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A new medical device for in-vivo isolation of circulating tumor cells in non small cell lung cancer (NSCLC) patients

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Abstract

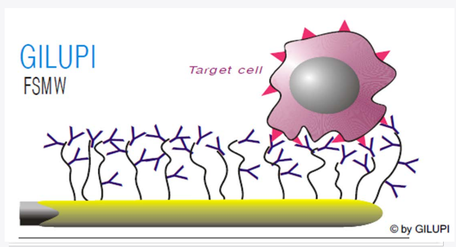
In NSCLC, the number of circulating tumor cells (CTCs) is discussed as a prognostic and stratification biomarker, and could also judge the treatment efficacy. Currently, CTCs are isolated in vitro from small limited volumes of blood samples. Furthermore, results for NSCLC are scarce. The aim of the study was to assess a functionalized and structured medical wire (FSMW) for in vivo isolation of CTCs directly from the blood of NSCLC patients.

The device was inserted in a cubital vein through a standard cannula for thirty minutes. The interaction of target CTCs with the FSMW was mediated by an antibody directed against the epithelial cell adhesion molecule (EpCAM). To confirm the CTCs binding to the wire, the immunohistochemical staining against EpCAM as well as CD45 for negative cell selection was performed. There were 72 applications of the wire in 48 stage I-IV NSCLC patients (12 double applications) and 12 non cancer patients. Enumeration data from 34 NSCLC patients with 46 applications and 7 non cancer patients (the other devices were not used for enumeration) were assessed. For 21 devices, results were compared to the Cell Search system.

The device was well tolerated in all 72 applications without side effects. We obtained in vivo isolation of CTCs in 32 of 34 NSCLC patients (94.1 %). The sensitivity was similar for early and late stage NSCLC patients. The median (range) of isolated EpCAM-positive CTCs was 13 (0-300). In the non cancer patients, no CTCs were detected (100 % specificity). In paired samples, only 1 patient with CTCs was detected by the Cell Search system.

Functional Structured Medical Wire

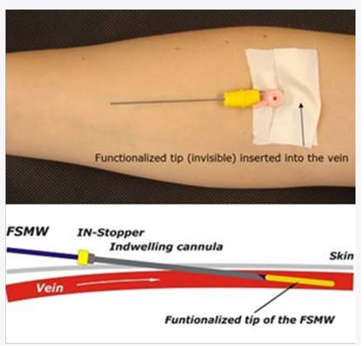
Figure 1. The biological functionalization of the wire is achieved using an antibody against the epithelial tumor marker EpCAM. EpCAM antibodies bound to a hydrogel coating of the wire mediate specific binding of EpCAM expressing target cells.



Nanodetector

Insertion into patient´s vein at the doctor´s office

30 minutes exposure time in a vein



Diagnostics
- *cytology*
- *PCR, etc.*

Result ← *Decision*

Patient population

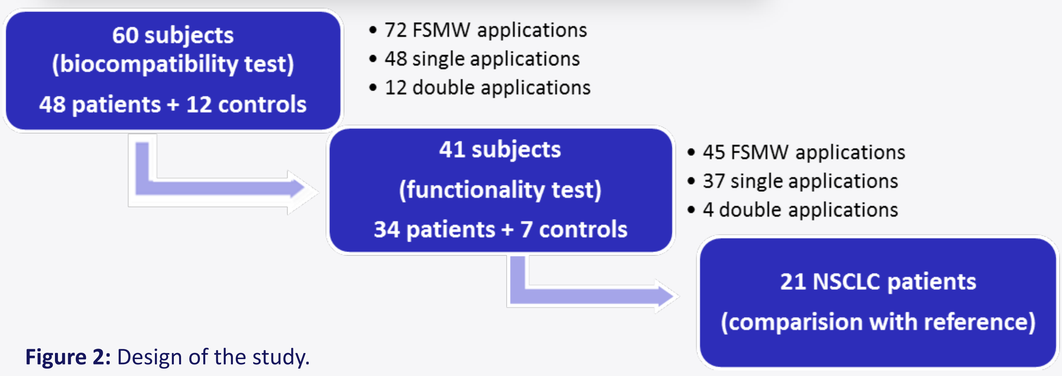


Figure 2: Design of the study.

