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Are metastases from metastases clinically relevant? A novel computer model helps understanding the metastatic progression

The process of metastasis formation remains enigmatic. Different models exist for predicting the metastatic spread of malignant tumors. However, it is difficult to evaluate these different models for their clinical relevance. Therefore a novel computer model was developed which permits comparison of the different models quantitatively with clinical data and which additionally predicts the outcome of treatment interventions. The computer model is based on a discrete events simulation approach. The growth of the primary tumor and the metastases is described via analytical functions, while a rate function models the intravasation events of the primary tumor and its metastases. Events describe the behavior of the emitted malignant cells until the formation of new metastases. With the help of the computer model it was evaluated whether metastases are able to metastasise and if late disseminated tumour cells are still capable to form metastases. The simulation results were compared with clinical data from an untreated patient with hepatocellular carcinoma and multiple metastases in the liver. Additionally, the resection of the primary tumour was simulated. The results of the computer simulations reveal that the number of metastases varies significantly between scenarios where metastases metastasise and scenarios where they not. In contrast, the total tumour mass is nearly unaffected by this mode of metastasis formation. Furthermore, the results provide evidence that late disseminated tumour cells are still capable of forming metastases. The simulation results show that in this particular case of hepatocellular carcinoma, carcinoma metastases exhibit the same growth pattern as the primary tumour. Simulations also allow estimating how the resection of the primary tumour delays or even prevents the patients death. The simulation results indicate that for this particular case of a hepatocellular carcinoma late metastases, i.e. metastases from metastases, are irrelevant in terms of total tumour mass. Hence metastases seeded from metastases are clinically irrelevant in our model system. Only the first metastases seeded from the primary tumour contribute significantly to the tumour burden and thus cause the patients death.