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Parallel AFM analysis of biopsies for cancer diagnosis

csem

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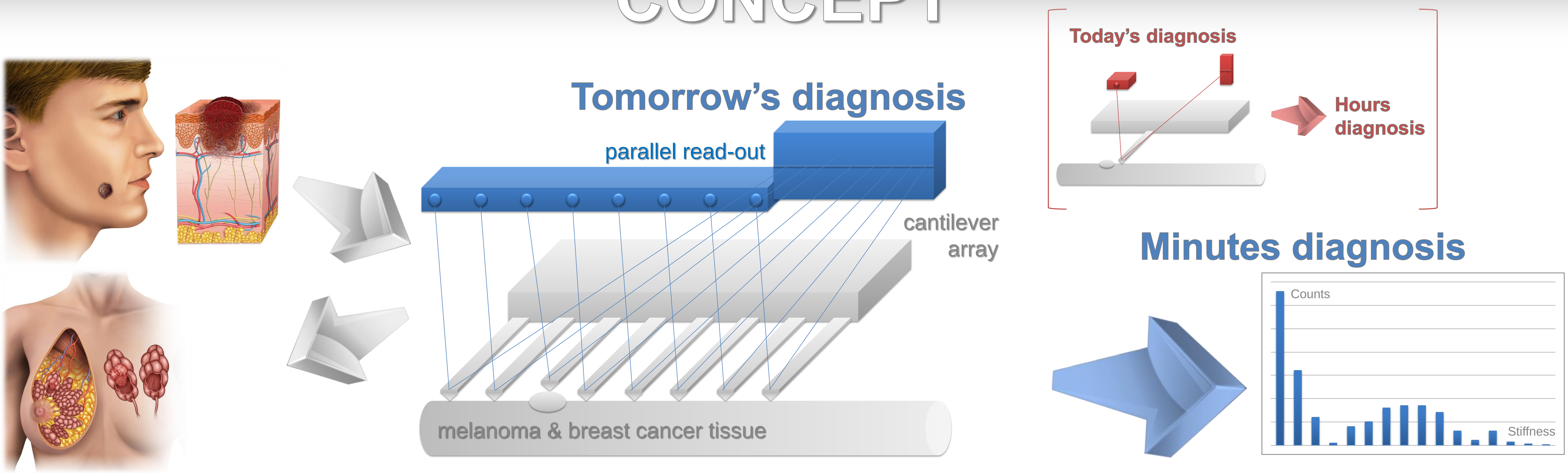
The aim is to develop a rapid diagnostic tool for cancer. Parallelized mechanical sensors are being developed to investigate biopsy samples in a fast and reliable way. A large number of force versus distance curves is acquired on the biopsy sample to get enough statistics for a representative value of the cell elasticity (Young's modulus) of the tissue under investigation. This process is highly automated, which will make the application by the medical doctor easier compared to the optical analysis of histologic preparations. The required time for this type of diagnosis will be reduced from hours to minutes. Therefore, the medical doctor will receive the information promptly and will be able to decide about the therapy.

