‘Technology’ Clinical Trial

A clinical trial methodology to formally assess the benefit of ‘technology’ as part of a clinical care pathway

PRISME Forum Technical Meeting

Dr. Dónal Landers, Nov 2020

Digital Experimental Cancer Medicine Team

MANCHESTER 1824 The University of Manchester

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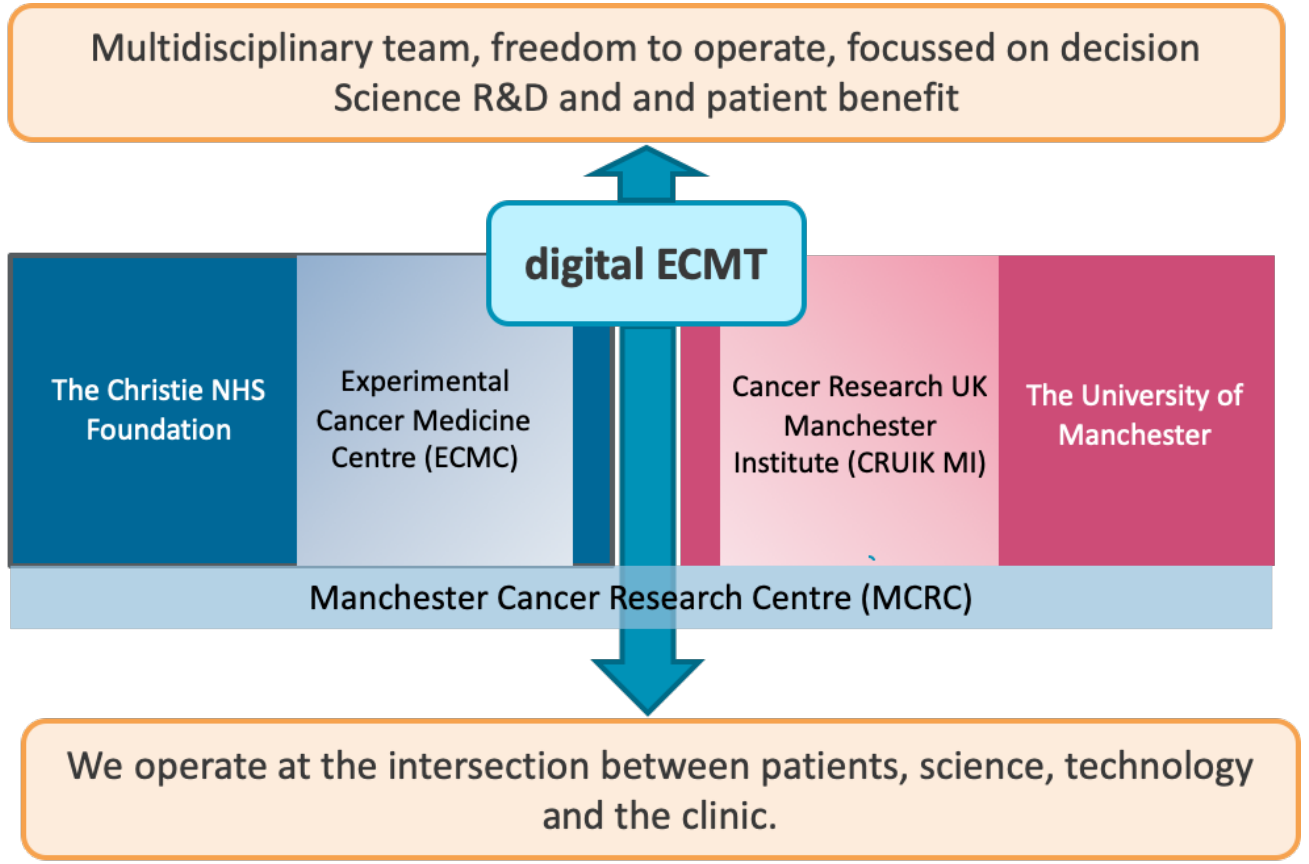
Who we are – clinical decision science research group

Digital Experimental Cancer Medicine Team

Our Vision – to digitally empower patients and healthcare professionals to innovate and design new cancer care pathways

Our Mission – To provide next generation patient cancer care through comprehensive data-driven evidence to enable:

- the transformation of clinical decision-making
- evolve the role of the patient
- improve patient outcomes



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‘Technology’ Clinical Trial

Overview

Examples:

