Breast Cancer Screening

Updates in research and liquid biopsy

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Key topics

- Status of breast screening: gaps and opportunities
- Status of lab tests for screening
- Clinical implementation considerations

Breast screening

Gaps and opportunities for new technologies

- Detect breast cancer before spreading to lymph nodes (99% 5 –year survival)
  - Many women not diagnosed at earliest invasive stage[1]
    - < 50% of women detected at stage 1
    - 25% of women under 35 and 36% of women 36-44 detected at stage 1

- Address underserved populations
  - Women with increased tissue density
  - Women under age 50 (20% of breast cancers)
  - Women not screening

[1]Freedman et al, *Cancer*, 124:2184-91, 2018

Mammography sensitivity decreases with increasing tissue density

Tissue density higher in young women

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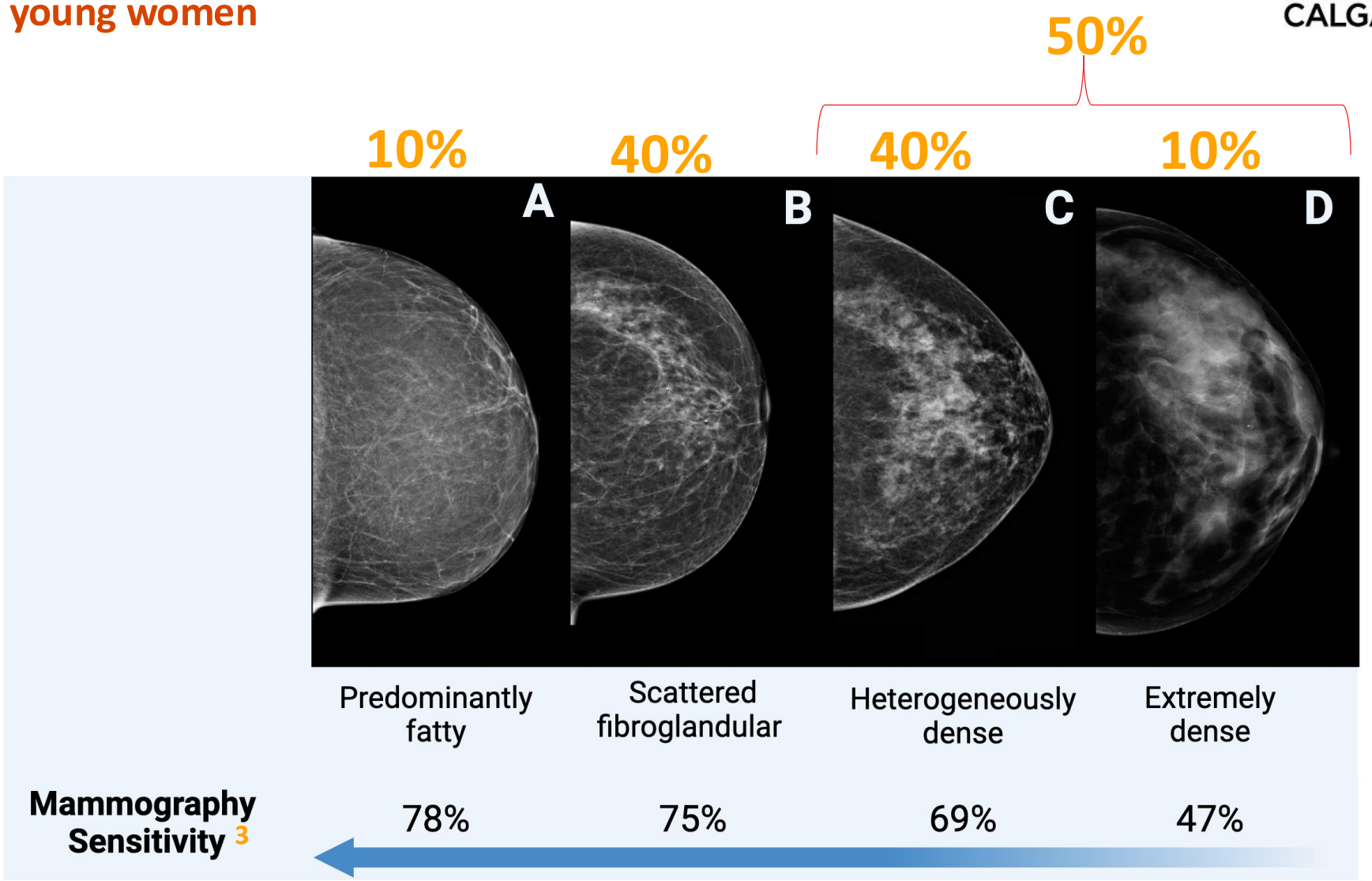
Prevalence[1,2]

64% of women 40-49 have C or D density[2]

