THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau
NEW ZEALAND

AUCKLAND BIOENGINEERING INSTITUTE

12 LABOURS DigitalTWINS Platform

EDITH Meeting January 18 2024

Thiranja Prasad **Babarenda Gamage** (tp.babarendagamage@auckland.ac.nz)

Auckland Bioengineering Institute (ABI)

2001-
30 Research Groups
300+ Researchers

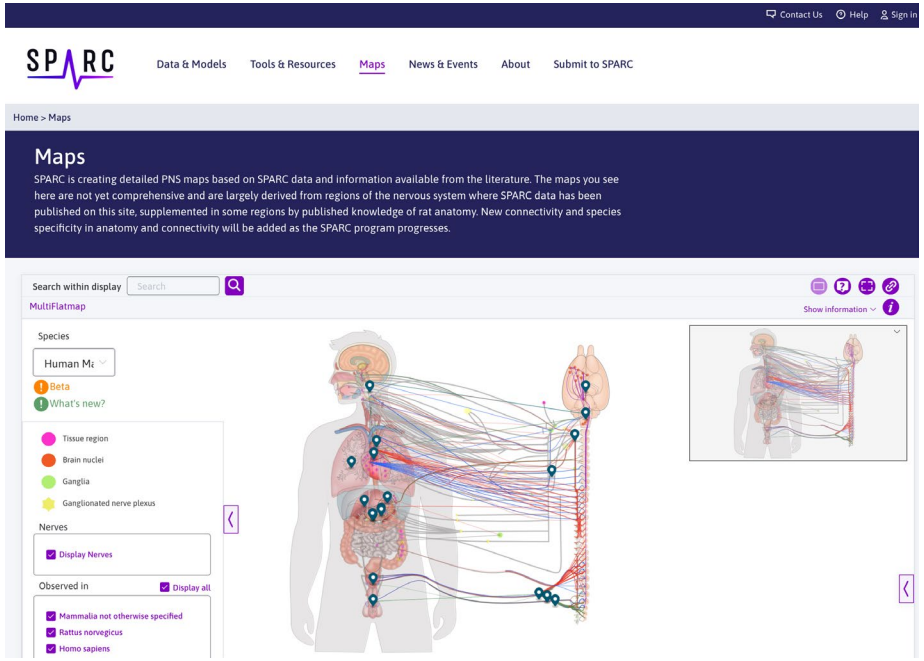
Physiome Project

SPARC

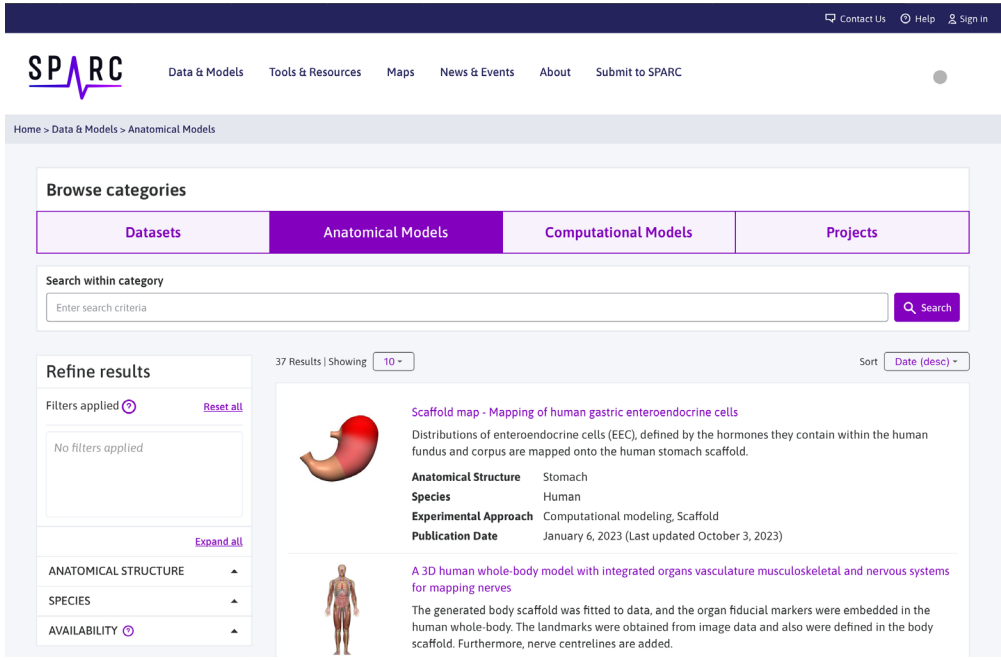
NIH
The Common Fund

2017-
60+ Research Groups in US
90 Institutions and companies
>15 organ systems
8 Species
>200 Curated datasets

Tools for mapping autonomic nervous system



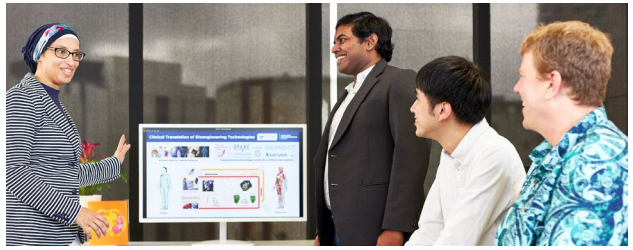
Web portal for presenting results (datasets etc)



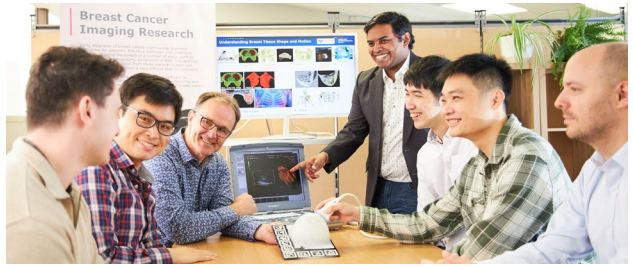
Auckland Bioengineering Institute (ABI)

