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## PRE-ACT: Prediction of Radiotherapy side Effects using explainable AI for patient Communication and Treatment modification

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### ABSTRACT

PRE-ACT leverages Artificial Intelligence (AI) to predict radiotherapy side effects in breast cancer patients, integrating complex imaging and genomics data. This Horizon Europe project aims to enhance shared decision-making by providing explainable predictions and tailored interventions, advancing personalised radiotherapy and improving patient outcomes.

### 1. Background

PRE-ACT is a multi-centre European study that uses Artificial Intelligence (AI) to predict side effects from radiotherapy in breast cancer patients. Radiotherapy side effects include skin ulceration, breast atrophy, arm lymphedema, and heart damage [1]. Some factors that increase risk for side effects are known, but current approaches mainly use low-dimensional statistical approaches and do not use all available complex imaging and genomics data [2]. AI is already used in some aspects of radiotherapy delivery, but PRE-ACT will leverage its huge potential towards prediction of side effects and provide an easily understood explanation to support shared decision-making between the patient and physician regarding radiation treatment options (see Figs. 1–3).

### 2. Methods

PRE-ACT is funded by Horizon Europe from October 2022 to 2027. The study consortium includes partners with expertise in computing, AI, radiation oncology, medical physics, genetics, psychology and health economics that is necessary to tackle this problem. The project has integrated rich datasets from three breast cancer patient cohorts (REQUIRE, CANTO and HypoG-01, N = 8924).

### 3. Results

In the first phase, the combined data was used to train a machine learning model that can predict which patients will get arm lymphoedema more accurately than previous approaches. The prediction accuracy for arm lymphedema is higher than any previously published approach (ROC AUC = 0.82). This predictive model forms the basis of an AI-based app with built-in explainability for key side effects of breast

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Fig. 1. Severe cases of late toxicity after radiotherapy for breast cancer (left; breast atrophy, centre: fibrosis, right: arm lymphedema).

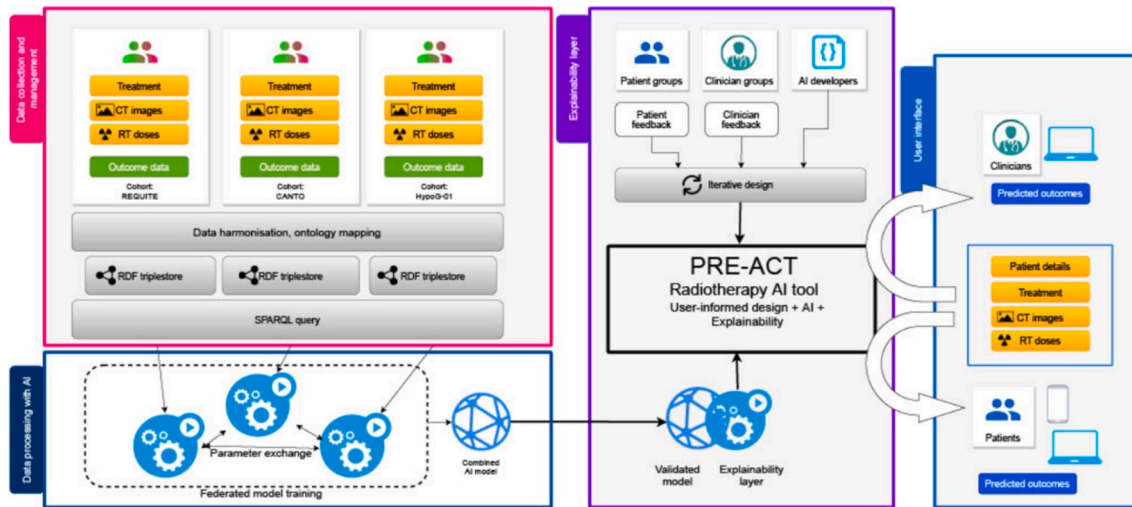


Fig. 2. Concept and structure of PRE-ACT.

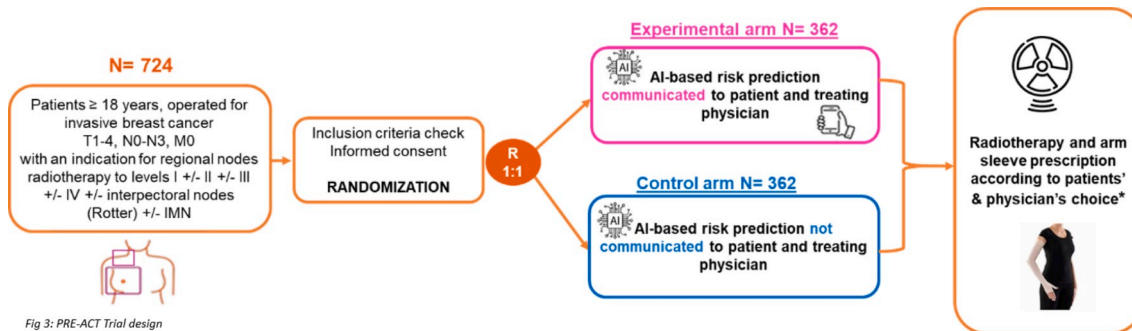


Fig 3: PRE-ACT Trial design

Fig. 3. PRE-ACT Trial design.

cancer radiotherapy after regional nodal irradiation (RNI).

The clinical impact of predicting side effects to support important treatment decisions in patients indicated for RNI will be investigated in an interventional randomized-controlled trial (PRE-ACT-01). A communication package has been co-designed with patients and stakeholders to ensure that predictions from the AI model are tailored to the user and communicated effectively. In the test arm of the PRE-ACT-01 trial, the personalised risk prediction will be communicated to physicians and patients in an assistive (rather than directive) manner and evaluated for its impact on the rate of arm lymphedema, use of supportive interventions, such as arm compression sleeves, and quality-of-life. In the standard arm, the personalised risk of side effects will not be communicated.

#### 4. Conclusions

PRE-ACT is designed to empower patients to make better decisions on their cancer treatment together with their physicians. It is doing this by providing an Explainable AI prediction of treatment side effects. The outcomes of this project will advance the personalised radiotherapy field and bring it closer to clinical implementation.

#### References

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- [2] G.E. Naoum, et al., Quantifying the impact of axillary surgery and nodal irradiation on breast cancer-related lymphedema and local tumor control: long-term results from a prospective screening trial, *J. Clin. Oncol.* 38 (2020) 3430–3438, <https://doi.org/10.1200/JCO.20.00459>.