

On Stable Fluctuation in Survival of Treated Breast Cancer PatientsA. Shutko^a, I. Akushevich^b, L. Ekimova^c, M. Karamullin^c and A. Yashin^b

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The earlier studies of some authors of this paper showed that, contrary to the theoretical expectations, the mortality rate of cancer patients treated with radio- or chemotherapy had not been changing monotonically with age, but experienced several repetitive cycles during the last 2-3 years of life [ESRB, 2004]. As the number of cases in this earlier investigation was limited, we tested the statistical validity of this finding using different data sets with a larger number of cases. For these purposes we investigated the survival curves for i) 3 different stages of breast cancer (T1N1-2M0 ,T2N1-2M0 ,T3-4N1-2M0) extracted from the Finnish Cancer Registry that covered a time period 1945-79(n=333) and ii) 12 different age groups of breast cancer (covering age interval 30-89 years) extracted from the U.S. Surveillance, Epidemiology and End Results (SEER) Registry (n=83536). Parametric methods were used to describe the survival curves by exponential functions (i.e., using one-compartment models with constant death rate k , or two-compartment models with k_1 and k_2 as death rates in each compartment), and harmonic function allowing for estimation of repetition period T_{cycle} of quasi-sinusoidal disturbances of the monotonic dumped exponential path. Nonparametric methods such as smoothing, spectral analysis, and a series of non-parametric tests were used to confirm the findings of parametric analyses and investigate statistical significance of the estimated periods. We found that there exists a life span region of 0-40 months in which fluctuations in survival curve and respective hazard rates are detectable. The period of such fluctuations, T_{cycle} , is in reciprocal relation with k value and varies within 5 - more, then 40 months. The T_{cycle} varies dependent on diagnosed cancer, or age at diagnosis. The T_{cycle} shows a maximum of 40-54 years-old subjects being described as n -order polynomial function of age. The T_{cycle} is shortening along as cancer stages increase. In the cases when the survival curves allow for decomposition into two compartments, associated with different rates of mortality k_1 and k_2 , the T_{cycle} can be associated with k corresponding to dominant compartment. In view of this, the phenomenon of stable fluctuations in survival can be understood if to assume an existence of certain physiological processes correlated with or even defined by the probability of death. We formulate respective hypotheses about the relation of this phenomenon with regular pre-death instabilities in physiological systems and first of all in stem and progenitor cells compartments of the hematopoietic system.