Scientists develop microscopic calibration tool with fluorescent nanodiamonds

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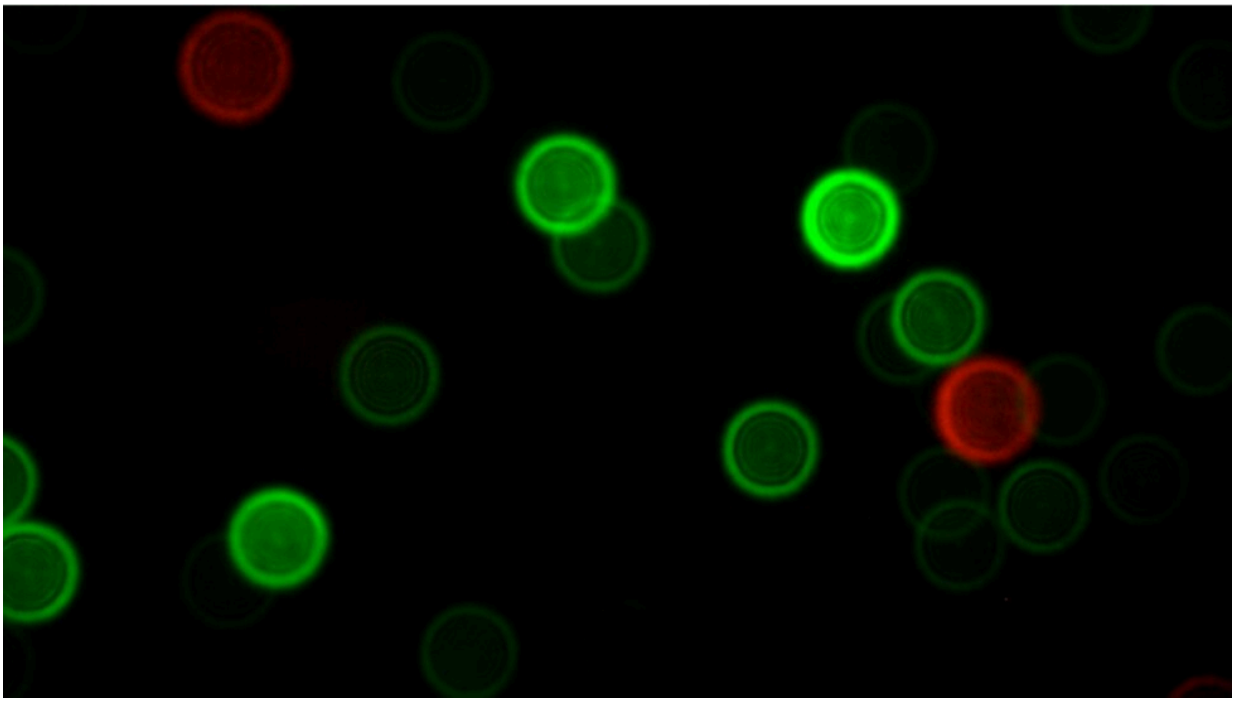

Microscopy image of fluorescent nanodiamonds, a calibration tool developed by researchers at the University of Illinois Urbana-Champaign in collaboration with industry partner GlaxoSmithKline. The nanodiamonds' longevity and durability make them a microscopic "first-aid kit" that stands the test of time. Credit: Beckman Institute for Advanced Science and Technology

Jewelers, geologists, and microscopists agree: diamonds are forever. Researchers at the University of Illinois Urbana-Champaign are using

microscopic nanodiamonds to calibrate and assess the performance of high-powered microscopes. Their longevity and durability make the tiny "first-aid kits" more than up to the task.

Advanced optical microscopy systems provide high-resolution views of the structure and function of cells and molecular compounds. Developing a stable fluorescent nanodiamond phantom promises wide-reaching applicability for microscopy research and quality control alike.

"There is potential that this is going to become a standard calibration tool in fluorescence microscopy worldwide. This sample is so convenient, and so easy to use, that it is hopefully going to make a large impact," said Mantas Žurauskas, an imaging research scientist for the GlaxoSmithKline Center for Optical Molecular Imaging at the Beckman Institute for Advanced Science and Technology, who led the research.

The team's paper, "Fluorescent nanodiamonds for characterization of nonlinear microscopy systems," was published in Photonics Research.

Fluorescent nanodiamonds are microscopic particles with small amounts of other chemical elements trapped inside as impurities. Žurauskas' research establishes their efficacy for producing stable microscopic images.

"[They] are unique in the way that they do not bleach," Žurauskas said. "Each time you look at them, they look the same. That's very rare in fluorescence microscopy."

Creating reliable calibration samples, called phantoms, is a challenge in biomedical microscopy imaging.

"There are changes each time you look at a fluorescent structure. As phantoms, I used fluorescent beads very often, these are like little beads

filled with fluorescent dye. Each time you look at them, they are a bit dimmer. It's really this fluorescence decay that is a big enemy in fluorescence microscopy," Žurauskas said.

The stability of a calibration sample is fundamental to assessing the optical system's day-to-day quality.

"It's kind of a first-aid kit for a microscope," said Žurauskas. "Ideally, we want to take the same object each time and see the same image."

Nanodiamonds' stability and longevity allows their continuous reuse as a calibration tool, eliminating the labor-intensive preparation researchers typically undergo.

Beckman's collaborative research environment was critical to engineering this robust, easy-to-use imaging phantom.

"[Professor and GSK Center Co-Director] Stephen Boppart created a unique environment, and a unique range of expertise so that people can meet in the corridors, can talk about the challenges they are facing daily, and find these unique solutions that are only possible in this sort of environment," Žurauskas said.

Boppart also emphasized the unique interdisciplinary nature of this research.

"We have this large interdisciplinary lab that does end-to-end development and application, so we develop laser sources, we develop microscopes, and we use those microscopes to do the biological and medical research, even clinical human studies. These nanodiamonds and phantoms are just one example where we also develop new tools to catch up with the development of the microscopy systems that we do.

"This interdisciplinary and highly collaborative element was extremely important for this research to happen," Boppart said.

How are the phantoms engineered?

Žurauskas explains: "The nanodiamonds are distributed randomly, and they are very sparse, so that you can look at individual particles, or on the opposite end of the spectrum you can look at dense distributions of these particles. A second plane contains a viewfinder grid, which is effectively a laser-machined grid with nanodiamonds embedded in it. This helps to find the same area each time."

Partners in industry are evaluating the imaging phantom for wider use.

"We currently have two companies evaluating the phantom. One company is LiveBx, a small spinoff of the university. That particular company is interested in how these phantoms can be used to improve their system," said Žurauskas.

Industry partner GlaxoSmithKline is also working to assess the new phantom for quality control applications in its own biomedical research labs.

The technology represents an important scientific advancement for calibrating microscopy systems and the images they generate, and points toward future research in creating more advanced and stable phantoms.

More information: Mantas Žurauskas et al, Fluorescent nanodiamonds for characterization of nonlinear microscopy systems, *Photonics Research* (2021). DOI: 10.1364/PRJ.434236

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