# Comparison of circulating tumor cell capture efficiency of the CellCollector™ technology *vs* CellSearch® in prostate cancer patients at multiple time points

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## ABSTRACT

Castration-resistant prostate cancer is the second most common cause of cancer-related death in men. Since most prostate cancer patients have a biopsy performed only at the time of diagnosis, representative tumor tissue samples giving real-time information about the disease status are generally missing. Therefore, the detection of circulating tumor cells (CTCs) in the blood of patients with castration-resistant prostate cancer might, in addition to their prognostic value, serve as liquid biopsy, complementing or replacing prostate-specific antigen determination in predicting and monitoring the response to different therapies. However, capturing these rare cells from whole blood is still a major challenge that needs significant improvement. Here we present the results of a comparison study, in which we compared CellCollector™, a unique *in vivo* approach for the isolation of CTCs, with CellSearch®, the current standard.

The comparison study included 25 prostate cancer patients (15 with localized [PCa-l] and 10 with metastasized prostate cancer [PCa-m]) and 29 individuals in the control group (24 men with benign prostate hypertrophy and 5 women). At multiple time points of treatment, CTCs were enumerated (42 applications for PCa-l and 29 for PCa-m). CellCollector™, a medical wire coated with epithelial cell adhesion molecule antibodies, was inserted in the cubital vein and incubated for 30 min. The captured CTCs were identified by immunofluorescence staining using cytokeratin- and DAPI-positive as well as CD45-negative as criteria. For the CellSearch® measurements, a blood draw of 7.5 mL blood was performed. We found that in 77.5% (55/71) of applications, the cancer patient was positive for CTCs using CellCollector™ (PCa-l: 55.2% [16/29]; PCa-m: 88.1% [37/42]). In contrast, CellSearch® resulted in only 42.2% (30/71) in the detection of CTCs (PCa-l: 17.2% [5/29]; PCa-m: 61.9% [26/42]). The counting after application to benign prostate hypertrophy patients resulted in 20.8% (5/24) in low numbers of CTCs and 12.5% (3/24) regarding CellSearch®. Two women showed a very low number of cytokeratin-positive cells (1 and 3, respectively). In addition, we found a correlation of the CTC levels detected by CellCollector™ and CellSearch® with the prostate-specific antigen level during treatment. In summary, our comparison study shows an improved sensitivity of CellCollector™ compared with the current standard regarding the isolation of CTCs from prostate cancer patients, and gives new insights in the value of CTCs for monitoring prostate cancer treatment.

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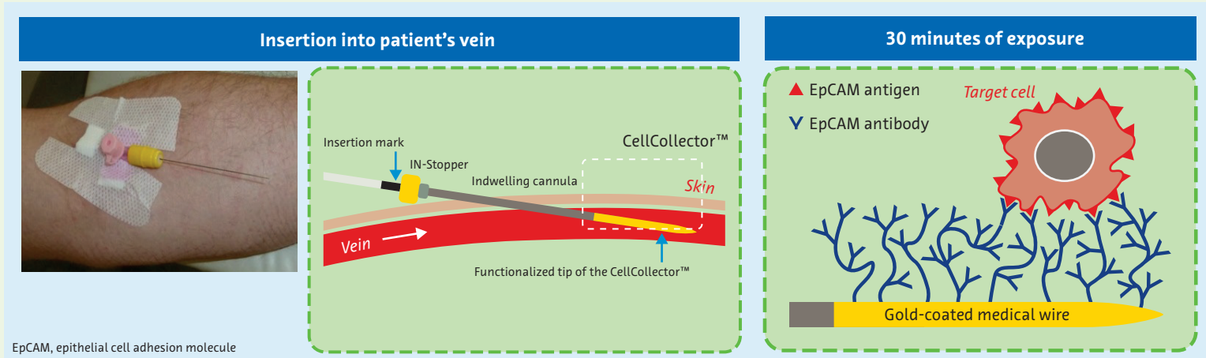
## INTRODUCTION

- Representative tumor tissue samples giving real-time information about the disease status are often missing in castration-resistant prostate cancer
- Circulating tumor cells (CTCs) in patients' blood might serve as a liquid biopsy, predicting and monitoring the response to different treatments
- However, capturing these rare cells from whole blood is still a major challenge, especially in the early setting, and efficient isolation methods are needed
- Here we present the results of a comparison study in which we compared CellCollector™, a unique *in vivo* approach for the isolation of CTCs (Figure 1), with CellSearch®, the current standard




EpCAM, epithelial cell adhesion molecule

**Figure 1.** Application procedure[1]

## METHODS

- The study included 25 prostate cancer patients (15 with localized and 10 with metastatic prostate cancer [PCa-l and PCa-m]) and 29 individuals in the control group (24 men with benign prostate hypertrophy [BPH] and 5 women) (Figure 2)
- At multiple time points of treatment, CTCs were enumerated and prostate-specific antigen (PSA) levels were determined
- CellCollector™, a medical wire coated with EpCAM antibodies, was inserted in the cubital vein and incubated for 30 min
- For the CellSearch® measurements, a blood draw of 7.5 mL blood was performed
- The captured CTCs were identified by immunofluorescence staining using cytokeratin- and Hoechst-positive as well as CD45-negative as criteria

