Utilizing Machine Learning for the Identification of Pre-Treatment Prognostic Non-Imaging Biomarkers of Cancer Therapy-Related Cardiac Dysfunction in Female Patients with Breast Cancer

COPEMHAGEN

47TH ANNUAL International Conference of the **IEEE Engineering in Medicine** and Biology Society

Mon-051 Poster No.

Eleni I. Georga¹, Adam D. Kypriadis¹, Georgia S. Karanasiou¹, Anastasia Constantinidou², Andri Papakonstantinou³, Kalliopi Keramida⁴, Dorothea Tsekoura⁵, Efrosini Kampouroglou⁶, Daniela Maria Cardinale⁷, Davide Mauri⁸, Lampros Lakkas⁸, Katerina Naka⁸, Dimitar Stefanovski⁹, Cameron Brown¹⁰, Athos Antoniades¹⁰, Grigoris Kalliatakis¹¹, Vasileios Skaramagkas¹², Kostas Marias¹¹, Manolis Tsiknakis¹², and Dimitrios I. Fotiadis^{1,13}, Fellow Member, IEEE

¹Unit of Medical Technology Intelligent Information Systems, Department of Materials Science and Engineering, University of Ioannina, Ioannina, Greece

²Medical School University of Cyprus, Bank of Cyprus Oncology Centre, Cyprus ³Unit of Breast Cancer, Endocrine tumors and Sarcoma oncology at the Karolinska Comprehensive Cancer Center, Karolinska University Hospital, and Karolinska Institute, Stockholm, Sweden ⁴2nd Department of Cardiology, National and Kapodistrian University of Athens Medical School, Athens University Hospital Attikon, and the Cardiology Department, General Anti-Cancer Oncological Hospital, Agios Savvas, Athens, Greece ⁵2nd Department of Surgery, Aretaieio University Hospital, National and Kapodistrian University of Athens, Athens, Greece

> ⁶2nd Department of Cardiology, National and Kapodistrian University of Athens Medical School, Athens University Hospital Attikon, Athens, Greece ⁷Cardioncology Unit, Cardioncology and Second Opinion Division, European Institute of Oncology, IRCCS, Milan, Italy

⁸Michaelideion Cardiac Center, Department of Cardiology in Medical School, University of Ioannina, Ioannina, Greece ⁹Institute of Oncology Ljubljana, Ljubljana, Slovenija ¹⁰Stremble Ventures Ltd, Limassol, Cyprus

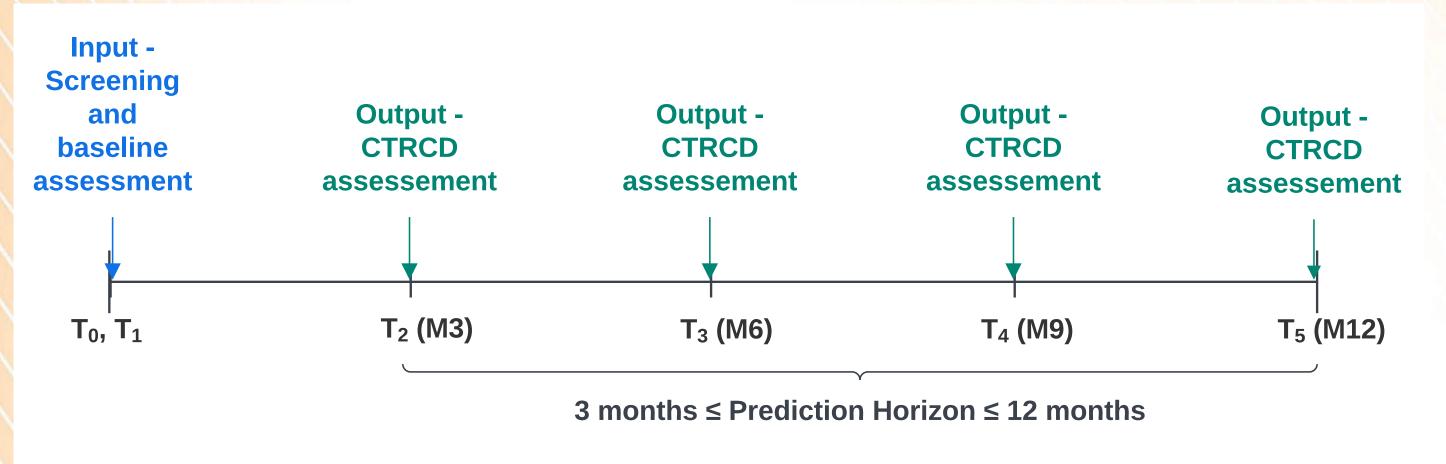
¹¹Institute of Computer Science, Foundation for Research and Technology - Hellas (FORTH), Heraklion, Greece ¹²Department of Electrical and Computer Engineering, Biomedical Informatics and eHealth Laboratory, Hellenic Mediterranean University, Heraklion, Greece ¹³Biomedical Research Institute, Foundation for Research and Technology-Hellas, Ioannina, Greece

