maintrac® Liquid Biopsy

Innovative Laboratory Diagnostics Before, During and After Cancer Therapy

maintrac

What is maintrac®?

maintrac® is a highly sensitive, minimally invasive laboratory test, that enables the detection of living **circulating tumor cells in the blood (Liquid Biopsy).** The test can be used **before, during and after therapy**[1]. Circulating tumor cells can thus be used as a **biomarker**[2].

Tumor cells can detach from the primary tumor or metastases at very early stages and can enter the bloodstream. These cells are called **circulating epithelial tumor cells** (CETCs/CTCs). They are responsible for the **recurrence of the disease**. Systemic therapy is designed to eliminate circulating tumor cells. During the course of disease, the number and characteristics of circulating tumor cells may change. The **maintrac®** method is **highly sensitive** for the **early detection** of these changes[3].

Approximately 90% of all tumors are of epithelial origin. Using **maintrac® Liquid Biopsy**, circulating tumor cells can be detected in a **blood sample** due to the expression of the surface protein EpCAM[4].

maintrac® Liquid Biopsy can be used for all **solid epithelial tumors**[1,5,6,7].

We offer the following examinations

- maintrac® **Cell Counting**
- maintrac® **Therapeutic Substance Testing**
- maintrac® **Therapy Relevant Tumor Cell Characteristics**
- stemtrac® **Tumorspheres**

Innovative Laboratory Diagnostics of Circulating Tumor Cells Before, During and After Cancer Therapy

maintrac® Quality Features

- **Highly sensitive** detection of living circulating tumor cells without enrichment steps[1]
- **Quantitative** determination of living tumor cells from peripheral blood[3]
- **Fast** and **reproducible**[1]
- Performed in a DIN EN ISO 15189 **certified laboratory**, accredited by DAkkS (ILAC approved)[8]

Recommendations for the time of blood sampling

- Before the start of neoadjuvant chemotherapy
- Before surgery
- 3 weeks after surgery
- 2-3 weeks after a chemotherapy cycle
- 2-3 weeks after completion of a therapy
- Blood samples can be taken at any time during hormone therapy or maintenance therapy.
- Blood samples can also be taken at any time during a therapy-free period.

Requisition

Shipping boxes including the lab request form can be ordered free of charge online at:
www.maintrac.de/en/order/order-maintrac-boxes

Only 15 ml EDTA blood is required for the examination.

Transmission of Results

The results are usually sent **digitally** (DSGVO-compliant) or **by post** within one week.

Costs

At present, the maintrac® diagnostics are not reimbursed by the statutory health insurances, but are a self-pay service. Whether and to what extent privately insured patients can receive reimbursement from their insurance company must be clarified with their own private health insurance company.

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maintrac® Cell Counting makes it possible to **monitor therapy** and **directly observe the activity of the remaining tumor burden** (minimal residual disease) in patients with primary and metastatic tumors prior to the detection by imaging methods[9].

Repeated analysis with **maintrac® Cell Counting** (every 3-6 months), captures the dynamics of the number of circulating tumor cells.

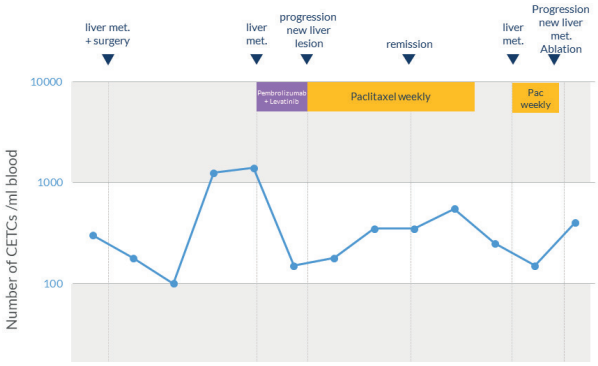
Application:

- **Progression measurements** during and after therapy
- **Monitoring tumour activity** in follow-up care, after the end of therapy and in metastatic situations

maintrac® Cell Counting provides an additional tool for personalized therapy.

