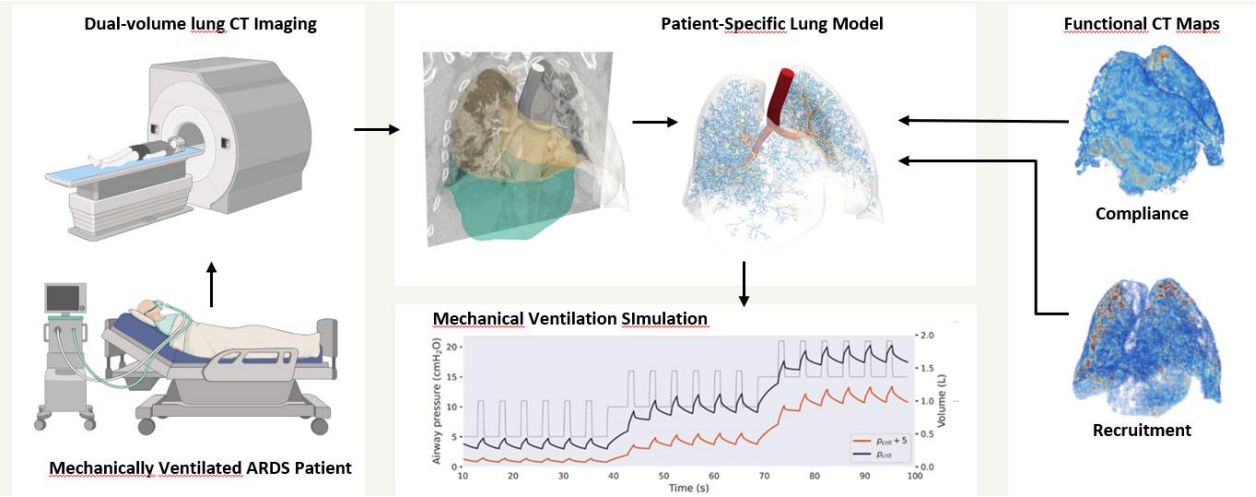


PhD subject proposal

Université Grenoble Alpes — Doctoral school ISCE

Engineering for Health, Cognition and Environment

Key information

Item	Details
Institution	Université Grenoble Alpes
Doctoral school	ISCE — Engineering for Health, Cognition and Environment
Specialty	BIS — Biotechnology, instrumentation, signal and imaging for biology, medicine and the environment
Research unit	STROBE — Synchrotron Radiation for Biomedicine, INSERM UA7
Thesis director	Prof. Sam BAYAT (MD, PhD, HDR) — sam.bayat@univ-grenoble-alpes.fr
Co-supervision	Dr Emmanuel Roux (PhD), CREATIS, INSA Lyon — co-supervisor (Grenoble–Lyon co-supervision) — emmanuel.roux@creatis.insa-lyon.fr
Funding	36-month doctoral contract on ANR resources — AAPG 2026 project OPTIVENT , partner 3 (STROBE INSERM UA7)
Funding source	ANR — French National Research Agency
Employer	Université Grenoble Alpes
Duration	36 months
Thesis start date	January 1, 2027
Application deadline	10 December, 2026

1. Thesis title

Patient-specific pulmonary digital twins from multi-volume CT: model construction and forward simulation of personalized protective mechanical ventilation in ARDS

Note on the title: thesis carried out within the ANR OPTIVENT project (work package WP1, partner 3), co-supervised between Grenoble (STROBE, INSERM UA7, UGA) and Lyon (CREATIS, INSA Lyon).

2. Keywords

acute respiratory distress syndrome, mechanical ventilation, digital twin, patient-specific modelling, reduced-order lung model, parameter identification, forward simulation, virtual clinical trial, lung computed tomography

3. Research field

Computational respiratory physiology / Patient-specific lung modelling and simulation / Functional medical imaging

Engineering for health: patient-specific modelling and numerical simulation applied to intensive care

4. Thesis abstract

Acute respiratory distress syndrome (ARDS) affects more than three million patients each year, with 30–50 % mortality. Mechanical ventilation is life-saving but aggravates lung injury through excessive strain (ventilator-induced lung injury, VILI). Because lung mechanics vary widely between patients, optimal ventilator settings remain largely empirical, and ventilation should be personalized.

