

TERMS OF REFERENCE



Pilot I Digital Twin System

Introduction

This pilot study will develop and validate a coupled lung-kidney digital twin capable of real-time simulation of these organ function in critically ill patients. Building on established in-silico models of respiratory mechanics, gas exchange and renal hemodynamics, the project will integrate these submodels into a unified framework. The digital twin will leverage patient-specific ICU data to personalize simulations, enabling in-silico evaluation of ventilator settings, fluid management strategies and novel therapeutics. By partnering with academic departments and specialized SMEs, this initiative aims to accelerate pre-clinical testing, reduce reliance on animal studies and support regulatory-grade virtual trials.

Purpose and scope

The primary objective is to demonstrate that a lung-kidney digital twin can (1) accurately reproduce patient trajectories of blood gases, urine output and hemodynamics; (2) suitable for bedside decision support to serve as a predictive platform for pharmaceutical and biotech R&D. Scope includes model adaptation, software integration, data-driven calibration and performance evaluation. Deliverables will encompass a validated coupling framework, user-interface prototypes, regulatory-compliant documentation and a pilot deployment package for SME partners.

Approach and methodology

We will develop and validate a coupled lung-kidney digital twin tailored to critically ill patients by integrating pre-existing, peer-reviewed organ models and patient data. First, we will adapt an established in silico model of respiratory mechanics and gas exchange and incorporate published, physiologically based mathematical models of renal filtration, reabsorption and hemodynamics. These submodels will be connected within a modular software framework so that changes in ventilation, perfusion, acid-base status or fluid balance in one organ appropriately influence

the other. Partnership with the Department of Computer Science to ensure computational performance suitable for bedside use.

To personalize and validate each patient's digital twin, we will assemble a de-identified dataset of ICU patients that includes demographics, laboratory values, ventilator settings and hemodynamic measurements. Advanced machine-learning technique will be employed to tune the model parameters until the twin accurately reproduces each patient's observed trajectory. We will then evaluate physiological accuracy by comparing model predictions of pulmonary, renal and hemodynamic markers against real measurements; assess computational performance and test predictive utility by simulating common interventions (for example, adjustments in ventilator settings, fluid challenges, or contrast-agent dosing).

Pre-requisite for participation

Upon successful validation, the lung-kidney digital twin will be offered as an in silico testbed for novel drug candidates and medical devices. Pharmaceutical and biotechnology partners will be able to use it to assess organ-level effects of therapies in a virtual critical-care environment before proceeding to animal or human trials, thereby reducing development time, cost and ethical burden.

Target partners include SMEs and technology providers with expertise in real-time simulation platforms, pharmacokinetic/pharmacodynamic profiling, or clinical data integration. Interested parties must be able to supply pharmacokinetic and pharmacodynamic parameters for investigational compounds or device effect profiles and access to de-identified preclinical or early clinical datasets.