Biologistics of lung cancer screening and management using field-effect of carcinogenesis and a novel biophotonics technique

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Abstract: According to the University of Memphis Biologistics Research Cluster, "biologistics is the management of the safe flow of high value, temperature sensitive and time-critical biological materials as they are delivered for patient care, analyzed for diagnostic purposes, processed to higher value products or stored to meet physical and data archival needs." In that context, the *biologistics* of early cancer detection and management is a preeminent challenge in modern medicine. In response, researchers are striving to understand biological structures and processes at the nanoscale, in particular the strong correlation between changes in intracellular nanoarchitecture related to basic cellular materials, such as DNA, RNA, lipids, and proteins, and the earliest stages of progressive carcinogenesis. Our group has recently developed an optical experimental technique based on a key principle of physics: mesoscopic light transport. This technique, termed partial wave spectroscopy, or PWS, is capable of detecting, for the first time, nanoscale alterations in a cell during early cancer progression. Preliminary results show that we can detect signs of ultra-early carcinogenesis in lung, colon, pancreas, esophagus and ovary cells by fast optical imaging. Moreover, we can quantify these nanoscale alterations, using mesoscopic base physics analysis. Importantly, based on the field effect of carcinogenesis, we can detect cancer from an easily accessible surrogate, far from the actual cancer site, but on the same epithelial track. For example, we were able to detect noninvasively lung cancer from buccal cells, colon cancer from rectal cells, and ovarian cancer from cervical cells.

The PWS optical technique is cost-effective and can be used for fast population-based mass screening of several cancers. Important to this proposal, it has shown sensitivity and specificity of ~80% for field effect detection from their corresponding surrogate sites. However, for practical and optimal use, we require ultra-sensitivity of the technique, ~99% sensitivity and specificity, to absolutely meet *biologistics* requirements for early cancer screening and management for a large population. To accomplish this, we propose further engineering to modify/improve the present PWS optical system to enhance light signals scattered from nanoscale alterations by using a thin metallic cavity incorporated into the present PWS technology. Using this optimized (enhanced) PWS (EPWS) platform, we will be well positioned to concentrate on the *biologistics* of early lung cancer detection and management. Lung cancer has one of the highest mortality rates in the U.S., justifying the urgency of this screening technology. Our research objectives are the following: (1) Develop enhanced partial wave spectroscopy (EPWS) instrumentation for the fast screening of early lung cancer: (i) design and incorporate a semi-transparent metallic cavity as a biological cell holder into the present PWS system and characterize this cavity-induced partial wave signal enhancement from nanoscale spatial refractive index fluctuations in the cell; (ii) optimize cavity, cell, and staining parameters for fast detection and screening. (2) Validate detection of lung cancer from buccal/cheek cells with high sensitivity and specificity to meet biologistics requirements for early cancer screening and cancer management: As a pilot study, we will use EPWS to detect lung cancer in human

subjects (n=50 lung cancer and n=100 normal) by collecting cells from (i) affected areas in lung biopsy (for cancer confirmation) and (ii) cheek /buccal cells, far from the affected areas, to test our method against the *"field effect"* of carcinogenesis.

Our approach to secure cells inside a metal cavity will be based on easy to manufacture effective cavity by using metal coated antireflection slides, and can be easily incorporated in EPWS technology. Lung cancer sample will be obtained from our collaborators.