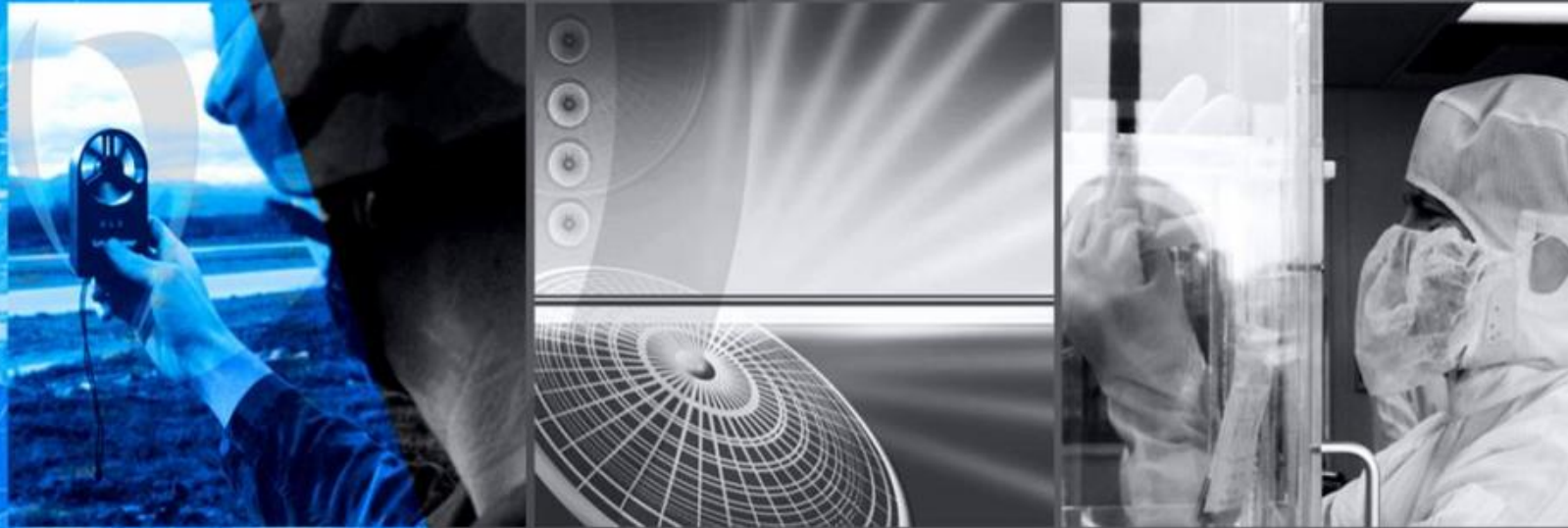


A Breathalyzer for Disease

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NEXT
GENERATION
DETECTION

#cancer-breathalyzer

Agenda



- Owlstone Medical
- Breath Biopsy
- Field Asymmetric Ion Mobility Spectrometry
- ReCIVA
- Medical applications
 - LuCID (Lung Cancer)
 - InTERCEPT (Bowel Cancer)
- Summary and Questions



Owlstone Medical Background



SPUN OUT OF
**CAMBRIDGE
UNIVERSITY**
IN 2004



PROVEN TEAM
75 EMPLOYEES



PROVEN TECHNOLOGY
\$38.3M INVESTMENT
\$32.7M MILITARY
CONTRACT / PRODUCTS
\$71M IN TOTAL



PROTECTED BY
16 PATENTS
(GRANTED AND PENDING)



ISO ACCREDITED
R&D AND MANUFACTURING
FACILITIES IN CAMBRIDGE UK



AWARD WINNING
MEDICAL XPRIZE
R&D100
MACROBERT



PROFITABLE
SECURITY AND INDUSTRIAL
BUSINESS



OWLSTONE MEDICAL
SPUN OUT WITH
\$18.55M INVESTMENT

A New Diagnostic Modality



Breath Biopsy™

A new modality in diagnostics

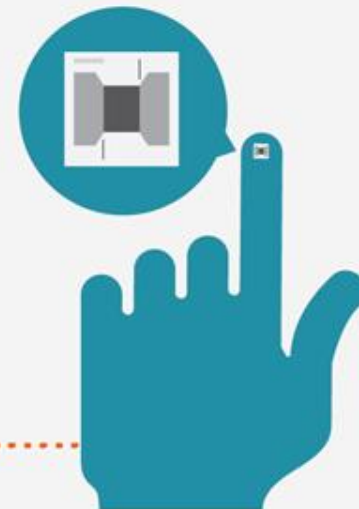
Volatile organic compound (VOCs) as biomarkers of cancer, inflammatory disease and infectious disease.



