

On Consolidated Predictive Model of the Natural History of Breast Cancer Considering Primary Tumor and Secondary Distant Metastases Growth in Patients with Lymph Nodes Metastases

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Abstract : This paper is devoted to mathematical modelling of the progression and stages of breast cancer. We propose Consolidated mathematical growth model of primary tumor and secondary distant metastases growth in patients with lymph nodes metastases (CoM-III) as a new research tool. We are interested in: 1) modelling the whole natural history of primary tumor and secondary distant metastases growth in patients with lymph nodes metastases; 2) developing adequate and precise CoM-III which reflects relations between primary tumor and secondary distant metastases; 3) analyzing the CoM-III scope of application; 4) implementing the model as a software tool. Firstly, the CoM-III includes exponential tumor growth model as a system of determinate nonlinear and linear equations. Secondly, mathematical model corresponds to TNM classification. It allows to calculate different growth periods of primary tumor and secondary distant metastases growth in patients with lymph nodes metastases: 1) 'non-visible period' for primary tumor; 2) 'non-visible period' for secondary distant metastases growth in patients with lymph nodes metastases; 3) 'visible period' for secondary distant metastases growth in patients with lymph nodes metastases. The new predictive tool: 1) is a solid foundation to develop future studies of breast cancer models; 2) does not require any expensive diagnostic tests; 3) is the first predictor which makes forecast using only current patient data, the others are based on the additional statistical data. Thus, the CoM-III model and predictive software: a) detect different growth periods of primary tumor and secondary distant metastases growth in patients with lymph nodes metastases; b) make forecast of the period of the distant metastases appearance in patients with lymph nodes metastases; c) have higher average prediction accuracy than the other tools; d) can improve forecasts on survival of breast cancer and facilitate optimization of diagnostic tests. The following are calculated by CoM-III: the number of doublings for 'non-visible' and 'visible' growth period of secondary distant metastases; tumor volume doubling time (days) for 'non-visible' and 'visible' growth period of secondary distant metastases. The CoM-III enables, for the first time, to predict the whole natural history of primary tumor and secondary distant metastases growth on each stage (pT1, pT2, pT3, pT4) relying only on primary tumor sizes. Summarizing: a) CoM-III describes correctly primary tumor and secondary distant metastases growth of IA, IIA, IIB, IIIB (T1-4N1-3M0) stages in patients with lymph nodes metastases (N1-3); b) facilitates the understanding of the appearance period and inception of secondary distant metastases.

Keywords : breast cancer, exponential growth model, mathematical model, primary tumor, secondary metastases, survival

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