have been identified by PCP, while most were self- (30%) or hospital-referred (50%). For 719 participants with 1 year follow-up, adherence to screening plans was > 90%, 41% improved their lifestyle (increase of WCRF score by >=1 point), but only 18% quit smoking. Perceived knowledge increased dramatically at day 8 (p= < 2.2 e-16). The global satisfaction rate was 93%. Since June 2024, the program has been extended to 5 additional French centers. In the early evaluation of this national implementation, local health care providers could be adequately trained to deliver the intervention in all centers, the One stop clinic could be delivered as planned in > 80% sessions, and the participants' satisfaction rates remained stable at 93%.

CONCLUSION
The two major issues encountered so far are low rate of PCP referral and over-representation of educated participants, which we plan to address through involvement of pharmacists and community nurses, broader information and training of HCPs, and future opening of centers in more deprived areas.

ABSTRACT NO.48

AI DETECTION PERFORMANCE ON PRE-DIAGNOSTIC PANCREATIC CANCER CECT SCANS

Tijmen de Haas, Dawid Rutkowski, Natália Alves, Megan Schuurmans, Matthias Löhr, Henkjan Huisman, John Hermans

RadboudUMC, Beeldvorming, Nijmegen, The Netherlands

BACKGROUND/OBJECTIVES

Early detection of pancreatic ductal adenocarcinoma (PDAC) improves survival, yet lesions remain undetected in 16% of cases 24–36 months and 85% of cases 3–6 months before diagnosis. The PANORAMA Grand Challenge establishes the state-of-the-art AI performance at pancreatic cancer detection in contrast-enhanced computed tomography (CECT). However, AI potential in aiding early diagnosis has yet to be evaluated. We hypothesize AI can help find PDAC in pre-diagnostic CECT scans.

METHODS

The AI algorithm is an ensemble of the top three performing models from the PANORAMA challenge and was evaluated on a pre-diagnostic cohort. The algorithm was trained on a publicly available dataset of 2238 cases. A set of 957 cases, including two external centers, was used for algorithm testing and ranking. The pre-diagnostic testing cohort includes over 300 CECT from an external center in Sweden, which was not used in development. The pre-diagnostic images are acquired 10 years to 3 months prior to clinica ldiagnosis and have histopathology confirmation. The pre-diagnostic imaging reports included in the cohort do not mention pancreatic cancer. Performance was evaluated using the area under the receiver operating characteristic curve (AUROC) for PDAC detection at each time point.

RESULTS

The top three algorithms achieved AUROC of 0.9263 (95%CI 0.9085-0.9429), 0.9239 (0.9068-0.9400), and 0.9090 (0.8876-0.9288) on the external testing set. AI performance in the pre-diagnostic time-cohort dataset is currently being evaluated and will be presented for the first time at the NKI early cancer diagnosis conference.

CONCLUSIONS

AI is capable of diagnosing patients with PDAC in early stages and can work in opportunistic screening to improve patient outcomes.

ABSTRACT NO.49

EXTERNAL VALIDATION OF BREAST CANCER RISK PREDICTION MODELS FOR PERSONALIZED SCREENING IN A PROSPECTIVE DUTCH SCREENING COHORT

Jim Peters[1], Danielle van der Waal[2], Carla H van Gils[3], Marjanka K Schmidt[4], Mireille JM Broeders[1,2], PRISMA consortium

[1]*Radboud University Medical Center, Department IQ Health, Nijmegen, The Netherlands*
[2]*Dutch Expert Center for Screening (LRCB), Nijmegen, The Netherlands*
[3]*Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands*
[4]*The Netherlands Cancer Institute, Division of Molecular Pathology and Division of Psychosocial Research and Epidemiology, Amsterdam, The Netherlands*

BACKGROUND

Tailoring breast cancer screening intensity to individual risk is expected to improve the harm-benefit ratio of screening compared to a 'one-size-fits-all' approach. Accurate risk prediction is essential for personalized screening. This study externally validates four established risk prediction models in a Dutch screening cohort.

