Forces and cytoskeletal dynamics during collective invasion of tumor spheroids

Ben Fabry[1] and Christoph W. Mark[1]

[1]*Department of Physics, University of Erlangen-Nuremberg, Erlangen, Germany*

Cell movements and associated cell-generated forces are of central importance in cancer metastasis where tumor cells leave a primary tumor and invade the surrounding tissue. This invasion process is driven by cells at the tumor boundary that collectively exert physical forces on the extracellular matrix. To study the physical forces arising from these collective effects, we embed invasive HT-1080 fibrosarcoma spheroids and non-invasive MCF-7 breast carcinoma spheroids in reconstituted collagen matrices. We measure the ongoing deformation of the collagen matrix over time by tracking embedded silica beads in the equatorial plane of the spheroids. We then compute the collective contractile forces from the matrix deformations with a non-linear finite element model. Invasive spheroids reach their maximal contractility after 30 min. Subsequently, overall contractile forces remain constant while cells at the spheroid border invade the matrix. Surprisingly, non-invasive spheroids also generate substantial contractile forces, but these forces rise slowly over the course of 12 hours, and no cells leave the spheroid. We conclude that overall contractility is a poor indicator for cell invasiveness, in contrast to dynamical changes of forces and cytoskeletal reorganization.