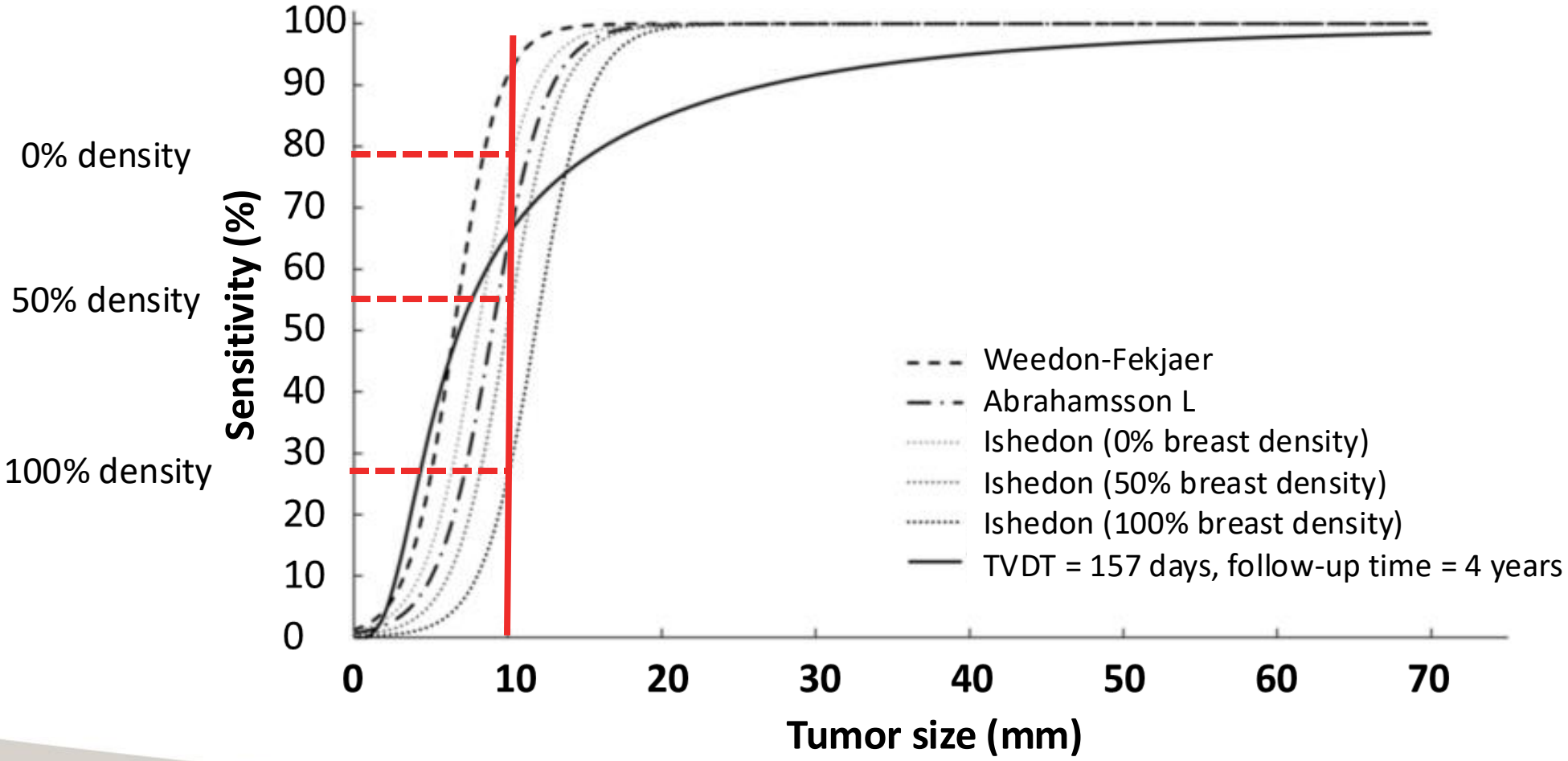


[1]CDC; [2]Sprague, 2019; [3]Lynge, 2019

*Breast density prevalence affected by ethnicity (Kerlikowske 2023)

Mammography sensitivity decreases with tumor size

And decreases with increasing breast density (computational modeling)



Wang et al, Breast 2021 55:69-74.

Mammography sensitivity low compared to MRI

Women at elevated risk

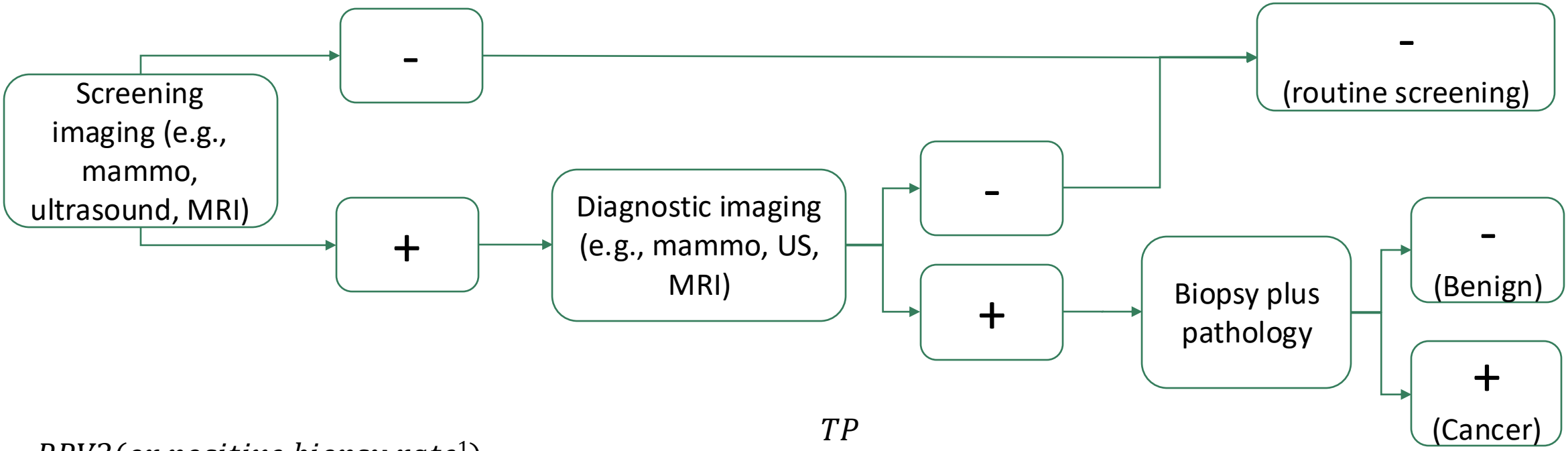
	The Netherlands	Canada	United Kingdom	Germany	United States	Italy
No. of centers	6	1	22	1	13	9
No. of women	1,909	236	649	529	390	105
Age range	25–70	25–65	35–49	≥30	≥25	≥25
No. of cancers	50	22	35	43	4	8
Sensitivity (%)						
MRI	80	77	77	91	100	100
Mammogram	33	36	40	33	25	16
Ultrasound	n/a	33	n/a	40	n/a	16
Specificity (%)						
MRI	90	95	81	97	95	99
Mammogram	95	>99	93	97	98	0
Ultrasound	n/a	96	n/a	91	n/a	0