METHODS

The Personalized Risk-based MAmmascreening (PRISMA) study is a prospective cohort study (inclusion 2014-2019) embedded in the Dutch biennial breast cancer screening program. Breast cancer risk was predicted for 27,804 participants using four established models: Gail, Breast Cancer Surveillance Consortium (BCSC) model, Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA), and the International Breast cancer Intervention Study (IBIS) model. We used questionnaire data (lifestyle, hormonal, family history) and mammogram-derived breast density -not included in Gail- to derive 5-year risk estimates (genetic information was set to unknown) Breast density was automatically measured on raw mammograms using Volpara version 1.5.0. Breast cancer diagnoses were ascertained through linkage with the Netherlands Cancer Registry until October 2023. Participants with screen-detected breast cancer at study entry (n=189) were excluded. Performance to predict 5-year breast cancer risk was evaluated using the concordance index (C-index), observed-expected (O/E) ratio and calibration slope.

RESULTS

After a median 4.3 years of follow-up (IQR 3.9-4.6), 361 breast cancer cases were observed. Prediction models reached the following performance metrics to predict 5-year breast cancer risk:
- Gail: C-index 0.56, O/E 0.91, calibration slope 0.68
- BCSC: C-index 0.60, O/E 1.07, calibration slope 0.90
- BOADICEA: C-index 0.59, O/E 1.23, calibration slope 0.59
- IBIS: C-index 0.60, O/E 0.67, calibration slope 0.70

CONCLUSION

In the Dutch screening population, breast cancer risk models based on questionnaires and density show moderate discriminative accuracy, slightly lower compared to their derivation cohorts, with only BCSC being well-calibrated. Better performing models are needed for personalized general population screening.

ABSTRACT NO.50

INSIGHTS FROM GENOMIC ANALYSES OF DUCTAL CARCINOMA IN SITU OF THE BREAST

Leon Wils[1], Lucia Chmelova[2], Lennart Mulder[1], Petra Kristel[1], Will Harley[1], Renee de Menezes[3], Johan Staaf[4], Therese Sorlie[5], Helen Davies[2], Serena Nik-Zainal[2], Jelle Wesseling[1], Esther Lips[1]

[1]*Division of Molecular Pathology, The Netherlands Cancer Institute, Amsterdam, The Netherlands.*
[2]*Early Cancer Unit, Hutchison/MRC Research Centre and Academic Department of Medical Genetics, Cambridge Biomedical Research Campus, University of Cambridge, Cambridge, UK*
[3]*Division of Psychosocial research and Epidemiology, The Netherlands Cancer Institute, Amsterdam, The Netherlands*
[4]*Division of Oncology, Department of Clinical Sciences Lund, Lund University, Lund, Sweden*
[5]*Department of Cancer Genetics, Institute for Cancer Research, Oslo University Hospital, Oslo, Norway*

BACKGROUND/OBJECTIVES

Ductal carcinoma in situ (DCIS) is a non-obligate precursor of invasive breast cancer. The PRECISION consortium aims to enhance understanding of the mechanisms underlying DCIS progression and to develop predictive markers for the risk of transformation to breast cancer. To date, the PRECISION studies have primarily relied on archival FFPE tissue material, which allows longitudinal outcome analysis but is often limited by the low quality and quantity of available material. To overcome these limitations, we aimed to explore the comprehensive genomic landscape of DCIS using whole-genome sequencing and RNA sequencing on high-quality fresh frozen DCIS samples, similarly to what was previously done for breast cancer[1].

METHODS

We collected fresh frozen biopsies and matched normal DNA from 113 DCIS patients from three institutions. Subsequently, we performed whole-genome sequencing and RNA-seq in order to elucidate the driver landscape of DCIS, identify molecular signatures and determine RNA-seq risk classifier scores[2].

