Postdoc Position
Analysing pulmonary transplant activity in France: Towards a prediction of chronic rejection

1 Project Presentation

1.1 Context

Lung transplantation is the ultimate treatment for end-stage respiratory failure. It is a heavy, costly treatment with pre-, peri-, and post-operative risks. In particular, 30% of lung transplant recipients develop chronic lung allograft dysfunction (CLAD) within 3 years, which, once diagnosed, results in a life expectancy of about 2 to 3 years. A recent report on the state of lung transplantation in France was conducted by the Académie de Médecine [1]. One of the points highlighted by this report is the mismatch in France between the needs and the capacities for lung transplantation, partly due to the low number of available grafts. One way to improve this situation could be to better target recipients based on the probability of graft rejection. The medical question is therefore: 'Is it possible to estimate the probability of lung graft rejection in a given patient, the potential organ recipient, in order to optimize graft allocation?'

1.2 Objectives

The aim of this project is to develop a tool to estimate the probability of the occurrence of CLAD. This requires mesoscopic and temporal modeling.

Preliminary analyses (univariate, multivariate statistics, and Bayesian approaches) have been conducted to identify causal links between variables. The goal is to build on these results to construct a prediction model for the onset of CLAD.

The first step will be to model the 'center effect,' that is, the biases related to the population pool managed by each transplant center (the typology of patients, including the pathologies that led to the transplant) and the specific care characteristics of the transplant centers (center expertise, care modalities).

In a second step, a model for estimating the probability of individual rejection based on this center effect and, among other factors, on the time series associated with the clinical follow-up of each patient will be proposed. In particular, it will be necessary to account for and correct the impact of practice evolution during the cohort formation.

1.3 COhort of Lung Tansplantation (COLT)

This cohort contains 1850 lung transplant patients across the national territory during the period 2010-2023, with follow-up for up to 10 years for most of them. It has resulted in a database aggregating pre-, peri-, and post-lung transplant information. The nature of the information is relatively varied and covers, for example, the patient's medical context, the practices of transplant centers, donor/recipient immunological matching, the evolution of respiratory function, etc. This represents approximately 450 variables of different types. In particular, the temporal evolution of respiratory function is studied. It is the largest European database on lung transplantation. We have access to and are authorized to use this database.

1.4 State of the art

The state of the art from the Académie de Médecine is exclusively descriptive. It does not propose any causal or predictive modeling of the observed phenomena. Furthermore, it only addresses the issue at the macroscopic level.

The state of the art is relatively poor in this field and has mainly focused on the immunological approach, assuming that graft rejection is primarily determined by the donor/recipient immunological confrontation [2].

1.5 Ethical issues

Ethical questions naturally arise on the legitimacy of having and using a tool that can contraindicate a potentially life-saving medical-surgical procedure (the transplant) for a patient otherwise doomed to short-term death (a few weeks) in favor of another patient whose medium- and long-term survival would be ensured. An ethical reflection will be conducted throughout the work, focusing on the medical explainability, which is necessary but may not be sufficient to convince doctors and patients, and on the patients' perception of such a model as a potential tool for medical decision support. For this, interviews with naïve patients, patients concerned with lung transplantation (waiting for a transplant, already transplanted), doctors, and project members will be conducted.

1.6 Work environment

Principal Investigators

- Mustapha Ouladsine is Full Professor at LIS, specializing in data science applied to diagnostics and prognostics in both industrial and medical contexts.
- Stéphane Delliaux is an Associate Professor and Hospital Practitioner. Trained as an anesthesiologist and intensivist, and a physician-physiologist in his daily practice, he specializes in the application of digital techniques, including artificial intelligence, for characterizing health states in general and physiological/pathological states in particular.

Team members

- Paul Chauchat is an Associate Professor in automatic control and signal processing at LIS, interested in hybrid estimation methods enhanced by machine learning.
- Raquel Urena is an Associate Professor in computer science and a specialist in AI for health at Sesstim, an expert in modeling medical time series data and creating predictive models based on machine learning techniques and their interpretability.
- Christophe Gonzales is a Full Professor at LIS, specializing in reasoning under uncertainty, particularly in the search for and exploitation of causal relationships. He was part of the preliminary analysis mentioned in 1.2.

Supervision team: Stéphane Delliaux, Raquel Urena, Paul Chauchat and Christophe Gonzales.

Collaborations : The recruited candidate will work at LIS-lab and C2VN, in Marseille. They will have access to the computing cluster of LIS. In addition to the supervising team, the postdoc will work in close collaboration with a junior hospital doctor, and will have the opportunity to supervise interns working on related topics.

2 Position details

2.1 General information

Starting date End of 2024

Duration 12 months

Salary Depending on Aix-Marseille Université scale

Hosting laboratory LIS (Laboratoire d'Informatique et des Systèmes), campus Saint-Jérôme, Marseille : https://www.lis-lab.fr

2.2 Requirements

We are looking for a person holding a PhD in mathematical modeling and/or machine learning/artificial intelligence, with a strong interest in applying these techniques in the healthcare field. Experience in the medical field would be appreciated but is not essential. Required skills:

- Strong programming skills in Python, with proficiency in libraries such as scikit-learn, PyTorch, Keras, and TensorFlow.
- Solid knowledge of machine learning and deep learning methods.
- A strong list of publications in international journals and conferences in the fields of mathematical modeling and/or artificial intelligence.
- Very good level of English (written and spoken)

2.3 How to apply

Apply by email to the supervising team members, with [post-doc CLAD] as subject. Attach a CV, motivation letter (2 pages max), and two references (letters of recommendation are appreciated).
Application limit date : 31/08/2024
Supervising team

- Stéphane Delliaux, stephane.delliaux@univ-amu.fr
- Raquel Urena, raquel.urena@univ-amu.fr
- Paul Chauchat, paul.chauchat@lis-lab.fr
- Christophe Gonzales, christophe.gonzales@lis-lab.fr

References

[1] Rapport de l'Académie Nationale de Médecine. Transplantation pulmonaire de l'adulte en france, état des lieux, 2023.

[2] Sabina Janciauskiene, Pierre-Joseph Royer, Jan Fuge, Sabine Wrenger, Joanna Chorostowska-Wynimko, Christine Falk, Tobias Welte, Martine Reynaud-Gaubert, Antoine Roux, Adrien Tissot, et al. Plasma acute phase proteins as predictors of chronic lung allograft dysfunction in lung transplant recipients. *Journal of Inflammation Research*, pages 1021–1028, 2020.