Lo 2017 (N=1249, screens = 1957) demonstrated mammogram sensitivity/specificity of 31%/89%.

Saslow 2007; Lo 2017; Berg 2012; For review see: Hollingsworth 2019

Imaging-based breast cancer detection

Positive Predictive Value (PPV) for imaging[1]



$$PPV3(or\ positive\ biopsy\ rate^{1}) = \frac{TP}{(TP\ +\ FP\ for\ those\ who\ received\ a\ biopsy)}$$

TP = True Positive (pathology confirmed)

FP = False Positive (no confirmed cancer)

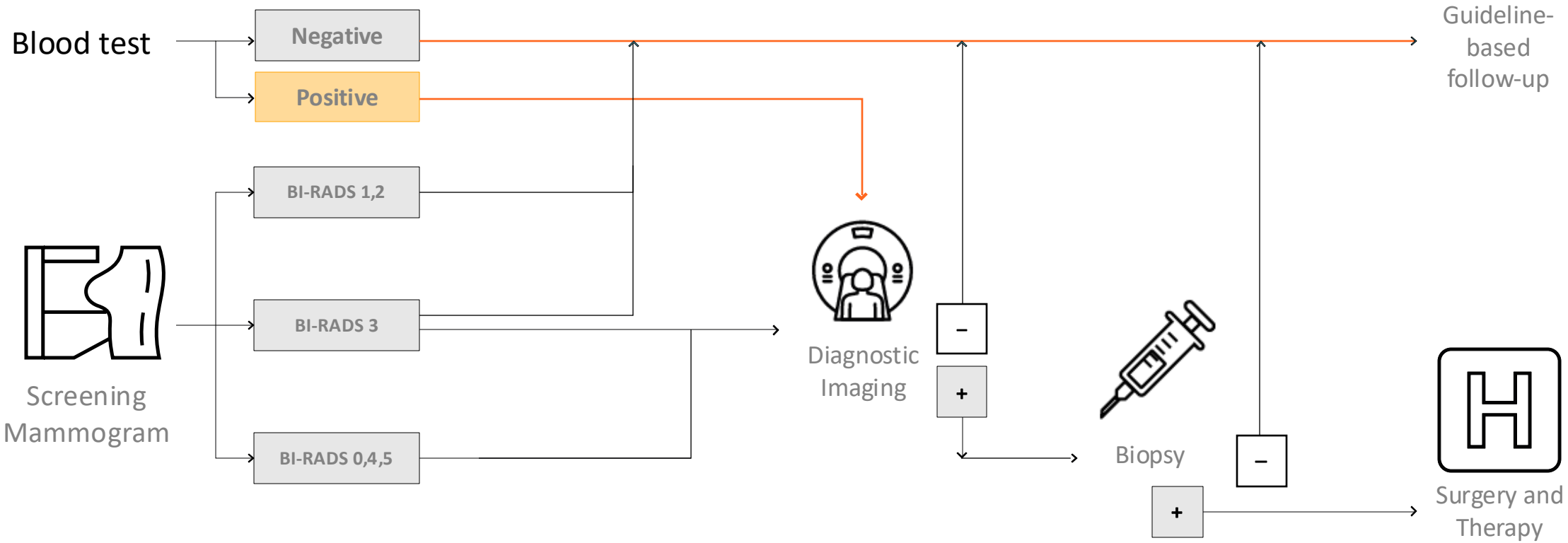
PPV3 = 12-41% depending on age and density[2]

[1]American College of Radiology BI-RADS Atlas
https://www.acr.org/-/media/ACR/Files/RADS/BI-RADS/FUOM-Basic-Audit.pdf