RESULTS

We observed driver mutations in the most commonly mutated breast cancer genes. ERBB2 amplification (50%) was the most frequent driver mutation, followed by TP53 (43%) and PIK3CA (27%) point mutations. In DCIS without ERBB2 amplification, we observed a diverse range of driver mutations. DCIS often harbors clustered structural rearrangements and substitution signatures linked to the APOBEC family of cytidine deaminases (48%). Additionally, DCIS lesions exhibit mutational signatures associated with germline defects in DNA repair pathways. Extrachromosomal DNA was present in 29 out of 60 HER2 positive DCIS, resulting in increased ERBB2 copy number in those samples. Seven samples had a high-risk DCIS RNA-seq risk score.

CONCLUSION

DCIS lesions share many genomic characteristics with invasive breast cancers, including driver mutations and mutational signatures, suggesting that many mutational processes involved in invasive breast cancer are already operational in pre-cancerous DCIS lesions.

[1]Nik-Zainal et al. Nature (2016)
[2]Lips et al. EACR (2024)

ABSTRACT NO.51

DEVELOPMENT AND CLINICAL IMPLEMENTATION OF A CELLULAR FUNCTIONAL ASSAY TO DETERMINE THE ACTIVITY OF VARIANT DNA MISMATCH REPAIR GENES

Iris Glykofridis, Marleen Dekker, Chantal Stoepker, Thomas van Ravesteyn, Hein te Riele & INVUSE consortium members

Division of Tumor Biology and Immunology, Netherlands Cancer Institute, 1066CX Amsterdam, The Netherlands

The rapid expansion of diagnostic sequencing in clinical genetics yields a growing pool of so-called Variants of Uncertain Significance (VUSs) in disease genes. These VUSs are often single base-pair alterations that substitute a single amino acid or a residue outside gene coding regions. In Lynch Syndrome, patients are predisposed to develop colorectal and endometrial cancer due to a germline mutation in one of the DNA mismatch repair (MMR) genes (MSH2, MSH6, MLH1 or PMS2). Sequencing of the DNA MMR genes, often reveals a VUS rather than a clearly pathogenic variant of the particular gene. As long as its functional consequences cannot be ascertained, the diagnosis Lynch Syndrome cannot be established or excluded, which precludes the identification of family members at risk or not at risk and therefore installment of targeted surveillance or curative treatment.

The KWF-sponsored consortium INVUSE ("Investigating Variants of Uncertain Significance for USE in clinical practice") unites the expertise of basic scientists, clinical laboratory geneticists, pathologists, gastroenterologists, gynecologists and surgeons from all Dutch academic medical centers and the Netherlands Cancer Institute-Antoni van Leeuwenhoek hospital. The aim of INVUSE is to develop and implement into routine diagnostics two complementary functional assays to determine the activity of DNA MMR VUSs. We here present the results of a cellular assay: oligonucleotide-directed mutation screening (ODMS) that interrogates VUS activity in a normal genomic and cellular environment. The assay results, in combination with all available functional and clinical data, will help to draw a robust conclusion on the phenotypic consequences of MMR VUSs.

ABSTRACT NO.52

THE EXTERNAL VALIDATION OF IMMUNOHISTOCHEMICAL MARKERS AS PROGNOSTIC FACTORS FOR SUBSEQUENT INVASIVE BREAST CANCER AFTER DUCTAL CARCINOMA IN SITU

C.V. Mulder, P. Kristel, L. Mulder, S. Cornelissen, R. Menezes, M. Schaapveld, M.K. Schmidt, J. Wesseling, E.H. Lips

Upon the inception of population-based screening programs, the incidence of ductal carcinoma in situ (DCIS) increased 6-fold. DCIS is a non-obligate precursor lesion of invasive breast cancer (IBC), of which the majority does not progress. This implies that women with non-progressive DCIS are overtreated. Several immunohistochemical markers have been identified as prognostic factors to distinguish progressive from non-progressive DCIS. Here we aim to externally validate these prognostic markers.

