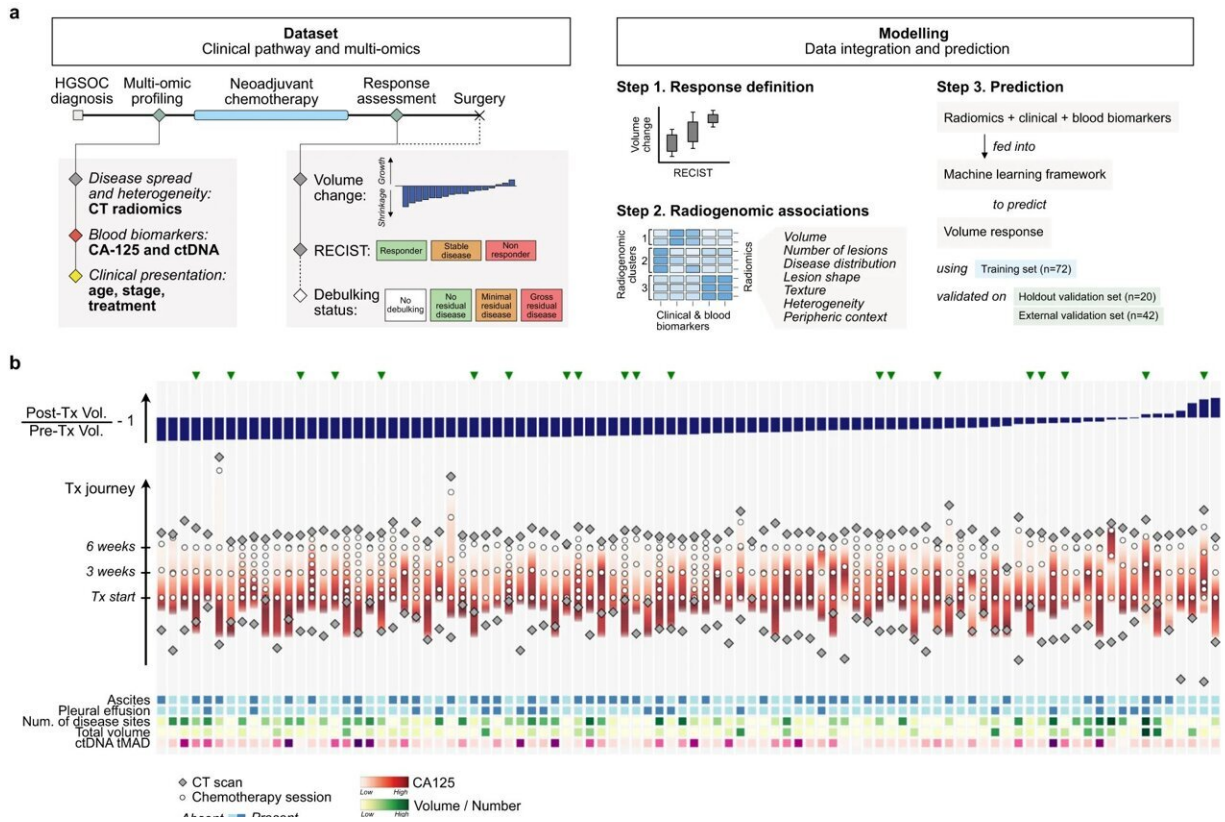
Ovarian cancer: Artificial intelligence predicts therapy responses

November 13 2023



Structure of the study and main characteristics of the training cohort. **a** Key time points and variables in the dataset (left) and steps of the modeling strategy (right). See also Supplementary Fig. S1 for additional information. **b** Treatment courses of all 92 patients in the NeOV cohort, ordered by decreasing volumetric tumor response following NACT. Patients analyzed in the hold-out validation set were randomly selected and are indicated with a green triangle. Treatment journeys progress vertically (bottom to top) and are aligned at the time of the first chemotherapy cycle. Additional biomarkers obtained at baseline are

