Information for health professionals

maintrac

Cancer cells in the blood

maintrac

The maintrac analysis method allows the quantification of circulating epithelial tumour cells in the blood.

Circulating epithelial tumour cells (CETC) determine the risk of haematogenous distant metastases and thus also the course of the disease. Consequently, it is of crucial importance to check the result during systemic treatment by monitoring the response of these cells..

Particularly in the adjuvant phase of treatment, only and cure is within therapeutical reach, individual optimisation of treatment is only feasible with adequate monitoring, and this is, for single tumour cells, using advanced microscopy. Since every live tumour cell in the blood counts.

The maintrac method was developed with this goal in mind.
It is based on simply collecting blood or body fluids in a standard EDTA tube. Tbe maintrac technique yields the EpCAM positive cells quantitatively, free of
lass, and highly reproducible.
The requirements ofthe highest European quality
criteria are fully met and the laboratory is accredited according to DIN EN ISO 15189
as has been stated by already several externa1 audits. The technical validations and clinical studies are pub1ished in worldwide highest ranked scientific journals (please press the Literature-button on Dur website maintrac.de).

Chemotherapy agents do not Act upon all cancer cells in the same way. The tumour releases cells into the patient's bloodstream, which increases the likelihood of metastasis with with increasing number of the cells. It is thus relevant for the treatment to identify, quantify and characterise the patient's tumour cells.

With maintrac, the response to various therapeutic interventions can be monitored, as the dynamics of the cell count has a highly significant correlation with the disease and/or metastatic growth.

maintrac cells and tumour markers?

maintrac gives an accurate representative control sample of vital cells with the characteristics of circulating tumour cells in the blood, while tumour markers rather reflect the disintegration of cancer cells throughout the body.

Three benefits for the patient

1. Individual efficiency control of adjuvant chemotherapy

Patients, whose circulating epithelial cells in the blood are completely eliminated or substantially reduced, rarely suffer a relapse.

2. Individual best use of hormone blockade:

As long as there is no increase of cell count in the blood, perhaps even a gradual reduction, relapses are rare.
The proliferation of circulating tumour cells depends on the number of their hormone receptors.
These receptors are blocked with hormone receptor blockers, thus preventing cell growth, for example with tamoxifen.
With HER2/neu this blocking ability sometimes only evolves over time.

3. Individual and targeted treatment where metastases are present

With statistically comparable treatments, we recommend those medications that affect the patient's cancer cells.

Gold standard

Circulating tumour cells

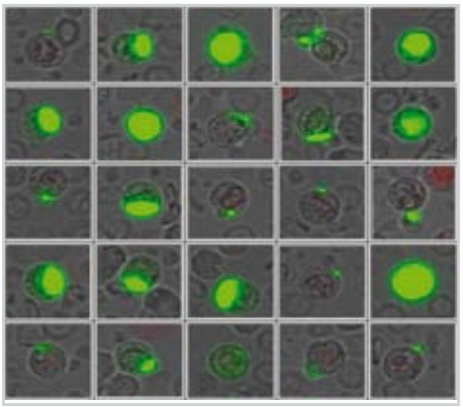
Methodology

Using the latest technology, the maintrac method opens up the new dimension of microscopic analysis of cancer cells that still live separately in the blood. **maintrac counts and characterises these cells contactless, without loss, and without destroying them.**

96% of cancer cells express cell surface EpCAM, 91% by using a further antigen in the case of sarcoma cells. EpCAM, the epithelial cytoadhesion molecule, initiates cell-cell contact, and stimulates cell growth. maintrac allows the monitoring of life and proliferation as well as death and disintegration of each individual cell and its quantitative evaluation, even in the presence of chemotherapy agents (chemosensitivity).

maintrac has also been able to open up the sub-cellular, molecular and nanoscale levels: gene variants are made visible with the maintrac FISH technique. By using a highly automated process even cells with a small number of EpCAM molecules can be captured in a reproducible manner – allowing the presentation of epithelial mesenchymal transition (EMT), which most likely plays a critical role in the process of metastasis. The stem cell assays are carried out routinely.