We conducted a case-cohort study nested in a Dutch population-based cohort of 8987 patients with DCIS treated with breast-conserving surgery (BCS) with or without radiotherapy between 2005 and 2015. Tissue blocks were requested for all 1237 women in the case-cohort, of which 940 were received and eligible for immunohistochemical analysis of ER, Her2, COX-2, Ki67 and p16. To assess the association of each marker and iIBC risk, weighted Cox proportional hazards models, with study time as underlying time scale, were implemented. All models were stratified by age at diagnosis and radiotherapy use, and adjusted for DCIS grade, size and margins status.

In our case-cohort, 316 women developed iIBC. The median follow-up time for the case-cohort was 7.2 years (interquartile range (IQR): 5.2-10.1). Cases were treated more frequently with radiotherapy than controls (76.0% vs 68.4%, p = 0.01) and were more often high grade DCIS (46.4% vs 38.0%, p = 0.04). In stratified cox proportional hazards models, ER, Her2, Ki67 and p16 were not statistically associated with subsequent iIBC. Interactions between ER and HER2, Her2 and Ki67, Ki67 and p16 and HER2, Ki67 and p16 were tested and were all not signifcantly associated with iIBC.

Currently we were unable to validate the aforementioned immunohistochemical markers as prognostic factors. Future work into morphological or molecular markers may shed light on the progression to iIBC in primary DCIS.

ABSTRACT NO.53

ONCOFETAL CHONDROITIN SULFATE ALLOWS IDENTIFICATION OF TUMOR-DERIVED EXTRACELLULAR VESICLES DIRECTLY IN BLOOD

Agustin Enciso-Martinez[1,2,3], Caroline Løppke[4], Joyce J. Koene[†,1], Jade Ebbelaar[†,3], Meike van der Geest[1], Mandy Los[3], Emma P.E.M. Boerrigter[1], Robert Dagil[4], Tobias Gustavsson[4,5], Elena Ethel Vidal-Calvo4, Ton G. van Leeuwen[2], Roman I. Koning[6], Nick van Es[7,8], Ali Salanti[4], Edwin van der Pol[‡,2,3], Rienk Nieuwland[‡,3], Mette Ø. Agerbæk[‡,4,9] and Peter ten Dijke[‡,1]

[1]Oncode Institute and Ten Dijke/Chemical Signaling Laboratory, Department Cell and Chemical Biology, Leiden University Medical Center, Leiden, The Netherlands
[2]Amsterdam UMC, University of Amsterdam, Biomedical Engineering & Physics; Amsterdam Cardiovascular Sciences, Cancer Center Amsterdam, Meibergdreef 9, Amsterdam, The Netherlands
[3]Amsterdam UMC, University of Amsterdam, Laboratory of Experimental Clinical Chemistry; Laboratory Specialized Diagnostics & Research, Department of Laboratory Medicine, Meibergdreef 9, Amsterdam, The Netherlands
[4]Centre for translational Medicine and Parasitology at Department for Immunology and Microbiology, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark
[5]VAR2 Pharmaceuticals ApS, Frederiksberg, Denmark
[6]Electron Microscopy Facility, Department of Cell and Chemical Biology, Leiden University Medical Center, Leiden, The Netherlands
[7]Department of Vascular Medicine, Amsterdam UMC location University of Amsterdam, Amsterdam, Netherlands
[8]Amsterdam Cardiovascular Sciences, Pulmonary Hypertension & Thrombosis, Amsterdam, The Netherlands
[9]VarCT Diagnostics, Frederiksberg, Denmark
[†,‡]These authors contributed equally

BACKGROUND

Tumor-derived extracellular vesicles (tdEVs) hold significant promise as biomarkers for early cancer detection through liquid biopsies. However, no tumor-specific markers are known that allow robust detection of tdEVs. Here, we show for the first time that oncofetal Chrondroitin Sulfate (ofCS), a malignancy-associated glycosaminoglycan modification, is present on tdEVs, and propose it as a novel biomarker. Unlike low-abundance protein markers, ofCS modifies multiple tdEV proteins, enhancing detection. Using the VAR2CSA protein, which selectively binds to ofCS, we successfully identified tdEVs from various types of cancer cells in vitro, as well as in blood plasma samples of pancreatic adenocarcinoma (PDAC) patients.