2. NOTION (iN-home Of cyTokines In immunOtherapy patieNts)

‘Technology’ clinical trial components

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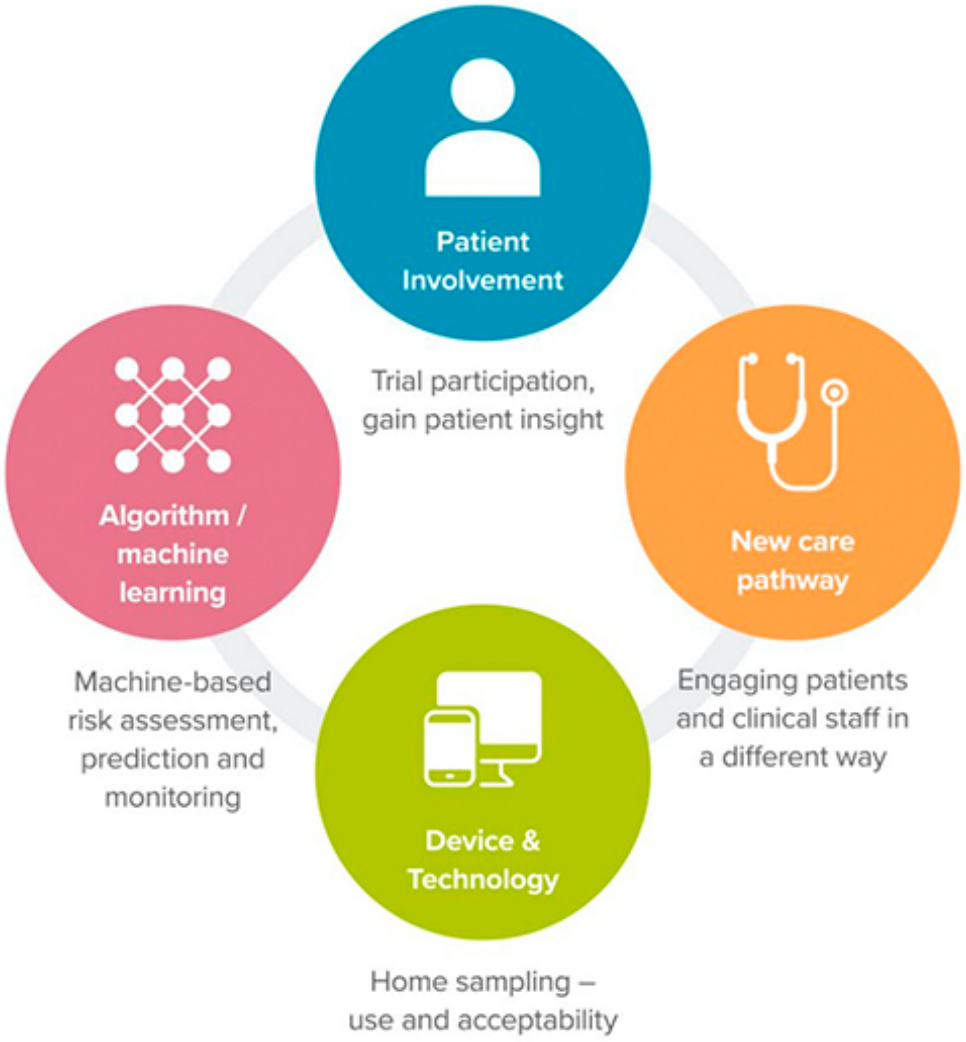

Driver – augmenting clinical decision making to benefit the patient

- Changing the design, delivery and interpretation in early clinical trials
- Developing new care pathways
- Changing the role of the patient
- Hypothesis testing, proof of concept and prototyping for new technology

Design Lab

Dedicated innovation space, located in the Phase 1 trials unit at The Christie, where we can gain insights from patients, carers and staff to:

- ensure that solutions and research designs are co-created form both a scientific and user perspective
- explore the use of technology to deliver aspects of an early clinical trial outside of the hospital and taking the clinical trial to the patient

Rationale for the ‘technology’ clinical trial

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Clinical care pathway development

- Ethical adoption of ‘technology’ - software, device, process and particularly AI through testing in a formal clinical trial
- Clinical solution is perceived as an IT problem and not as a clinical care pathway problem affecting patients

Clinical culture

- Patients and healthcare professionals to-date are not sufficiently involved in defining the clinical problem being addressed
- Building patient and healthcare professional trust