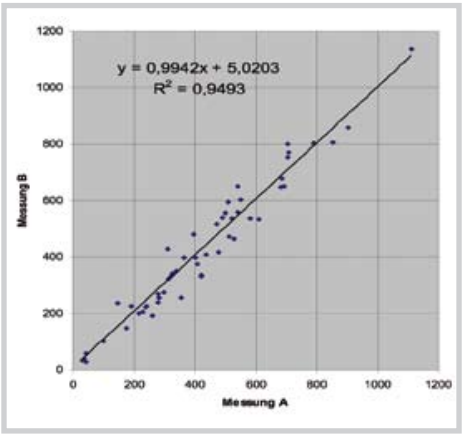
Appearance of tumour cells



There is a high variation of the amount and 10cal densitiy of EpCAM on the cells. With maintrac, even cells with a very low EpCAM expression can be can be captured. This is especially important since these cells are potentially crucial in the process of metastasis.

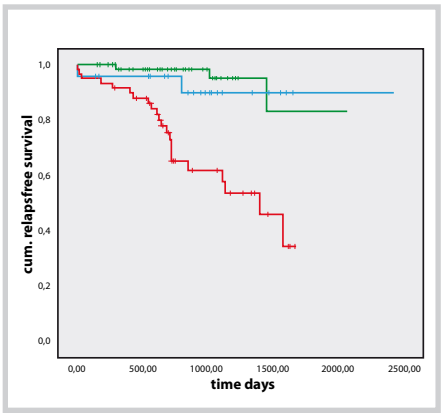
Similarly, the reproducibility of the cell counting results is excellent and has been recognised by **DAkkS, the German Accreditation Centre GmbH, for more than 6 years.**

Reproducibility



Clinical relevance

Patients with increasing cell numbers under treatment have a higher risk of recurrence (red Kaplan Meier curve). The course oft he cell number thus is clinically relevant and can be documented using the maintrac technique. **This enables to optimize personally the therapy of patients with increased cell numbers.**



Paradigm shift

Targeted treatment

maintrac

maintrac proof

Proof of efficacy

Every live tumour cell in the blood is significant.

Adjuvant chemotherapy is an attempt to kill any tumour cells remaining in the body after surgical resection of a malignant tumour.

Malignant tumours release epithelial tumour cells into the patient's bloodstream, and they then in turn attempt to form metastases in other essential organs.

Less cancer cells means less tumour burden

With maintrac proof you can check whether the chemotherapy agent used against the circulating tumour cells in your patient's blood are working, i.e. whether the chemotherapy is effective. A drop in cancer cells means the treatment is effective.

Comparing the number of circulating epithelial tumour cells (CETC) in a blood sample taken at the start of chemotherapy with the number after a period of time determined by your treatment indicates whether treatment has resulted in a reduction of cancer cells.

maintrac monitoring

Monitoring of cell numbers

Tumour cells can change during treatment or grow again after treatment has been completed. Monitoring the long-term success of treatment by monitoring the epithelial tumour cells circulating in the blood is thus advisable. The number of tumour cells is determined regularly at appropriate intervals, compared, and the overall change in cell numbers evaluated. Additional assays carried out concurrently over the entire course of the illness improve the prospects of optimised, timely, adjusted and personalised treatment.

Monitoring of maintenance treatment and alternative therapies is also possible.

With some tumours adjuvant chemotherapy (or without chemotherapy) is followed by maintenance treatment. Examples include hormone blockade treatment, small-molecule agents or, where requested, alternative therapies with appropriate agents.

Even with these treatments the behaviour of circulating epithelial tumour cells (CETCs) in your patient's blood can be monitored, allowing a raid response in case of changes. By testing circulating epithelial tumour cells for particular properties (maintrac characterisation) the treatment can be optimised for each patient.

maintrac sensitivity

Sensitivity to medications

Each patient is unique, each tumour individual.

The drug sensitivity of tumour cells is different for each medication.