REQUIREMENTS

 Pre-treatment risk assessment of cancer therapy-related cardiovascular toxicity (CTR-CVT) can inform cardiovascular prevention strategies and cancer treatment choices, mitigating CTR-CVT risk and improving adherence to effective cancer treatments and overall survival [1].

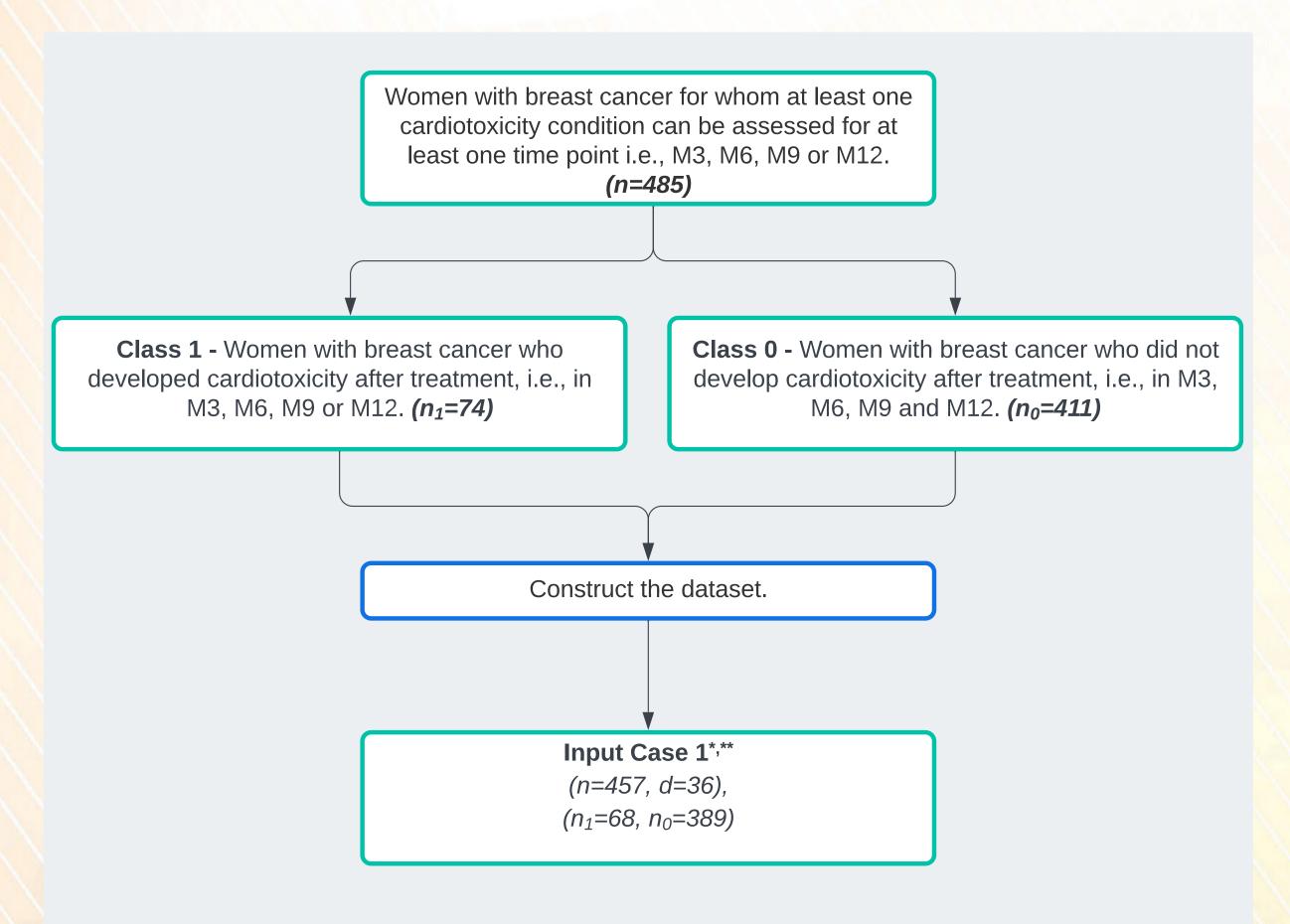
STUDY OBJECTIVE

 To identify pre-treatment prognostic biomarkers of asymptomatic cancer therapy-related cardiac dysfunction (CTRCD) in women aged ≥55 years diagnosed with breast cancer [2,3].