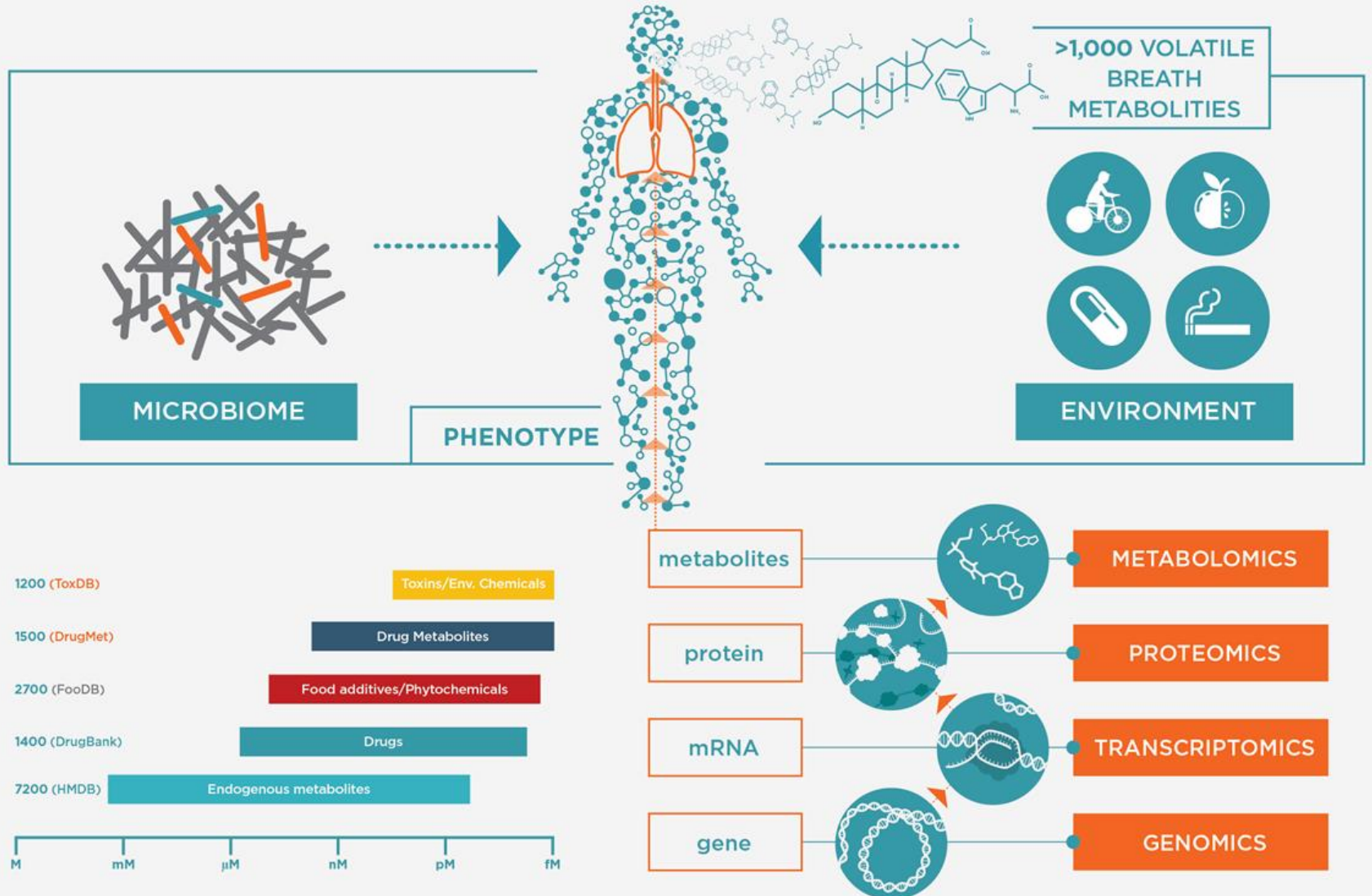
The Owlstone FAIMS Platform

Next generation detection (NGD)

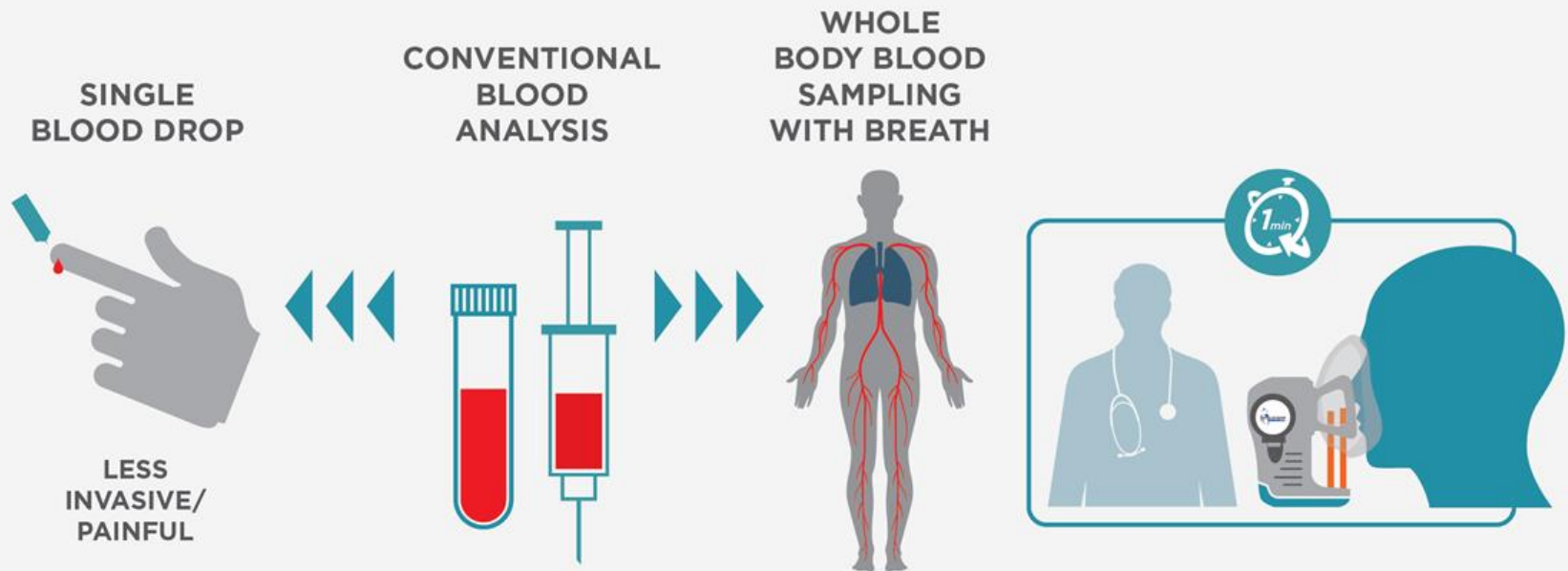
Software programmable microchip spectrometer for detection of disease VOCs.



The Science of Breath Biomarkers



Whole body blood sampling



- Your lungs are very effective at exchanging chemicals with your blood, including volatile metabolites and biomarkers that are generated even at the earliest stages of disease.
- It takes ~1 minute for your entire blood volume to circulate around your body once.
- By continuously preconcentrating exhaled chemicals we can sample and analyze the entire circulating blood volume.
- This is completely non-invasive and pain free.

Where are we in Breathomics?



- Modern breath testing commenced in 1971, with the work of Nobel Prize winner Linus Pauling.
- Hundreds of scientific papers published suggesting the presence of VOC biomarkers across a range of diseases.

SOME PUZZLING QUESTIONS

1 Why is there very little agreement in identified biomarkers within a disease?



2 Why is breath testing not used routinely in clinical setting?



SOME HISTORICAL CHALLENGES



- Maturity of breath sampling hardware and protocols for robust, repeatable sampling.

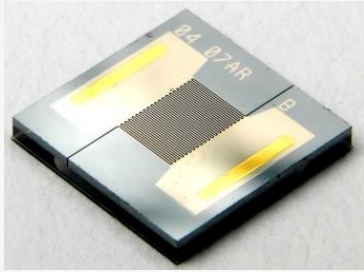
- High end, expensive spectrometer vs low performance enose.
- Different analytical techniques required in biomarker discovery and clinical translation.



- Study design and size - small patient numbers in pilot studies and lack of blinded validation studies.

WITHOUT SOLVING THESE YOU CAN'T HAVE CONFIDENCE IN INITIAL BIOMARKER DISCOVERY AND VALIDATION

FAIMS Programmable Chemical Sensor



- Field Asymmetric Ion Mobility Spectrometry
- Highly sensitive and selective
 - < ppb level
- Tunable for untargeted and targeted detection
- Simultaneous detection of multiple biomarkers.
- Small size - suitable for point of care (POC) or central lab.



Ion Mobility



- FAIMS = Field Asymmetric Ion Mobility Spectrometry (or DMS)
- Variant of Ion mobility spectrometry (IMS)
 - Distinguishing ions according to differences in the speed that they move through a buffer gas under the influence of an electric field.