2001-
30 Research Groups
300+ Researchers

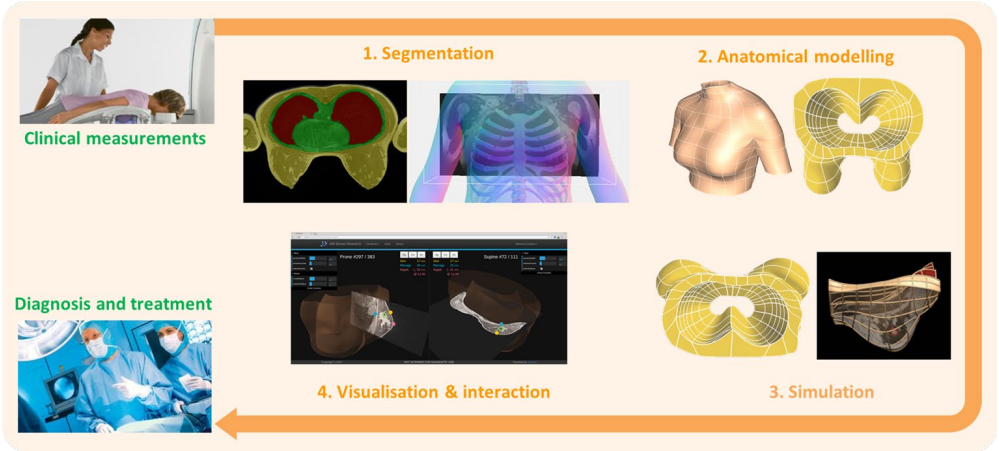
- 2005- Undergrad/PhD Bioengineering (ABI)
- 2017- Research Fellow



- Clinical Translational Technologies Group
- Breast Biomechanics Research Group
- Cardiac Mechanics
- Lung Mechanics



- Soft tissue biomechanics/FEM
- Automated clinical workflows
- Clinical studies
- Statistical shape analysis
- Image registration
- Computer vision & AR
- Parameter estimation
- Optimal experimental design
- UQ
- HPC software development
- Teaching



2019 Babarenda Gamage et al Royal Society Interface Focus

Physiome Project

SPARC

NIH The Common Fund

2017-
60+ Research Groups in US
90 Institutions and companies
>15 organ systems
8 Species
>200 Curated datasets

5 years R&D
Fully automated

Te Whatu Ora Health New Zealand

Aotearoa New Zealand

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UNIVERSITY OF AUCKLAND
Waipapa Taumata Rau
NEW ZEALAND

AUCKLAND BIOENGINEERING INSTITUTE

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Physiome Project

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- Automated clinical workflows
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60+ Research Groups in US
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>15 organ systems
8 Species
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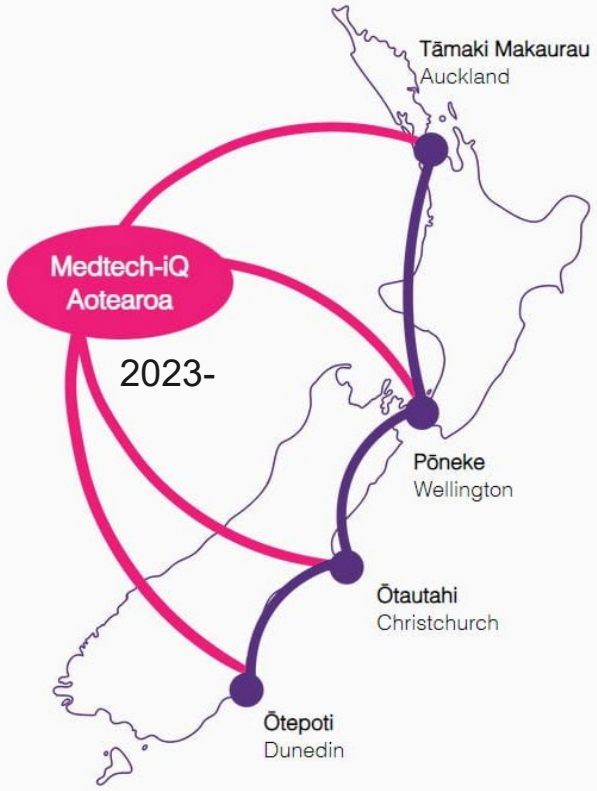
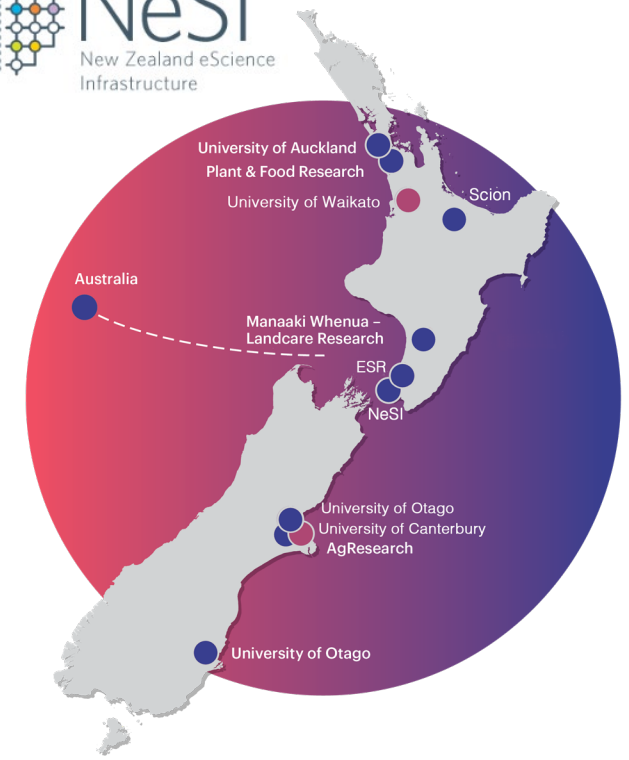
MedTech CMDT
RESEARCH NETWORK
CONSORTIUM FOR MEDICAL DEVICE TECHNOLOGIES

2012-



Linking researchers, healthcare systems, communities, and industry affiliates

NeSI
New Zealand eScience Infrastructure



rakeiora
GENOMICS PLATFORM

GEN3 DATA COMMONS

NIH
The Common Fund

AAI REMS

CSC

12 LABOURS Project – Translation of Digital Twins

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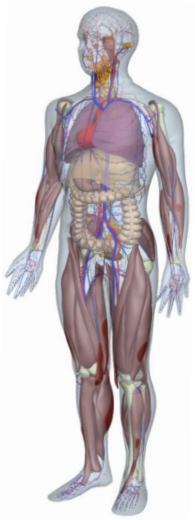
2021-2025

12 Labours

MINISTRY OF BUSINESS, INNOVATION & EMPLOYMENT
HIKINA WHAKATUTUKI

Peter Hunter

David (Andre) Nickerson



Tech Platform 1

Systems Medicine Modelling Framework
Accounting for Energy Conservation

1. Units

Joule (J)
Second (s)
Metre (m, m^3) → Mechanics
Coulomb (C) → Electromagnetics
Mole (mol) → Chemistry
Entropy (S) → Heat flow

2. Physics approach

Port-Hamiltonian framework
(0D=Bond graphs)

Tools

3. Protein classes

4. BG model (full) (reduced)

Metabolic enzymes
SLC transporters
ABC transporters
Ion channels
Receptors: TRKs
Receptors: GPCRs
Signal transduction
Muscle contraction
Cell cycle
Immune cytokines
Gene transcription & translation

5. FCU

Intracellular glucose transport
Intracellular pH
Intracellular metabolism
Myofilament mechanics
...
...
...