[2]Conant et al., JAMA Oncology, 2019

Blood tests for screening

Blood-based testing would complement imaging



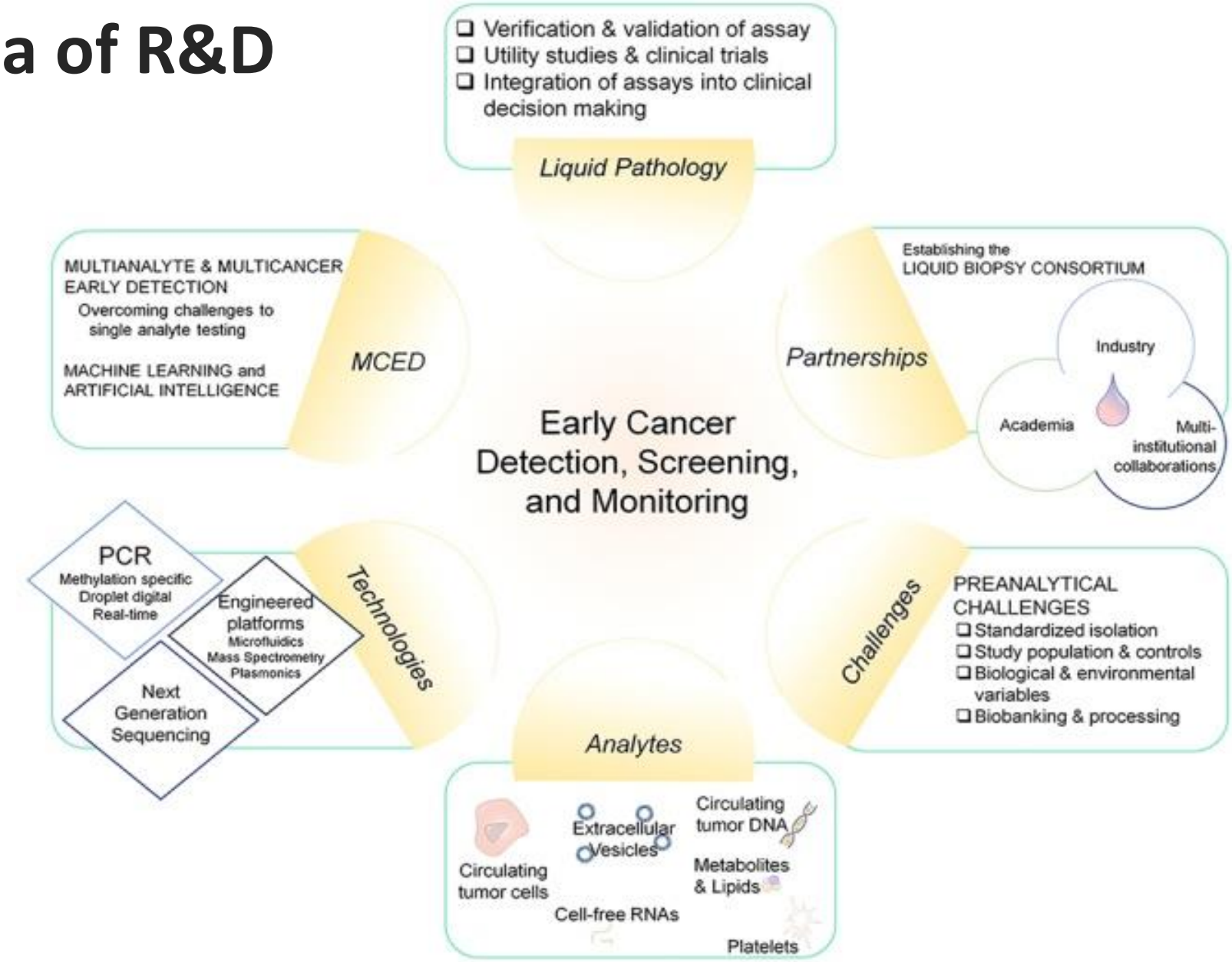
*Definitive breast cancer diagnosis provided by pathology analysis of biopsy specimen

Blood-based screening

- Focus: blood tests aimed at use in breast screening
- Many technologies in various stages of development and validation[1,2]
- Stages:
  - Biomarker identification and validation
  - Clinical test development
  - Clinical test validation
  - Utility and economic validation