METHODS

The recombinant VAR2CSA (Malaria-encoded) protein (rVAR2) was fluorescently labelled, and used to detect tdEVs from cancer cell lines, tdEVs spiked into healthy plasma, and tdEVs in plasma from advanced-stage PDAC patients. For validation, we used orthogonal single EV detection methods, including calibrated flow cytometry and super-resolution fluorescence microscopy. The staining specificity was validated using a non-ofCS binding rVAR2 mutant, and enzymatic digestion of ofCS chains by chondroitinase treatment prior to staining.

RESULTS

We identified ofCS+ tdEVs in conditioned media from multiple cancer cell lines. Furthermore, we detected tdEVs spiked into healthy donor plasma, as well as ofCS+ tdEVs in plasma from PDAC patients. In contrast, only minimal rVAR2 levels were detectable in plasma samples from healthy controls. These findings were consistent across the different methods, and the ofCS specificity of the rVAR2 staining was validated using

the rVAR2-mutant controls and chondroitinase treatment, both of which led to a significant decrease in particle counts and fluorescence signal.

CONCLUSION

Our study demonstrates that tdEVs display ofCS on their surface, allowing for selective targeting by the malarial VAR2CSA protein. Thus, this approach offers a tool to identify tdEVs, and can be used to explore their function and biomarker potential in cancer.

ATTENDEE LIST

NAME ATTENDEE	JOB TITLE	INSTITUTE / COMPANY
Eddymurphy Akwiwu	Doctoral researcher	Amsterdam UMC
Soha Allioui	Intern	UMC Utrecht
Diana Andreoli	PhD candidate	University of Twente
Philip Awadalla	Professor and Senior Group Leader	Nuffield Department of Population Health, Big Data Institute, University of Oxford
Svetlana Bajalica Lagercrantz	MD, Professor	Karolinska Institutet
Jan Willem Beijer	CCO	Sirius Medical
Jacques Bergman	Professor of Gastrointestinal Endoscopy, Head of Innovation, dept of Gastroenteroloy Amsterdam UMC	Amsterdam UMC
Hans Berkhof	Head of department Epidemiology and Data Science	Amsterdam UMC
Doreth Bhairosing	Research Coordinator	NKI Center for Early Cancer Detection
Patrick Bier	BDM	Olink Proteomics
Mara Blonden	Business Director	Netherlands Cancer Institute
Stig Egil Bojesen	Clinical professor	Herlev and Gentofte Hospital
Jillian Bracht	Postdoctoral Researcher	Amsterdam UMC
Mireille Broeders	Professor Personalized Cancer Screening	Radboud University Medical Center
Esther Brouwer	Projectleader	RIVM-CvB
Ipek Bulut	Postdoctoral Researcher	Koc University
Ronald Burggrave	Director	Genetic Tools Europe B.V.
Sarah Carden	International Alliance for Cancer Early Detection (ACED) Programme Manager	Cancer Research UK
Sigrid Carlsson	Associate Attending Epidemiologist	Memorial Sloan Kettering Cancer Center
Beatriz Carvalho	Senior Scientist	Netherlands Cancer Institute