FTU

6. Primary FTU

Kidney tubule, glomerulus, etc
Lung acinus
Myocardial sheet
Liver lobule components
Bone osteon
Fibre, neuromusc jnctn, etc
...

7. Secondary FTU (including 3D structure)

nephron
alveoli
tissue block
lobules
osteon
Fascicle
...

8. FE + constitutive laws (●); Scale up with scaffolds (▼)

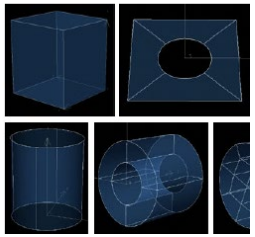
surrogate
surrogate
surrogate

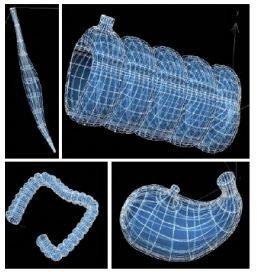
9. Organs

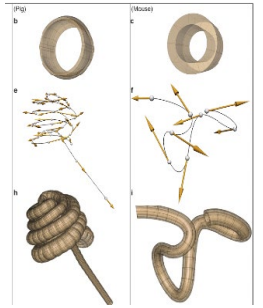
Kidney
Lung
Heart
Liver
Bone
Skeletal muscle
...

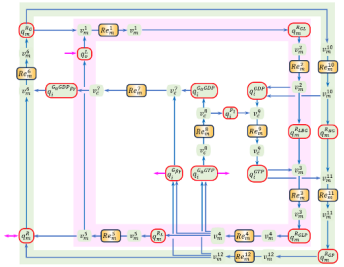
10. Systems physiology

3D anatomical model of the body
Regulation of fluid volume
Regulation of arterial blood pressure
Regulation of pH
Regulation of electrolyte balance
Regulation of glucose
Regulation of O_2 and CO_2
Regulation of calcium
Regulation of phosphate
Regulation of body temperature
...



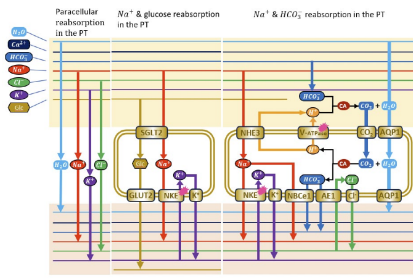


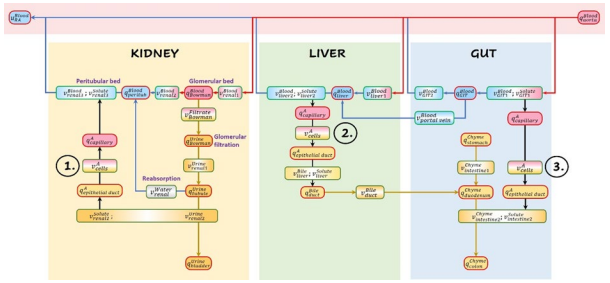


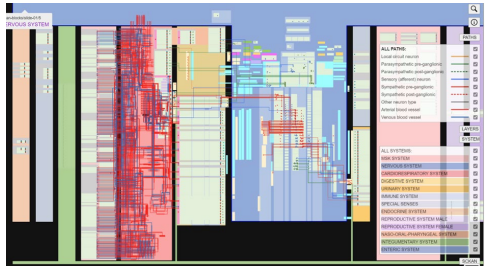


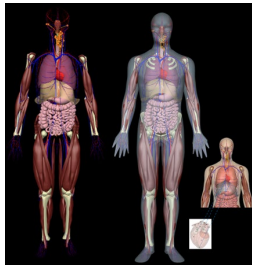
Models

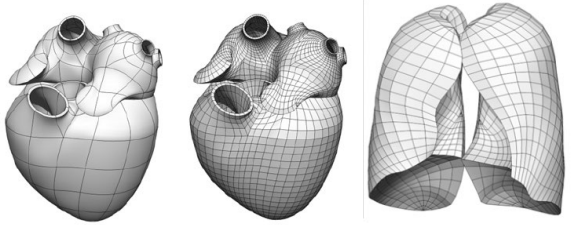
Tools











12 LABOURS Project – Translation of Digital Twins

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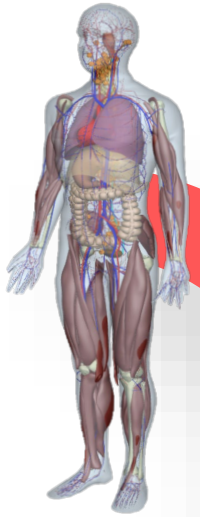
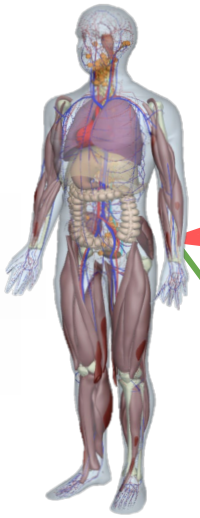


Tech Platform 1

Personalisation Workflows

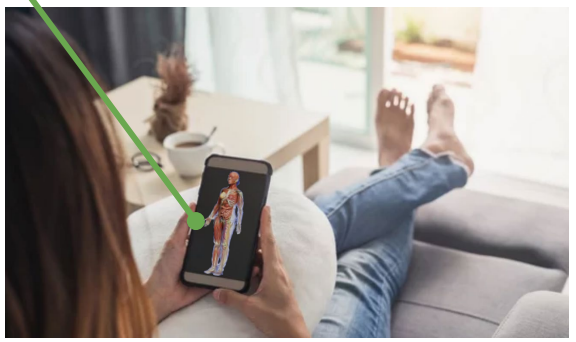


Personalised Digital Twin

Tech Platform 2

Prasad Babarenda Gamage

Clinical Healthcare



Home-based Healthcare

Poul Nielsen

Implantables Wearables Surface Imaging

Tech Platform 3

Clinical Recordings Lab Tests

12 LABOURS – Exemplar Workflows

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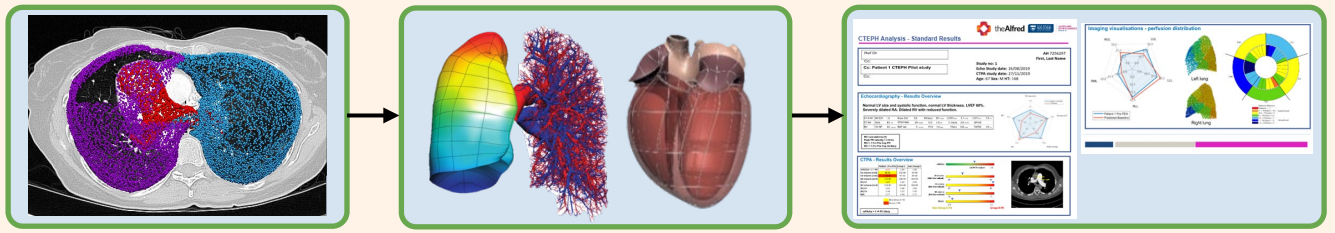
AUCKLAND BIOENGINEERING INSTITUTE