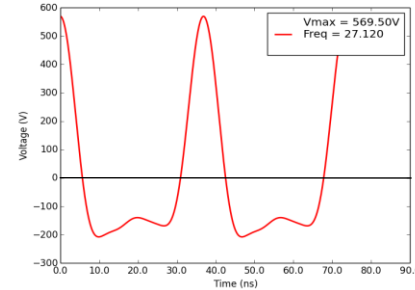
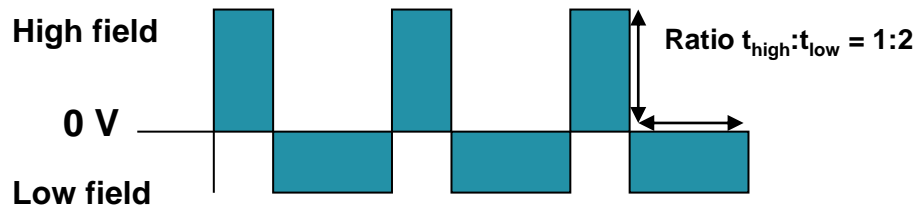
The diagram shows the equation $V_d = K E$ with three blue boxes connected to it by lines. The box labeled "Ion mobility" is connected to the letter 'K'. The box labeled "Electric field strength" is connected to the letter 'E'. The box labeled "Ion velocity" is connected to the V_d term.

- At low fields, an ion's mobility (K) is constant and is a function of charge (z) and collision cross-section (Ω)
- Ions with a larger cross-section are more likely to collide with gas molecules, travelling more slowly than smaller ions.

FAIMS Basics

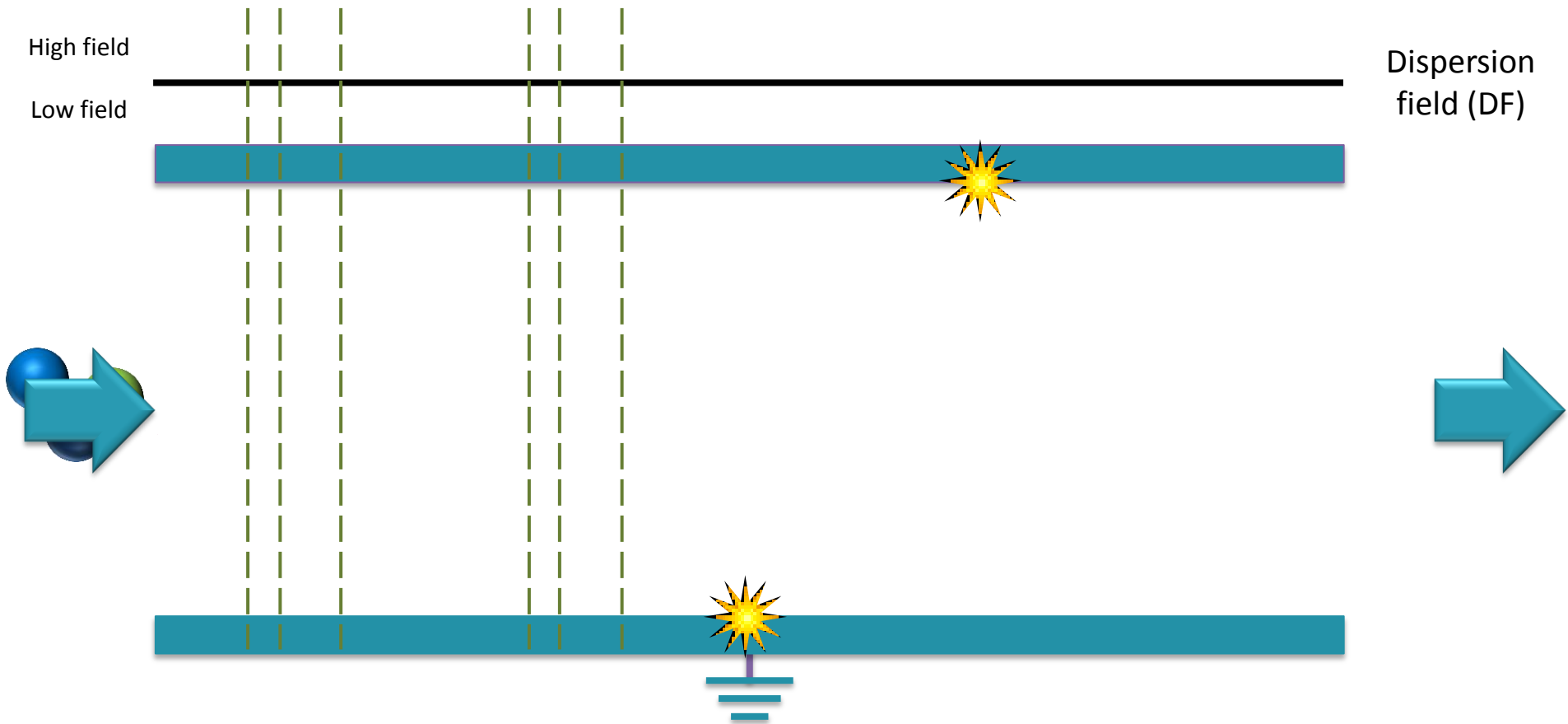


- FAIMS uses an asymmetric alternating electric field, perpendicular to the direction of travel.



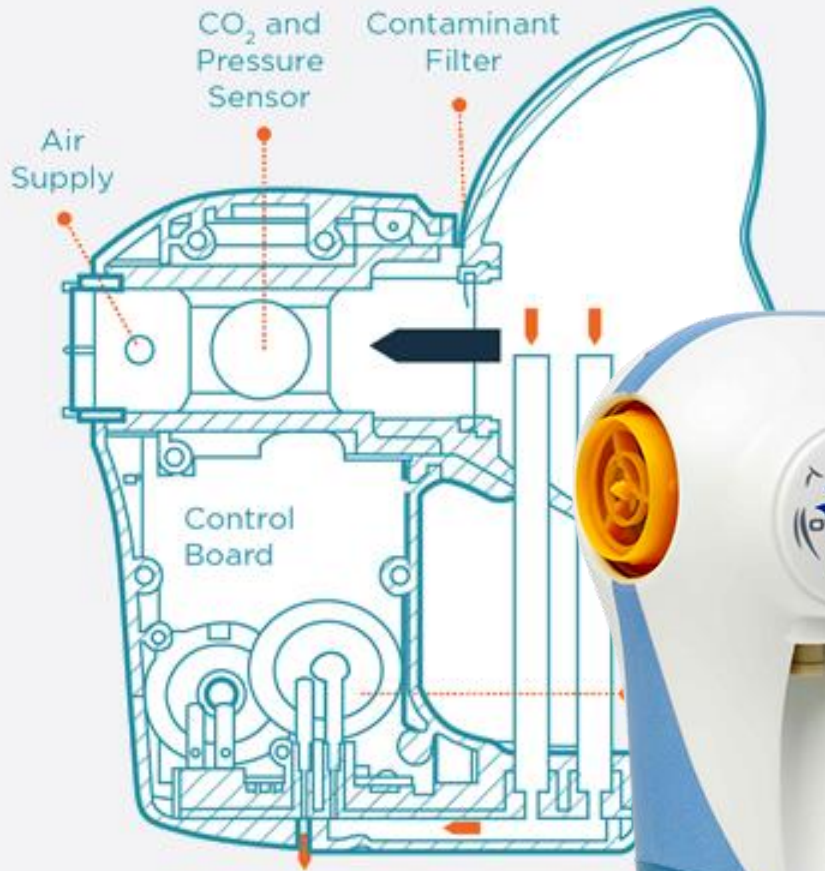
- Ions will be subjected to an electric field condition which causes them to drift in one direction at a velocity based on its ion mobility.
- As the field is reversed in direction and magnitude, the ion changes direction and speed based on its new mobility at the new electric field conditions.
- This is repeated at a rate based on the operating frequency of the device and usually results in a net drift towards an electrode.
- By applying an additional compensation field (CF), this sideways drift can be cancelled out, correcting for the drift and focusses ions through the device.