Kim Chu	Statistician	Queen Mary University of London
Greg Clemenceau	Intern	UMC Utrecht
Kiana Collins	DPhil student	University of Oxford
Monserrat Conde	Researcher	University of Oxford
Victoria Cooley	Doctoral Researcher	German Cancer Research Center (DKFZ)
Veerle Coupé	Hoogleraar	Amsterdam UMC
Tatjana Crnogorac-Jurcevic	Professor of Molecular Pathology and Biomarkers	Barts Cancer Institute- Queen Mary University
David Crosby	Head of Prevention and Early Detection Research	Cancer Research UK
Edwin Cuppen	Scientific Director	Stichting Hartwig Medical Foundation
Behdad Dasht Bozorg	Senior Scientist	Netherlands Cancer Institute
Elspeth Davies	Qualitative Researcher	University of Oxford
Silvana Debernardi	Senior Postdoctoral Research Assistant	Barts Cancer Institute- Queen Mary University of London
Sjoerd Elias	Associate Professor of Clinical Epidemiology	UMC Utrecht, Julius Center
Agustin Enciso	Postdoctoral Researcher	Leiden and Amsterdam University Medical Centers
Athurva Gore	Associate Director of Bioinformatics	Singlera Genomics, Inc.
Rosa de Groot	Project coordinator Hebon	Netherlands Cancer Institute
Tijmen de Haas	PhD candidate	RadboudUMC
Miranda Kleijn	Head of Clinical Research	Qurin
Harry de Koning	Professor of Public Health and Screening Evaluation	Erasmus Medical Center Rotterdam
Chris de Korte	Chair Medical Ultrasound Imaging Center	Radboudumc
Margot de Looff	Senior onderzoeker POCT	Hanze
Frederique Denijs	MD	Erasmus MC
Johan De Rooij	CSO	you2yourself BV
Peter Devilee	Professor	LUMC
Meike de Wit	Senior Postdoc	Netherlands Cancer Institute

Caroline Drukker	Surgical oncologist	Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital
Bruno Duso	Clinician-Scientist	Gustave Roussy
Clara Frick	Doctoral researcher	German Cancer Research Center (DKFZ)
Duco Gaillard	PhD candidate	Netherlands Cancer Institute
Yuan Gao	Postdoctoral Researcher	Netherlands Cancer Institute
Vanessa García López-Mingo	PhD candidate	AmsterdamUMC
Peter Gardner	Professor of Analytical and Biomedical Spectroscopy	University of Manchester
Iris Glykofridis	Postdoctoral Researcher	Netherlands Cancer Insititute
Marjolein Greuter	Assistant Professor	Amsterdam UMC
Stuart Griffiths	Director of Research, Services & Policy	Yorkshire Cancer Research
Rick Groeneweg	Junior Researcher	Erasmus MC
Eltjo Heddema	Product Development & Research	OncoInv
Daniëlle Heideman	KMBP	UMCG
Samuel Hervas Gomez	Postgraduate Researcher / PHD Student	University of Manchester
Bart Hesselink	Scientist	Self-screen
Juul Hubert	PhD candidate	Erasmus MC
Joost Huiskens	CMIO	Microsoft
Joep IJspeert	MDL-arts	Antoni van Leeuwenhoek Hospital
Colin Jacobs	Associate Professor	Radboudumc
Heinz Jacobs	Division Head, Group Leader	NKI-AVL
Peter Kapitein	Patient Advocate	Inspire2Live
Leon Klimeck	PhD candidate	DKFZ Heidelberg
Lindy Kregting	Postdoctoral epidemiologist	Radboudumc
Agne Krilaviciute	Postdoctoral Researcher	DKFZ
Nicole Kukutsch	Dermatologist	Antoni van Leeuwenhoek Hospital
Evelyn Kurotova	Research Technician	Barts Cancer Institute, Queen Mary University of London
Liza Maria Kurucz	PhD candidate	The Netherlands Cancer Institute - Antoni van Leeuwenhoek Hospital
Satomi Kuwahara	Verpleegkundige in opleiding tot specialist	Antoni van Leeuwenhoek