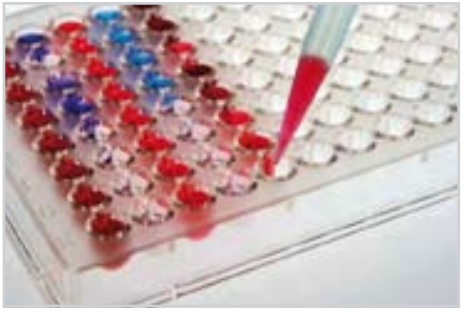
The degree of efficacy of medications administered can therefore vary. Using a simple blood sample, the maintrac chemosensitivity test can determine which therapeutic agent is most effective against the tumour cells of the individual patient your patients.

Genetic tumour profiles

Psycho-oncology benefits

Which drug has the best personal efficacy?

With maintrac sensitivity any number (usually up to 6) of commonly used cytostatic drugs or other medications (small-molecule agents or alternative medications) can be tested for their power against circulating tumour cells in the blood. In most cases the medication with the highest efficacy will be selected for treatment. Whenever treatment has to be adjusted, you can check in appropriate intervals whether the new medication is still effective.



The assay can be used to test for properties of the cell surface, intracellular markers, switching individual genes on and off as well as testing for genetic variants of single / the majority of circulating tumour cells.

maintrac characterisation

Treatment-relevant properties of tumour cells

What are the properties of circulating tumour cells?

There are a number of treatments that are only advisable if the tumour cells have the relevant target structures. Previously, such tests have predominantly been carried out on primary tumours. Difficulties arise because the primary tumour is frequently made up of different cells at varying stages of maturity. It is often not clear which of these cells are able to form metastases. In addition, primary tumours or biopsy material from the primary tumour may no longer be available after surgical resection of the tumour. The langer ago the primary tumour has been removed the less reliable is to assume its properties have not changed.

With maintrac it is now possible to characterize the actual circulating tumour cells and identify the most suitable treatment, according to their actual properties.

Which treatments are more successful depending on the actual properties of the CETCs?

Examples include the blockade of various hormone receptors from oestrogen to progesterone, EGFR and HER2/neu, as well as androgen receptors, small-molecule agents or even immunological er naturopathic or so called complementary therapies with.

Whether these methods will be effective for your patient can be determined with special tests for circulating tumour cells. The percentage of growing or sleeper cells can also be determined, which is particularly important, since rapidly growing cancer cells are treated with different agents compared to slow-growing or sleeper cells.

With adenocarcinoma of unknown primary origin (ACUP) it is possible, similar to a nodular mass, to identify where these cells originated, based on the characterisation of the circulating tumour cells.

Sound results

Personalised treatment

maintrac

Paradigm shift

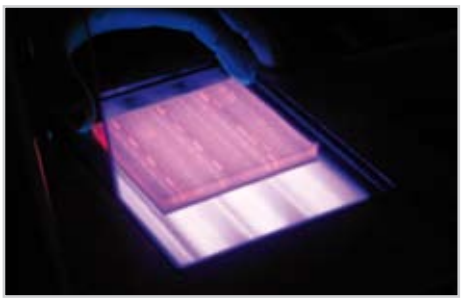
Targeted treatment

In addition to the guidelines, the targeted treatment of individual patients with the individually most effective drug has become the focus of an optimal, personalised treatment.

The relevant and sound results of the maintrac chemotherapy sensitivity assay allow for an informed decision when selecting a drug for cancer treatment.

Genetic tumour profiles

By focusing on the genetic profile of individual live tumour cells in the patient's blood, new forms of treatment become possible, new paths and approaches are opened up in the treatment of cancer, which so far has eluded patients due to their complexity.



Psycho-oncology benefits

Cancer patients not only suffer their illness, but also the uncertainty of whether the treatment is effective and whether they have really beaten the cancer at the end of treatment. All cancer patients live with the fear that their cancer will recur or spread.
With diagnostic imaging tumours as small as 1cm can be detected. However, already a tumour the size of 1mm emits up to 100,000 cancer cells per day into the blood. maintrac detects changes in cell numbers from approximately 50,000 cells in the entire blood stream. As such, long-term monitoring with maintrac can be considered as a "screening test as part of the follow-up". Being aware of the dynamics of their cell numbers can help alleviate the patient's fear of unnoticed recurrence and, with this psycho-oncology benefit, give them a better quality of life.