Project 1

Biomarkers for pulmonary hypertension

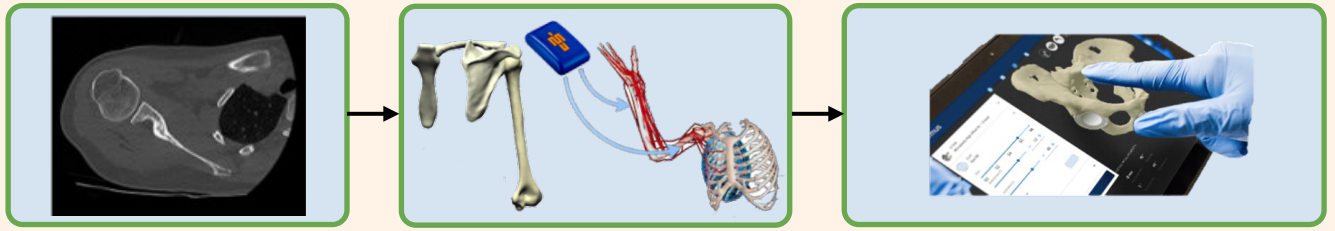


Merryn Tawhai

Martyn Nash

Project 2

Personalised rehabilitation of upper limb disorders

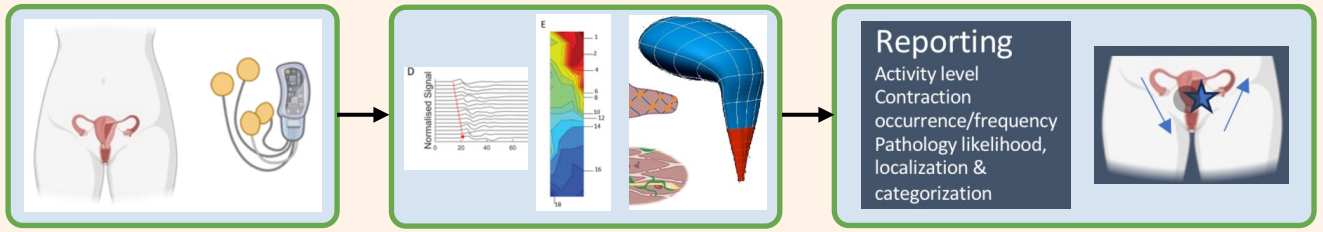


Thor Besier

Julie Choisne

Project 3

Control of organ function by the autonomic nervous system (Uterus & Stomach)