Michel Leenders	Director of Real Estate and Services	Antoni van Leeuwenhoek
Renée Leenen	MD, PhD Candidate	Erasmus MC Cancer Institute, Urology
Deborah Ligtenberg	Patient advocate	Stichting Erfelijke Kanker Nederland
Esther Lips	Associate Staff Scientist	NKI-AVL
Jeroen Lodder	PhD candidate	Netherlands Cancer Institute
Carin Louis	Patient Advocate	NFK
Marieke Louwman	Senior Researcher Epidemiology	IKNL
Mao Mao	CEO	SeekIn
Gerrit Meijer	Professor of Oncologic Pathology	Netherlands Cancer Institute
Renee Menezes	PI	Netherlands Cancer Institute
Laura Meulenbroeks	PhD student	Amsterdam UMC
Fin Milder	Lector	Hanzehogeschool Groningen / Hanze University of Applied Sciences
Lot Mulder	MD, PhD student	Netherlands Cancer Institute
Tiziano Natali	PhD Candidate	NKI - AvL
Henrik Nygaard	Senior Business Development Manager	Singlera Genomics
Marek Oerlemans	PhD student	Netherlands Cancer Institute
Govind Pai	Research lab manager	University Hospital Düsseldorf
David Palmer	Chief Scientific Officer	Dxcover
Vincent Pappalardo	Postdoctoral Researcher	Netherlands Cancer Institute
Jasika Paramasamy	PhD Candidate and Technical Physician	Erasmus MC
Line Pedersen	Consultant, PhD	Danish Cancer Society
Maikel Peppelenbosch	Head of the Laboratory	Erasmus Medical Center
Liudmila Peppelenbosch-Kodach	Pathologist	Netherlands Cancer Institute
Adam Perrett	Research Associate	University of Manchester
Jim Peters	Postdoctoral Researcher	Radboud
Maud Plantinga	Lead Risk-based Screening	KWF Kankerbestrijding
Anna Plym	Researcher	Karolinska Institutet
Jos Poell	Staff Scientist	Amsterdam UMC
Bas Pouw	Lead Early Detection	KWF Kankerbestrijding
Bram Pronk	PhD Candidate	Delft University of Technology

Lucia Pueyo Valles	Research Technician	Barts Cancer Institute- Queen Mary University of London
Mrsilda Qyli	Doctor of Science in Molecular Biology	Western Balkans University
Albert Rocabruna	Senior Clinical Sales Executive	SOPHiA GENETICS
Monique J. Roobol	Professor Decision Making in Urology	Erasmus University Medical Center, Cancer Institute
Stephen Rosenberg	Director of Science Programs	Stand Up To Cancer
Caryn Ross-Innes	Senior Research Associate	University of Cambridge
Theo Ruers	Med. Head Center for Early Cancer Detection	NKI Center for Early Cancer Detection
Amir Ata Saei	Assistant professor	Karolinska Institute
Phil Sanders	Head of Genomics Department	Flomics Biotech
Ilona Schelle	Board member	Stichting Inspire2live
Marjanka Schmidt	Professor of Genetic Epidemiology of (Breast) Cancer (LUMC); Research Theme Lead Early Detection (NKI-AVL)	Netherlands Cancer Institute
Ton Schumacher	Director of Research a.i.	Netherlands Cancer Institute
Ioannis Sechopoulos	Professor	Radboud University Medical Center
Loes Segerink	Prof./Group leader BIOS	University of Twente
Dmitry Sergeev	PhD candidate	DKFZ
Jayni Shah	Research Technician	Barts Cancer Institute, Queen Mary University of London
Mehrnoosh Shokouhi	PhD candidate	Netherlands cancer institute
Michiel Sinaasappel	Medical Physics Expert	Antoni van Leeuwenhoek
Jasleen Singh	PhD candidate	Erasmus MC
Kim Smits	Associate professor	Maastricht University
Renske Steenbergen	Professor	Amsterdam UMC
Mei-Chee Tai	Deputy Head	Cancer Research Malaysia
Madeleine Tilanus	Researcher	ErasmusMC Rotterdam
Esther Toes	Assistant professor	Erasmus MC
Piotr Twardowski	PhD candidate	Amsterdam UMC
Kristel van Asselt	Associate professor, GP	UMC Utrecht
Irma van de Beek	Clinical geneticist	Antoni van Leeuwenhoek
Tilja van den Berg	Projectmanager	Nederlands Kanker Collectief
Eef van den Borst	PhD candidate	University of Antwerp

