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Consolidated Predictive Model of the Natural History of Breast Cancer Considering Primary Tumor and Secondary Distant Metastases Growth

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Abstract : This study is an attempt to obtain reliable data on the natural history of breast cancer growth. We analyze the opportunities for using classical mathematical models (exponential and logistic tumor growth models, Gompertz and von Bertalanffy tumor growth models) to try to describe growth of the primary tumor and the secondary distant metastases of human breast cancer. The research aim is to improve predicting accuracy of breast cancer progression using an original mathematical model referred to CoMPaS and corresponding software. We are interested in: 1) modelling the whole natural history of the primary tumor and the secondary distant metastases; 2) developing adequate and precise CoMPaS which reflects relations between the primary tumor and the secondary distant metastases; 3) analyzing the CoMPaS scope of application; 4) implementing the model as a software tool. The foundation of the CoMPaS is the exponential tumor growth model, which is described by determinate nonlinear and linear equations. The CoMPaS corresponds to TNM classification. It allows to calculate different growth periods of the primary tumor and the secondary distant metastases: 1) 'non-visible period' for the primary tumor; 2) 'non-visible period' for the secondary distant metastases; 3) 'visible period' for the secondary distant metastases. The CoMPaS is validated on clinical data of 10-years and 15-years survival depending on the tumor stage and diameter of the primary tumor. The new predictive tool: 1) is a solid foundation to develop future studies of breast cancer growth 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. The CoMPaS model and predictive software: a) fit to clinical trials data; b) detect different growth periods of the primary tumor and the secondary distant metastases; c) make forecast of the period of the secondary distant metastases appearance; d) have higher average prediction accuracy than the other tools; e) can improve forecasts on survival of breast cancer and facilitate optimization of diagnostic tests. The following are calculated by CoMPaS: the number of doublings for 'non-visible' and 'visible' growth period of the secondary distant metastases; tumor volume doubling time (days) for 'non-visible' and 'visible' growth period of the secondary distant metastases. The CoMPaS enables, for the first time, to predict 'whole natural history' of the primary tumor and the secondary distant metastases growth on each stage (pT1, pT2, pT3, pT4) relying only on the primary tumor sizes. Summarizing: a) CoMPaS describes correctly the primary tumor growth of IA, IIA, IIB, IIIB (T1-4N0M0) stages without metastases in lymph nodes (N0); b) facilitates the understanding of the appearance period and inception of the secondary distant metastases.

Keywords : breast cancer, exponential growth model, mathematical model, metastases in lymph nodes, primary tumor, survival
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