Reproducibility of Pathologist-read and AI-based ER scoring in ER-low breast cancer

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- Estrogen receptor-low (ER-low) HER2-negative breast cancer (BC) has been treated as ER positive breast cancer in accordance with the current international guidelines (ASCO Hormone Receptor–Positive Breast Cancer guideline 2018 and ESMO Early breast cancer: Clinical Practice Guidelines for diagnosis, treatment and follow-up 2019)
- Recent studies showed that ER low BC has similar outcomes as triple negative breast cancer (TNBC) (PMID: 38745990, 34419555) . Moreover, 82% of the St. Gallen Consensus Panel would treat ER low BC patients as TNBC patients.

- However, the analytical validity of the altered ER cut-off has not been confirmed yet in large round-robin setting.
- **AIM: To investigate the reproducibility of AI based ER scoring among independent operators/AI platforms and compare that of pathologist-read ER scoring among pathologists**

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Specimen collection and participants

- Specimen collection: HE and IHC-ER images of 60 whole slide resection specimens from Karolinska cohort
  - ER negative, ER low and ER positive cases
  - Send out invitation to pathologists/breast cancer research experts representing several countries/institutions for round robin pathologist reading and AI ER scoring
  - Divide participants into three groups according to slide #3.
  - Pathologist reads: All participants shall follow the ASCO-CAP guidelines for ER scoring
  - AI reads:
    - Participants can use any AI tool (CE-IVD, FDA approved, LDTs, open-source tools) to score ER-IHC images
    - Participants should use an already existing AI tool/pipeline for the ER-IHC scoring: Images of the current dataset cannot be used as training set for this study aim.
    - Basic details of AI tool used in the study will be collected for transparency reasons however publishing the AI model is not mandatory

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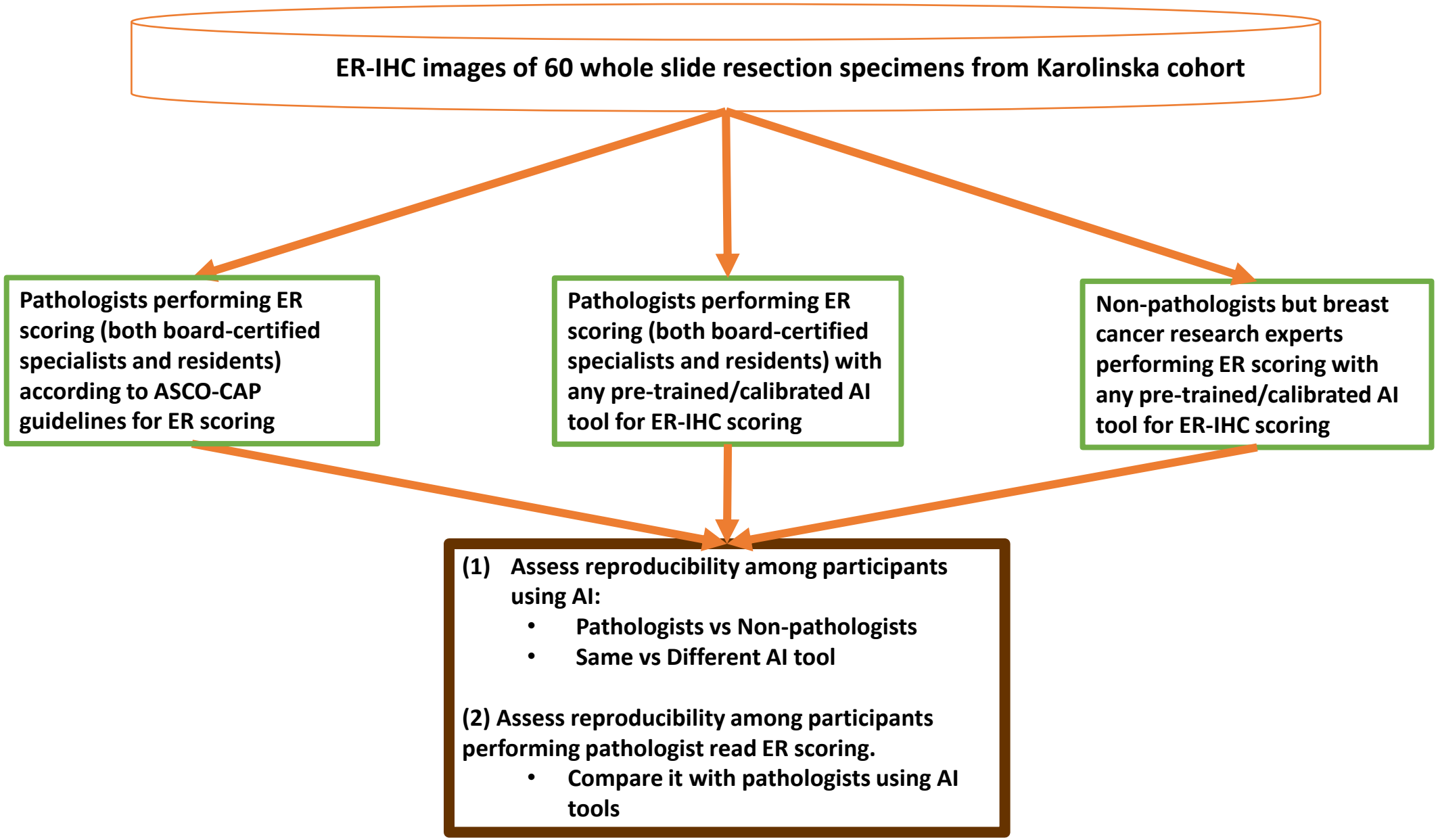

Analysis plan

- Reproducibility of operators using the same AI tool/algorithm.
- Reproducibility of operators using different AI tools.
- Reproducibility of pathologists performing ER scoring compared to pathologists using AI tool
- Reproducibility of pathologists using AI tool compared to non-pathologists but breast cancer research experts using AI tools
- SAP:
  - The reproducibility will be estimated with intra-class correlation coefficient (ICC). The pre-specified success criteria used in this study should be achieving an ICC with the lower bound of the 95%CI > 0.80
  - The exact statistical power of the study will be calculated.
  - Data will be visualized using ONEST plots, boxplots, spaghetti plots and heatmaps

How to join the study?

If you would like to join study, please register on this link

If you have any questions, please contact:

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Co-authorship is granted for study participants who submitted pathologist-read or AI-based ER scores for the entire study set