[1]Keup et al., Cancers, 2023; [2]Rubinstein et al., CA Cancer J Clin, 2024

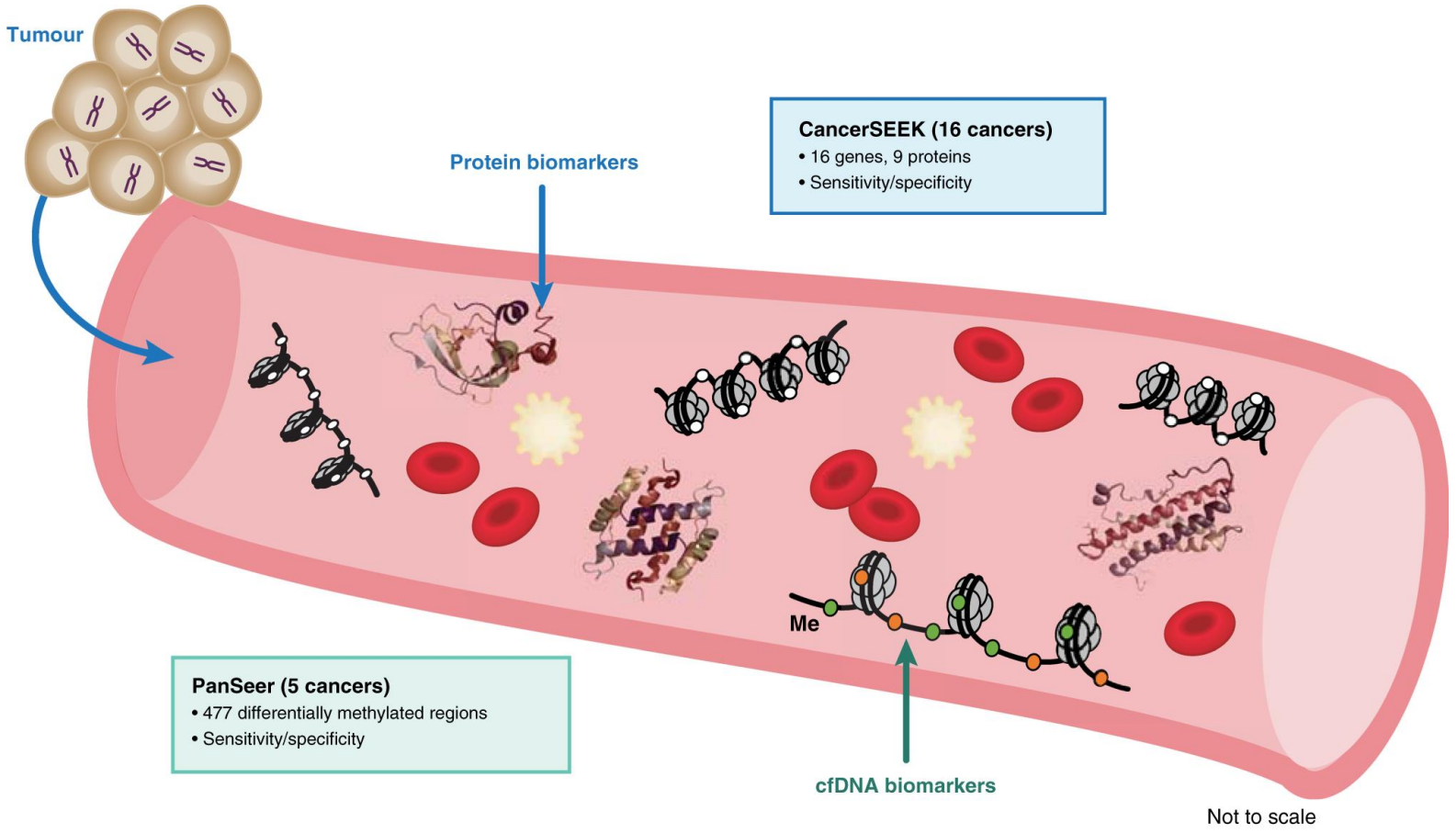
Active area of R&D



Batool et al, Cell Rep Med. 2023 Oct 17; 4(10): 101198.

Multi-Cancer Early Detection Tests

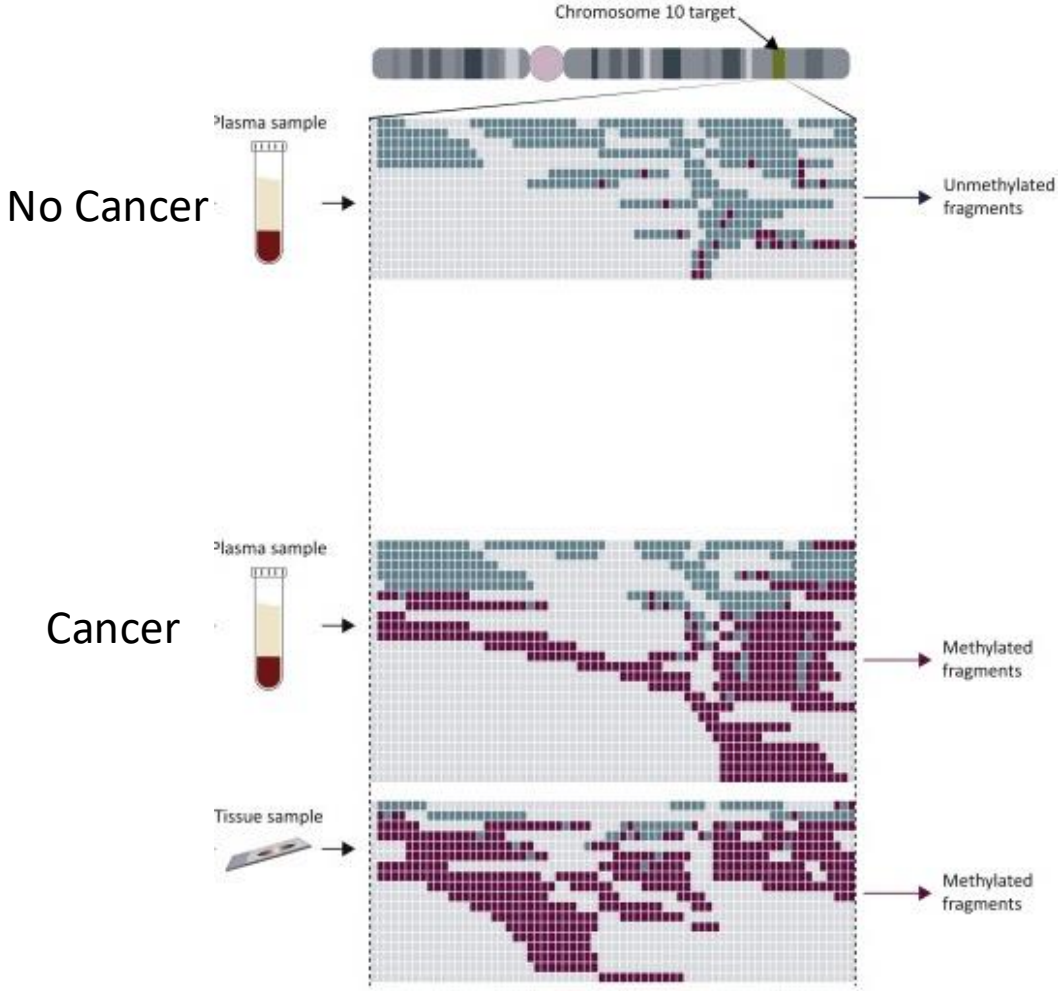
Look for pieces of cancer (e.g., ctDNA) and the tissue of origin (TOO)