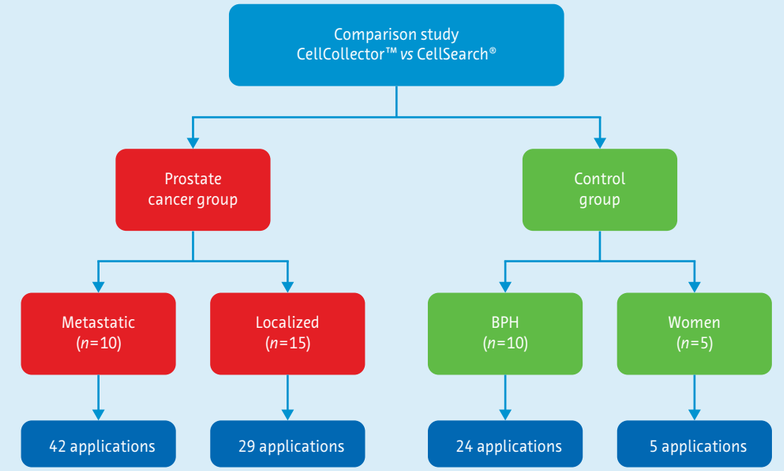
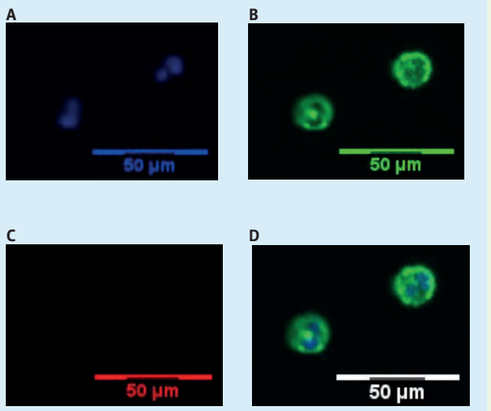



**Figure 2.** Trial design

## RESULTS

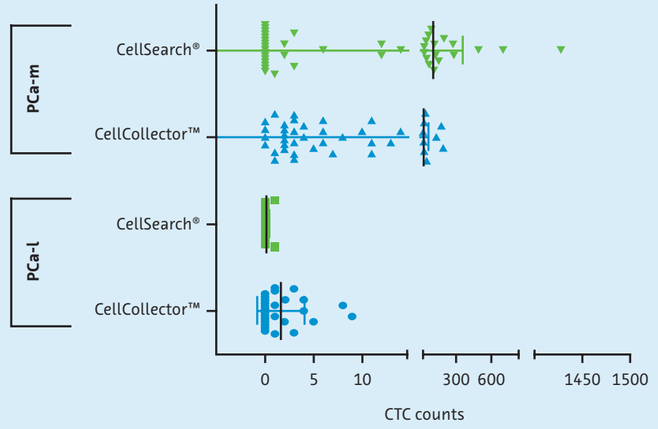
### Application of CellCollector™ led to the isolation of CTCs in prostate cancer patients (Figure 3)




The CTCs were identified and enumerated by positive nuclear staining (Hoechst) (A), positive cytokeratin (B), negative CD45 staining (C), and overlay of all images, size, and morphological characteristics (D)

**Figure 3.** Immunofluorescence images of the CTCs captured with CellCollector™ in the blood of prostate cancer patients

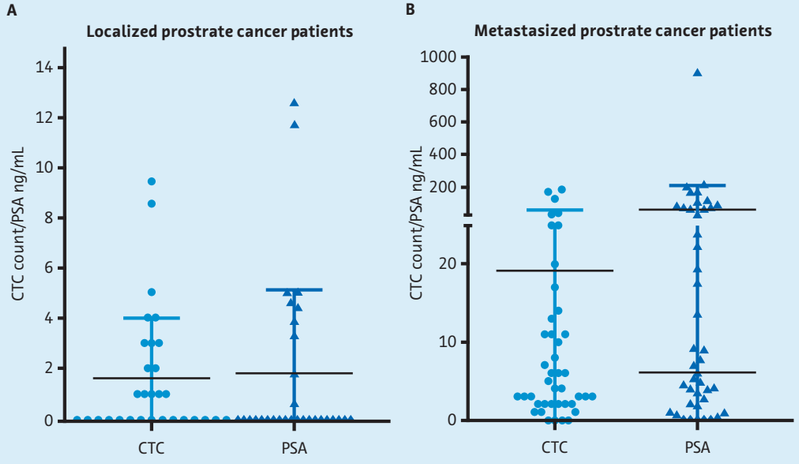
### CellCollector™ showed a higher sensitivity than the CellSearch® system, especially in localized prostate cancer patients (Figure 4)




We found that in 77.5% (55/71) of applications (PCa-l: 55.2% [16/29]; PCa-m: 88.1% [37/42]), the cancer patient was positive for CTCs using CellCollector™. In contrast, CellSearch® resulted only in 42.2% (30/71) in detecting CTCs (PCa-l: 17.2% [5/29]; PCa-m: 61.9% [26/42]). In rare cases, the control groups showed very low numbers of cytokeratin-positive cells

**Figure 4.** Comparison of the CTC counts obtained with CellCollector™ and CellSearch® in prostate cancer patients (PCa-l and PCa-m)

### The detected CTC levels correlated with the PSA level




(A) In localized prostate cancer patients, we detected a mean of 1.43 CTCs. The mean PSA level was 0.04 ng/mL. (B) In metastatic prostate cancer patients, we detected a mean of 19.9 CTCs. The mean PSA level was 61 ng/mL

**Figure 5.** CTC counts and PSA levels using CellCollector™

## CONCLUSIONS

- **This comparison study shows an improved sensitivity of CellCollector™ compared with the current standard regarding the isolation of CTCs from prostate cancer patients**
- **The detected CTC levels correlated with the respective PSA levels**
- **CTCs hold great promise as liquid biopsy for monitoring prostate cancer treatment**

### Reference

1. GILUPI. 2014. Available at: http://www.gilupi.de/gilupimethod.html.

### Acknowledgments

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