# Motility Contrast Tomography of Multicellular Tumor Spheroids

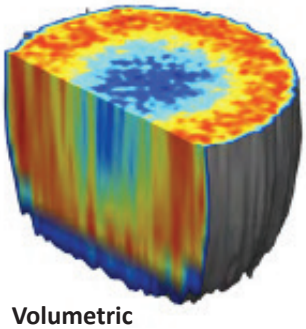
Multicellular tumor spheroids are ideal targets for biodynamic imaging (BDI). The penetration depth of BDI into tissue is approximately 1 mm, which is a typical large spheroid size that supports a necrotic core. Because BDI is depth-gated, it can take a mid-section that cuts across the proliferating shell, through the region of quiescence, and into apoptotic and necrotic regions.

Motility contrast tomography (MCT) provides a simple and fast assessment of the degree of motion in living tissue. It generates an activity map of the tissue by constructing a motility metric that combines all the intracellular motions into a single quantitative value. It takes only a few seconds to generate a motility map at a single section plane, which makes it an ideal mode for high-throughput applications.

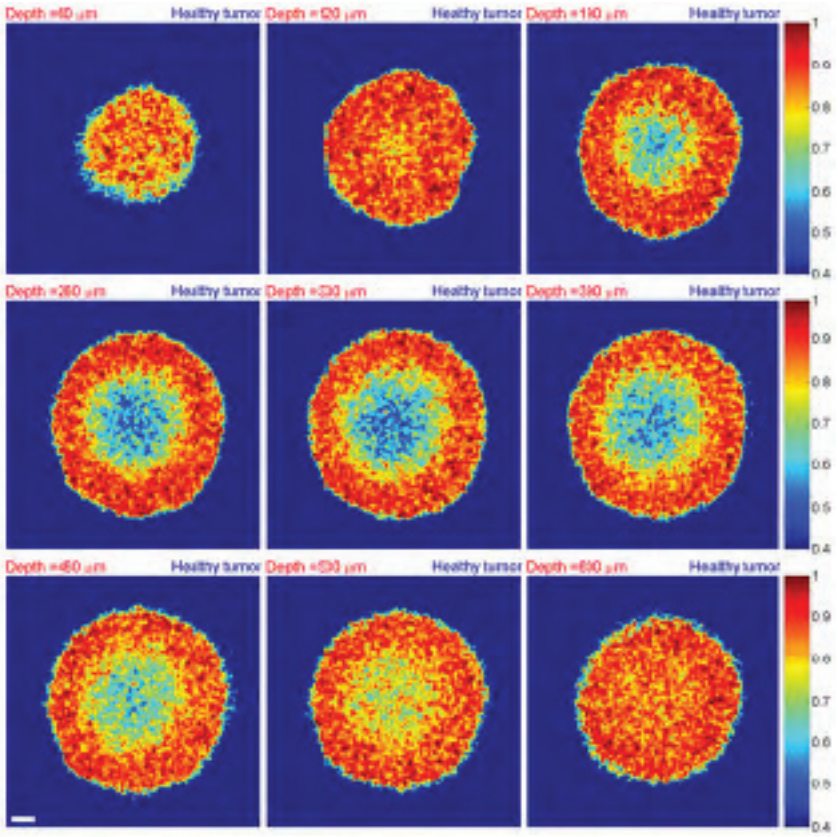
## *Biodynamic Imaging Platform*

### KEY FEATURES

- Measures heterogeneous activity of a tumor spheroid throughout its volume.
- Real-time measurements of drug efficacy and transport in 3D tissue.



**Volumetric**



**Optical Sections**

**Fig. 1** Volumetric motility contrast tomography of an 800 micron diameter multicellular tumor spheroid. Selected sections are shown on the left color-coded to motility metric. Red denotes high intracellular motility, while blue is weaker motion. The proliferating shell is approximately 200 microns thick and exhibits strong intracel-luar motility. The core is hypoxic, acidic and the central core is necrotic. The sections are combined into the three-dimensional cut-away on the right.

Volumetric motility maps capture the entire tumor spheroid volume up to 1 mm in diameter, including the inner quiescent shell and the hypoxic and acidic core. Be-cause MCT is fast (only a few seconds for a single section) transport and drug effects are captured in real time.