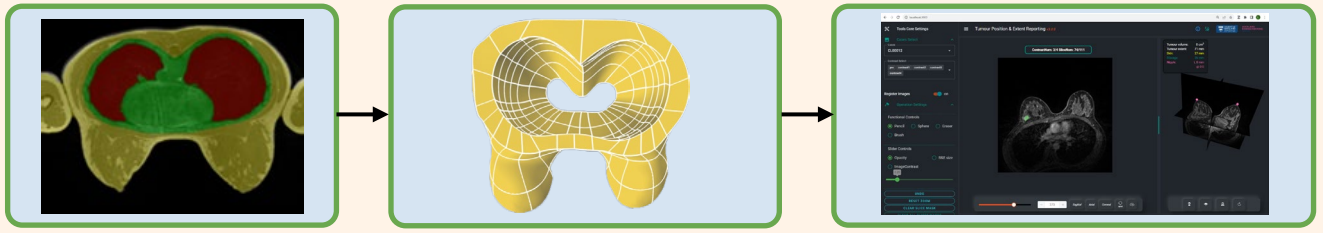


Alys Clark

Leo Cheng

Project 4

Automated reporting of breast cancer



Prasad Babarenda Gamage

Martyn Nash

Poul Nielsen

- Implemented in phases

Common Elements for Enabling End Users

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NEW ZEALAND

AUCKLAND BIOENGINEERING INSTITUTE

Data Objects

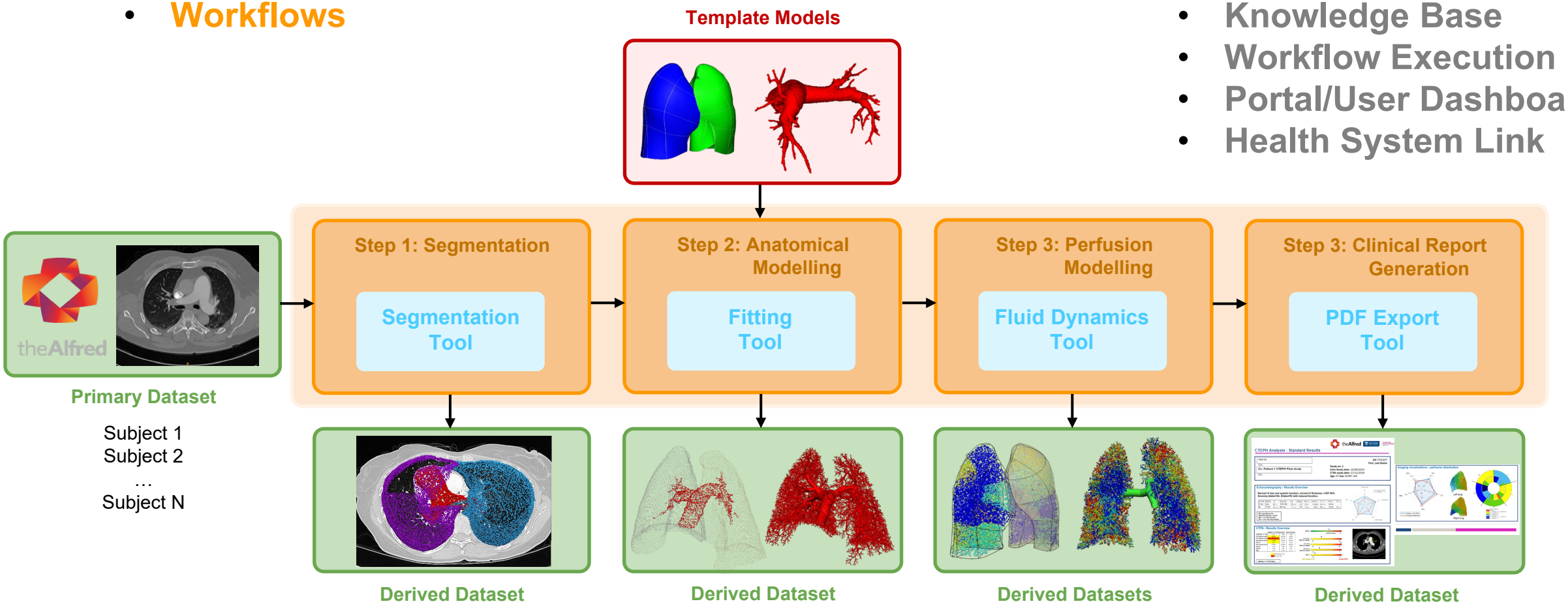
- Models
- Datasets
- Tools
- Workflows

Guidelines & Resources

- Documentation
- Data Management Plans
- Ethics Application Templates

Core Services

- Harmonised Database
- Data Ingress/Egress
- Data Catalogue
- Knowledge Base
- Workflow Execution
- Portal/User Dashboards
- Health System Link

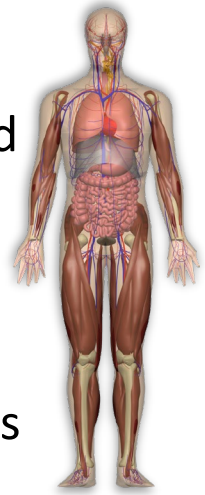


12 LABOURS DigitalTWINS Platform

(Digital **T**ranslational **W**orkflows for **IN**tegrating **S**ystems)

- **Guiding principles:**
  - Standardisation for interoperability (common terminologies, ontologies, annotations …)
  - Infrastructure-agnostic
  - Modular and extensible services

- **Foster ecosystem:**
  - Support FAIR and reproducible research outcomes
  - Provide foundation for integrating research efforts and assembling multi-scale, -physics, -organ digital twins
  - Meet data sovereignty requirements
  - Efficiently conduct clinical trials
  - Adopt standards to send workflows between platforms



Timeline:

2021-2025

1. Develop & deploy prototype
   - Core services
   - Guidelines & resources
2. Demonstrate its clinical application in exemplar projects

2026-

- Production deployment
- Adoption across ABI
- Adoption nationally via Medtech IQ

Clinical Translational Technologies (CTT) Group

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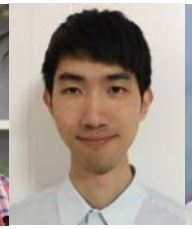
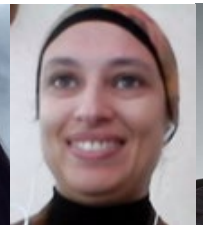
AUCKLAND BIOENGINEERING INSTITUTE

Prasad Babarenda Gamage (lead)

David (Andre) Nickerson


Chinchien Lin

Jiali Xu


Ayah Elsayed

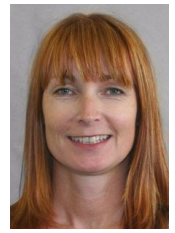
Linkun Gao

Yuan (Frances) Feng

Jianwei (David) Yu

Alan Wu

Clinical Collaborators & Advisors


Robyn Whittaker

Penny Andrew

Anthony Doyle

Te Whatu Ora
Health New Zealand

MINISTRY OF HEALTH
MANATŪ HAUORA

Research/Community Collaborators & Advisors

Diana Siew (ABI)

David Hawkes (UCL)

Alistair Young (KCL)

Tom Gillespie (UCSD)

NeSI
New Zealand eScience Infrastructure

Nick Jones

Claire Rye

Nathalie Giraudon

Jun Huh

Physiome Project

12 Labours

EDITH

VPH Institute
Building the Virtual Physiological Human

GEN3
DATA COMMONS

Misty Edmonds

Cris Print

Annette Lasham

Nick Knowlton

- ABI Research Groups
- ABI Software Team

Centre for eResearch

SPARC

Center for Translational Data Science
AT THE UNIVERSITY OF CHICAGO

Iwi United Engaged Limited

THE UNIVERSITY OF AUCKLAND
NEW ZEALAND
MEDICAL AND HEALTH SCIENCES

Funding
MINISTRY OF BUSINESS, INNOVATION & EMPLOYMENT
HIKINA WHAKATUTUKI

Clinical Translational Technologies (CTT) Group

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NeSI
New Zealand eScience Infrastructure

uniservices
IDEAS TO LIFE RANGAHAUA KIA WHAI HUA

Iwi United Engaged

SPARC

GEN3
DATA COMMONS

Center for Translational Data Science
AT THE UNIVERSITY OF CHICAGO

UNSW
Tyree Foundation Institute of Health Engineering

Te Whatu Ora
Health New Zealand

genomics aotearoa

UC San Diego

Mātai
Te Mata Mātai Hura

Centre for eResearch

TE AHO O TE KAHU
CANCER CONTROL AGENCY

THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau
NEW ZEALAND
MEDICAL AND HEALTH SCIENCES

MedTech CMDT
RESEARCH NETWORK
CONSORTIUM FOR MEDICAL DEVICE TECHNOLOGIES

upf. Universitat Pompeu Fabra Barcelona

EDITH
VPH Institute
Building the Virtual Physiological Human

TE TĪTOKI MATAORA
MEDTECH RESEARCH TRANSLATOR

i3 institute for innovation + improvement

healthAlliance
Right behind better healthcare

DigitalTWINS Platform – Vision

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Models

- Physiome Model Repository
- BioModels
- SPARC
- etc

Datasets

- NIH National Cancer Institute Imaging Data Commons
- European Genome-Phenome Archive
- Biomedical Research Hub
- Mātai
- REDCap (Research Electronic Data Capture)

- etc

Tools

- OpenSim
- etc

Workflows

- BioSimulations (Reproducing & Reusing Biomodels & Simulations)
- Dockstore
- etc

Health System

Patient EHR

Clinical Trials

DigitalTWINS Platform

Harmonised Database

2

Repositories

- Models
- Tools
- Datasets
- Workflows

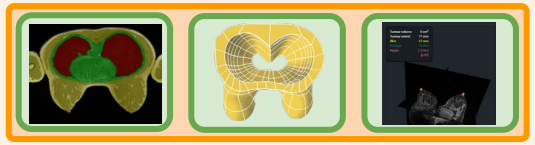
Knowledge Base

5

Workflow Execution

3

- Clinical Workflows



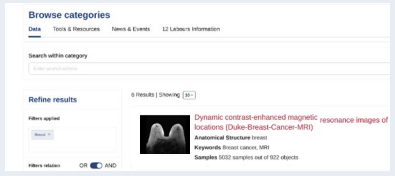
- Insilico Trial Workflows
- Digital Twin Assembly Workflows
- etc

