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An EU-funded project has shown that high-resolution fluorescence microscopy allows doctors to make a diagnosis on whether cancer is present or not from tiny samples. This means smaller needles can be used for extracting the samples, with less side effects for patients.

The survival chances of cancer patients can be dramatically increased by an early diagnosis. For people with suspect breast or prostate cancer, a common approach is to remove a sample for diagnosis of the suspected tumour with a large needle (cross-section area of about 10 mm$^2$) inserted into the breast or prostate gland.

However, this method, known as a ‘core-needle biopsy’, can be painful and lead to severe side effects – such as infections. The risks also include the accidental transfer of cancerous cells in a tumour to the bloodstream and other parts of the body, a process known as “seeding”.

The use of a thinner needle would be preferable, but the smaller sample amounts removed are often not enough to provide clear results – until now, says Jerker Widengren, project coordinator for the EU-funded FLUODIAMON[2]project and a professor at the KTH Royal Institute of Technology in Sweden.

FLUODIAMON has opened the way to using thinner needles (cross-section area of about 0.1mm$^2$) by demonstrating that high-resolution fluorescence microscopy allows doctors to get the diagnostic information they need from smaller tissue samples.

The technique involves marking molecules with fluorescent chemicals – called ‘fluorophores’ – which glow when light is applied. The wavelength, intensity and polarisation of the fluorophores allow scientists to image the spatial distributions of target molecules in sampled cells at a resolution much higher than was possible before. The higher resolution provides them with much more information, enabling them to make an accurate diagnosis.

**Less sample, more information**
FLUODIAMON advanced and adapted this technique for diagnostic purposes, devised fluorescent marker molecules with unique features to bind to target molecules on cells in the samples, and developed new software to analyse the acquired images. In parallel, the project developed new types of fine needles to improve their ability to obtain representative tissue samples and reduce the risk of cancer cell seeding.

“Altogether the project’s techniques represent a new way to combine diagnostic reliability with safe, minimally invasive sampling,” says Widengren.

He cautioned that it may take time before the medical profession starts using the technique as an alternative to core-needle biopsies.

“The medical profession is very conservative,” he explains. “But as use of florescence imaging technology becomes easier and the costs go down I am sure it is just a matter of time.”

**Breakthrough image technique**

FLUODIAMON took advantage of a relatively recent breakthrough in imaging techniques developed by Stefan Hell of the Max-Planck Society’s Institute for Biophysical Chemistry in Germany.

Hell, who participated as a researcher in FLUODIAMON, was a joint winner of the 2014 Nobel Prize in chemistry for his development of STED microscopy. This provides super-resolution imaging by selectively deactivating fluorophores in a sample.

STED microscopy was one of the main types of florescence imaging techniques investigated by the project. The researchers also employed other florescence imaging techniques – multi-parameter detection imaging (MFDi), transient state (TRAST) imaging and two-photon excitation (TPX) spectroscopy.

Each technique provides additional information to help doctors diagnose whether cells are cancerous, says Widengren. For example, the project demonstrated that TRAST imaging is able to detect the differences in metabolic activity typically occurring in cancer cells.

With the end of the project in May 2012, the former partners have continued working on the florescence imaging techniques developed during FLUODIAMON. Widengren, for example, is developing the TRAST system further to investigate if differences in oxygen consumption in cells could provide a sign of cancer.

He is also leading a locally funded project in Stockholm to examine whether STED imaging of proteins in the blood’s platelets could be a sign of cancer.

**See also:**
CORDIS [3]

**Project:**
Ultra-high resolution and ultra-sensitive fluorescence methods for objective sub-cellular diagnosis of early disease and disease progression in breast and prostate cancer

**Project Acronym:**
FLUODIAMON

**Project website:**
http://www.biomolphysics.kth.se/fluodiamon [2]

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