“PRE-ACT – PREDICTION OF RADIOTHERAPY SIDE EFFECTS USING EXPLAINABLE AI FOR PATIENT COMMUNICATION AND TREATMENT MODIFICATION”

Iordanis Koutsopoulos[1]

[1]Athens University of Economics and Business, Greece

Keywords: AI, Explainability, Prediction of radiotherapy side effects

Project Outline and Objectives

The medical community is actively seeking opportunities to apply Artificial Intelligence (AI) towards automating and optimizing notoriously difficult predictive tasks so as to provide tangible benefits to society. Examples include personalized healthcare, patient monitoring, drug development, and advanced prognosis tools, among others.

The Horizon Europe PRE-ACT project (https://preact-horizoneurope.eu/) aims to deliver a framework, grounded on solid and novel AI concepts, for prediction of radiotherapy side effects, and subsequently utilize it to inform and support the decision-making of stakeholders about optimal treatment. The AI framework will feature:

- explainability by design in the AI models;
- distributed training of AI models, using Federated Learning algorithms;
- transferrable and generalizable AI models to different side effects and other cancer types, through Transfer Learning methods.

The project will leverage data from *three multi-centre patient European cohorts* to train AI models for risk prediction of side effects. Data include patient medical records such as comorbidities, anatomy, demographics, as well as treatment data, radiotherapy dose distribution data, Computerized Tomography (CT) scans, auto-contouring of critical organs in CT scans, and genetic data. A communication package that will emerge through a systematic participatory co-design methodology with patients and physicians, will ensure that predictions from the AI model will be presented in a meaningful, explainable manner to patients and clinicians to inform their joint decision-making regarding the choice of radiation treatment option.

Different stakeholders (patients, clinicians, AI developers) will be involved from the beginning in the co-design process of intelligent user interfaces for presenting the AI results in an effective manner, with careful consideration of possible biases and attendance to ethical issues. A health economics analysis will be used to examine the cost-effectiveness of the approach to regulatory bodies, with the aim of enhancing clinical treatment guidelines for patient benefit.

In terms of measureable objectives, the main aims are:

- Primary outcome: change of at least 6% in incidence of arm lymphoedema.
- Prediction of radiotherapy toxicity with sensitivity > 85%;
- At least 80% of physicians and patients become aware of algorithm predictions after the completion of the co-design process are satisfied with the information obtained through the communication package.

There exist four threads pertaining to AI and computing: (i) Explainable AI techniques to make the risk prediction interpretable for the patient and the clinician; (ii) Fair AI techniques to identify and explain potential biases in clinical decision support systems; (iii) Training of AI models from distributed data through Federated Learning algorithms to ensure data privacy; (iv) Mobile/web applications, so as to provide the patients and clinicians with an interface for the side effect risk prediction. Collectively, these four threads enforce *Trustworthy* AI and pave the way to transparent and responsible AI systems that are adopted by end-users and may thus unleash the full potential of AI.

Project Partners and their Roles

The involved partners and their roles are:

- Athens University of Economics and Business-Research Center (GR): Coordination; Distributed/ Federated Learning, Transfer Learning, Explainable AI, Mobile/web app design and implementation.
- University of Leicester (UK). Technical coordination, harmonisation of genomics and clinical data, clinical trial site, end-user focus groups, access to patient database, clinical interpretation of AI predictions.
- UNICANCER (FR). Access to two patient databases, patient recruitment and follow-up, clinical trial planning and implementation.
- University of Maastricht (UM): Health economics analysis.
- Consiglio Nazionale delle Ricerche (IT): Co-design of communication package, usability and acceptance studies.
- MAASTRO Radiation Oncology Clinic (NL): Pre-processing of clinical, imaging, and genomic data, infrastructure design and implementation, distributed learning for image-based data mining, patient recruitment.
- Medical Data Works (NL): design, standardization, and implementation of federated repositories, federated external validation of prediction models.
- University of Applied Sciences of Western Switzerland (CH) explainability of AI models.
- CENTAI Institute (IT). Fairness and bias in clinical decision support systems, explainable AI.
- Therapanacea (FR): auto-contouring and dose estimation/prediction; toxicity prediction; contouring variation. Deployment and commercialization.

Project Use Cases and Expected Outcomes

The project's prime focus is on *arm lymphoedema*, since it is one of the most disabling side effects in the commonest cancer type, with comparatively high long-term survival. Other side effects are acute skin toxicity, late breast toxicity (e.g., breast atrophy), and cardiac toxicity.

The impact of explainability of the AI model will be assessed in a clinical trial that comprises two arms, namely two disjoint subsets of recruited patients. In the first arm, the personalised risk prediction will be communicated to physicians and patients, while in the second arm, it will not. In the patient followup period, the impact of explainability will be assessed through the rate of occurrence of arm lymphoedema, and other quality of life indicators. The ultimate goal is to demonstrate that risk communication in an explainable manner improves patient quality of life and that it can lower treatment costs.

Sustainability and future work

The main exploitable outcomes/assets of the project are:

1. Rapid uptake of methodology and software solutions by others in the scientific and clinical fields to apply it to other oncology patient data, extending beyond just radiotherapy research.
2. Commercial radiotherapy software providers e.g. Therapanacea and others, will incorporate AI-based risk prediction in their platforms.
3. A gradual change in radiotherapy clinical practice, in response to changing guidelines, to include explailable-AI-based risk prediction in treatment decisions.
4. A growing awareness among cancer patients and doctors that personalised risk prediction can empower them to jointly make better treatment decisions

Further developments will explore transferability of the predictive models of treatment response and/or prognostic models with other cancer types, particularly for urinary and rectal side effects in prostate cancer patients. Many more possibilities exist beyond the scope of PRE-ACT e.g. for assessing dysphagia in head and neck cancers.