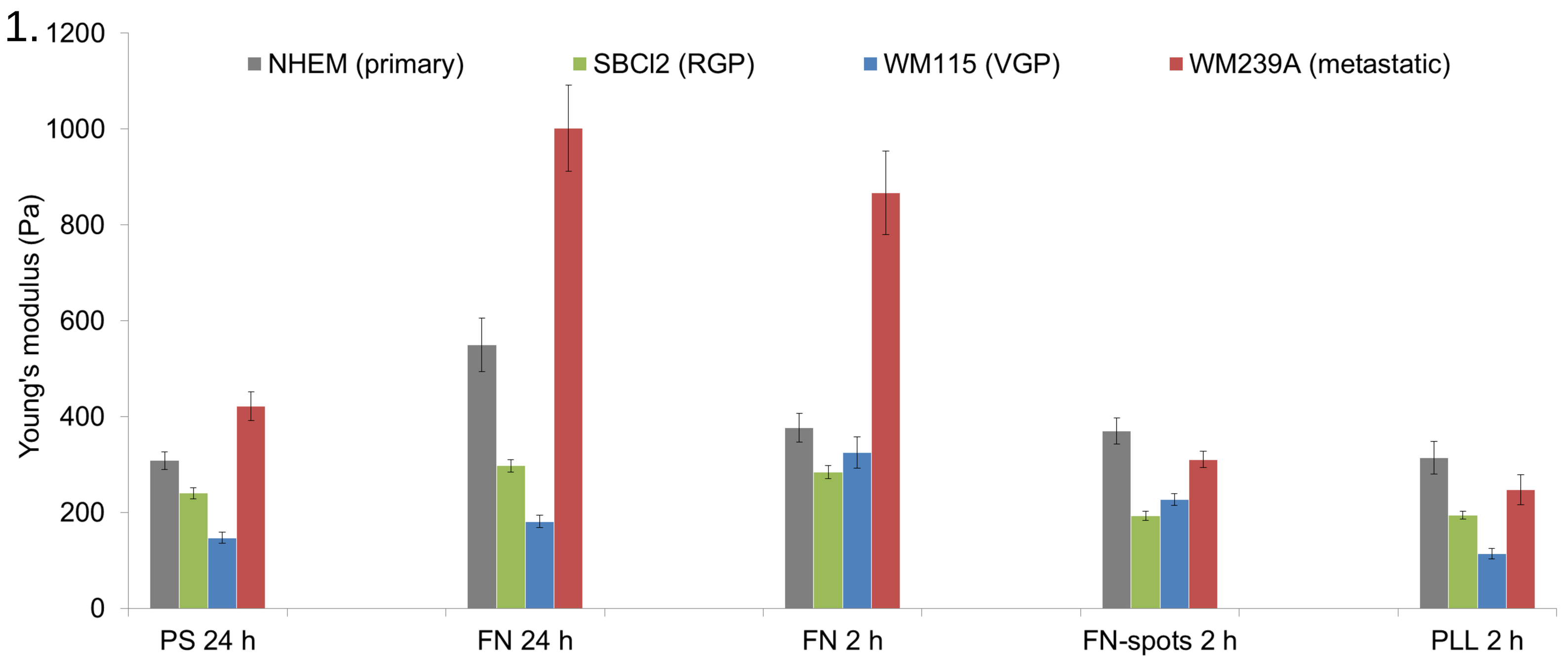
CONCEPT



"A rapid diagnostic tool for cancer dignosis based on parallelized mechanical sensors to investigate melanoma and breast cancer biopsies"

The stiffness of tumor cells varies during cancer progression. Using a single AFM (Atomic Force Microscopy) cantilever, we examined how the stiffness of melanoma cells varies during progression from non-invasive Radial Growth Phase (RGP) to invasive Vertical Growth Phase (VGP) and to metastatic tumors. We showed that transformation of melanocytes to RGP and to VGP cells is characterized by decreased cell stiffness. However, further progression to metastatic melanoma is accompanied by increased cell stiffness and the acquisition of higher plasticity by tumor cells, which is manifested by their ability to greatly augment or reduce their stiffness in response to diverse adhesion conditions.

1.



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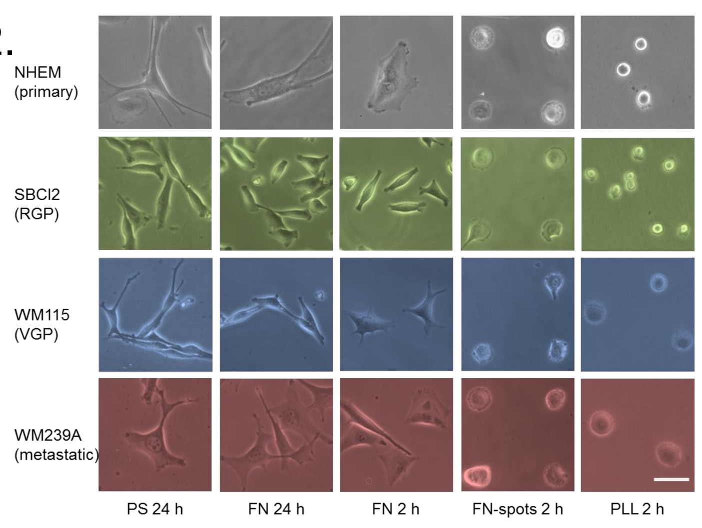

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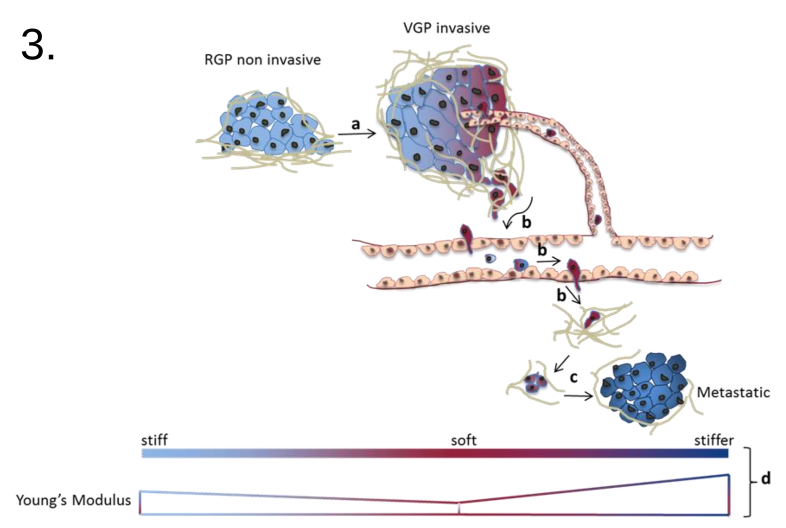


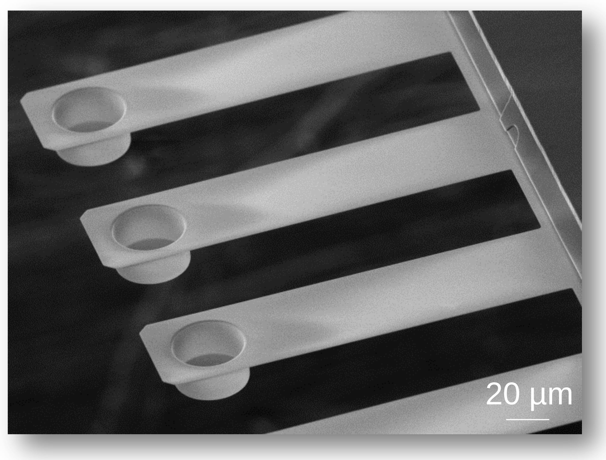
1. Melanoma cell elasticity is influenced by adhesion substrate and correlates with cell morphology. Histograms of average Young's Modulus of normal human epidermal melanocytes (NHEM) and melanoma cells plated on polystyrene (PS), fibronectin (FN) or poly-L-lysine (PLL) for 2 hours or 24 hours; error bars indicate the standard error.
2. Phase-contrast images of the analyzed cells on the different substrates; scale bar is 50 µm.
3. Model showing the increased plasticity of melanoma cells during malignant progression. Transformation of RGP melanoma cells into VGP cells is associated with decreased cell stiffness which promotes cell deformation, invasion, and intravasation (a, b, d). After extravasation, metastatic melanoma cells have to adapt to a new tissue environment and this final step of metastatic colonization is characterized by additional changes in cell stiffness (c, d).

Weder *et al.* Nanomedicine, 2014, 10(1):141-8.

Cancer diagnosis has now to be extended on ex vivo tissue in a fast and reliable way

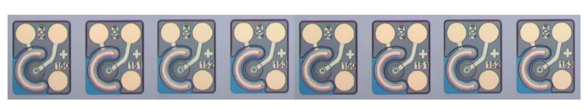
Probe

- 8-cantilevers array
- 100-250 µm pitch
- 50-100 µm wide
- 200-500 µm long
- 0.05 N/m
- 10 µm pyramidal tip
- Silicon nitride



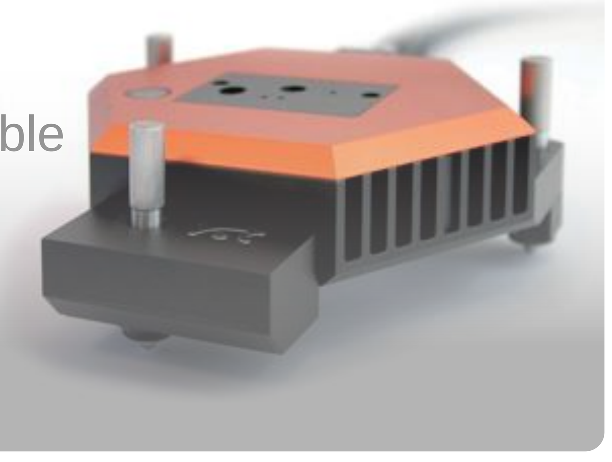
Read-out

- 8-VCSELs array
- 850 nm emission
- 10 Gb/s
- [Vertical Cavity Surface Emitting Laser]



Integration

- FlexAFM
- Commercially available
- Nanosurf AG



A new AFM instrument including cantilever array microfabrication and read-out, positioning and scanning mechanics, and prototyping is coming out to reduce the diagnosis time of melanoma and breast cancer by the parallelization of mechanical sensors. Data acquisition and processing will deliver quantitative elasticity numbers for future therapy.

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