# NUMERICAL ASSESSMENT OF THE EFFICIENCY OF A NEW MINIMALLY INVASIVE PROBE FOR THE ISOLATION OF CIRCULATING TUMOR CELLS

Felix Hehnen (1,2), Henri Wolff (1,2), Sophia Krakowski (1,2), Gabi Bondzio (3), Michael Lommel (1,2), Ulrich Kertzscher (1,2) and Paul Friedrich Geus (1,2)

1. Deutsches Herzzentrum der Charité, Institute of Computer-assisted Cardiovascular Medicine, Biofluid Mechanics Laboratory, Augustenburger Platz 1, Berlin 13353, Germany;

2. Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Institute of Computer-assisted Cardiovascular Medicine, Charitéplatz 1, 10117 Berlin, Germany

3. Invicol GmbH, Köpenicker Straße 325, Berlin 12555, Germany

### **Isolation of CTCs**

Liquid biopsy, particularly the isolation of circulating tumor cells (CTCs) from blood, is a promising approach in the fight against cancer. CTCs are cells that have been shed from the primary tumor or metastatic deposits and circulate through the bloodstream. The analysis of CTCs and their quantification in blood can be used to diagnose cancer, for prognostic evaluation, treatment stratification and treatment monitoring, as shown in the review by Lin et al. [1]. However, the reliable isolation of CTCs continues to be a technical challenge [2,3]. This is due to their rarity in blood: it is assumed that there are less than 10 CTCs / mL in cancer patients [4].

To overcome the limitations of current isolation methods, screening large blood volumes in vivo was recommended to increase CTC yield [5]. Therefor the company Invicol (Berlin, Germany) developed the BMProbe<sup>TM</sup>: A minimally invasive device with a twisted geometry to increase the interaction with blood and the screened blood volume.

## **CFD study**

In this study, using multiple Computational Fluid Dynamics (CFD) simulations, the efficiency of the BMProbe<sup>™</sup> is quantified. In the following, the term efficiency refers to the ability of the probe to isolate CTCs from the bloodstream. Since a direct simulation of cell attachment has many limitations, high computational costs and is usually associated with inaccuracies, the efficiency in this study is determined indirectly via three parameters that are known to have an influence on cell attachment. These parameters include the screened blood volume, the residence time of cells near the probe's surface and the transport of cells to the probe's surface (negative wall normal rate). Further, the influence that the geometry of the BMProbe<sup>™</sup>, the vein diameter and the blood flow velocity have on the efficiency of the BMProbe<sup>TM</sup> is presented.

#### Results

The numerical data suggests that the geometry has a strong influence on cell binding efficiency. Increasing the number of windings improves the transport of cells to the surface (negative wall normal rate) and the screened blood volume but decreases the residence time of particles in the close vicinity of the probe. When compared to experimental data, the screened blood volume and the wall normal rate indicate cell attachment very well, whereas the residence time does not show a significant impact on the attachment of cells. For the 32-windings BMProbe<sup>TM</sup>, the screened blood volume is determined to be 130 mL – 313 mL, depending on the vein diameter, which is a multiple of the volume achieved by common CTC isolation techniques.

#### References

- Lin, D.; Shen, L.; Luo, M.; Zhang, K.; Li, J.; Yang, Q.; Zhu, F.; Zhou, D.; Zheng, S.; Chen, Y.; et al. Circulating Tumor Cells: Biology and Clinical Significance. Signal Transduct. Target. Ther. 2021, 6, doi:10.1038/s41392-021-00817-8.
- Raufi, A.G.; May, M.S.; Hadfield, M.J.; Seyhan, A.A.; El-Deiry, W.S. Advances in Liquid Biopsy Technology and Implications for Pancreatic Cancer. Int. J. Mol. Sci. 2023, 24, doi:10.3390/ijms24044238
- Vidlarova, M.; Rehulkova, A.; Stejskal, P.; Prokopova, A.; Slavik, H.; Hajduch, M.; Srovnal, J. Recent Advances in Methods for Circulating Tumor Cell Detection. Int. J. Mol. Sci. 2023, 24, doi:10.3390/ijms24043902.
- Haber, D.A.; Velculescu, V.E. Blood-Based Analyses of Cancer: Circulating Tumor Cells and Circulating Tumor DNA. Cancer Discov. 2014, 4, 650–661, doi:10.1158/2159-8290.CD-13-1014.
- Batool, S.M.; Yekula, A.; Khanna, P.; Hsia, T.; Gamblin, A.S.; Ekanayake, E.; Escobedo, A.K.; You, D.G.; Castro, C.M.; Im, H.; et al. The Liquid Biopsy Consortium: Challenges and Opportunities for Early Cancer Detection and Monitoring. Cell Reports Med. 2023, 4, 101198, doi:10.1016/j.xcrm.2023.101198

## Acknowledgements

This research was funded by the Investitionsbank Berlin and the European Regional Development Fund (grant no. 10194288).

