Purpose: Modeling tumour control probability (TCP) in breast conserving therapy (BCT) with the classic Webb-Nahum radiotherapy model can not explain the outcomes of treatments without radiotherapy (65% TCP at 10 years) from the Fifth Cycle data of the Early Breast Cancer Trialists' Collaborative Group (EBCTCG). The TCP model was extended to solve this inconsistency.

Methods: We proposed a statistical model originating from the Webb-Nahum model, but also considered tumour cell quantity as a heterogeneous variable and introduced a new heterogeneity factor: indolent-cell fraction (ICF). With assumed Beta distribution, this ICF factor describes the proportion of tumour cells remaining after primary surgery which do not cause local recurrence even if radiotherapy is omitted. The residual microscopic tumour cell quantity was estimated using detailed digital analysis of the microscopic slides from breast-cancer resection specimens (60 patients, 1818 slides). The ICF factor together with an approximation of radiosensitivity was estimated using Shor-Zhurbenko optimization to fit data from the EORTC boost-vs-no-boost trial to the new model. Uncertainties were incorporated using bootstrapping. The analysis was performed separately for younger (age = 50 years) and older patients. Finally, the radiotherapy dose-TCP responses of two groups were compared.

Results: The estimated number of residual microscopic tumour cells after surgery was significantly larger in younger patients (9.1e7) than in older patients (1.6e7, P<0.001). Using ICF increased the modeling accuracy at 0Gy for younger and older patients by 40% and 29%, respectively. The estimated tumour radiosensitivity was larger in younger patients than in older patients (0.060Gy-1 vs 0.054Gy-1, P<0.001), but the Beta parameter of ICF for younger patients was smaller (1.4e7 vs 1.8e7), which means older patients have a larger fraction of indolent tumour cells (P<0.001). This combination accurately described the TCP differences between these groups.

Conclusions: The accuracy of TCP modeling in BCT was improved with our model.

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