depicted in the bottom heatmap. **c** Sites of primary and metastatic disease in HGSOC. **d** Distribution of tumor volumes by site for patients in the training cohort. **e** Distribution of tumor sites by patient. **f** Volume changes of the omental and pelvic/ovarian disease for all patients in the training cohort. *p* value obtained from the two-sided Mann-Whitney *U* test. **g** Total and site-specific volume change stratified by RECIST 1.1 response status for the training cohort. *p* value obtained from the point biserial correlation coefficient, two-tailed. **h** Total and site-specific volume change stratified by *BRCA* mutation status. These figures are restricted to the $n = 45$ patients in the training cohort for whom the *BRCA* mutation status was known. *p* value obtained from the two-sided Mann-Whitney *U* test. Boxes indicate the upper and lower quartiles, with a line at the median. Outliers are shown as circles and identified via the interquantile range rule. Source data are provided as a Source Data file. Credit: *Nature Communications* (2023). DOI: 10.1038/s41467-023-41820-7

A model based on artificial intelligence is able to predict the therapy outcome (measured by volumetric reduction of tumor lesions) in 80% of ovarian cancer patients. The AI-based model has an accuracy of 80%, significantly better than current clinical methods.

The tool, named IRON (Integrated Radiogenomics for Ovarian Neoadjuvant therapy), analyzes various patient clinical features, from circulating tumor DNA in the blood (liquid biopsy) to general characteristics (age, health status, etc.), tumor markers, and disease images obtained through CT scans. Based on this analysis, it provides a prediction of the therapy's likelihood of success.

This achievement stems from a recent study published in *Nature Communications*, conducted on 134 high-grade ovarian cancer patients. The study was coordinated by Professor Evis Sala, Chair of Diagnostic Imaging and Radiotherapy at the Faculty of Medicine and Surgery of the Catholic University and Director of the Advanced Radiology Center at

the Policlinico Universitario A. Gemelli IRCCS. The AI model was initially developed by the team of professor Sala at the University of Cambridge.

Ovarian cancer affects over five thousand women annually in Italy, adding to the thirty thousand patients who have already received a diagnosis. Due to its lack of specific early symptoms, diagnosis often occurs in advanced stages of the disease. High-grade serous ovarian carcinoma, constituting 70–80% of ovarian tumors, is particularly aggressive and frequently resistant to chemotherapy. Currently, therapy response prediction for this type of tumor is only 50% accurate.

Additionally, there are few clinically useful biomarkers for this type of cancer due to its high heterogeneity, varying significantly from patient to patient. This led to the development of an artificial intelligence-based tool capable of accurately predicting chemotherapy responders.

The study

"We compiled two independent datasets with a total of 134 patients (92 cases in the first dataset, 42 in the second independent test set)," Professor Sala and Dr. Mireia Crispin Ortuzar from Cambridge explained. For all patients, clinicians collected clinical data, including demographic information and treatment details, as well as blood biomarkers like CA-125 and circulating tumor DNA (ctDNA). Quantitative characteristics of the tumor derived from CT scan images of all primary and metastatic tumor sites were also obtained.

Omental and pelvic/ovarian locations (common for ovarian cancer spread) represented the majority of the disease burden initially. Omental deposits showed a significantly better response to neoadjuvant therapy compared to pelvic disease. Tumor mutations (e.g., TP53 MAF assessed on circulating DNA) and the marker CA-125 were correlated with the

overall disease burden before treatment and therapy response.

Furthermore, advanced analysis of CT scan images revealed six patient subgroups with distinct biological and clinical characteristics, indicative of therapy response. All these tumor features were used as input data for artificial intelligence algorithms that collectively form the tool. The developed model was then trained, and its effectiveness was validated on an independent patient sample.

"From a clinical perspective, the proposed framework addresses the unmet need to identify patients unlikely to respond to neoadjuvant therapy and may be directed to immediate surgical intervention," Professor Sala emphasized.

"The tool could be applied to stratify the risk of each individual patient in future clinical research conducted at Policlinico Gemelli in collaboration with Professor Giovanni Scambia's team, Chair of Gynecology and Obstetrics at the Faculty of Medicine and Surgery of the Catholic University and Scientific Director of the Policlinico Universitario Agostino Gemelli IRCCS Foundation," professor Sala concludes.

More information: Mireia Crispin-Ortuzar et al, Integrated radiogenomics models predict response to neoadjuvant chemotherapy in high grade serous ovarian cancer, *Nature Communications* (2023). DOI: 10.1038/s41467-023-41820-7

Provided by Universita Cattolica del Sacro Cuore