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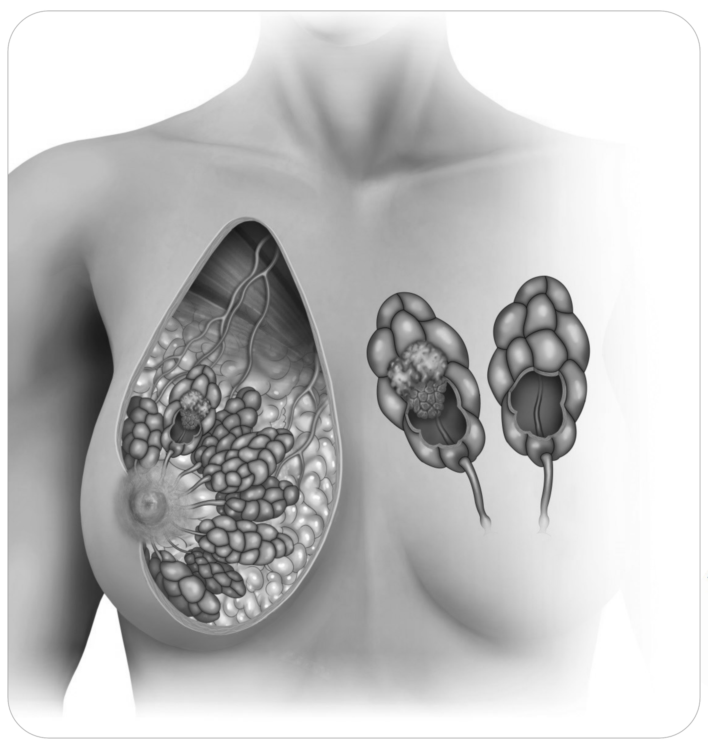
Demonstration of Parallel AFM Read-out for Rapid Sensing of Cancer