The FAIMS device, a tunable filter



- As the field reverses direction and magnitude, the ion changes direction and speed
- Each ion has a specific net sideways drift velocity
- The sideways drift can be cancelled out by applying the CF

ReCIVA - Breath Collector



- **Flexible**
 - Breath volume
 - Alveolar and/or bronchial fraction.
 - Multiple samples for duplicate analysis
- **Reliable**
 - Reduces environmental contamination
 - CE marked
- **Non-invasive**
 - Adult and paediatric masks
 - Comfortable for all
- **Reusable**
 - Disposable masks and filters



Flexible breath collection




Main screen | Collection settings

Pump A

2 Tubes

Flow rate per tube A: 200 ml/min

Collection volume per tube A: 250 ml



Pump A breath section

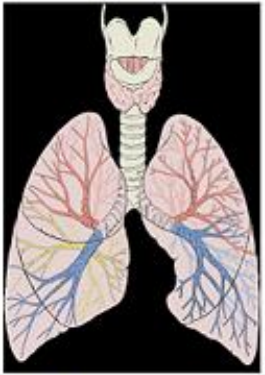
Upper airways only

Pump B

2 Tubes

Flow rate per tube B: 200 ml/min

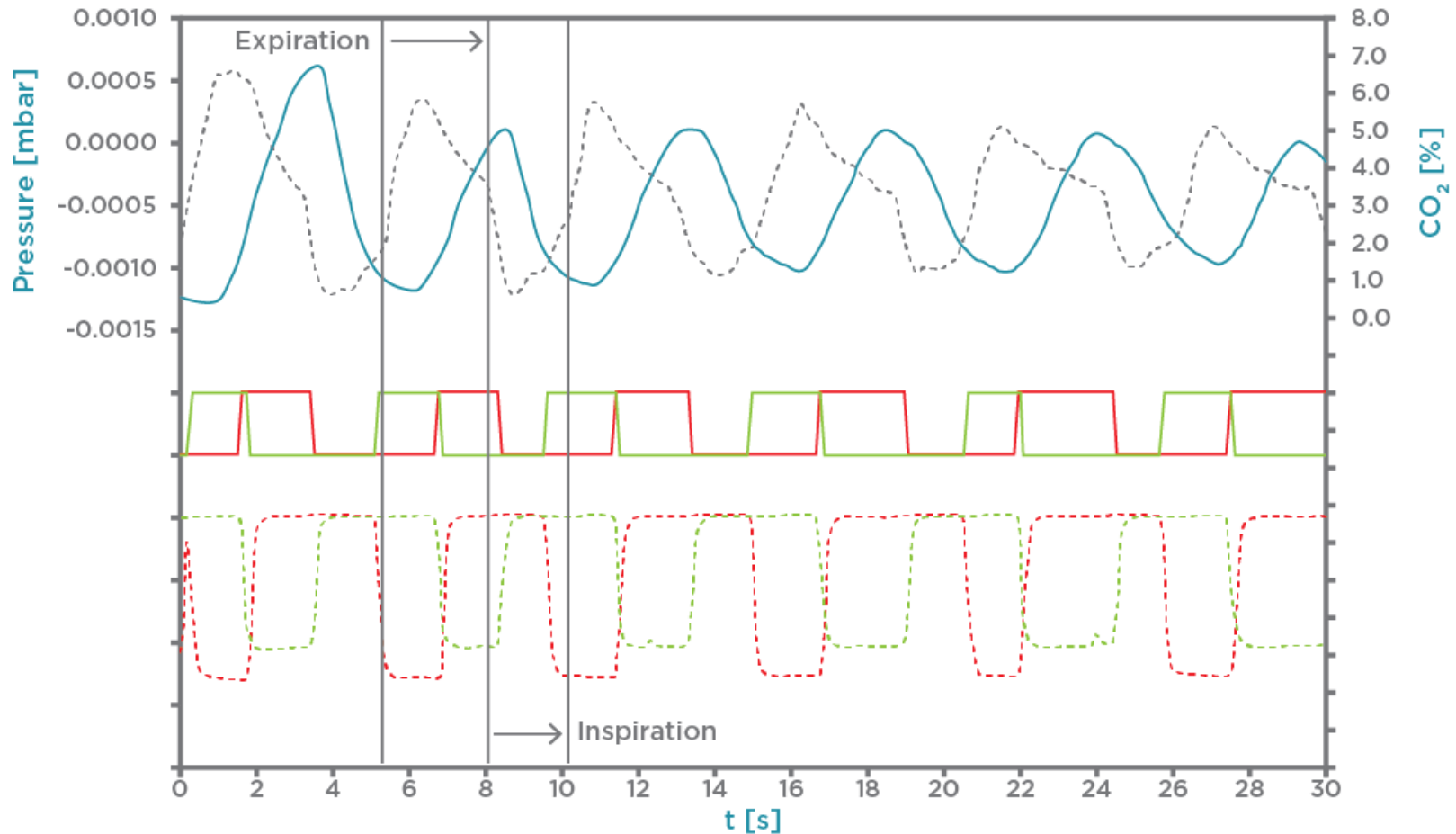
Collection volume per tube B: 500 ml



- Upper airways only
- Lower airways only
- ✓ Upper and lower airways
- Whole breath (including mouth air)
- Upper airways including mouth air
- Fixed CO₂
- Fixed pressures
- Always on

Save | Advanced Settings

ReCIVA Sampler

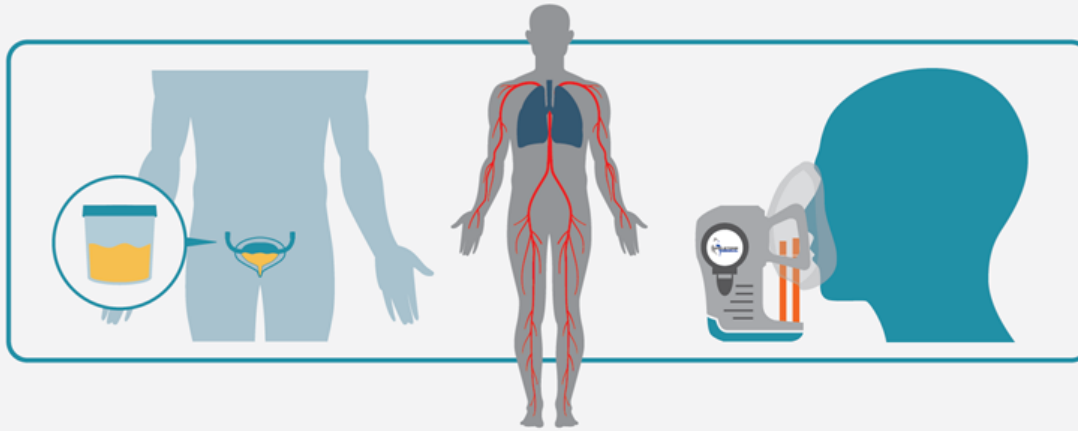


---- Pressure (Mask) — Trigger (L Pump) — Trigger (R Pump) - - - - Pressure (L ΔTube) - - - - Pressure (R ΔTube) — CO₂

