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Generalization of a deep learning model for HER2 status prediction on H&E-stained whole slide images from 3 neoadjuvant clinical studies

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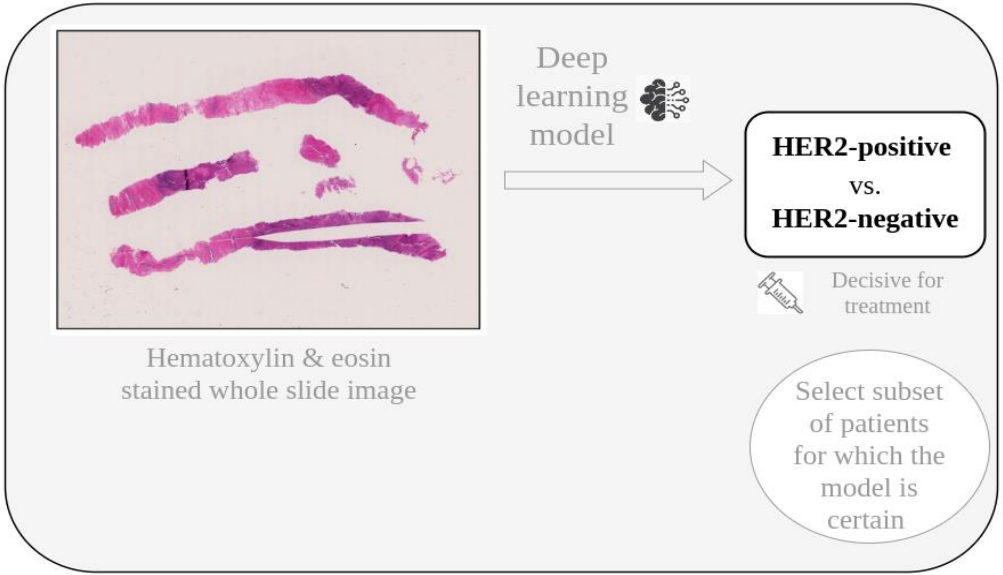
Disclosure

Miriam Hägele

Part-time employment at Aignostics GmbH.

Background and Aim

- Predict HER2 status in breast cancer from routine diagnostic histological slides via deep learning algorithms
- Develop model to generalize across clinical studies



Materials and Methods

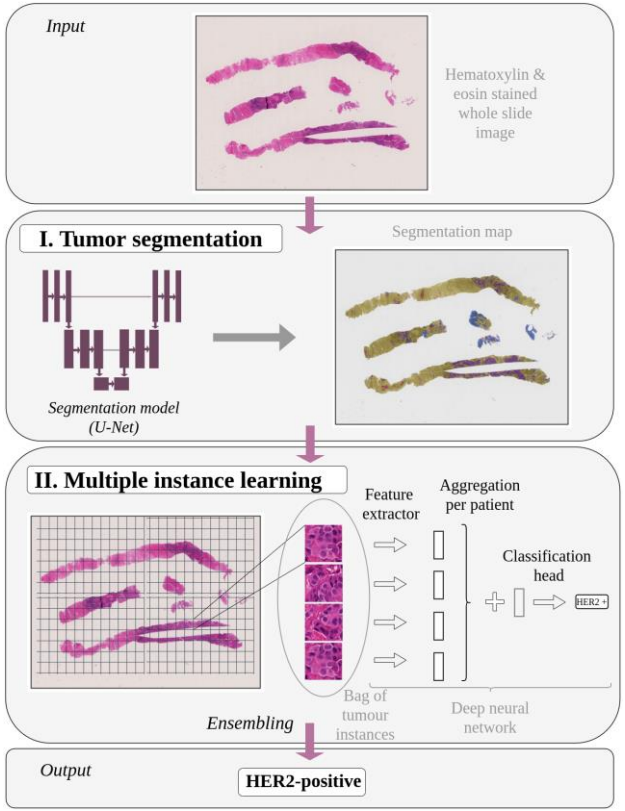
Data

- Three neoadjuvant clinical studies[1,2,3]

Two-step machine learning approach

1. Extract tumor regions: *Segmentation model*
2. Weakly supervised approach: *Multiple instance learning model*

- Selective prediction evaluation



GeparSixto: Von Minckwitz et al. Lancet Oncol (2014).
GeparSepto: Untch et al. Lancet Oncol (2016).
GeparOcto: Schneeweiss et al. Eur J Cancer (2019).

Results

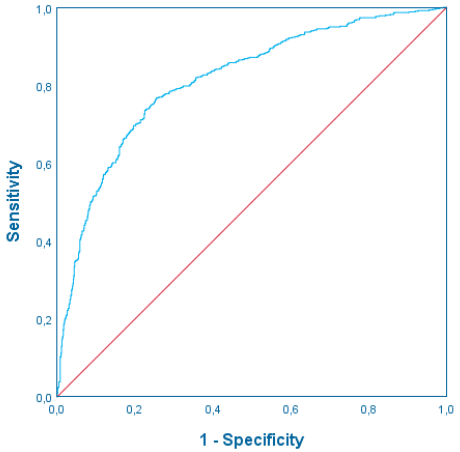
- Validated on 1567 independent patients
- Tested generalization to independent clinical study GeparOcto[3]

	Training	Validation
GeparSixto[1]	205	156
GeparSepto[2]	639	496
GeparOcto[3]	-	915

	ROC AUC (CI 95%)	**Balanced accuracy***
Test cohorts (GeparSixto, GeparSepto, GeparOcto)	81.2 (79.0-83.4)	73.1%
Independent study cohort (GeparOcto)	79.9 (76.9-82.9)	70.4%

Balanced accuracy = (Sensitivity + Specificity) / 2

ROC curve *(overall)*



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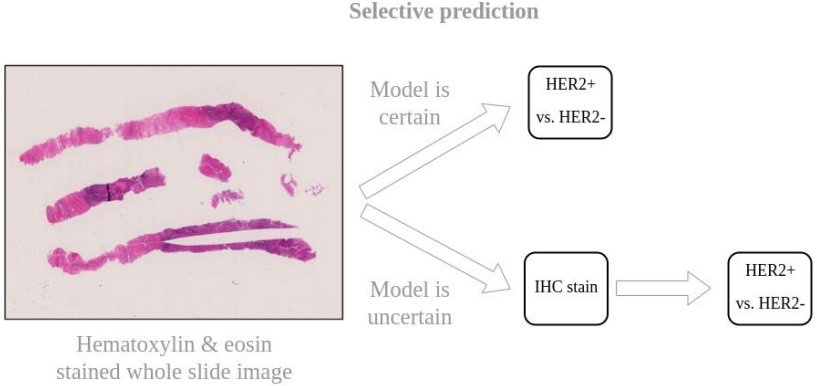
Selective Prediction

- *Concept:* Automatically select cases for which the model is very certain, i.e. define a subset with high predictive performance
- Trade-off between predictive performance and coverage

	Total	Selection with guaranteed risk[1]	Ensemble tail
Coverage	100%	32%	13%
Balanced accuracy	0.73	0.81	0.85



[1] Geifman et al. (2017).

Conclusion

- Our deep learning model predicts HER2 status with state-of-the-art performance
- We validate the performance of our deep learning model on an independent clinical study
- Substantial performance increases can be achieved for subsets of patients based on the model's confidence via selective prediction

Acknowledgments

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