Octavian Bucur

BIDMC, USA

Expansion pathology: Physical tissue expansion for nanoscale imaging and investigation of clinical specimens

Background: In pathology, examination of cellular structures and molecular composition using diffraction-limited microscopy is key to diagnosis. Recently, a new approach, Expansion Microscopy, was developed to enable physical magnification and high resolution imaging of cell lines and mouse brain sections with conventional optical microscopes, by embedding them in a dense swellable polymer and adding water to swell the polymer after the enzymatic digestion of the proteins. The purpose of our study is to develop a pathology-optimized physical tissue expansion method for nanometer imaging and investigation of clinical tissue samples and to analyze its utility in diagnostic pathology and research.

Methodology: We developed a pathology optimized physical tissue expansion method called Expansion Pathology (ExPath), which uses clinically optimized chemistry, labeling and imaging methodologies to enable the expansion and visualization of both human FFPE and frozen clinical samples, including previously stained/unstained, mounted/unmounted and whole tissue slide/tissue microarrays sections, of a wide variety of fixed human tissue types and pathologies.

Findings: This ExPath protocol enabled expansion of human normal and cancer tissues ~4.5x in linear dimension and ~100x in volume, with a post-expansion measurement error of 3-7%. Physical tissue expansion pushes the optical microscopes beyond their limits (currently 250 nm in resolution), by enabling for the first time ~70 nm resolution imaging of diverse biomolecules in intact tissue with an optical microscope. With ExPath, certain lesions and pathologies of the kidney previously diagnosed with an electron microscopy (EM) can now be diagnosed with a conventional optical microscope after physical tissue expansion, an inexpensive, faster and reliable strategy. It also enables high-fidelity computational discrimination between early breast neoplastic lesions that to date have challenged human judgment.

Conclusion: ExPath offers new approaches for assessing pathologically important features in human tissue. It may eliminate the need for EM in diagnosis of certain diseases for which EM is required for diagnosis and it can improve the computational discrimination between pathological lesions that are hard to distinguish with existing techniques. ExPath may enable routine use of nanoscale imaging in molecular pathology and research.

Speaker Biography

Octavian Bucur is working as an Instructor in the Departments of Pathology and Medicine at the Harvard Medical School, BIDMC, in Boston, MA, focusing on the development and application of new experimental and computational technologies with significant impact in molecular, diagnostic pathology and personalized medicine. He is also a member of the Ludwig Cancer Center at Harvard and Broad Institute of MIT and Harvard. In collaboration with Dr. Edward Boyden's laboratory at MIT, he has developed a pathology-optimized physical tissue expansion method called Expansion Pathology that enables ~100 times expansion in volume of any type of clinical specimen and visualization of 70-80 nm structures with conventional optical microscopes (currently limited to ~250 nm resolution). Expansion Pathology has the potential of replacing electron microscopy in diagnosis and investigation of certain pathologies and nanometer structures (Nature Biotechnology, in press; 3 patents filed).

e: obucur@bidmc.harvard.edu

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