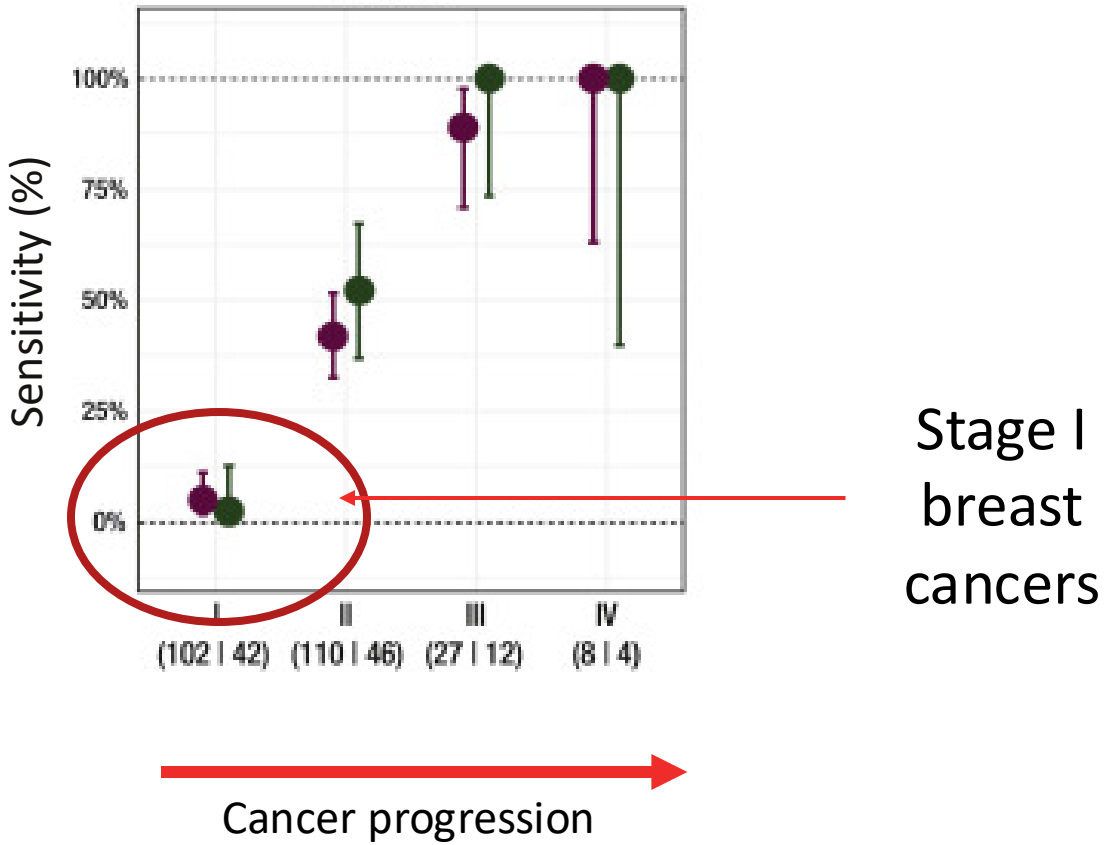


Liu, M., 2021, British Journal of Cancer (Br J Cancer) ISSN 1532-1827 (online)

MCED ctDNA-based test: breast screening

Sensitivity affected by breast cancer stage





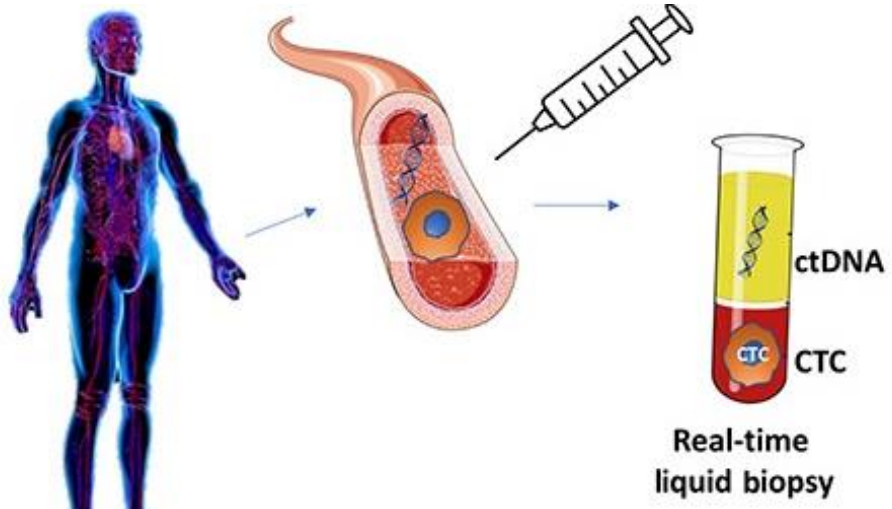
Stage I breast cancers

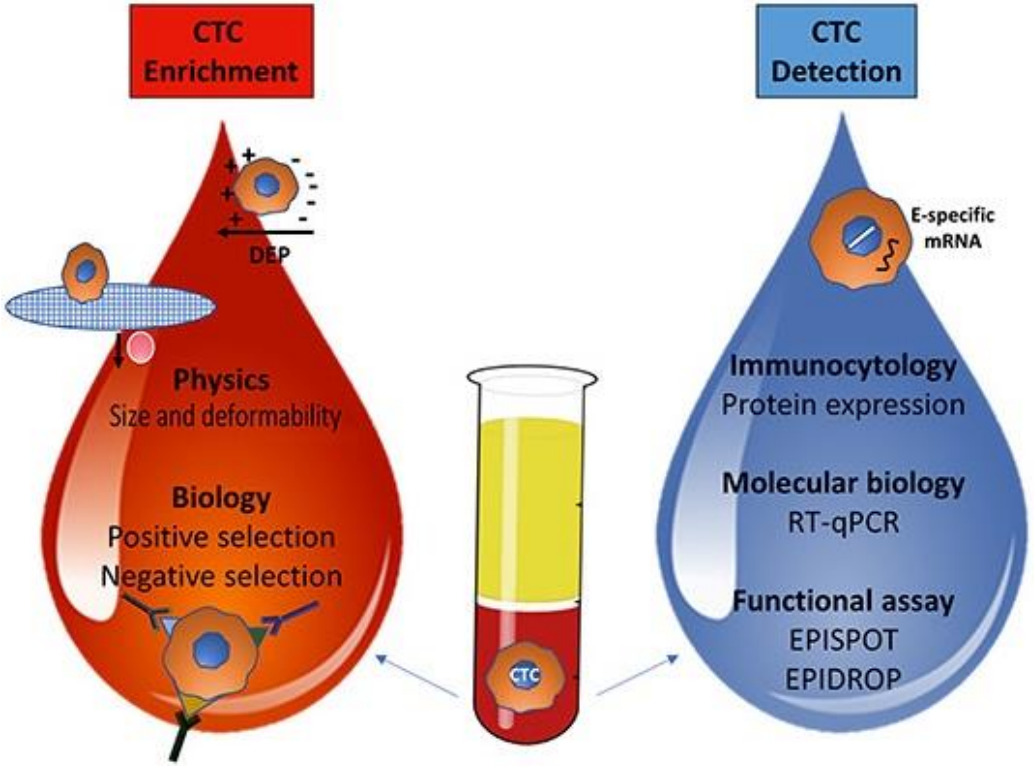
Liu et al., Ann Oncol 2020; The Circulating Cell-free Genome Atlas Study - ClinicalTrials.gov; Klein et al., 2021

Circulating Tumor Cells

Over two decades of research[1]

Screening application limited by low levels in early breast cancer





[1]Reduzzi et al, Crit. Rev. Oncol. Hem., 2024; Heidrich et al., Int. J. Cancer, 2021

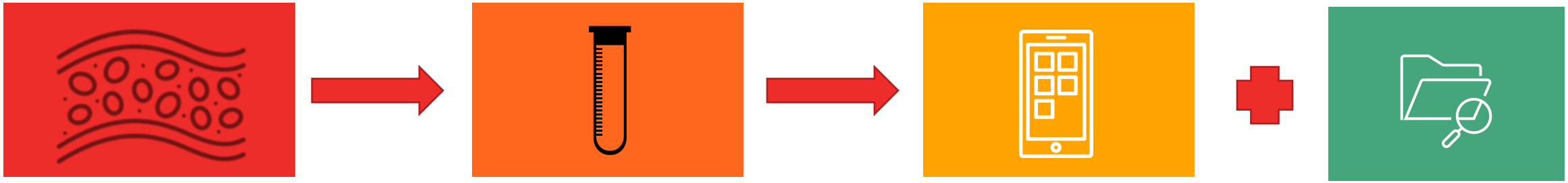
Blood tests for breast screening

Key factors

- Robust, reproducible, scalable test platform
- Simple, stable sample collection and transport
- Clinical performance in target population

New blood test platform– proprietary IP

We developed a new blood test platform based on RNA from whole blood



Specific RNA biomarkers from lysed whole blood

- 15 transcripts (proprietary)
- Involved in several key cancer mechanisms (IP)

Target Quantification System (TQS) –

- PCR instrument-based
- Proprietary molecular assay
- Custom reagents and use specifications