Medical Applications



NON-INVASIVE PATIENT SAMPLING IN BREATH OR URINE



APPLICATIONS

CLINICAL
DIAGNOSTICS



PRECISION
MEDICINE

CANCER



INFECTIOUS
DISEASE



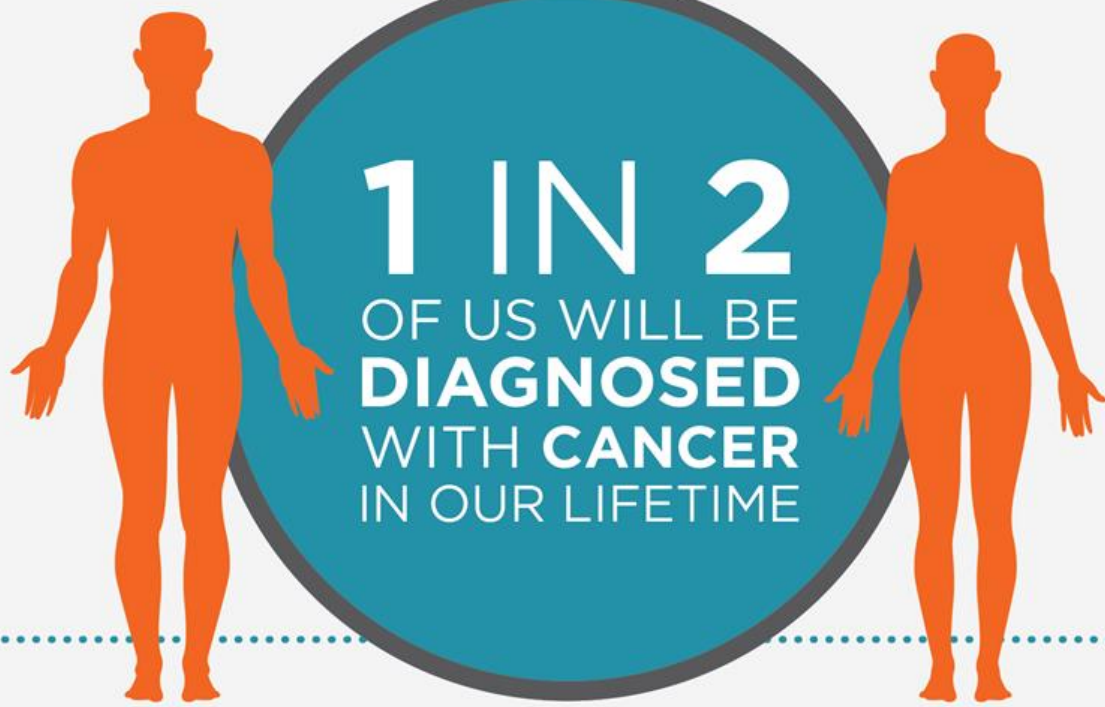
INFLAMMATORY
DISEASE



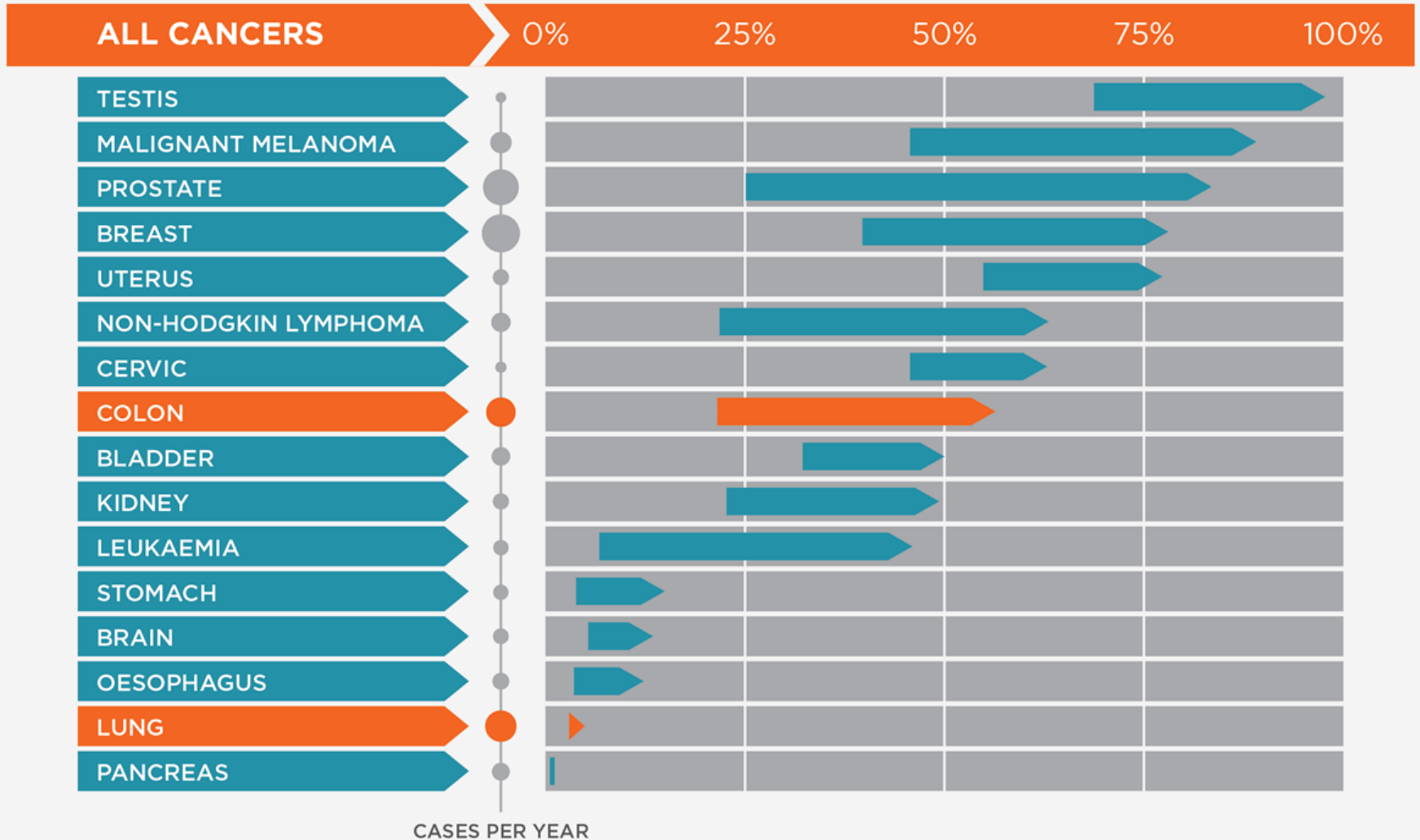
1 in 2 of us will be diagnosed with cancer



