Poster #25

Early detection of breast cancer by liquid biopsy exploiting the DNA damage sensitivity (DDS)

Rahel Nussbaumer[1], Julia Godau[2], Rosanna Zanetti-Daellenbach[3], Arne Faisst[2], Zeinab Barekati[2], Oliver Schicht[2], Frank Staedtler[2], Bettina Woelnerhanssen[4]
[1]University Hospital Basel, Basel, Switzerland
[2]4D Lifetec AG, Cham, Switzerland
[3]Gynecology, St. Claraspital, Basel, Switzerland
[4]St. Clara Research Ltd., Basel, Switzerland

Background

Breast cancer represents the most frequent cancer in women in Europe, with 27.8% of all newly diagnosed cancer per year and accounts for 16.4% of all annual cancer deaths for females[1]. Although the risk for breast cancer increases significantly after the age of 50 years, it can also affect younger women. Mammography and self-detection are most widely used for breast cancer detection, followed by a biopsy. To a lower degree, liquid biopsy methods are applied to detect mutated tumour DNA. Even where cancer screening methods have evolved, they show limitations in terms of sensitivity and the detection of early cancer stages. We address this gap by developing a completely new, cell-based biomarker assay for early cancer detection and started to assess the assay's performance in clinical practice.

Method

The biomarker assay itself is based upon *ex vivo* UV-B radiation of peripheral blood mononuclear cells (PBMCs) combined with high-performing single-cell gel electrophoresis[2] (Fig 1 and Fig 2). In an observational study, 'Prospective Evaluation of 4D Lifetest™ Parameters to Develop a Universal Early Cancer Diagnosis Test', blood samples from 45 participants were collected (42% patients with newly diagnosed, untreated breast cancer and 58% non-cancer).

Results

Evaluation of the DNA damage sensitivity (DDS) comparing non-cancer with cancer samples resulted in 100% sensitivity at 95% specificity (95% CI: 81.1% to 99.8%) across all stages (Table 1). The mean DDS for early-stage breast cancer 0,I and II did not differ significantly from late-stage III and IV, suggesting high performance also for early detection (Fig 3).

Conclusion

In summary, we demonstrate DDS biomarker assay's potential in detecting breast cancer with high accuracy in a simple, non-invasive way. These data suggest that the DDS biomarker assay is expected to become a practical method to support clinical diagnostics.

Biomarker DNA damage sensitivity

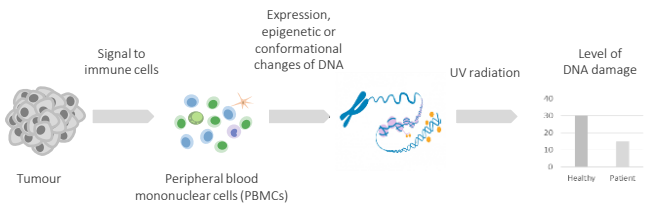

Figure 1. Overview of the potential underlying mechanism of the biomarker DNA damage sensitivity (DDS) in liquid biopsy to distinguish cancer patient-derived samples from healthy donors.

Lifetest™ work flow

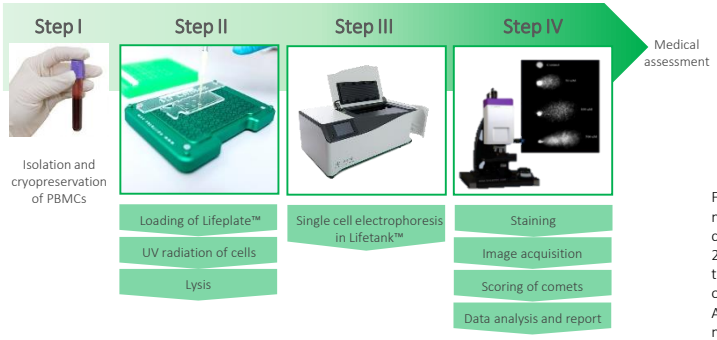

Figure 2. DNA damage sensitivity (DDS) assay workflow. Lifeplates™ are designed in a 12 or 96 spot format. Per patient two spots are loaded. Single cell electrophoresis is performed using the Lifetank™ allowing simultaneous processing of six 12 or 96 spot Lifeplates™, respectively.

High sensitivity for early detection

Table 1: Assay sensitivity at 95% specificity (95% CI: 81-100)

	Sensitivity%	95% CI	Specificity%
Overall	100	83.2 - 100	95
Clinical Stage			
Stage 0-II	100	78.5 - 100	95
Stage III-IV	100	56.6 - 100	95

Detection of breast cancer

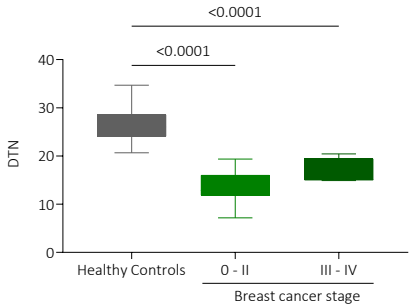

Figure 3. The graph illustrates the DTN (%DNA tail after UVB exposure normalized with baseline values) of samples derived from 26 healthy donors compared to 19 breast cancer patients (UICC stage 0-II: 74%, stage III-IV: 26%). Patient samples with >80% viability were analyzed. Box plots display the 25-75% percentile and whiskers represent the minimum and maximum of the values. Statistical significance was calculated with ordinary one-way ANOVA and Tukey's multiple comparisons. Age and gender differences were not found.

References

[1] European Commission. European Cancer Information System. https://ecis.jrc.ec.europa.eu. Accessed 20 April 2021.
[2] Cassano, Juan C et al. "A novel approach to increase robustness, precision and high-throughput capacity of single cell gel electrophoresis." *ALTEX* vol. 1,37 (2019): 95-109.

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Contact: rahel.nussbaumer@gmx.ch or julia.godau@4dlifetec.com