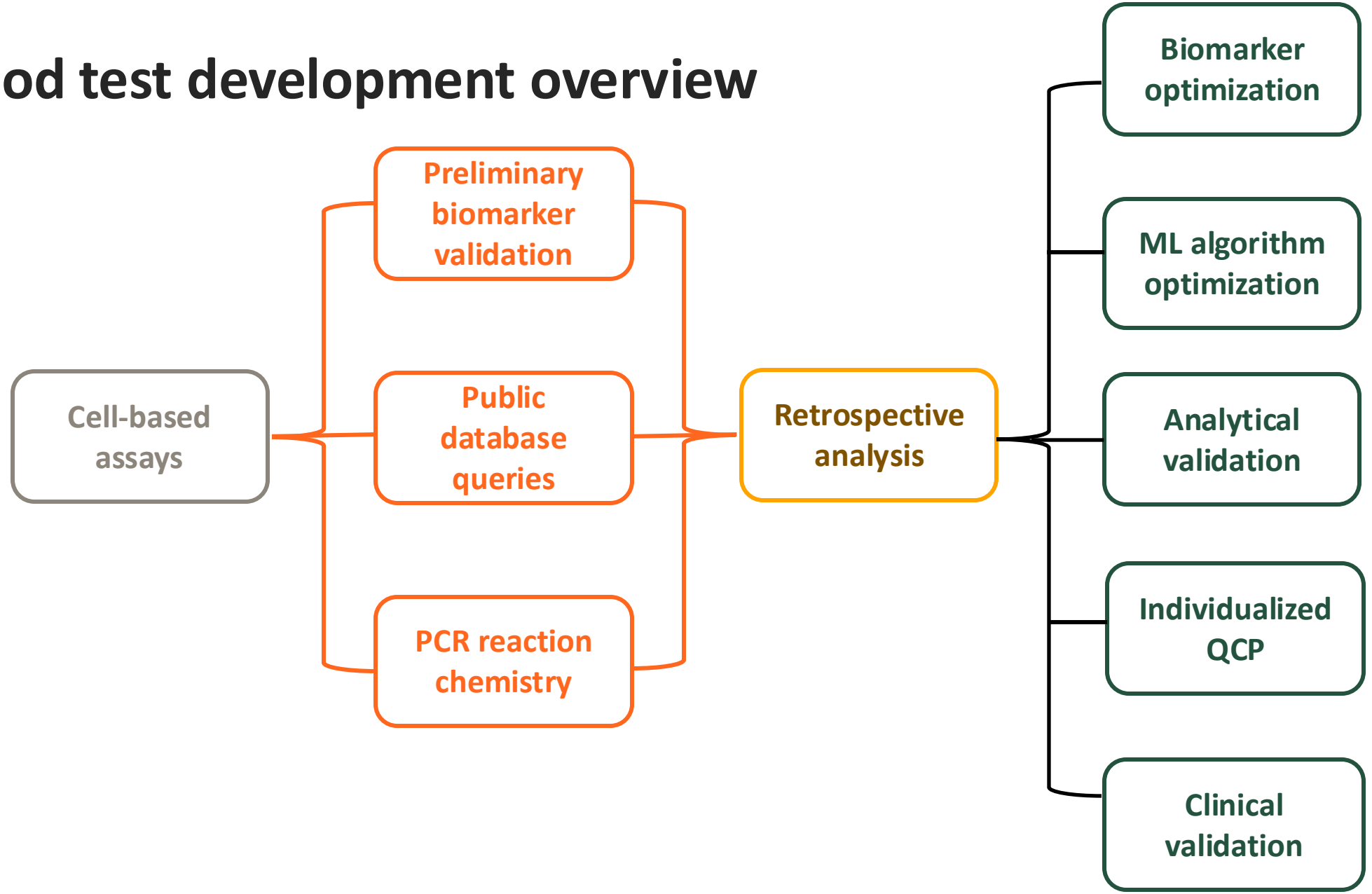
Expression Signal Assessment Software (ESAS) –

- Processes raw data from samples and controls
- Proprietary AI/ML algorithms

Secure anonymized data sets-

- Clinical studies

Blood test development overview



ISO 13485:2016

- CE-IVD
- CLIA/COLA
- CPSA

Clinical validation study

Investigation of a Novel Blood Test to Identify Breast Cancer (IDBC)

Recruitment group: Women 25-80

Exclusion Criteria: cancer diagnosis, male

Methodology: Blood collected near the time of mammogram or clinical breast exam. Medical records for imaging, surgical, and pathology data.

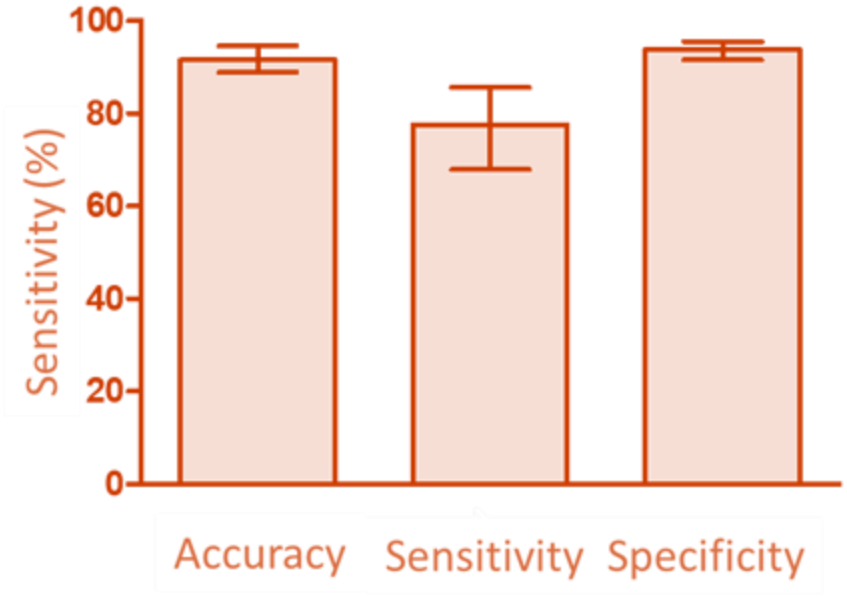
Primary Endpoint: Clinical sensitivity and specificity
Determined in blinded analysis; results for Syantra test compared to pathology or absence of breast cancer diagnosis

Supported by funding from Alberta Innovates ASBIRI Award
with Alberta Cancer Foundation and DynaLIFE Medical Labs

Blinded clinical study blood test results

84% of samples with cancer at stage 1 or 2

Specificity 94%
Sensitivity 79%



- **High specificity**
- **Detection of breast cancer, including**
  - **before lymph node involvement**
- **Detection in women 25-80, including**
  - **in women with dense tissue**
  - **in young women**
- **Robust, scalable process**

Newly funded DoD study: new sites addressing diverse populations

Fuh, EBCC, 2022; Bundred et al., SABCS, 2021; Fuh et al., submitted

Summary

New multi-biomarker, high complexity blood tests have potential to complement imaging and address gaps in screening and early detection

- Women with dense tissue
- Younger women
- Women not currently screening

Summary-Cont

- ***Critical factors***
  - ***Sensitivity*** for detection of invasive breast cancers before lymph node involvement
  - ***Specificity*** high enough to enable economically viable implementation
  - Robust, reproducible results
  - Validation in target populations
- ***Future***
  - Expansion of validated populations
  - Expansion of clinical and economic utility studies

Thank you!

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Reach out for more information

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