Immunocytochemical analysis

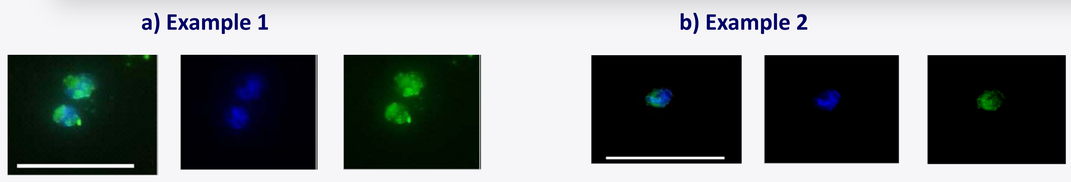
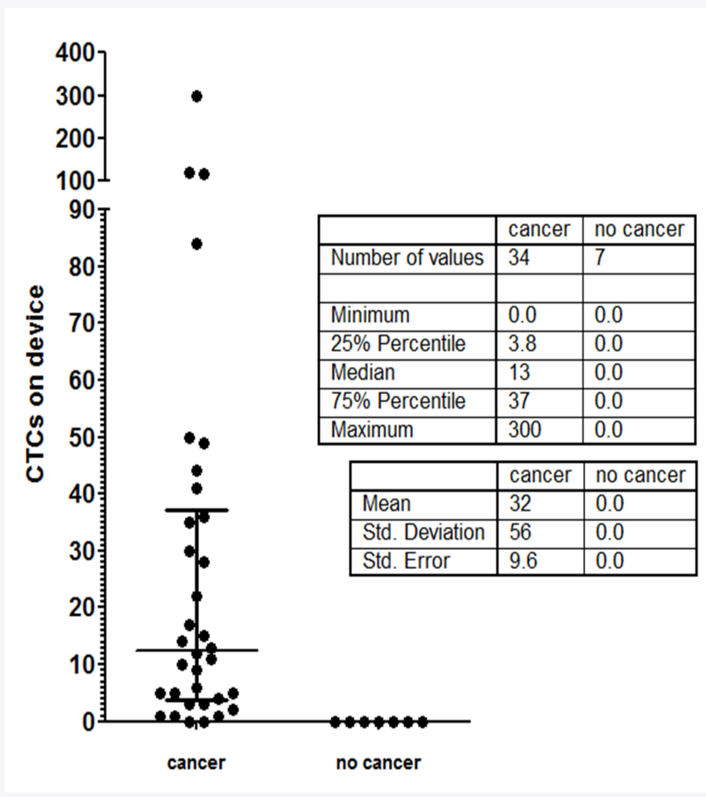


Figure 3: Immunocytochemistry analysis of CTCs captured *in vivo* with the FSMW in the blood of lung cancer patients. The CTCs were identified and enumerated via positive EpCAM and DAPI staining (respective green and blue staining in top panels), size and morphological characteristics. The white scale bar corresponds to 50µm.

Results *in vivo* captured CTCs



	cancer	no cancer
Number of values	34	7
Minimum	0.0	0.0
25% Percentile	3.8	0.0
Median	13	0.0
75% Percentile	37	0.0
Maximum	300	0.0

	cancer	no cancer
Mean	32	0.0
Std. Deviation	56	0.0
Std. Error	9.6	0.0

Figure 4: Results of CTCs captured *in vivo* with the FSMW in the blood of NSCLC patients.

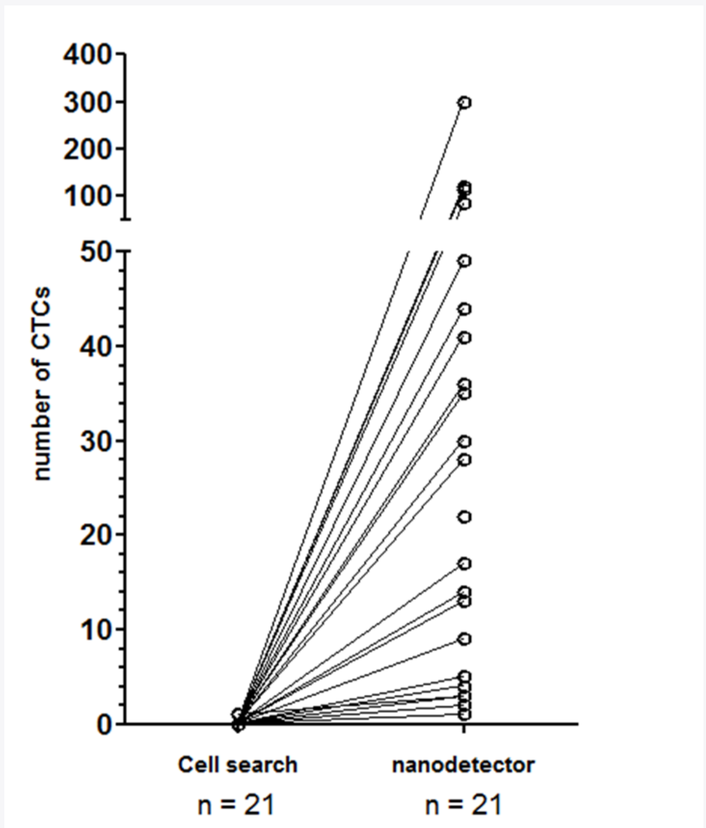


Figure 5: Comparison of the methods, the FSMW *in vivo* and the Cell Search® method *in vitro*.

- In 100% of paired samples:
  FSMW >= Cell Search

Summary

- There were no AEs. All patients showed very good biocompatibility and no side effects.
- FSMW sensitivity for in vivo isolation of CTCs in NSCLC patients was **94.1 %** (32/34)
- In paired samples, only 1 patient with CTCs was detected by the Cell Search system.
- Detection of CTC´s could be shown in **all occurred tumor stages** (especially early stages)
- The implementation of FSMW into clinical practice may improve early detection, prognosis and therapy monitoring of NSCLC patients as well as the molecular analysis of the CTCs, resulting in personalized treatment regiments

Also founded by: