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### Title

A quantitative study of breast cancer glucose and lipid metabolism with nonlinear optical microscopy

### Permalink

<https://escholarship.org/uc/item/59m5f9n3>

### Journal

JOURNAL OF NUCLEAR MEDICINE, 56(2)

### ISSN

0161-5505

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### Publication Date

2015

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Peer reviewed

**A quantitative study of breast cancer glucose and lipid metabolism with nonlinear optical microscopy.** J. Hou, A. Paul, E. Gratton, E. Botvinick, E.O. Potma, B. Tromberg; University of California, Irvine, Irvine, CA

We study the correlation of breast cancer cell glucose and lipid metabolism with cancer proliferation and metastasis by nonlinear optical microscopy (NLOM). The cellular glucose metabolism is assessed by imaging the metabolic coenzymes (NADH and FAD+) through two photon excited fluorescence (TPEF) microscopy and fluorescence lifetime microscopy (FLIM). We evaluate the oxidative/glycolytic rate from fluorescence lifetime of NADH and from redox ratio calculated as the intensity ratio of FAD+/(NADH+FAD+). We map out the lipid distribution by coherent anti-Stokes Raman scattering (CARS) microscopy and develop a Matlab program based on machine learning algorithm to compute the lipid percentage from CARS images. Commercial cell lines (MCF10A, T47D, MB231 and PME) and cells extracted from patient biopsies are suspended in Matrigel/collagen mixture and are dynamically monitored for 2-3 weeks. In the 3D environment, we observed that different cell types show different metabolic rates and morphological patterns corresponding to their proliferation and metastatic status. Normal breast cells and non-malignant cells show highest redox ratio and lipid percentage and form polarized structures (acini) with a hollow center. The malignant cells, which form solid spheroids, are the most glycolytic and have less lipid storage in cytoplasm. The metastatic groups, with a moderate glucose metabolic rate and lowest lipid percentage, do not form any growth arrested structure. A shift from glycolytic to oxidative and an increase in lipid content have also been observed during the acini formation. The results of this study have the potential to enhance the understanding of the correlation of cell metabolism and cancer progression and can lead to novel strategies and targets for therapy and prevention.