DATASET

- CARDIOCARE's Retrospective Data: The dataset utilized in this study was generated via the CARDIOCARE's retrospective study [4].
- Patients were treated with anthracyclines and/or anti-HER2 therapies in adjuvant, neoadjuvant, or metastatic settings.
- Clinical, cardiac imaging, biochemical markers, demographics, and medical history were systematically collected at screening, baseline, and at 3, 6, 9, and 12 months following treatment initiation, when available.



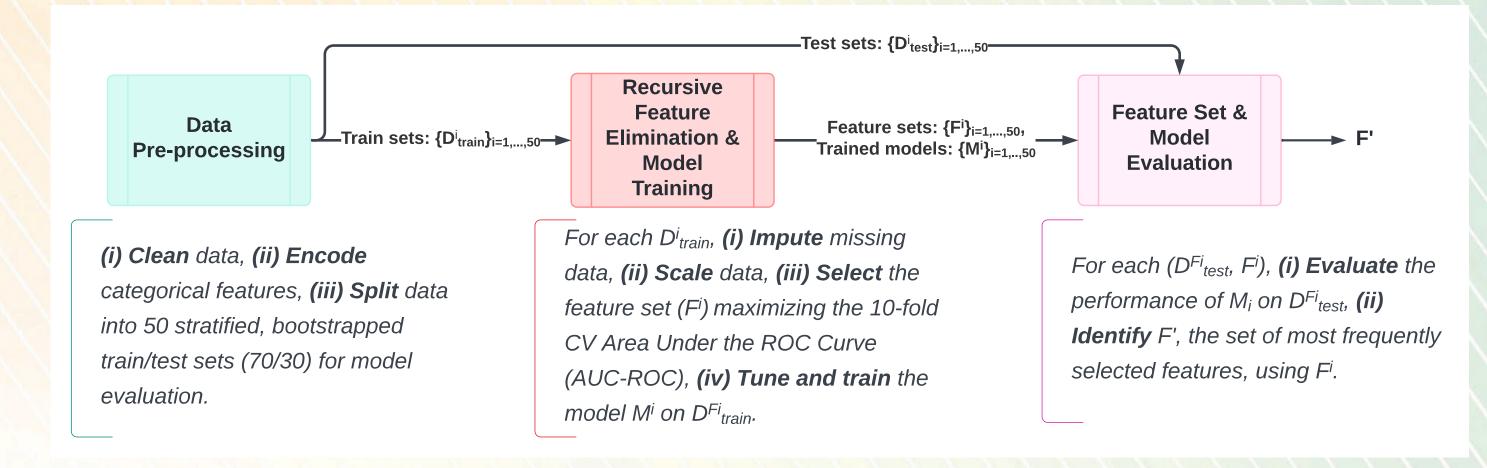
n: number of patients; d: number of features; *Features with >40% missing values are removed; **Samples with >50% missing values are removed.



Research supported by CARDIOCARE project funded under the framework of HORIZON 2020 (GA ID: 945175).

