147P - Blind validation of an AI-based tool for predicting distant relapse from breast cancer HES stained slides

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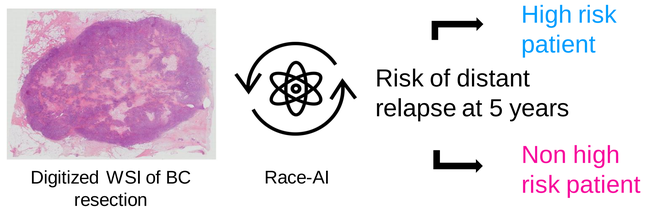
Background & objectives

- Breast cancer (BC) is a heterogeneous disease encompassing several subtypes associated to a wide range of prognosis.
- Risk determination is crucial for treatment decision. We developed RlapseRisk™ BC, an AI-based tool that assesses the risk of distant relapse at 5 years of ER+/HER2- early invasive (ei)BC patients from HES (hematoxylin-eosin-safran)-stained whole slide images (WSI) and clinical data. Preliminary results of this tool were presented last year (Abstract 2392/1124O - ESMO2021).
- RlapseRisk™ BC was conceived as a companion diagnostic tool, applicable everywhere, able to help treatment decisions in clinical practice.

In the current study, we present a one-shot blind **external validation** of RlapseRisk™ BC.

Model

- RlapseRisk™ BC model was developed on the **GrandTMA** cohort with 1800 HES WSIs.
- It combines Self-Supervised Learning (Moco v2) to extract features from images, and a multiple instance learning model (Deepmil) to predict a risk of distant relapse.



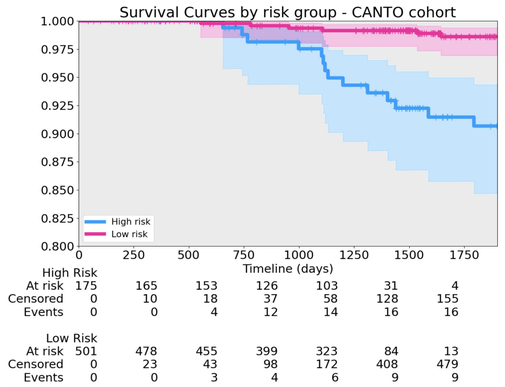
Validation study

- RlapseRisk™ BC validation dataset included 676 HES-stained WSIs from ER+/HER2- eiBC patients diagnosed at Gustave Roussy between 2012 and 2017, included in the CANTO cohort (NCT01993498, comprising 25 patients who relapsed at 5 years).
- We compared RlapseRisk™ BC performance to the two most relevant clinical scores: **Predict Breast and CTS0**.
- Model performances were evaluated through their cumulative sensitivity and dynamic specificity at 5 years to assess the accuracy of the scores to identify distant relapses.
- Each score has been dichotomized into low risk/high risk with respect to a threshold that has been set beforehand (5% for predict Breast, 1.40 for CTS0).

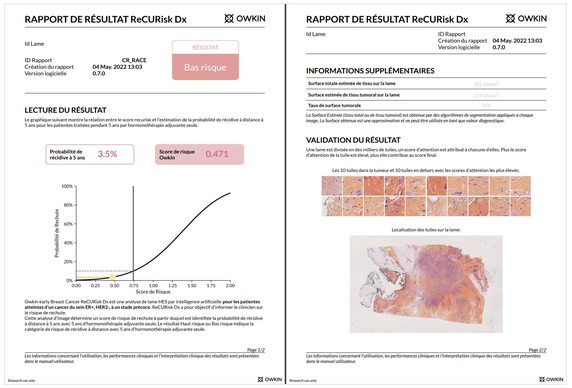
Results

Scores	Cumulative Sensitivity @5Y	Dynamic Specificity @5Y
RlapseRisk™ BC	**0.64 [0.57-0.72]**	**0.78 [0.76-0.80]**
Predict Breast	0.61 [0.52-0.70]	0.77 [0.75-0.79]
CTS0	0.43 [0.34-0.52]	0.80 [0.78-0.82]

- Among the non high risk population treated **without adjuvant chemotherapy**, **the distant relapse rate was 0.3%** (1 out of 324).
- The obtained results showed the ability of RlapseRisk™ BC to generalize on independent data and thus endorses the robustness of the method.



Patient report and interpretability



- High relapse risk tiles displayed **high tumor cell content, strong nuclear atypia and massive architecture**.
- Most contributive tiles of low risk corresponded to **fibrotic stroma with a few low-grade tumor cells**.

Conclusion

We performed the **first fully blind validation of RlapseRisk™ BC**, an AI-based tool to assess the risk of distant relapse.

Additional analyses validate the clinical value of RlapseRisk™ BC and suggest that it could be used for therapeutic de-escalation purposes. **RlapseRisk™ BC has been CE marked in May 2022.**

Future work

- Extension of validation to mutli-site and multi-scanner eiBC WSIs from the CANTO cohort (under completion).
- Development of algorithms adapted to different slide conditions (such as HE staining or biopsy specimens) increasing the generalization capacities of our model.
- In-depth tiles analysis centered on the spatiality notion.

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