Quantification of the re-growth of previously sensitive subpopulations is possible as well as of one or the other drug-refractory subpopulation.

Single Cell Picking - The single cell analysis

Expect precision

Cells from solid tumours washed out into the blood may be heterogeneous.

You have completed the first step of metastasis. Of course, not all of these cells will be able to form a metastasis.
With maintrac and EpCAM, the human epithelial antigen, circulating tumour cells in the blood can be detected, marked and quantitatively proven.

The SINGLE CELL PICKING method is used for the isolation and molecular genetic analysis of individual pure circulating tumour cells, for example for genetic research with regard to suitability for treatment. Some of these cells can be propagated and then used for immunisation. These cells may also be cryopreserved for further research.

Long-term monitoring

Ease of use

Advantages of single cell analysis

- Determination of the tumour cell expression status before and during treatment (transcriptomics)
- Detection of mutations and genomic changes (genomics)
- Determination of heterogeneity of washed out populations before and during the treatment
- Analysis of the effect of cytotoxic drugs, and, where appropriate, with precise identification of metastases-enabling cells

Benefits for the patient

This analysis is increasingly and successfully used with targeted and personalised treatment approaches.

Testing request

On the Web: www.maintrac.de
(Form completed with all details, including patient's signature)

... for maintrac cell counting

Quantitative determination of circulating tumour cells for treatment follow-up and monitoring

Material required:
15ml EDTA blood (tubes labelled with patient's name, date of birth, date of collection)

...for chemosensitivity testing

Material required:
Please submit one daily treatment dose of the medication, agents, or homeopathic remedies after consultation with our lab.

(15ml EDTA blood is sufficient for the testing of up to 7 agents)

Shipping of samples

If the patient is undergoing currently chemotherapy:

Please send blood samples before the next cycle of chemotherapy (Minimal two weeks after chemotherapy) and every further blood drawing at the same time interval.

Transport:
In a save/stable box/letter, without ice

Transportation Company:
FEDEX or comparable companies. Please include the official Papers (e.g. label with human material, toll papers)

German toll number:
Labor Dr. Pachmann: 7489552

Duration of shipping:
The blood must arrive in our lab within 72 hours

Shipping Address:

Labor Dr. Pachmann
Kurpromenade 2
95448 Bayreuth
Germany

Results:

Normally within 1 week per fax

Bank details:
IBAN:
DE52 7607 0024 0882 6984 00

BIC:DEUTDEDB773 – Deutsche Bank

Working Group
Transfusion Medicine Center Bayreuth TZB

Your competent partner for oncology and haemostaseology

Dr. Pachmann Laboratory and Practice provides outpatients and inpatients of all health insurers with diagnostic services and treatment. The laboratory specialises in blood stasis disorders, particularly thrombocytopenia, von Willebrand disease, thrombosis and pulmonary embolism and their individual prophylaxis. The lab also hosts the quarterly meeting of the Bavarian Quality Circle for Thrombosis and Pulmonary Embolism. Like all other blood tests at the lab, the determination of tumour cells in the blood for the monitoring of results in adjuvant chemotherapy, for hormone therapy and personalised treatment optimisation once metastases have occurred are carried to the highest standard. The lab also competently handles any issues relating to transfusion immunology. The practice is barrier-free and child-friendly.

SIMFO Spezielle Immunologie Forschung + Entwicklung GmbH Bayreuth is a medical-biological research facility, offering professional research management and methodology development, coupled with highly specialised expertise in oncology, haemostasiology and transfusion medicine. We are committed to developing the most current, state-of-the-art procedures for you through ongoing continuing education, structured knowledge transfer and a successful culture of innovation.

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Dr. Pachmann

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