Isabelle van den Bosch	PhD candidate	Erasmus MC
Daan van den Broek	Specialist in Laboratory Medicine	Netherlands Cancer Institute
Anton van den Ouden	QC and Compliance	DeSenexResearch
Yuri van der Burgt	Associate Professor	Leiden University Medical Center
Paul van der Leest	Postdoctoral Researcher	Netherlands Cancer Institute
Daniëlle van der Waal	Epidemiologist	Dutch Expert Centre for Screening (LRCB)
Sandra van Dijk	Head of Department	RIVM Dutch National Institute for Public Health
Carla van Gils	Professor Clinical Epidemiology of Cancer	UMC Utrecht
Sophie van Grinsven	PhD candidate	UMC Utrecht, Julius Center
Meike van Harten	PhD candidate	Erasmus MC
Severien van Keer	Assistant Professor	Centre for the Evaluation of Vaccination; University of Antwerp
Henk van Kranen	Patient Advocate	Inspire2live
Monique van Leerdam	Gastroenterologist	Netherlands Cancer Institute
Lotte van Leeuwen	PhD candidate	Erasmus MC
Pim van Leeuwen	Urologist	Netherlands Cancer Institute
Ton van Leeuwen	head department of Biomedical Engineering & Physics	Amsterdam UMC
Nikki van Loenen	PhD candidate	University of Twente
Nanette van Roermund	MD PhD candidate	Amsterdam UMC
Huub van Rossum	Specialist in Laboratory Medicine	Netherlands Cancer Institute
Lucas van Schaik	PhD candidate	Netherlands Cancer Institute
Willem van Snippenberg	Scientist	Self-screen
Marieke van Wel-Stoffels	Projectmanager CVV	NKI Center for Early Cancer Detection
Francine van Wifferen	Postdoctoral Researcher	Amsterdam UMC
Lisanne Verhoef	Projectmanager Early Detection	Netherlands Cancer Institute
Emma Vieveen	Datamanager Hebon	Netherlands Cancer Institute
Pradeep Virdee	Senior Medical Statistician	University of Oxford
Lieke Visser	Belangenbehartiger Preventie	NFK
Emile Voest	Senior Group Leader, Oncoloog NKI	Netherlands Cancer Institute
Adri Voogd	Clinical Epidemiologist, Associate Professor	Universiteit Maastricht

Jonathan Wan	Academic Clinical Fellow in Medical Oncology	University College London
Xin Wang	Postdoctoral Researcher	Netherlands Cancer Institute
Matty Weijenberg	Professor of Molecular Epidemiology of Cancer	Department of Epidemiology, Maastricht University
David Weinberg	Chair, Department of Medicine; Weg Chair in Medical Science	Fox Chase Cancer Center
David Weller	Professor of General Practice	University of Edinburgh
Jean Marie Wernet	Student	Netherlands Cancer Institute
Jelle Wesseling	Groepsleider	Netherlands Cancer Institute
Vera Wesselink	Postdoctoral Researcher	Netherlands Cancer Institute
Sanne Westerhout	MD PhD candidate	Antoni van Leeuwenhoek Hospital / Erasmus MC
Marianne Wezeman	Business Development Manager	Olink Proteomics
Oliver White	PhD candidate	Erasmus MC
Leah Wilk	Postdoctoral Researcher	Amsterdam UMC
Caroline Willems	Patient advocate	Stichting Erfelijke Kanker Nederland
Leon Wils	Postdoctoral Researcher	Netherlands Cancer Institute
Saskia Wilting	Assistant Professor	Erasmus MC Cancer Institute
Bea Wisman	Researcher	University Medical Center Groningen
Mark Witteveen	PhD candidate	Netherlands Cancer Institute - Antoni van Leeuwehoek Hospital
Stuart Wright	Research Fellow in Health Economics	The University of Manchester
Lianlian Wu	Research Associate	Cambridge University
Derya Yakar	Radiologist	UMCG & AvL