This thesis is the methodological foundation of the ANR OPTIVENT project. Its core objective is to build functional pulmonary digital twins — patient-specific models reproducing the mechanical response of an individual lung — and to use them for forward simulation of mechanical ventilation. It builds on a framework demonstrated by our group, in which regional properties derived from CT images at two lung volumes are embedded in a model coupling an anatomically realistic bronchial tree, regional compliance and recruitment/derecruitment dynamics. Lung segmentation and deformable registration are already established and serve as input tools: the thesis concentrates on the model and on what it predicts.

Three challenges are addressed: **model construction** — a reduced-order (0D) regional lung model whose parameters are identified for each patient by solving an inverse problem constrained by the measured regional deformation and respiratory mechanics, then verified and validated; **forward simulation** — exposing each twin to a broad range of ventilation strategies to map, patient by patient, the relationship between settings and recruitment, overdistension and regional strain; and **scale-up** — running construction and simulation reproducibly on >200 ARDS patients of the multicentre CT4ARDS-2 study (NCT06113276) and on public multi-volume CT collections. The thesis delivers the validated twin cohort and the virtual clinical trial corpus on which the project's explainable predictive model depends.

5. Objectives and context

Objectives

- Formulate a reduced-order regional lung model (viscoelastic tissue, regional compliance, recruitment/derecruitment thresholds, airway tree, chest wall), building on the group's existing framework.
- Calibrate it per patient by inverse problem against the regional deformation (from the existing registration pipeline) and global pressure–volume data, with plausibility bounds and parameter uncertainty.
- Verify and validate the twins: numerical verification, identifiability and sensitivity analyses, comparison with data not used for calibration (additional CT volumes, bedside mechanics, recruitment-to-inflation ratio).
- Run forward simulations of ventilation strategies (PEEP, tidal volume, plateau/driving pressure, timing) and quantify recruitment, overdistension, regional stretch and mechanical power.
- Scale up to the CT4ARDS-2 cohort and public datasets (TCIA, DIR-Lab), add physiologically constrained virtual patients, and deliver a FAIR, documented virtual clinical trial dataset and pipeline.

Context

Protective ventilation rests on standardised rules, whereas mechanical properties in the injured lung are highly heterogeneous: recruitable collapsed regions coexist with overdistended aerated regions, and existing ventilation simulators ignore this heterogeneity. We have shown that a patient-specific in silico lung model — anatomically accurate bronchial tree, regional compliance from registration of CT images at two pressures, regional recruitment/derecruitment dynamics — plausibly reproduces global pressure–volume curves and local behaviour, and can simulate a change in PEEP. With the CT processing chain now established, the open questions lie in the model: how to identify its regional parameters robustly from two volumes, how far its predictions can be trusted, and what it predicts when ventilation is changed.

Building and simulating each model is too slow for bedside use. OPTIVENT therefore first makes twin construction and forward simulation systematic, validated and scalable, then uses the resulting virtual clinical trials to train an explainable predictive model — an approach proven in diabetes and cardiology (Living Heart Project) but never applied to mechanical ventilation. The thesis, mainly hosted at STROBE (INSERM UA7, UGA; partner 3, WP1 lead), occupies this upstream, critical position. A mobility period at the CREATIS laboratory (Lyon) is also planned.

6. Methodology and work plan

Phase 1 — Model formulation and verification (months 1–8). Appropriation of the existing framework and CT4ARDS-2 data; registration inputs used with automated quality-control flags (Jacobian, overlap, inverse consistency). Formulation of the regional model and numerical verification (convergence, time-stepping, regional resolution) on pilot patients.

Phase 2 — Parameter identification and validation (months 6–18). Inverse-problem calibration matching simulated to measured regional deformation and global pressure–volume behaviour, with hard plausibility bounds and Bayesian or ensemble uncertainty. Identifiability and global sensitivity analyses (Sobol indices); validation against independent data.

Phase 3 — Forward simulations: virtual clinical trials (months 12–30). Incremental/decremental PEEP trials, tidal volume, plateau and driving pressure, timing; main outcome combined recruitment and overdistension, plus regional strain and mechanical power. Comparison of twin-optimal settings with clinical PEEP-setting methods; space-filling sampling and constrained virtual patients.

Phase 4 — Scale-up and multi-site deployment (months 16–28). Automated twin construction and simulation for >200 patients and public collections, deployed locally at each site so only de-identified derived models leave it; parallel computing on GRICAD; confidence level per twin.