14.1 MILLION
DEATHS



10 Year Survival, Changes Since 1971



Early Detection "Our Greatest Opportunity"



DIAGNOSED EARLIER

AT STAGE 1



More than 5 in 10 survive 5 or more years

DIAGNOSED LATER

AT STAGE 4



Less than 1 in 10 survive 5 or more years



DIAGNOSED EARLIER

AT STAGE 1



More than 9 in 10 survive 5 or more years

DIAGNOSED LATER

AT STAGE 4



Less than 1 in 10 survive 5 or more years

- Largest breath biomarker trial ever undertaken in the world
- Early detection of lung cancer
- 21 sites across UK, Europe.
- Target recruitment 3,000 patients (1,500 cases, 1,500 controls)
- Chief Investigator: Dr Robert Rintoul, Papworth Hospital



THIS YEAR
LUNG
CANCER
WILL COST

US HEALTHCARE
PROVIDERS

\$ **12.1**
Billion

THIS YEAR
221,200
PEOPLE

will be
DIAGNOSED
with
LUNG CANCER
and

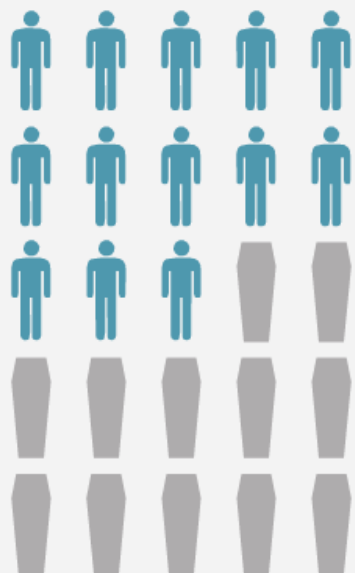
158,040
WILL DIE
IN THE **US**



STAGE I

IF DETECTED AT

STAGE IV



54%

OUT OF 100

54

4

PEOPLE WILL SURVIVE LUNG CANCER



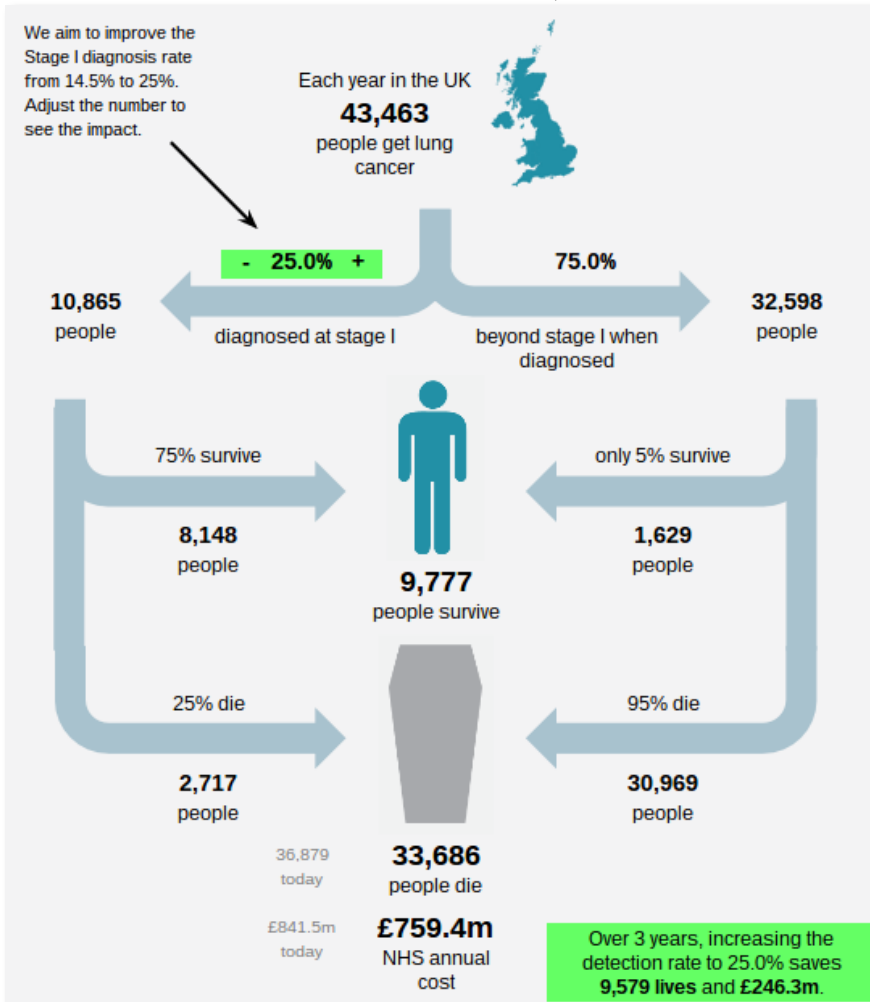
4%

UNFORTUNATELY
ONLY



OF
PATIENTS
ARE DETECTED
AT STAGE I

An increase in detection rates to 25% would save 9,547 lives and £246M over three years



InTERCEPT

EARLY DIAGNOSIS OF COLORECTAL CANCER

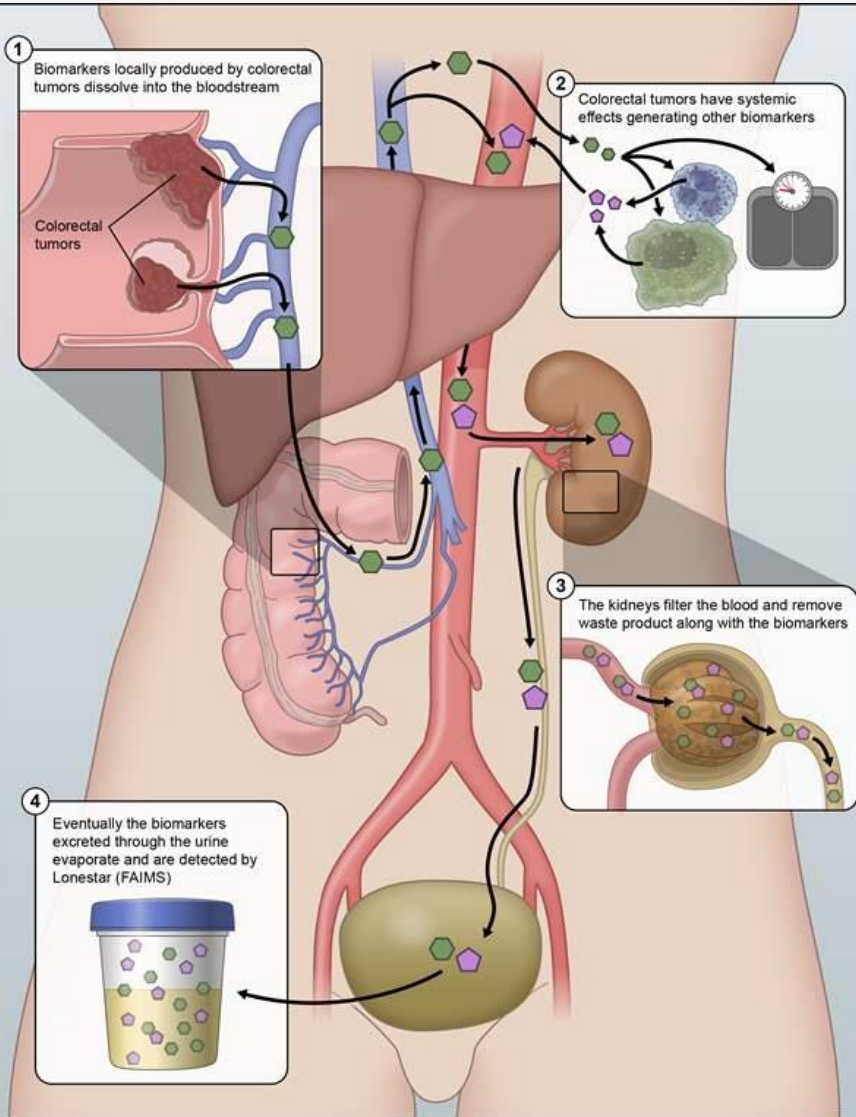


Bowel Cancer
Screening by
Analyzing Volatile
Biomarkers in Urine



InTERCEPT

EARLY DIAGNOSIS OF COLORECTAL CANCER



- Biomarkers locally produced by colorectal cancer dissolve in the bloodstream
- Colorectal tumors have systemic effects generating other biomarkers
- The kidneys filter the blood and remove waste products along with the biomarkers
- Eventually the body excretes these biomarkers through the urine where they can be detected by Lonestar FAIMS analyzer

InTERCEPT

EARLY DIAGNOSIS OF COLORECTAL CANCER



APPROXIMATELY
450,000
PEOPLE IN EUROPE
ARE DIAGNOSED WITH
**COLORECTAL
CANCER**
EACH YEAR



IT IS RESPONSIBLE
FOR AROUND
215,000
DEATHS
ANNUALLY



IT IS THE
SECOND
MOST COMMON
CAUSE OF DEATH
FROM CANCER
FOR BOTH
MEN AND WOMEN¹

THE GLOBAL
ECONOMIC BURDEN
IS ESTIMATED TO BE
\$99
BILLION

IF IT IS
DETECTED EARLY,
THERE IS A



5 YEAR
SURVIVAL RATE²

EVEN WITH CURRENT
SCREENING METHODS, ONLY



OF CANCER
IS DIAGNOSED
AT STAGE 1
IN THE UK²

THERE IS AN **URGENT**
AND **GROWING NEED**
TO **IMPROVE EARLY DIAGNOSIS**
IN **COLORECTAL CANCER**



InTERCEPT

EARLY DIAGNOSIS OF COLORECTAL CANCER



UK



60% of 10 million population screened with FIT
Age range* 60-75 years old

FRANCE



42% of 19 million population screened with FIT
Age range* 50-74 years old

GERMANY



18% of 28 million population screened with FIT
Age range* >56 years old

ITALY

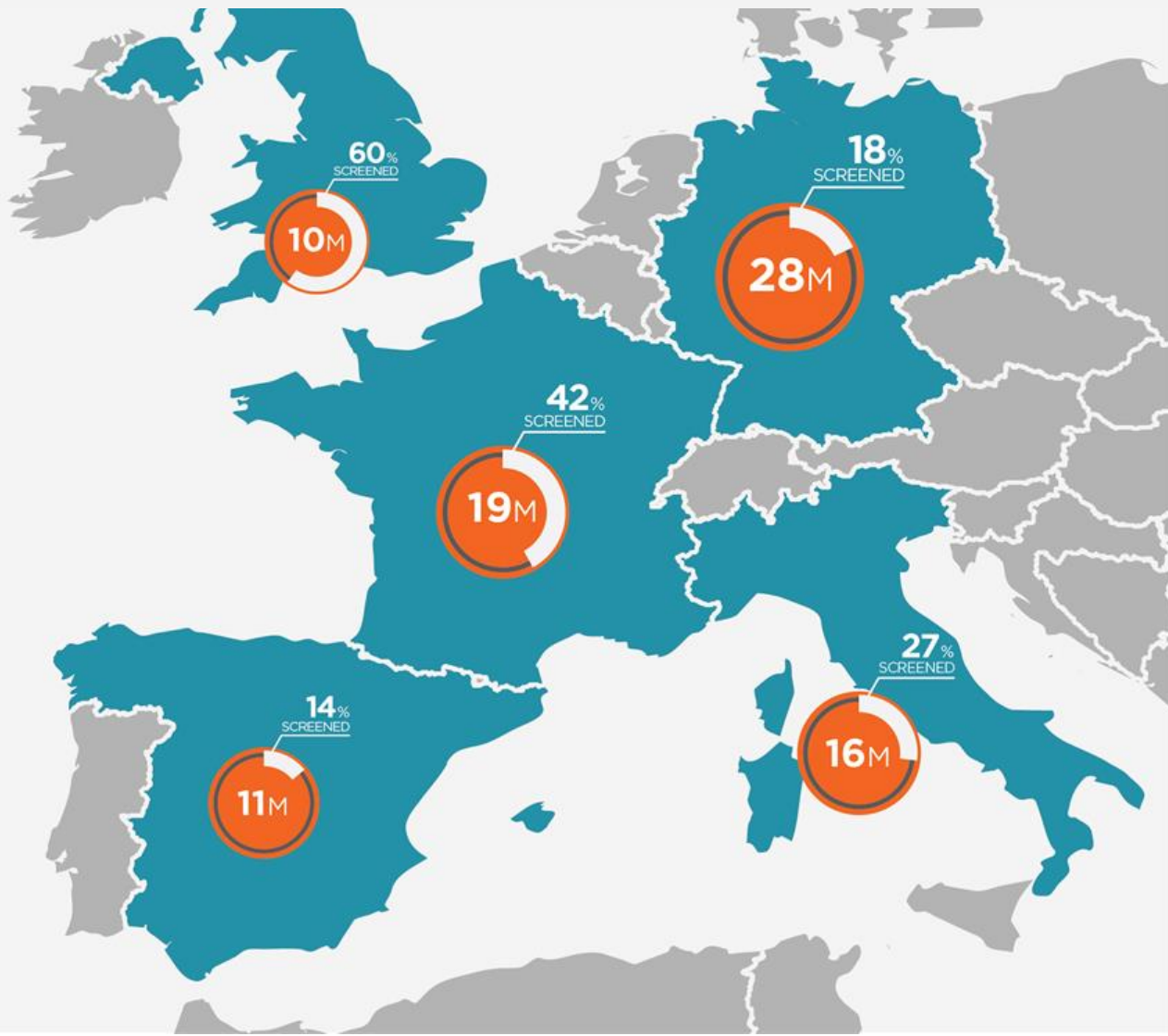


27% of 16 million population screened with FIT
Age range* 50-69 years old

SPAIN



14% of 11 million population screened with FIT
Age range* 50-69 years old



*Defined by the age range obtained from identified source for national screening program or recommendations.

