DOES EXTIRPATION OF THE PRIMARY BREAST TUMOR GIVE BOOST TO GROWTH OF METASTASES? EVIDENCE REVEALED BY MATHEMATICAL MODELING

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In the 1970s a number of oncologists brought forward a hypothesis that extirpation of the primary tumor may give boost to proliferation of dormant or slowly growing metastases, trigger their vascularization, and accelerate the growth of vascular secondary tumors. It was supported by epidemiological analyses of the time course of post-surgery recurrence for various categories of cancer patients and corroborated by an experimental study of accelerated growth of metastases after resection of the primary Lewis lung carcinoma in mice.

In this work, we provide a dramatic confirmation of this hypothesis based on a comprehensive mechanistic model of cancer natural history developed in [1, 2]. This model leads to an explicit formula for the distribution of the volumes of detectable metastases in a given secondary site at any time post-diagnosis. The model provided an excellent fit to the volumes of $n = 31, 20$ and $15$ bone metastases observed in three breast cancer patients $8$ years, $5.5$ years and $9$ months after primary diagnosis, respectively. The model with optimal parameters allowed us to reconstruct individual natural history of cancer for the first patient. According to the model, resection of the primary tumor was followed by a 32-fold increase in the rate of metastasis growth. The model and our conclusions were validated by the analyses of the other two patients.
