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Mathematical modelling for cancer recurrence caused by premalignant lesions formed before the first treatment

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Residual premalignant lesions after the first treatment such as surgery and chemotherapy are considered to be a cause of cancer recurrence. A previous study showed that the presence of premalignant lesions surrounding the primary tumour drives the high rate of local cancer recurrence. If cancerization requires m specific mutations in one cell, cells which have less than m mutations are still not cancer cells but have higher risk of cancerization than normal cells. In this study, we constructed a mathematical model of cancer recurrence caused by premalignant lesions (m=2 in this model). There are three populations in the model: (i) normal cells with no mutation, (ii) premalignant cells with one mutation, and (iii) cancer cells with two mutations. The total number of a healthy tissue is kept constant and there is a rare chance of mutation every time cell divides. Once a cancer cell with two mutations arises, the population proliferates exponentially, ignoring the number restriction. Under this assumption, we investigated the dynamics of accumulating mutations by combining Moran process and branching process. As a result, we derived analytical solutions for the probability distribution of the number of cancer cells over time and confirmed the accuracy by comparing them to the results from stochastic simulations. Finally, we found that premalignant lesions have a greater effect on time to recurrence when patients are older or growth rate of cancer cells is lower.

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