Results to date show[9]:

- **Decreasing cell numbers** under systemic therapy indicate a **positive response to therapy**.
- If **cell numbers remain constant** with or without therapy, it can be concluded that the **tumor dynamics** is currently **low**.
- **Repeated increase** of cell numbers indicate an **increased risk of recurrence**



Innovative Laboratory Diagnostics of Circulating Tumor Cells Before, During and After Cancer Therapy

maintrac® Therapeutic Substance Testing

Using **maintrac® Therapeutic Substance Testing,** the **effectiveness of a planned therapy** can be individually **tested in advance** on circulating tumor cells[10].

Depending on tumor type, stage of disease, pretreatments and patient, the **degree of response** of different substances **can vary** considerably.

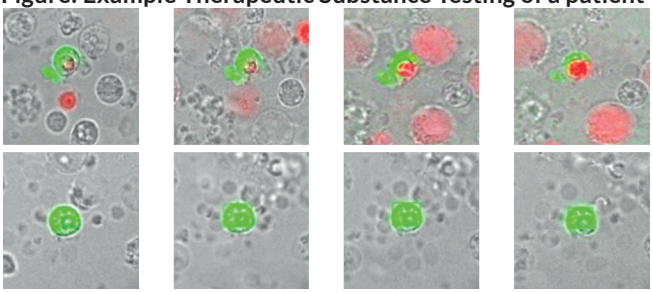
maintrac® Therapeutic Substance Testing shows the **response** (sensitivity) or **nonresponse** (resistance) of **cytotoxic substances** on living circulating tumor cells. These substances can be tested individually or in combination, as well as in different concentrations.

Application:

- **Following the initial diagnosis** of a malignant tumor, before therapy is initiated
- **In the metastatic situation** before a new therapy is started
- In case of **progression** of the disease under treatment

In addition, the effect of **hyperthermia** on circulating tumor cells can also be examined (with or without cytotoxic substances)[10].

Figure: Example Therapeutic Substance Testing of a patient



The upper row shows the **death of a tumor cell** under a **cytotoxic substance** that is **effective** for the patient. In the bottom row, the cytotoxic substance shows no effect.

maintrac® Therapy Relevant Tumor Cell Characteristics

maintrac® Therapy Relevant Tumor Cell Characteristics provide indications of a possible **response** oder **nonresponse** to a chosen therapy.

A series of therapies is only useful if the tumor cells exhibit the respective characteristics. Testing of specific tumor characteristics on circulating tumor cells can provide **additional information** about the **aggressiveness** of the tumor and the **response** to a potential targeted therapy[7].

Both the surface characteristics and the genetic characteristics of the tumor can change during the **course of the disease**. This can influence the efficacy of the therapies applied.

Application:

- When a **tissue biopsy** to obtain information on tumor characteristics is **not possible**
- When a **recurrence/progression** occurs during the course of targeted therapy
- When the **origin of a tumor** is unknown (CUP)

List of biomarkers:

- Hormone receptors (ER, PR, AR)
- Growth factor receptors (Her2/neu amplification, EGFR, EGFR amplification, VEGFR2, c-Kit, IGFR)
- Prostate-associated markers (PSA, PSMA)
- Proliferation markers (Ki67)
- Immunomodulatory molecules (PD-L1, B3-H7)
- Others (apoptosis detection, Mel A / Melan A, PLAP)

stemtrac® Tumorspheres

Tumors release cells into the surrounding tissue and into the blood. They are called circulating epithelial tumor cells (CETCs/CTCs). Amongst them are the so-called **circulating cancer stem cells**, which can be identified with **stemtrac®**. During a period of up to **21 days**, the cancer stem cells grow into **tumorspheres** in vitro. A tumorsphere is a **spherical structure** that results from the cell division of a cancer stem cell[11].

Clinical relevance[11]:

The more stemtrac® Tumorspheres found, **the more aggressive** the tumor and **the higher the risk of metastasis**.