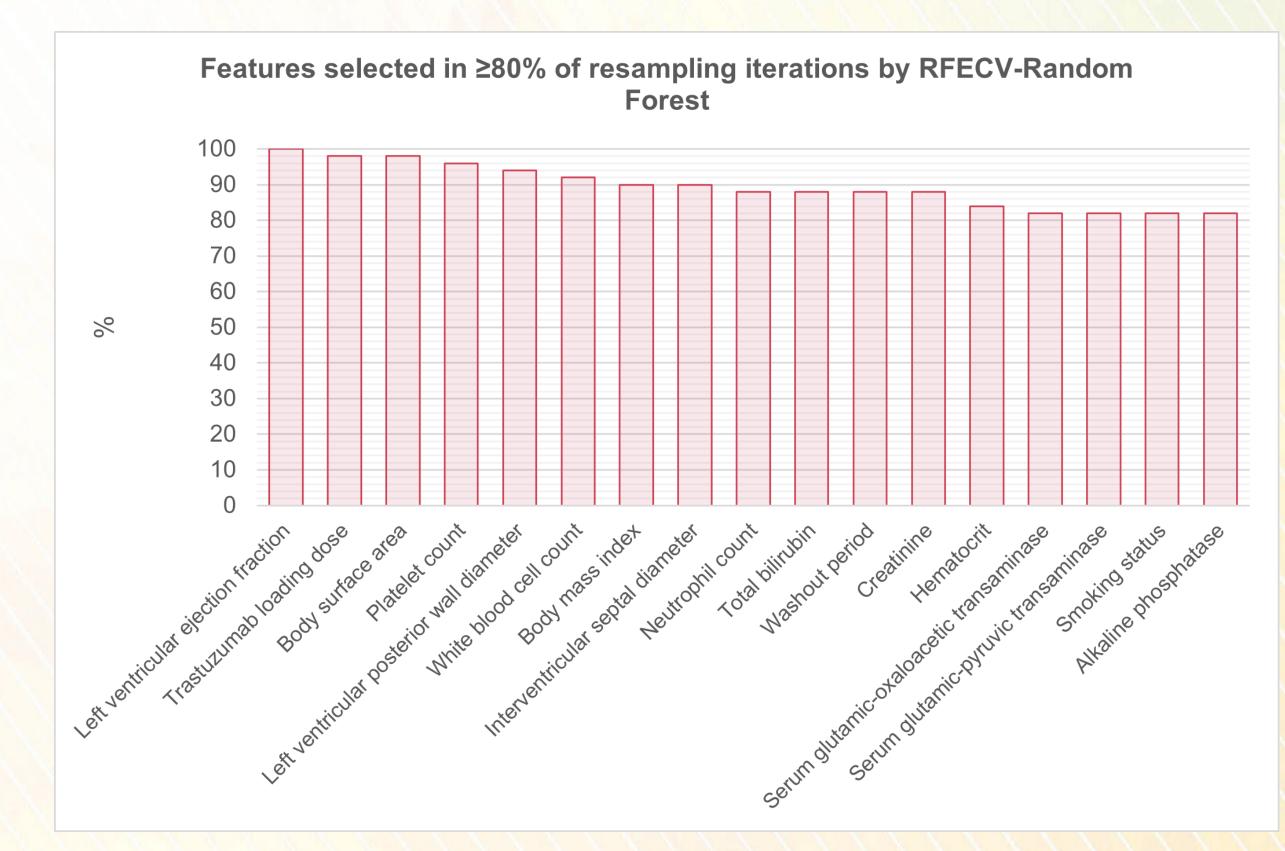
METHODS

 The identification of significant features acting as prognostic biomarkers of asymptomatic CTRCD is framed as a feature selection problem, addressed using a Recursive Feature Elimination with Cross-Validation (RFECV) strategy.



RESULTS

- RFECV-Random Forest model achieved the highest prognostic performance (ROC-AUC = 0.75 ± 0.07) among six classifiers.
- Features selected in >90% of iterations, including LVEF, trastuzumab loading dose, body surface area, BMI, platelet count, WBC count, and cardiac imaging parameters (LV posterior wall and interventricular septal diameters), emerged as strong prognostic biomarkers for asymptomatic CTRCD.



CONCLUSION

- An ML-based feature selection approach identified a reproducible set of pretreatment biomarkers predictive of asymptomatic CTRCD in women aged ≥55 years with breast cancer, achieving a mean ROC-AUC of 0.75 ± 0.07.
- The results support the utility of integrating clinical, biochemical, and cardiac imaging data into ML models for pre-treatment risk stratification in cardiooncology, aligning with recent ESC and IC-OS recommendations.

REFERENCES

[1]. A. R. Lyon et al., "2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS): Developed by the task force on cardio-oncology of the European Society of Cardiology (ESC)," Eur. Heart J., vol. 43, no. 41, pp. 4229-4361, Nov. 2022.

[2]. C. Brown et al., "A systematic review of miRNAs as biomarkers for chemotherapy-induced cardiotoxicity in breast cancer patients reveals potentially clinically informative panels as well as key challenges in miRNA research," Cardio-Oncol., vol. 8, no. 1, p. 16, Sep. 2022.

[3]. A. Alexandraki et al., "New Insights in the Era of Clinical Biomarkers as Potential Predictors of Systemic Therapy-Induced Cardiotoxicity in Women with Breast Cancer: A Systematic Review," Cancers, vol. 15, no. 13, 2023. [4]. G. Karanasiou et al., "A multimodal approach for the management of co-morbid cardiotoxicity in the elderly breast cancer patients," Eur. J. Cancer, vol. 175, p. S40, Nov. 2022.