

Epigenetic aging differ in breast cancer discordant twin pairs – Same life but different disease status.

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Breast cancer discordant twin pairs have been analyzed for intra-pair differences in epigenetic aging linked to the cancer diagnosis. Epigenetic aging is an aging status prediction based on blood DNA methylation levels. It has been shown that these prediction models show correlation with an individual health and disease status. Here it is investigated whether and when the diagnosed twins show different epigenetic age from the healthy co-twins.

1 MATERIAL AND METHODS

DNA methylation was quantified from 24 breast cancer discordant all female twin pairs, 11 monozygotic and 13 dizygotic, from the Finnish twin cohort [Kaprio, 2019]. These twin pairs were age 38 to 82 at the time point of sampling. A total of 10 pairs were sampled up to 15 years before the diagnosis, 14 pairs up to 30 years after the diagnosis. DNA methylation based epigenetic age and its deviation from chronological age, called epigenetic age acceleration (EAA) were calculated based on the Horvath [Horvath, 2013] and Phenoage [Levine, 2018] models.

Paired t-tests were applied to investigate differences in EAA between the healthy and cancer diagnosed twin in each pair. This was done separately for twin-pairs sampled before (Fig. 3 and Fig. 4, left), and after the diagnosis (Fig. 3 and Fig. 4, right).

Linear regression was used to assess any within-pair differences in EAA, and whether that relates to the time of diagnosis (Fig. 1 and Fig. 2).

2 RESULTS

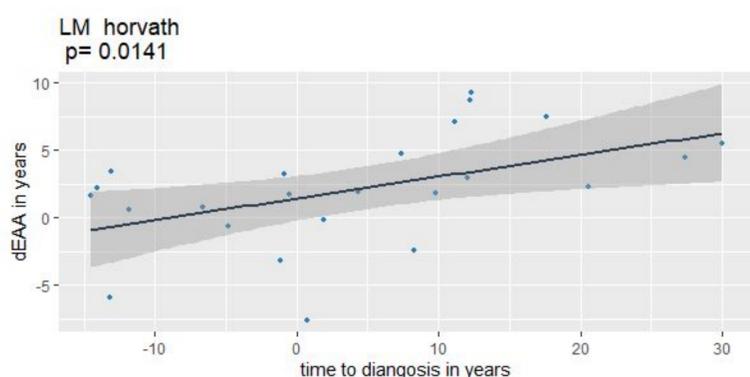


Fig.1 Linear regression of intra-pair differences in EAA (Horvath) by time to diagnosis, including the 95% confident band.

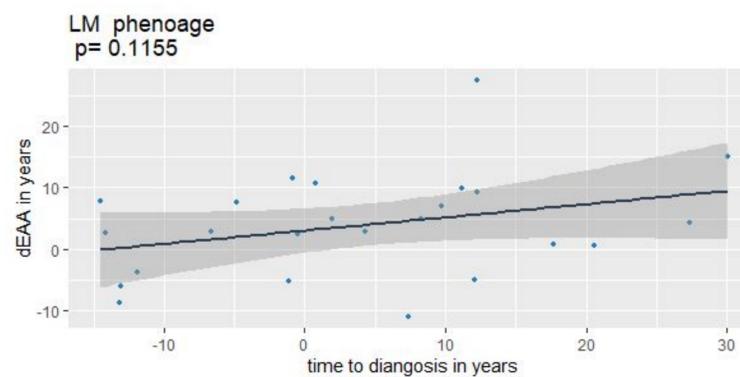


Fig.2 Linear regression of intra-pair differences in EAA (Phenoage) by time to diagnosis, including the 95% confident band.

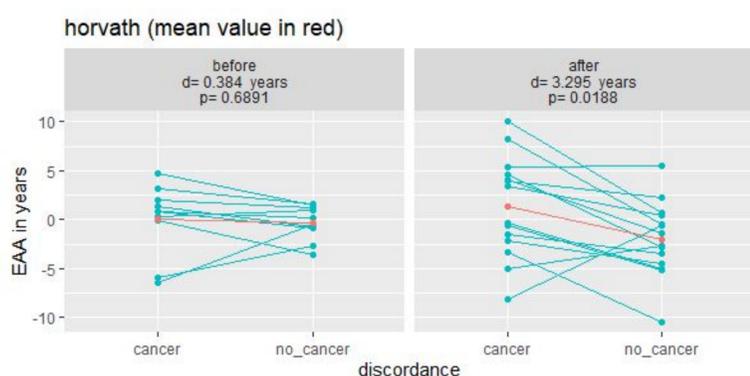


Fig.3 Plot of EAA (Horvath) of twin samples taken before and after the diagnosis. The p-values and dEAA refer to the within-pair differences from a paired t-test.

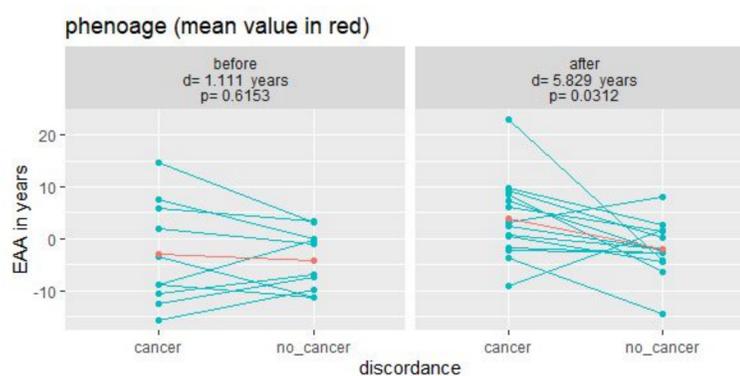


Fig.4 Plot of EAA (Phenoage) of twin samples taken before and after the diagnosis. The p-values and dEAA refer to the within-pair differences from a paired t-test.

3 Discussion

Breast cancer discordant twin pairs sampled before the diagnosis **do not show differences** in their epigenetic age acceleration. (Fig. 3 and Fig. 4, left)

Breast cancer discordant twin pairs sampled **after** the diagnosis **show differences** in their epigenetic age acceleration. (Fig. 3 and Fig. 4, right)

- The breast cancer diagnosed twin seem to undergo faster epigenetic aging.
- However, EEA is only significantly different after the time of diagnosis, and epigenetic alterations related to cancer treatment could explain the accelerated aging rate.

The intra-pair difference in EAA is larger after the diagnosis compared with before the diagnosis. (Fig. 1 and Fig. 2) However, longitudinal data is needed to confirm if the difference in EAA increases linearly over time.

- A possible underlying effect of breast cancer might be already present shortly before the diagnosis.

An additional number of samples of about 100 breast cancer discordant twin pairs are currently measured for their blood DNA methylation levels, to increase the cohort and enable further analysis.

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