G. Weder, J. Cottet, M. Favre, R. Ischer, L. Le Reste, M. Liley and H. Heinzelmann

CSEM SA, Neuchâtel

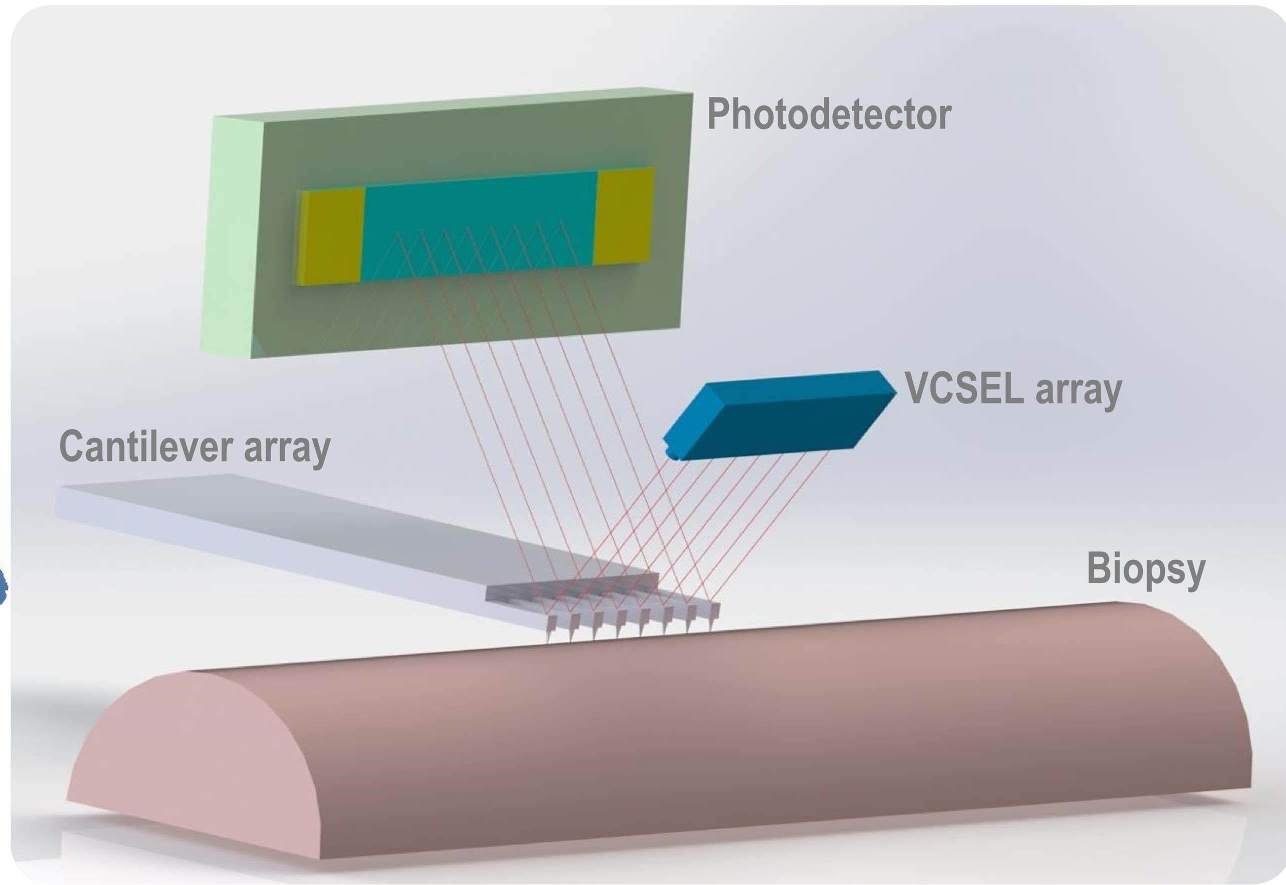
The development of cancer is associated with mechanical changes in both cells and extracellular matrix in living breast tissue. Atomic force microscopy (AFM) is an ideal tool to investigate the mechanical properties of cells in biopsy samples in a reliable way. It is, however, slow. This is a significant limitation since a large number of measurements (force-distance curves) on the biopsy sample is required for a statistically meaningful set of data. CSEM is developing a new rapid diagnostic tool using parallelized AFM cantilevers to investigate breast biopsy samples. The major innovation of this development is to reduce the analysis time of the tissue mechanical profile from hours to minutes for clinical use.

