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An illustration of patient-specific cancer modelling: from microscopic data to macroscopic, quantitative predictions

Ductal carcinoma in situ (DCIS)—a type of breast cancer whose growth is confined to the duct lumen—is a significant precursor to invasive breast carcinoma. DCIS is commonly detected as a subtle pattern of calcifications in mammograms. Mammograms are also used to plan surgical resection (lumpectomy) of the tumour, but multiple surgeries are often required to fully eliminate DCIS. This highlights deficiencies in current surgical planning. Immunohistochemical measurements have been proposed to assess DCIS and plan treatment, but no standard has emerged to quantitatively predict a patient's clinical progression (i.e., macroscopic measurements such as the growth rate) based upon such microscopic measurements.

We present a mechanistic, agent-based model of solid-type DCIS with comedonecrosis and calcification [1]. Each agent has a lattice-free position and phenotypic state. Cells move by exchanging biomechanical forces with other cells and the basement membrane. Each phenotypic state has a "submodel" of changes in cell volume and composition. Phenotypic transitions from the quiescent state are regulated by proteomic- and microenvironment-dependent stochastic processes. We combine a model analysis, a mathematically-oriented literature search, and a new patient-specific calibration protocol to fully constrain and calibrate the model to an individual patient's immunohistochemical and morphometric data [2].

The model predicts linear growth at approximately 7–10 mm per year, consistent with mammography [3]. It also predicts a linear correlation between the calcification size (as in a mammogram) and the tumour size (post-operative pathology measurement), in excellent quantitative agreement with 87 clinical data points [4]. These results suggest that hybrid multiscale models can be rigorously calibrated to molecular data by upscaling mechanistic cell-scale models. Such multiscale models can potentially bring mathematics to the clinic to improve patient care.

References

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