AI

- Blind adoption of non-peered reviewed AI as part of a clinical care pathway
- Belief in the ‘noise’ and ‘hype’ of technology and AI – technology ‘hype’ cycle curve
- Belief that AI is intelligent and has ‘built-in’ internal ‘ethical’ reasoning methods in the maths
- Assuming that the algorithm has trained properly on a high data fidelity and fully representative data sets and is generalizable

‘Technology’ clinical trial – future clinical trial framework

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Technology assessment

Clinical Benefit

‘Technology’ Clinical Trial

Right Hypothesis
Right way

Regulatory
& Ethical Navigation

Trial Delivery

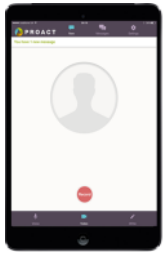
Proven approach

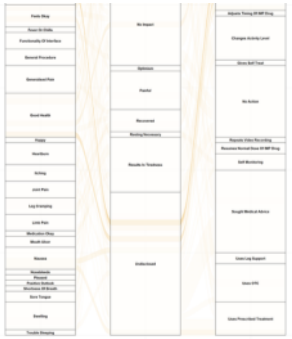
Decision Science and Analytics

Patient as co-researcher

Current projects

PROACT thematic analysis: oncology clinical trial experience



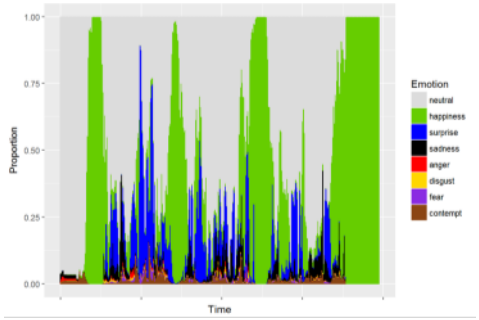


IN-HOME: Home measurement of creatinine

NOTION: remote monitoring of patient cytokine levels

PROACT video analytics: automated emotion detection

Manual transcript	Sentiment analysis
Hi, it's me again, umm … it is day 5 after my fasenra injection and … things are going well i .. err … feel much better, much clearer … I am able to enjoy the outside without wheezing … umm … and any major asthma symptoms so .. umm … looking forward to the weeks ahead, thanks	91%



‘In-Home’ nephro-oncology study

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Primary objectives of the study:
Part A) assessing the feasibility and acceptance of patients measuring at home
Part B) understanding the potential for earlier diagnosis of changes in renal function through intensive home-monitoring.

Purpose: enable patients with renal dysfunction to participate in Phase 1 clinical studies by:

- Integrating the expertise of both oncologists and nephrologists and providing enhanced renal monitoring and risk mitigation in early oncology trials
- Changing the selection criteria for trials in a data-driven and risk-stratified way so that individuals with both renal-impairment and cancer, who are currently excluded, to have the option of taking part in an early cancer study

Population: Head and Neck cancer patients

Nephrologists: Prof. Sandip Mitra and Dr. Leanne Philips at Manchester NHS Foundation Trust

Clinical use case – predictive AKI monitoring

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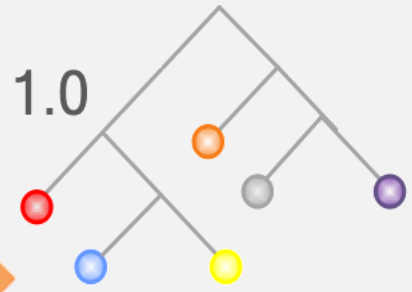
Home monitoring

Patients use a point of care test kit at home to measure their creatinine – Nova Biomedical Creatinine StatSensor

Ease of data transfer

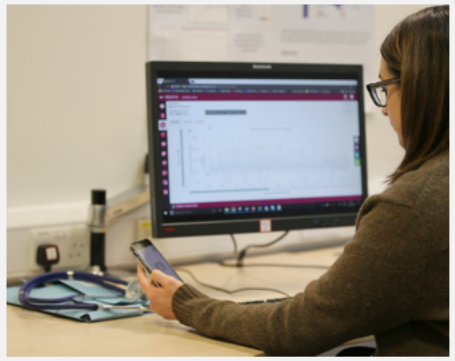
Patients send in their results using a nephro-oncology app to a secure Microsoft Azure cloud platform