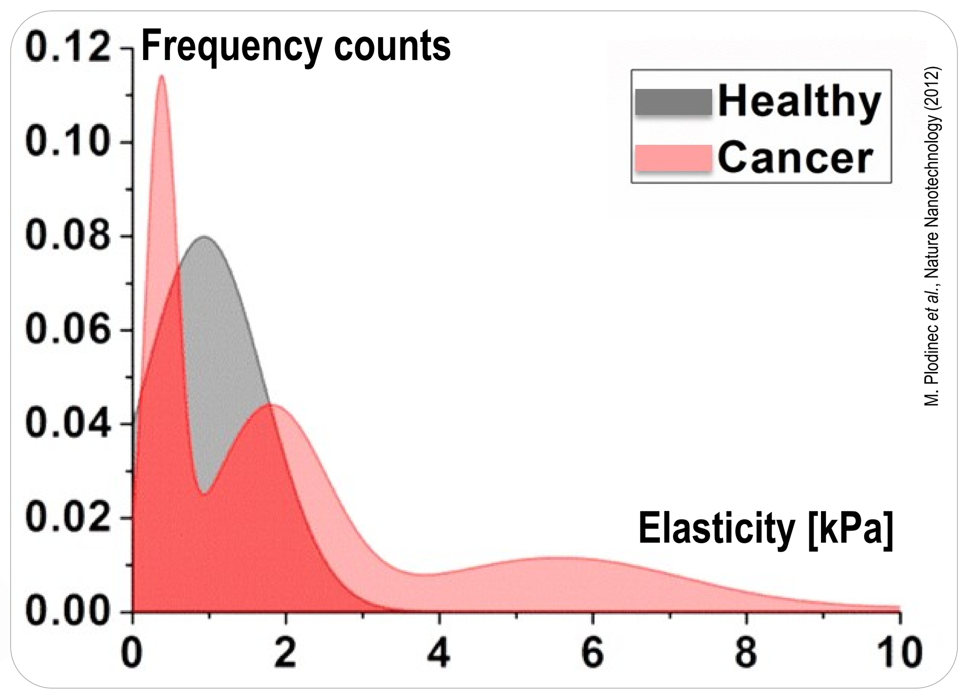
CONCEPT



I. BREAST BIOPSY SAMPLES

II. PARALLEL AFM NANOINDENTATION





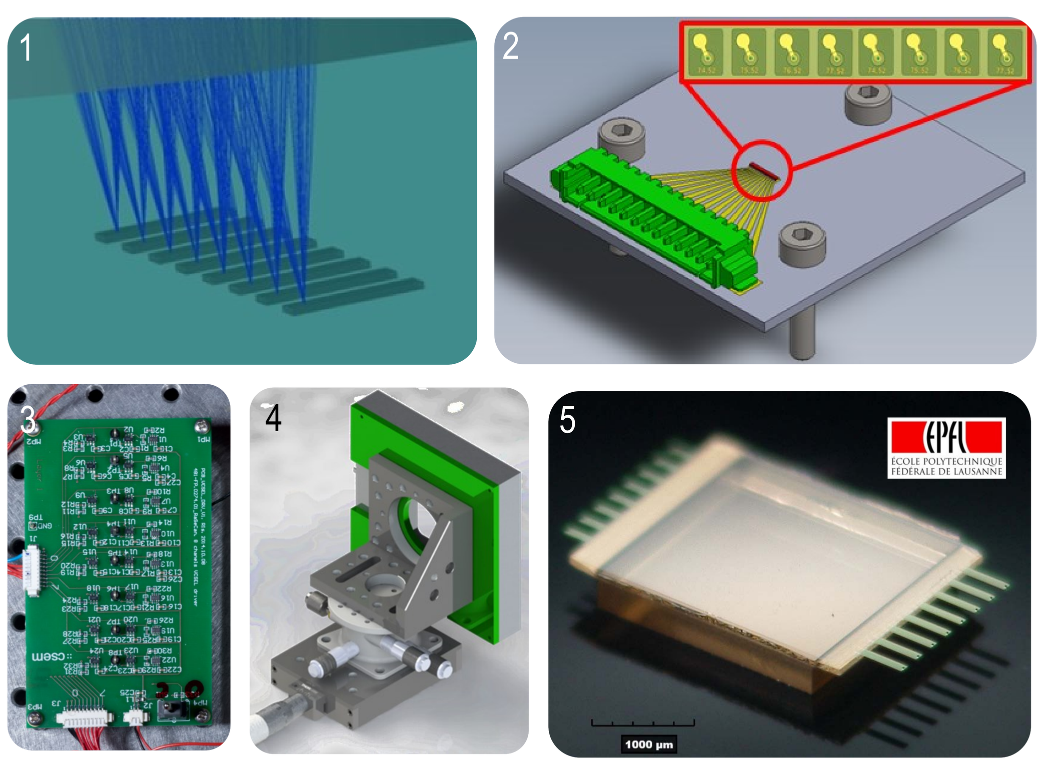
III. TYPICAL HEALTHY AND CANCER ELASTICITY PROFILES

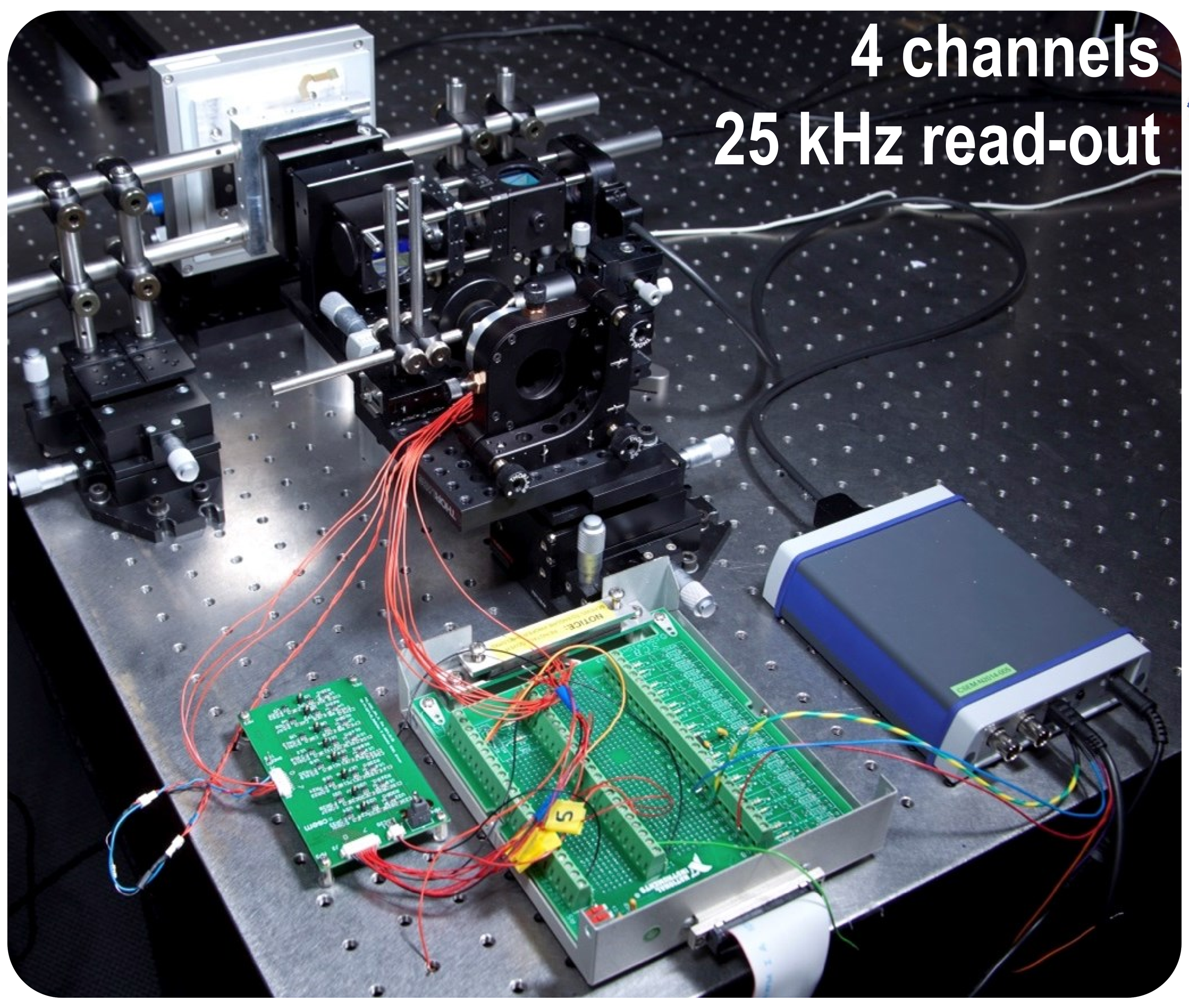
Results DEMONSTRATOR phase 1

The standard procedure uses a single AFM cantilever to acquire multiple elasticity maps across the entire biopsy sample. To fill this need of reducing analysis time, CSEM worked on the replacement of this single AFM cantilever by a cantilever array of several AFM cantilevers operating in parallel. It involves an innovative parallel read-out of the probes. The strategy consists in reading a cantilever array with a VCSEL array (Vertical Cavity Surface Emitting Laser). Each laser beam is focused at the end of one cantilever of the array, and the reflected light is detected using a photodetector. The proof of concept of parallel AFM read-out was demonstrated on agarose gels showing soft tissue-like mechanical properties.

IV. INTERDISCIPLINARY APPROACH

OPTICS simulations[1]
PACKAGING vcsel array[2]
ELECTRONICS vcsel driver[3]
INSTRUMENTATION micropositioners & scanners[4]
MEMS MICROFABRICATION cantilever array[5]
SIGNAL PROCESSING photodetector & software





V. INTEGRATION

VI. PARALLEL FORCES-INDENTATION CURVES

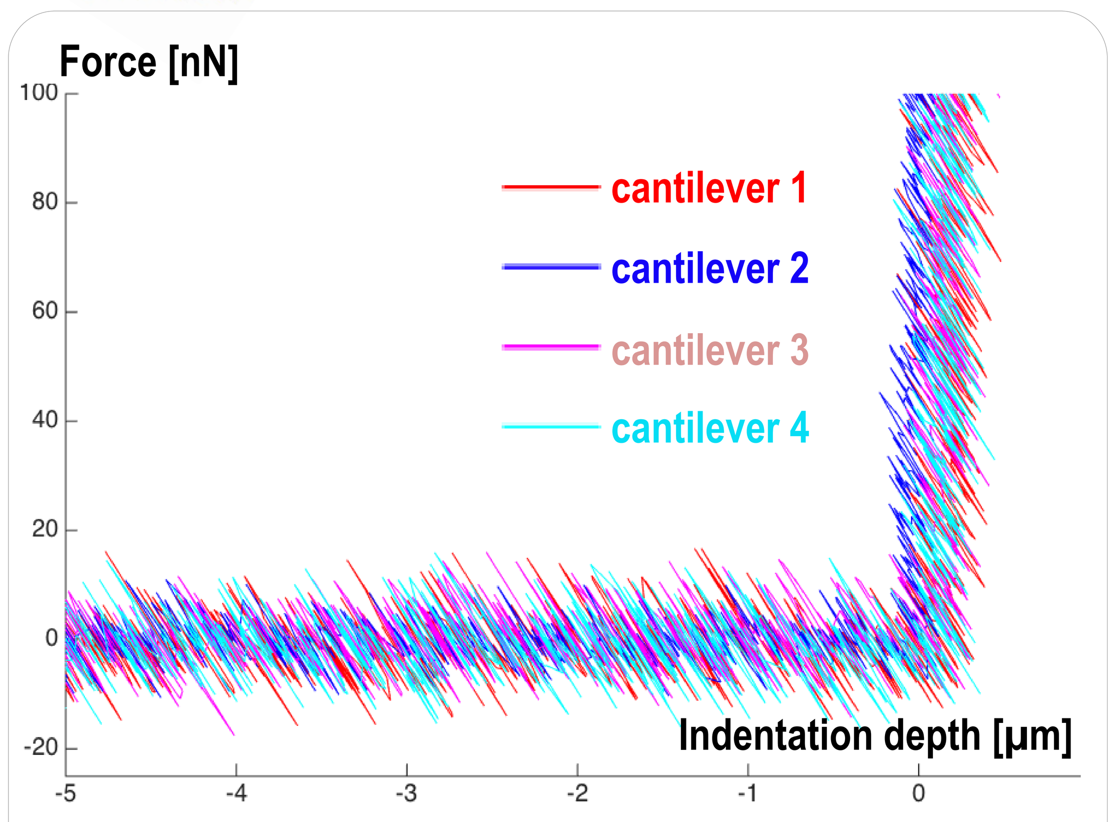


Figure: Typical force-indentation curves on glass for calibration

Outlook PROTOTYPE phase 2

The demonstrator will be improved in a second phase towards a prototype. Parallelized AFM measurements in combination with the commercial AFM-based diagnostic tool called ARTIDIS® (Automated and Reliable Tissue DIagnosticS – developed by Nanosurf) should open new perspectives for clinical application: data acquisition time will be reduced to minutes.

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