ADI

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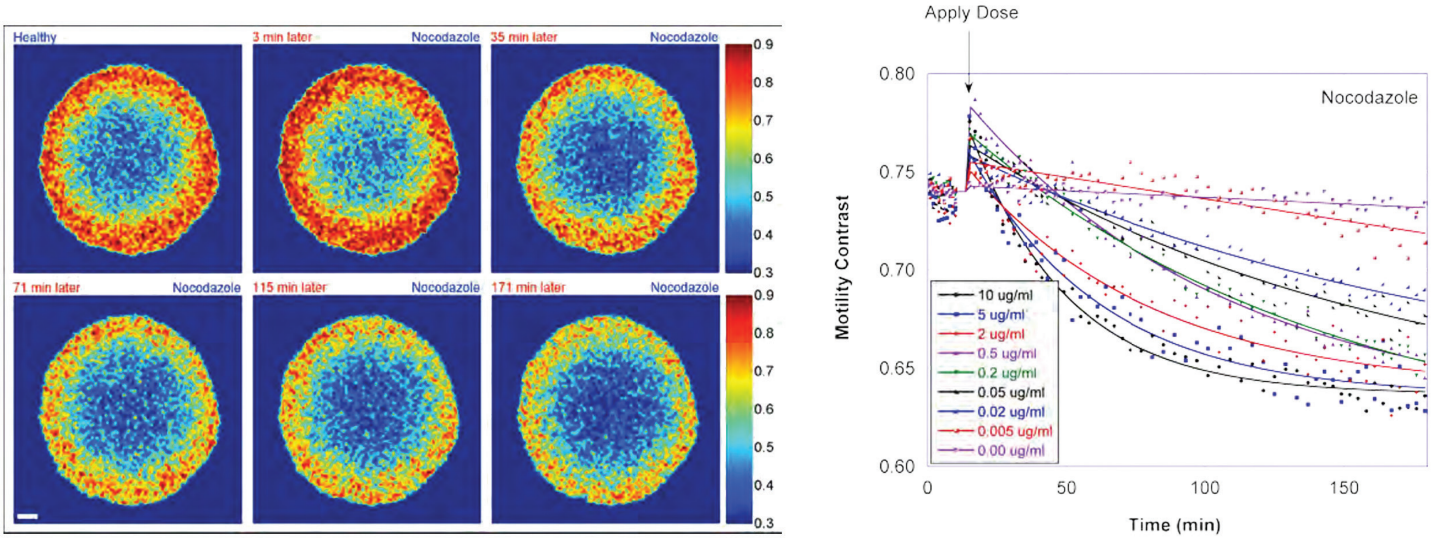
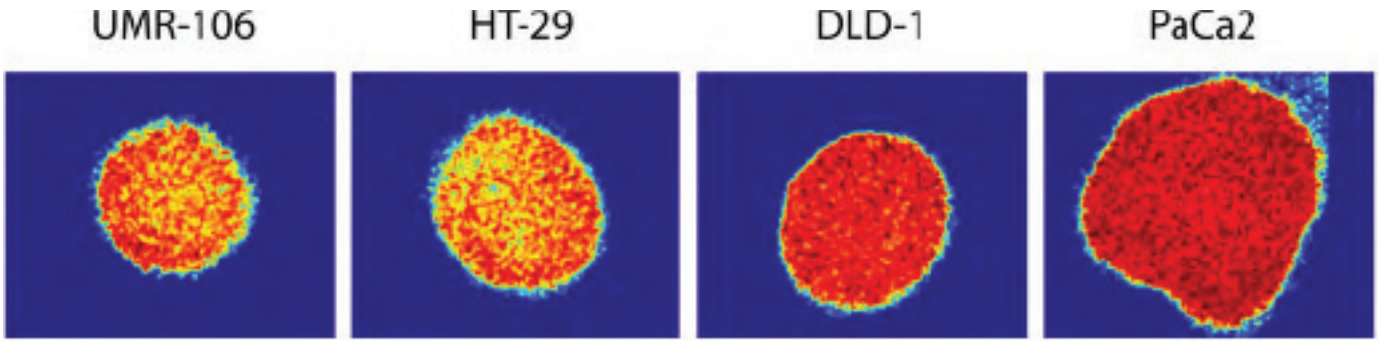



**Fig. 2** Motility Contrast Tomography of the mid section of an osteogenic sarcoma spheroid responding to nocodazole. White bar is 50 microns. The motility in the proliferating shell decays in time. The dose dependence of the motility metric is shown in the graph.




**Cell Line Motility Images**

**Fig. 3** Different cell lines have different degrees of motility, or activity. The UMR is an osteogenic sarcoma with the lowest motility metric around 80%. HT-29 and DLD-1 are colon adenocarcinomas with intermediate motility. PaCa2 is a pancre-atic cell line showing the highest motility metric of around 95%.

The capability of MCT to monitor drug effects in real time throughout a 1 $mm^3$ volume of living tissue provides the customer with a new handle on drug transport and drug efficacy monitoring in three-dimensional tissue culture. The differing activities of different cell lines provide a measure of metabolic rates and proliferation rates that change in response to applied drugs. Early toxicity is reflected in alteration of these rates, and provides a means to monitor toxicity through the heterogeneous regions of an avascular tumor, including quiescent cell layers. Motility Contrast Tomography requires no fluorescent tags and is non-invasive, enabling long-term longitudinal studies.


***References:***

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