AI - Acute Kidney Injury Algorithm (AKI)



AI/Machine Development

Home creatinine data are interwoven with their hospital data using the AKI algorithm



Fast interpretation & intervention

Medical team and patient receive notification advising whether intervention is required

NOTION (iN-home Of cyTokines In immunOtherapy patieNts)

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Primary objective: To evaluate feasibility of collecting and measuring cytokine concentrations obtained by in-home Dry Blood Spot sampling in patients receiving CPI therapy

- Proof of concept, non-CTIMP, medical device Investigator led study
- Patient population: Renal Cell carcinoma and Metastatic Melanoma patients on first line combination checkpoint inhibitors
  - 20% of patients experience high grade toxicities on CPI and those on combination CPI are 55% likely to experience grade 3-4 toxicity
  - Cytokines are released during an inflammatory response and have been shown in a number of studies to correlate with immune related adverse events (irAE)
- Closer monitoring of cytokines could help with earlier detection of irAEs and allow for earlier intervention, improved immune-related complications and allow patients to stay on treatment longer -> **Steppingstone to the ATMP studies**

Immune related toxicity detection

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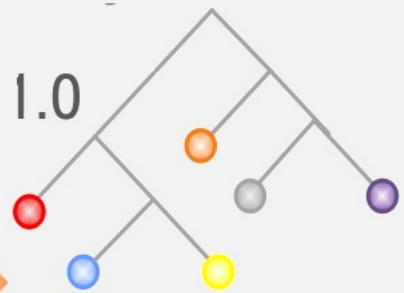
Home monitoring:

Patients use a point of care test kit at home to measure their cytokines – Neoteryx device

Ease of sample transfer:

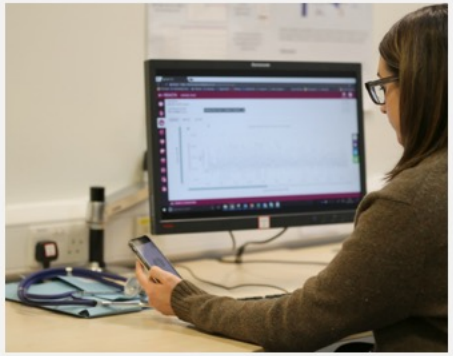
Patients send in their samples to the lab by post

AI – immune related toxicity detection



AI/Machine Development & Learning

Home cytokine data will be used to help predict the onset of immune related toxicities



Fast interpretation & intervention

Medical team and patient receive notification advising whether intervention is required

COVID-19 risk in oncology evaluation tool

- Establish a tool to identify patients suitable for immediate discharge versus those likely to have severe infection
- Inform clinicians and patients about likely COVID-19 severity

12 UK hospitals

299 patients with cancer and confirmed COVID-19

Main cohort	Validation cohort

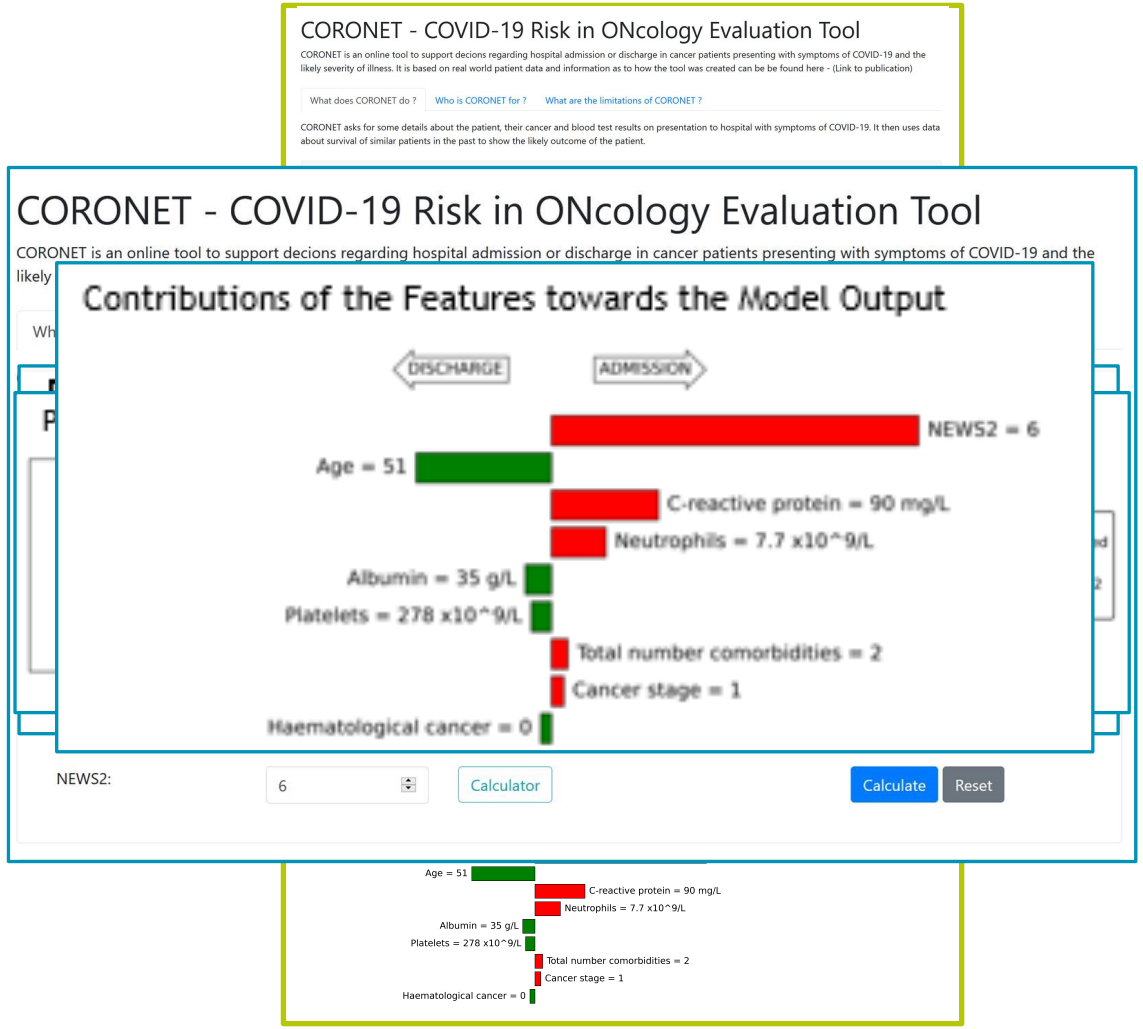
Clinical characteristics and cancer treatment history

Worst COVID outcome reviewed

Discharge <24 hours	Supplementary O2	Death

Methods compared

Logistic regression	Random forest



REACT Observational Study in COVID-19 patients in collaboration with the University Hospital Southampton

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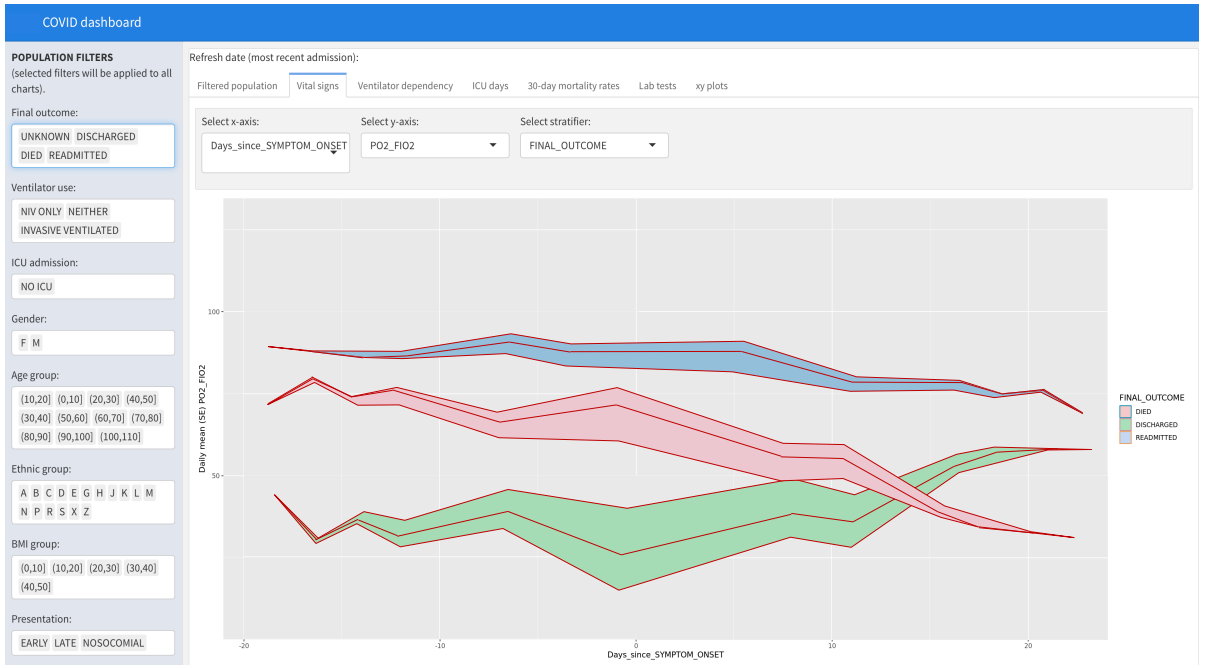
University Hospital Southampton

