

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

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Abstract : Finding algorithms to predict the growth of tumors has piqued the interest of researchers ever since the early days of cancer research. A number of studies were carried out as an attempt to obtain reliable data on the natural history of breast cancer growth. Mathematical modeling can play a very important role in the prognosis of tumor process of breast cancer. However, mathematical models describe primary tumor growth and metastases growth separately. Consequently, we propose a mathematical growth model for primary tumor and primary metastases which may help to improve predicting accuracy of breast cancer progression using an original mathematical model referred to CoM-IV and corresponding software. We are interested in: 1) modelling the whole natural history of primary tumor and primary metastases; 2) developing adequate and precise CoM-IV which reflects relations between PT and MTS; 3) analyzing the CoM-IV scope of application; 4) implementing the model as a software tool. The CoM-IV is based on exponential tumor growth model and consists of a system of determinate nonlinear and linear equations; corresponds to TNM classification. It allows to calculate different growth periods of primary tumor and primary metastases: 1) 'non-visible period' for primary tumor; 2) 'non-visible period' for primary metastases; 3) 'visible period' for primary 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-IV model and predictive software: a) detect different growth periods of primary tumor and primary metastases; b) make forecast of the period of primary metastases appearance; c) have higher average prediction accuracy than the other tools; d) can improve forecasts on survival of BC and facilitate optimization of diagnostic tests. The following are calculated by CoM-IV: the number of doublings for 'nonvisible' and 'visible' growth period of primary metastases; tumor volume doubling time (days) for 'nonvisible' and 'visible' growth period of primary metastases. The CoM-IV enables, for the first time, to predict the whole natural history of primary tumor and primary metastases growth on each stage (pT1, pT2, pT3, pT4) relying only on primary tumor sizes. Summarizing: a) CoM-IV describes correctly primary tumor and primary distant metastases growth of IV (T1-4N0-3M1) stage with (N1-3) or without regional metastases in lymph nodes (N0); b) facilitates the understanding of the appearance period and manifestation of primary metastases.

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

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