A mathematical model for metastatic growth: numerical resolution and confrontation with preclinical data

Niklas HARTUNG, I2M, Aix Marseille Université, Marseille, France

Joseph CICCOLINI, Faculté de Pharmacie, Aix-Marseille Université, Marseille, France

Florence HUBERT, I2M, Aix Marseille Université, Marseille, France

Séverine MOLLARD, University of Cambridge, Cancer Research UK Cambridge Institute, UK

Classification of cancer as localized or metastatic disease remains the mainstay for determining the best therapeutic strategy to be undertaken at the bedside. Despite major progresses in imaging methods, these technologies still cannot detect metastatic lesions under 10^8 cells in patients. Developing a mathematical tool to better assess the metastatic risk, in cases where no evidence of metastasis is available yet, would help clinicians to decide on the most adequate therapeutic strategy.
A metastatic model by Iwata *et al.* [1] has been shown to describe the metastatic growth dynamics visible on CT scans of a patient with a metastatic hepatocellular carcinoma very accurately. It has further been confronted with published clinical data on metastatic relapse in 3,500 patients with breast cancer and has shown to accurately predict the risk of a metastatic disease when calibrated properly [2].
In the first part of this work, based on [3], we will show how a family of metastatic models with 1D or 2D structuring variables, based on the Iwata model, can be reformulated into an integral equation counterpart, a Volterra equation of convolution type, for which a rich numerical and analytical theory exists. Furthermore, we will show how this approach permits to reduce the computational cost of the numerical resolution.
In the second part, we have adapted the Iwata model to the preclinical context and confronted it with experimental data. The fast and precise simulation of the metastatic model presented in the first part make advanced statistical methods feasible.

Acknowledgements Coworkers of the model confrontation to preclinic data were Dominique Barbolosi, Assia Benabdallah, Guillemette Chapuisat, Christian Faivre, Sarah Giacometti, Gerard Henry et Athanassios Iliadis.
The authors were partially supported by the Agence Nationale de la Recherche under grant MEMOREX-PK ANR-09-BLAN-0217-01, by the Cancéropôle PACA (PROCAN project), Project PhysCancer 2009-2013 (n^o101194), GEFLUC Marseille-Provence and the French Association pour la Recherche contre le Cancer (ARC, subvention n^o5009).

Références

[1] Iwata, K., Kawasaki, K. and Shigesada, N., *A dynamical model for the growth and size distribution of multiple metastatic tumors*, J Theor Biol 203: 177-186, 2000.

[2] Barbolosi, D., Verga, F., You, B., Benabdallah, A., Hubert, F., Mercier, C., Ciccolini, J. and Faivre, C., *Modélisation du risque d'évolution métastatique chez les patients supposés avoir une maladie localisée*, Oncologie 13 (8): 528-533, 2011.

[3] Hartung, N., *Efficient Resolution of Metastatic Tumour Growth Models by Reformulation into Integral Equations*, preprint: http://hal.archives-ouvertes.fr/hal-00935233

Niklas HARTUNG, Aix Marseille Université, CNRS, Centrale Marseille, I2M, UMR 7373, 39 rue Frédéric Joliot-Curie 13453 Marseille cedex 13
niklas.hartung@univ-amu.fr