Unraveling cancer cell migration in 3D

Reto Fiolka, Claudia Schaefer, Erik Welf and Gaudenz Danuser
Department of cell biology
University of Texas Southwestern Medical Center
5323 Harry Hines Boulevard, Dallas, TX 75390
Reto.Fiolka@UTSouthwestern.edu

KEY WORDS: Live cell imaging, light-sheet microscopy, two-Photon excitation, time-lapse imaging, 3D microenvironments, cell migration

A critical step towards identifying cures for cancer is to understand what enables certain cells to metastasize efficiently while others do not. We investigate cancer cell motility in 3D microenvironments by combining cutting edge microscopy technology and computer vision. To provide minimally invasive high-resolution 3D imaging deep within hydrogels, we adopted two-Photon light-sheet microscopy [1] with a larger field of view. The system provides isotropic resolution in the range of 300 nm while rapidly covering large volumes of 300x300x100 microns. We present the 3D morphology and dynamics of different cancer cells in collagen gels. We could observe that often most actin structures were localized in the cortex of a cell (Fig.1), a feature that is obscured in conventional assays using cells spread on coverslips. The light-sheet microscope enables us to image rapid dynamics like blebbing or the formation of filipodia with great spatiotemporal detail, but also to conduct long term observations spanning many hours. We are now implementing systematic experiments to map out the relation between the dynamics of molecular composition of the cortex and single cell morphogenesis. We also envision scaling-up light-sheet microscopy for the purpose of drug screening in 3D microenvironments.

Figure 1: Maximum intensity projections (left two panels) of a HBEC cell in collagen gel labeled with tracrin-eGFP and corresponding central cross-sections (right two panels). The images belong to a time-lapse series encompassing 75 time points and over 12000 raw images. Scale bar: 10 microns.