- Commenced following offer of help in March
- Set up REACT Observational Study in Patients with COVID-19
- 600+ patients with over 250k data points including clinical, ICU, cytokines, labs and symptom onset date
- Application of statistical, AI and ML methods to the data to identify novel ways to predict outcome from early presenting data



ACUITY
PERSONALISED ANALYSIS & INSIGHT

Developing a line-of-sight to a new clinical care pathway

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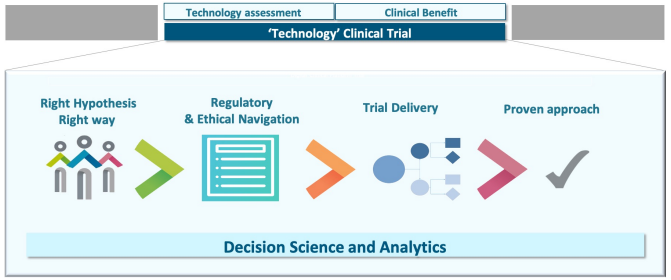
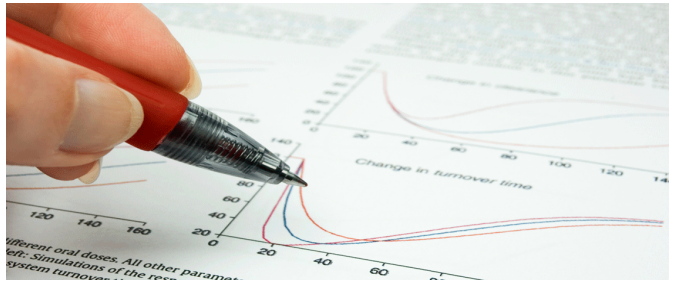
1



- Identify clinical need
- Design the experiment
- Components
  - Patient involvement
    - Design lab
    - F2F meetings
  - Define the current 'as-is' process and the new 'to-be' process
  - Technology
    - Algorithm (ethical)
    - Software
    - Device
    - Technology platform

2



- Complete and publish the experiment (CSR, manuscript etc.)
- Full peer review
- Provide transparency
  - Data
  - Validity
- Algorithm (AI development)
  - Explainable (XAI)
  - Interpretable
  - Reproducible
- Demonstrate design of care pathway is ethical across all components

3

- Translate to clinical care pathway:
  - All technology components
  - Ensure scalability and reliability
  - Validate process
  - Continual clinical process improvement

Summary

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- Relatively new research team building a ‘technology’ clinical trial capability at CRUK MI and The Christie – ECMT Phase I Unit
- The ‘technology’ clinical trial model provides a robust framework for assessing clinical feasibility and clinical benefit
- COVID-19 accelerating new interest and new grant funding opportunities in accelerating technologies in the management cancer patients

CORONET

- Designing the clinical care pathways based on patient ergonomics is delivered through their direct involvement as a co-researchers in our work - digital lab and F2F meetings
- Understanding the full ethical implications of a technology implementation in a clinical setting requires a robust clinical trial design, transparency, open development, publication of methods and datasets for peer review – builds trust and clinical confidence
- Our goal is to transfer our knowledge and experience throughout the CRUK/ECMC network through the UpSmart Award (CRUK Accelerator Award) and Cancer Core Europe (CCE) and also to collaborate with interested third parties

UpSMART digital clinical trials

Cancer Core Europe

- Ultimately, our goal is to build better patient-centred clinical care pathways through our research by listening to their clinical needs and proactive involvement in our ‘technology’ clinical trials – COVID-19 has demonstrated how our health systems need to adapt and change to exploit advances in technology

Thank you

Engaging patients, driving decisions

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