Phase 5 — Delivery and writing (months 28–36). Corpus delivery to the machine learning partners, analysis of the determinants of the simulated response, pipeline release, articles and thesis.

Risks. Non-identifiable parameters → model reduction guided by identifiability analysis; delayed data access → local deployment, CNIL/DPO procedures from month 1; computing load → GRICAD and parallelisation; poor-quality cases → quality flags and exclusion from full modelling.

7. Expected results

- A validated, documented patient-specific lung model and calibration procedure, with identifiability, sensitivity and validation analyses.
- A cohort of >200 ARDS digital twins with regional parameter distributions, uncertainty and confidence levels (deliverables D1.1, D1.2).
- A forward simulation and augmentation framework with documented physiological constraints, and the virtual clinical trial dataset linking patients, ventilation strategies and predicted recruitment/overdistension (D2.1, D2.2).
- A mechanistic characterisation of how regional heterogeneity determines the response to ventilator settings, identifying phenotypes that benefit most from personalisation.
- Two to three first-author publications and international conference communications.

8. Candidate profile

Master's or engineering degree in biomedical engineering, computational mechanics, applied mathematics, physics or medical image processing. Strong Python scientific programming is required. Experience in numerical modelling — ODE or reduced-order models, finite elements, parameter estimation, inverse problems, sensitivity analysis — is a major asset; deformable registration expertise is not required, as the pipeline exists. Autonomy, rigour, well-documented code and the ability to work with clinicians and machine learning researchers are essential. English B2 minimum.

Taught during the thesis: respiratory mechanics, ARDS pathophysiology, protective ventilation and the group's modelling framework (STROBE, partner ICUs, Eindhoven team); simulation and HPC training (GRICAD).

9. Supervision arrangements

Director: Prof. Sam Bayat (Professor of Physiology, UGA; head of the Lung Function Laboratory, CHU Grenoble Alpes; Director of STROBE, INSERM UA7, host laboratory). Co-supervisor: Dr Emmanuel Roux (CREATIS, INSA Lyon; image processing, Lyon CT4ARDS site), providing a Grenoble–Lyon co-supervision; the thesis will mainly take place at STROBE, with a mobility period at CREATIS (Lyon). Day-to-day support: Cécile Olivier, research engineer (WP1 CT inputs, workflow and data management). Weekly team meetings in Grenoble with regular Grenoble–Lyon video meetings, monthly WP1/WP2 partner meetings, six-monthly OPTIVENT committees, annual follow-up (CSI) as required by ED ISCE, mandatory ED modules and budgeted visits to partner sites.

10. Scientific, material and financial conditions

36-month doctoral contract funded by ANR (OPTIVENT, AAPG 2026), employer Université Grenoble Alpes. The partner budget covers a GPU workstation, open-access publication and travel (partner meetings, international conferences). Access to GRICAD computing and to CT4ARDS-2 data within the project's regulatory framework.

Data protection. Imaging and clinical metadata only, pseudonymised at source; raw CT never leaves the clinical sites (local pipeline deployment); HDS-certified storage; FAIR data management plan; no processing before the required authorisations.

11. Dissemination and valorisation objectives

- Two to three first-author articles (e.g. Medical Image Analysis, J Appl Physiol, Critical Care, IEEE TBME) and communications at ERS, ESICM/LIVES, MICCAI, ISBI, CPLF, SRLF.
- Open-source release of the pipeline and deposition of de-identified derived and synthetic data (Zenodo, GitHub); contribution to OPTIVENT deliverables and ANR reports. No patent or confidentiality constraint envisaged.

12. Planned collaborations

- **Prof. Adrien Bartoli** — CHU Clermont-Ferrand / Institut Pascal, OPTIVENT coordinator: digital twins, virtual clinical trials.
- **Prof. Omar Ait Aider** — LEME : Laboratoire Energétique Mécanique Electromagnétisme, Université Paris Nanterre.
- **Dr Emmanuel Roux** — CREATIS, INSA Lyon: thesis co-supervisor; image processing, Lyon CT4ARDS site.
- **Prof. Wouter Huberts** — TU Eindhoven: co-development of the lung simulation framework, model formulation and calibration.
- **Prof. Guillaume Dumas, Dr Florian Sigaud** (CHU Grenoble Alpes) and **Prof. Jean-Christophe Richard** (HCL Lyon): ventilation scenarios, physiological envelopes, recruitability, Lyon cohort.

13. References

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