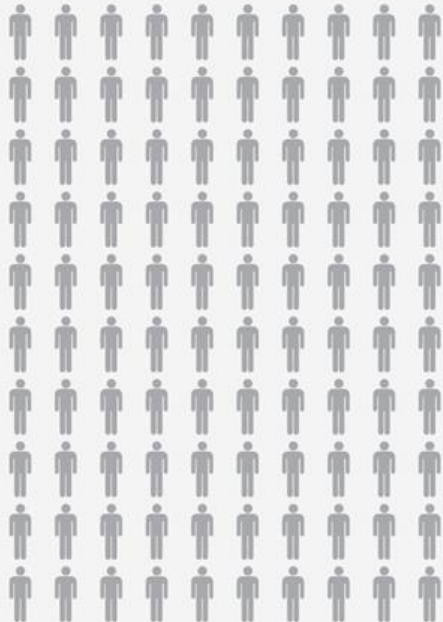
InTERCEPT

EARLY DIAGNOSIS OF COLORECTAL CANCER

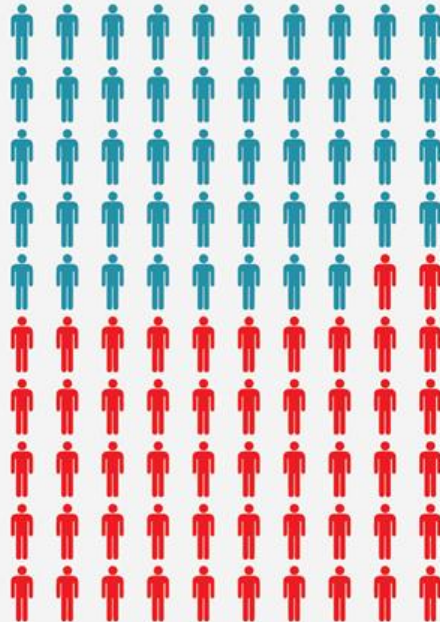


FECAL IMMUNOCHEMICAL TEST (FIT)

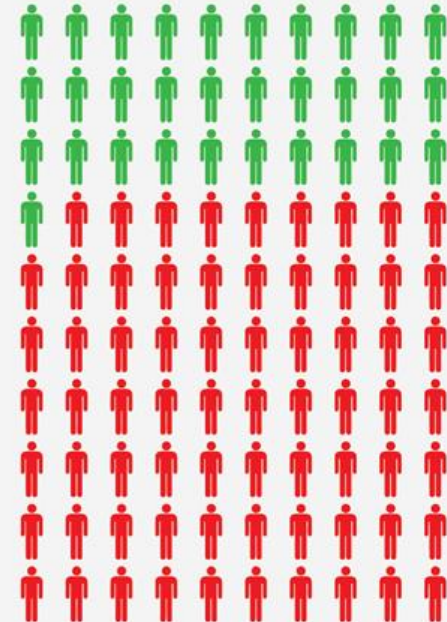
100 PATIENTS
WITH COLON CANCER



COMPLIANCE
RATE **48%**



TEST
SENSITIVITY **66%**



OUT OF 100 PATIENTS
ONLY 31 CANCERS ARE DETECTED

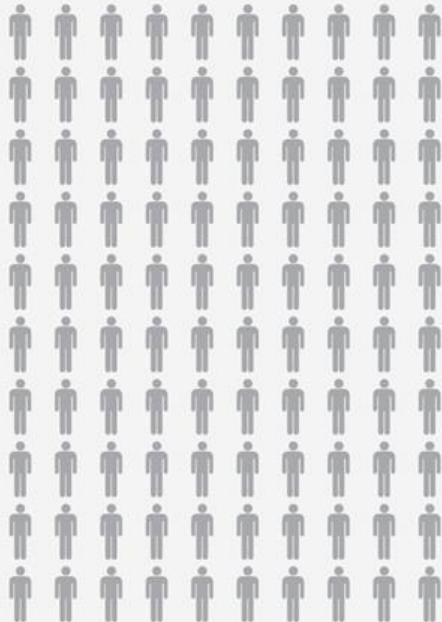
InTERCEPT

EARLY DIAGNOSIS OF COLORECTAL CANCER

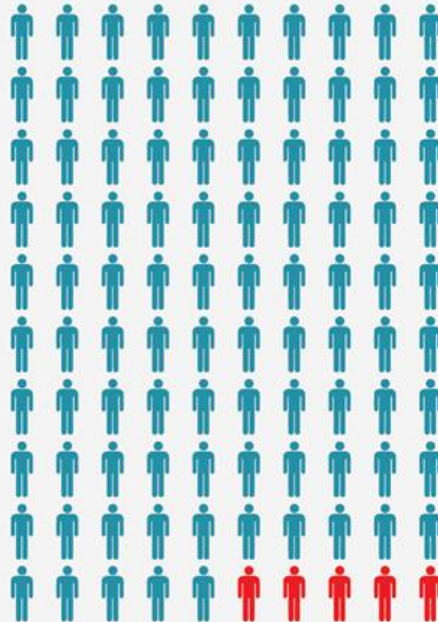


OWLSTONE FAILS

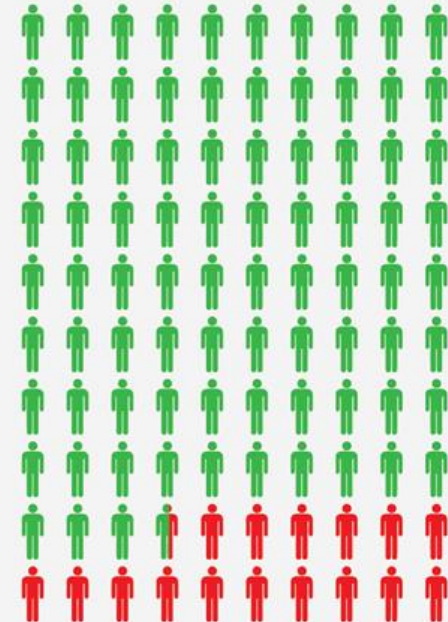
100 PATIENTS
WITH COLON CANCER



COMPLIANCE
RATE **95%**



TEST
SENSITIVITY **88%**



OUT OF 100 PATIENTS
84 CANCERS ARE DETECTED



InTERCEPT

EARLY DIAGNOSIS OF COLORECTAL CANCER



**OWLSTONE FAIMS INCREASES
RATE OF CANCER DETECTION BY**

↑ 170%

FIT

31

OUT OF **100** PATIENTS
WITH **COLON CANCER**
ARE **DETECTED**

FAIMS

84

OUT OF **100** PATIENTS
WITH **COLON CANCER**
ARE **DETECTED**

A Breathalyzer for Disease



- **Our Vision:** Owlstone Medical will become the global leader in non-invasive diagnostics for cancer, infectious disease and inflammatory disease
- **Our Goal:** Save 100,000 lives and save \$1.5B in health care costs.
- Platform technology.
- Pipeline of medical applications, including multi-billion dollar opportunities in colon cancer and lung cancer screening.
- **Clinical trials:** Commenced in lung cancer (LuCID), colon cancer (InTERCEPT) and planned in stratification of therapy response for Asthma

#cancer-breathalyzer