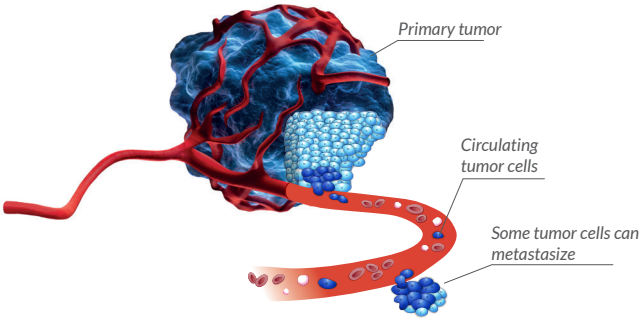
- Metastasized patients have more tumorspheres than non-metastasized patients.
- The number of tumorspheres can be used as a **biomarker** for the presence of already **existing metastases**.
- No tumorsphere growth was observed in subjects without diagnosed cancer.

Application:

The number of **stemtrac® Tumorspheres** can be used in combination with **maintrac®** to monitor the activity of the remaining tumor burden:

- **After the end of therapy** to estimate the aggressiveness and metastatic risk of the remaining tumor cells.
- **In complete remission** when CETCs are increasing.
- **In disease progression** when CETCs are low or undetectable (loss of EpCAM expression, i.e. dedifferentiation of tumor cells)

Your competent partner in oncology.



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[1] Pachmann, Katharina et al. "Standardized quantification of circulating peripheral tumor cells from lung and breast cancer." Clinical chemistry and laboratory medicine vol. 43,6 (2005): 617-27. doi:10.1515/CCLM.2005.107

[2] Pachmann, Katharina et al. "Assessing the efficacy of targeted therapy using circulating epithelial tumor cells (CETC): the example of SERM therapy monitoring as a unique tool to individualize therapy." Journal of cancer research and clinical oncology vol. 137,5 (2011): 821-8. doi:10.1007/s00432-010-0942-4

[3] Pizon, M et al. "Heterogeneity of circulating epithelial tumour cells from individual patients with respect to expression profiles and clonal growth (sphere formation) in breast cancer." Ecancermedicalscience vol. 7: 343 (2013). doi:10.3332/ecancer.2013.343

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[5] Gold, Madeleine et al. "Monitoring of circulating epithelial tumor cells using the Maintrac® method and its potential benefit for the treatment of patients with colorectal cancer." Molecular and clinical oncology vol. 15,4 (2021): 201. doi:10.3892/mco.2021.2363

[6] Pachmann, Katharina et al. "Circulating epithelial tumor cells as a prognostic tool for malignant melanoma." Melanoma research vol. 28,1 (2018): 37-43. doi:10.1097/CMR.0000000000000407

[7] Schott, Dorothea Sonja et al. "Sensitive detection of PD-L1 expression on circulating epithelial tumor cells (CETCs) could be a potential biomarker to select patients for treatment with PD-1/PD-L1 inhibitors in early and metastatic solid tumors." Oncotarget vol. 8,42 (2017): 72755-72772. doi:10.18632/oncotarget.20346

[8] The maintrac method is a method produced in the Dr. Pachmann laboratory (in-house production). It is used exclusively in the Dr. Pachmann laboratory and is therefore not marketed.

[9] Pachmann, Katharina et al. "Monitoring the Response of Circulating Epithelial Tumor Cells to Adjuvant Chemotherapy in Breast Cancer Allows Detection of Patients at Risk of Early Relapse." Journal of Clinical Oncology vol. 26,8 (2008): 1208-1215. doi: 10.1200/JCO.2007.13.6523

[10] Rüdiger, Nadine et al. "Chemosensitivity Testing of Circulating Epithelial Tumor Cells (CETC) in Vitro: Correlation to in Vivo Sensitivity and Clinical Outcome." Journal of Cancer Therapy vol. 4, 2 (2013): 597-605. doi: 10.4236/jct.2013.42077

[11] Pizon, Monika et al. "The number of tumorspheres cultured from peripheral blood is a predictor for presence of metastasis in patients with breast cancer." Oncotarget vol. 7,30 (2016): 48143-48154. doi:10.18632/oncotarget.10174

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