Digital Twins

4

1 Data Ingress

Data Catalogues

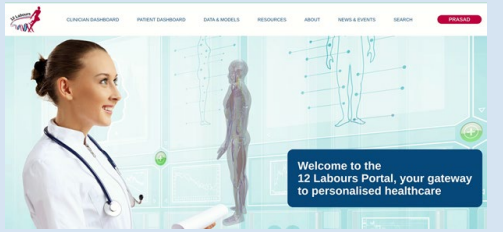


Education Dashboard

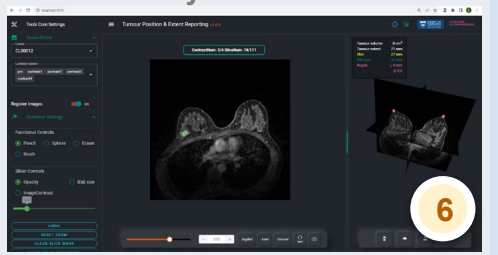
Patient Dashboard

Data Egress

Portal

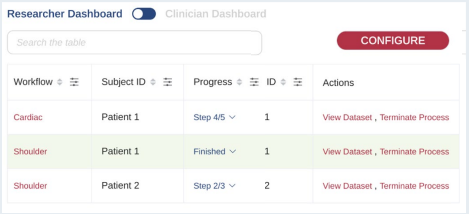


Clinical Study Dashboard



6

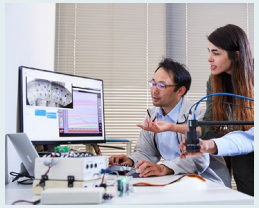
Researcher Dashboard



End users

Clinicians

Researchers



Patients

Public

Industry

- etc

DigitalTWINS Platform – Implementation

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NEW ZEALAND

AUCKLAND BIOENGINEERING INSTITUTE

SPARC Dataset Structure*

Findable Accessible Interoperable Reusable

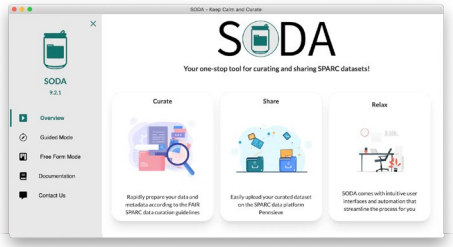
*Bandrowski et al biorxiv

uberon

ARDC Nectar Research Cloud

Datasets

- primary
  - dataset_Description.xlsx
  - samples.xlsx
  - subjects.xlsx
  - submission.xlsx
  - CHANGES.txt
  - README.txt
  - code
  - derivative
  - docs
  - protocol
  - source



SPARC-me

digitaltwins

pypi

DigitalTWINS Platform

Harmonised Database

2 Repositories

Datasets

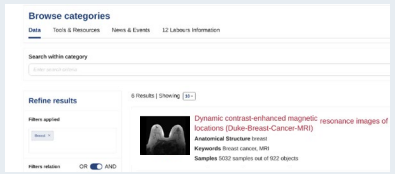
GEN3 DATA COMMONS

iRODS

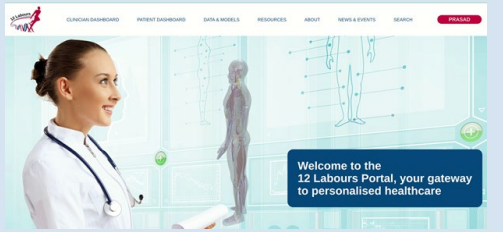
ORTHANC

1 Data Ingress

Data Catalogues



Portal



Nuxt

Element

FastAPI

DigitalTWINS Platform – Implementation – EP4

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NEW ZEALAND

AUCKLAND BIOENGINEERING INSTITUTE

Datasets

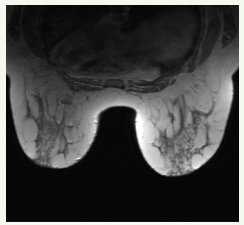
THE CANCER IMAGING ARCHIVE

922 cancer patients*

- Clinical MRI
- EHR data
- Clinical reports
- Molecular data

Duke UNIVERSITY

SDS Dataset



*Saha et al 2018 Br. J.Cancer

DigitalTWINS Platform

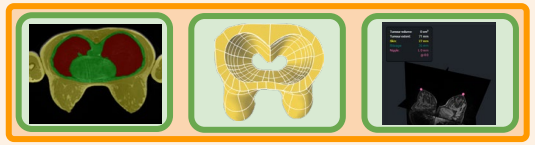
Harmonised Database

2 Repositories

Datasets

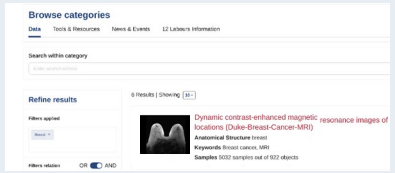
Workflow Execution 3

Clinical Workflows

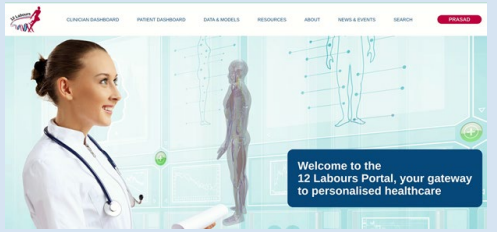


1 Data Ingress

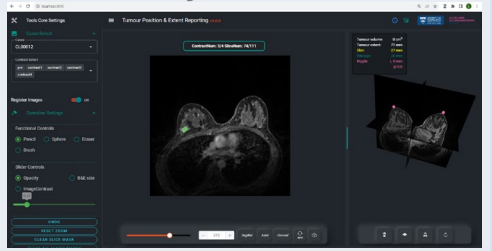
Data Catalogues



Portal

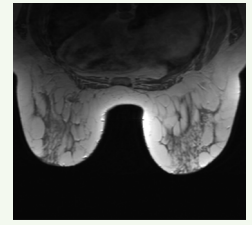


Clinical Study Dashboard



Data Egress

SDS Dataset



DigitalTWINS Platform – Workshop 1 – September 2023

- Describing and storing data in the DigitalTWINS platform

- Learning outcomes
  1. Connecting to DigitalTWINS platform via portal or Python API
  2. Creating SDS datasets programatically using sparc-me
  3. Uploading/downloading datasets via Python API

- Materials
  - Independent instance of DigitalTWINS platform for each exemplar project
  - Pre-workshop reading material
  - Workshop documentation
  - 5 Tutorials
  - Feedback forms

- **Updated Plan:**
  - We will implement all exemplar project workflows in platform
  - Generate documentation & tutorials from these implementations

DigitalTWINS Platform – Current Developments

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NEW ZEALAND

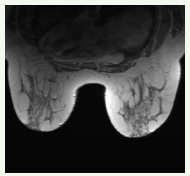
AUCKLAND BIOENGINEERING INSTITUTE

Te Whatu Ora Health New Zealand

REDCap Research Electronic Data Capture

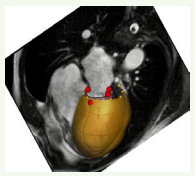
Remote monitoring via IEEE 11073 (Platform 3)

SDS Dataset 1



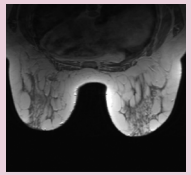
Patient 1
Patient 2
…
Patient N

SDS Dataset 2

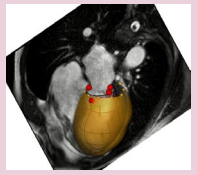


Patient 1
Patient 2
…
Patient N

Patient 1



Imaging Study 1



Imaging Study 2

DigitalTWINS Platform

Harmonised Database

2 Repositories

Datasets
Tools
Workflows

HL7 FHIR
SNOMED CT
HAPI FHIR

Workflow Execution 3

Clinical Workflows

COMMON WORKFLOW LANGUAGE
docker

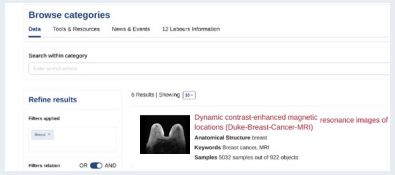
Workflow Manager
MAP Client Scaffold
Mapping Tool

Digital Twins

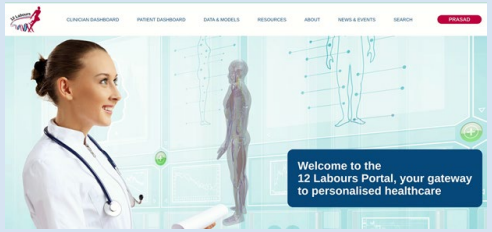
4

1 Data Ingress

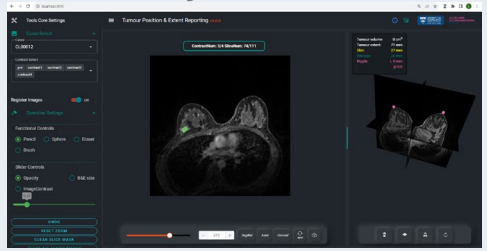
Data Catalogues



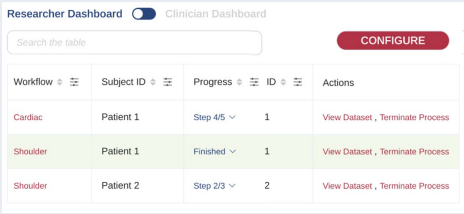
Portal



Clinical Study Dashboard



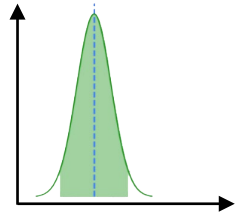
Researcher Dashboard



Credibility Assessment Tools

- Generalised Modular Bayesian Uncertainty Quantification Framework

- Measurements
- Model Parameter Estimation



- Accounting for surrogate model approximation errors
- Optimal experimental design

Engineering Science

Oliver Maclaren

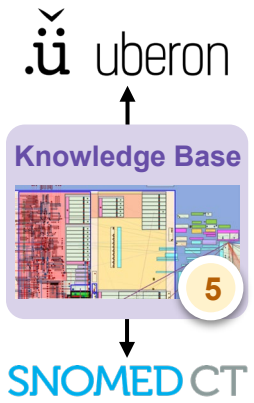
Ruanui Nicholson

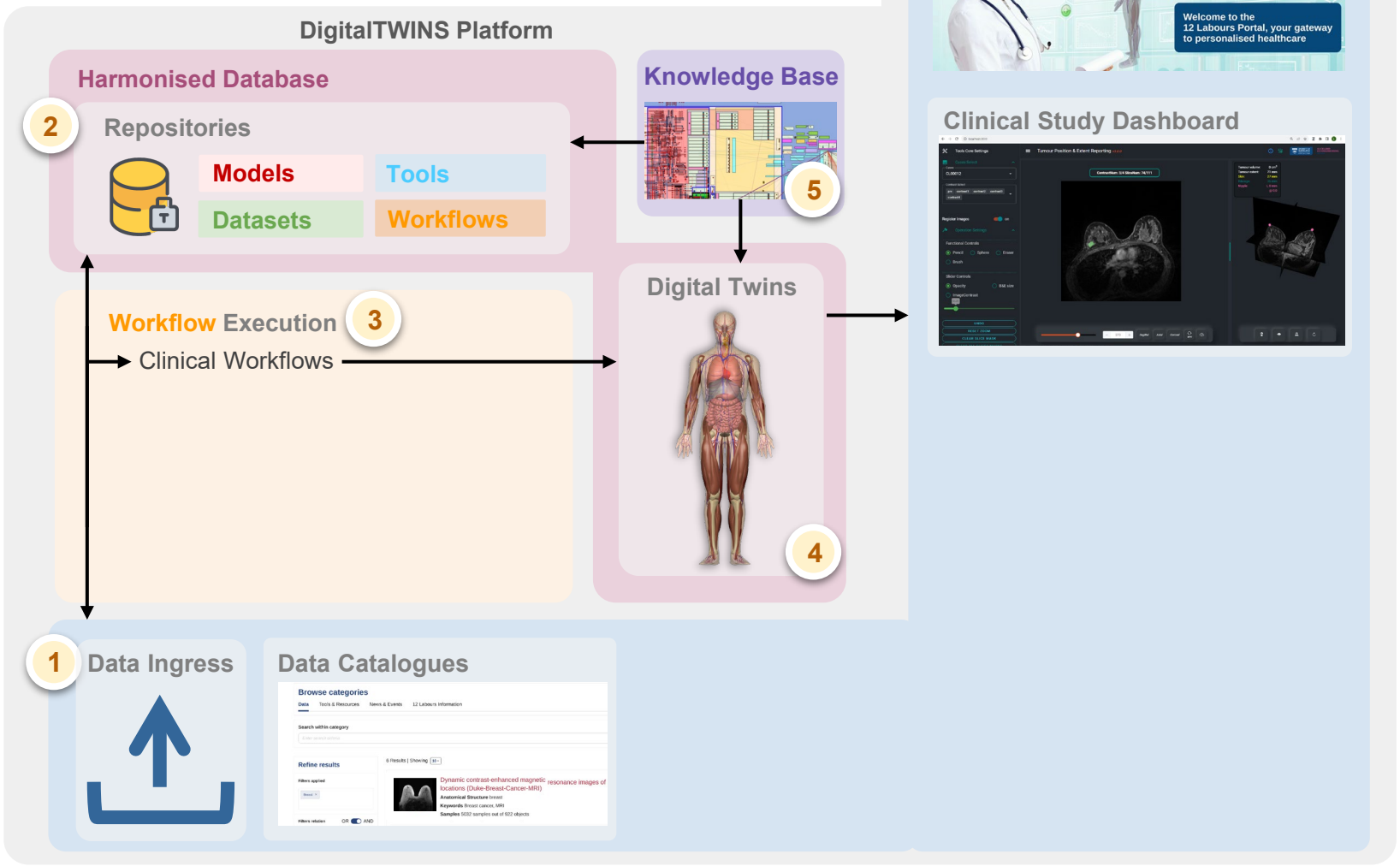
Prasad

Finbar Argus

David Wu

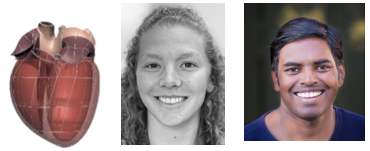
DigitalTWINS Platform – Current Developments





Automated Workflow Assembly Tools

- Personalise model parameters e.g. stiffness
- Assess added prognostic value

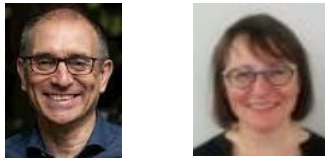


Mathilde Verlyck | Prasad

David Nickerson | Martyn Nash | Debbie Zhao

MEDICAL AND HEALTH SCIENCES

Te Whatu Ora
Health New Zealand



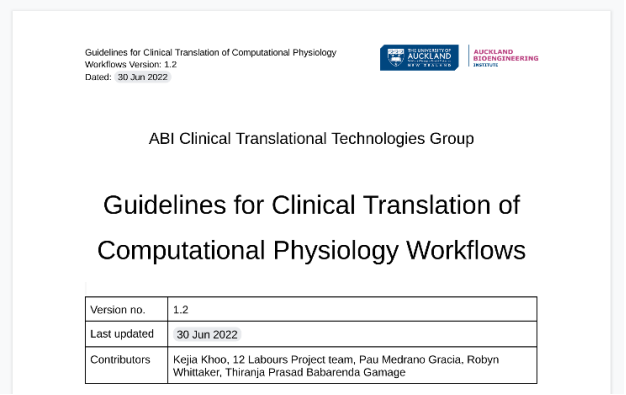
Rob Doughty (Cardiologist) | Katrina Poppe (Biostatistician)

Guidelines & Resources

THE UNIVERSITY OF AUCKLAND
Te Whare Wānanga o Tāmaki Makaurau
NEW ZEALAND

AUCKLAND BIOENGINEERING INSTITUTE

- Guidelines for Clinical Translation of Computational Physiology Workflows


Guidelines for Clinical Translation of Computational Physiology Workflows Version: 1.2
Dated: 30 Jun 2022

ABI Clinical Translational Technologies Group

Guidelines for Clinical Translation of Computational Physiology Workflows

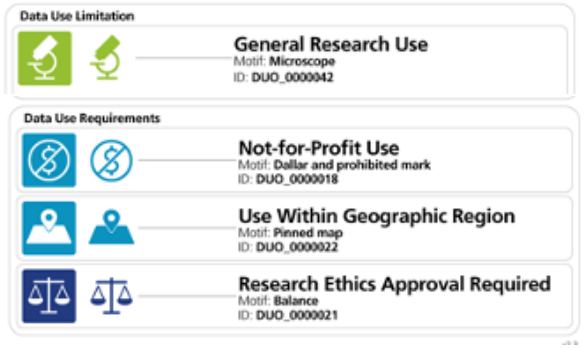
Version no.	1.2
Last updated	30 Jun 2022
Contributors	Kejia Khoo, 12 Labours Project team, Pau Medrano Gracia, Robyn Whittaker, Thiranja Prasad Babarenda Gamage

Contents

Executive summary
Glossary
Abbreviations
Resources and referenc
Introduction
Is it a medical device?
Phases of clinical translation
Phase 1: Initiation
Phase 2: Pre-clinical research
Phase 3a: Clinical research
Phase 3b: Commercialisation activities
Phase 4: Regulatory review
Phase 5: Launch and post-market
Intellectual property protection
Venture creation
Data policies
Data protection
Future developments
Regulatory considerations
Examples

Include Data Use Descriptions

Data Use Ontology



2016 Dyke et al PLOS Genetics
2018 Woolley et al NPJ Genomic Medicine

Indigenous Data Sovereignty Descriptions

ENRICH Local Contexts

2021 Liggins et al Molecular Ecology

- Unified Ethics Application Templates

ABI Clinical Translational Technologies Group

Guidelines for Ethics Applications

Version no.	1.0
Last updated	7 Jul 2022
Contributors	Kejia Khoo, Pau Medrano Gracia, Thiranja Prasad Babarenda Gamage

- Consistent:
  - Consent form
  - Data management plan
  - etc
- Emphasise data reuse/linking to enable vision for creating integrated digital twins

TE AKA MĀTAURANGA MATEPUKUPUKU CENTRE FOR CANCER RESEARCH

TE TĪTOKI MATAORA MEDTECH RESEARCH TRANSLATOR

Te Whatu Ora Health New Zealand

uniservices IDEAS TO LIFE RANGAHAUA KIA WHAI HUA

Iwi United Engaged

Jiali Xu

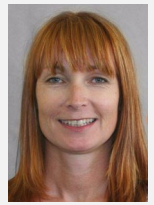
Pau Medrano-Gràcia

Misty Edmonds

Kent Lee

Annette Lasham

Nick Knowlton


Robyn Whittaker

Summary

- Outlined vision for 12 LABOURS DigitalTWINS platform
  - provide foundation and common infrastructure for:
    - integrating systems to assemble virtual human twins
    - efficiently reproduce, reuse, and integrate research efforts

- Guidelines - to support researchers increase their awareness and understanding

- Keen to collaborate

- All infrastructure presented is opensource/permissive license (github.com/ABI-Software)

Thiranja Prasad *Babarenda Gamage* (tp.babarendagamage@auckland.ac.nz)