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Informationsportal zu Krebserkrankungen bei Kindern und Jugendlichen

Embryonal, non-rhabdoid CNS tumours (former CNS-PNET) and pineoblastoma – Brief information

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1. General information on the disease

Embryonal, non-rhabdoid tumours of the *central nervous system* (until recently known as primitive neuroectodermal tumours of the central nervous system, CNS-PNET) and pineoblastoma are *solid tumour*s that arise from *brain* tissue or *spinal cord* tissue. Since they directly originate from the CNS, they are also called *primary CNS tumour*s, thereby differentiating them from malignant tumours of other organs that have spread (metastasised) to the CNS.

Both, embryonal CNS tumours and pineoblastoma originate from extremely immature (*undifferentiated*) cells of the central nervous system, which divide at a high rate. Therefore, these tumours grow very fast. They look very alike under the microscope and also share various features with medulloblastoma, an *embryonal* tumour of the *cerebellum*.

Embryonal, non-rhabdoid CNS tumours and pineoblastoma differ, for example, with regard to their location in the CNS: non-rhabdoid CNS tumours usually grow in the upper part of the brain (*supratentorial*ly), mostly in the cerebral hemispheres [see *cerebrum*]; hence they were previously called supratentorial PNET (stPNET) in order to differentiate them from the also embryonal medulloblastoma. Very rarely, they develop in other areas of the CNS. Pineoblastoma usually grows in the area of the *pineal gland*, a small endocrine organ in the centre of the brain (pineal region).

Both tumour types show an aggressive growth pattern. Embryonal non-rhabdoid CNS tumours often spread from one cerebral hemisphere into the other and/or into the *meninges*, from where they invade additional CNS tissue. Pineoblastoma may spread from the area of the pineal gland into other regions of the brain and spine as well. Metastasis outside the CNS, for instance to bones, *bone marrow*, lung, or *lymph nodes*, is rare.

2. Tumour types

The group of embryonal, non-rhabdoid CNS tumours (prior to the update of the *WHO classification* known as CNS-PNET) includes different tumour types, which differ regarding their histological and, partly, also to their molecular features.

According to the current classification of the World Health Organization (*WHO*) for tumours of the central nervous system (WHO classification 2016), the tumours considered here include, above all, the “embryonal tumours with multilayered rosettes (ETMR)”, which – depending on harbouring or not harbouring a certain *genetic* alteration on *chromosome* 19 (the so-called C19MC amplification) – are called either ETMR C19MC-altered or ETMR NOS (short for: not otherwise specified). Additional

tumours of this group are, for example, the rare medulloepithelioma and other embryonal, non-rhabdoid CNS tumours that have not been otherwise specified.

Due to their rarity and similarity regarding the course of the disease, many authors considered pineoblastomas and embryonal, non-rhabdoid CNS tumours as one group in the past. Today, however, it is well-known that a pineoblastoma differs substantially from other embryonal CNS tumours on the molecular level and, therefore, needs to be dealt with as an independent tumour type.

Embryonal, non-rhabdoid CNS tumours as well as pineoblastoma are defined as high-grade malignant tumours (WHO grade IV).

3. Incidence

Embryonal, non-rhabdoid CNS tumours and pineoblastoma are rare: they account for approximately 2 % of all CNS tumours in childhood and adolescence. In Germany, about ten children and adolescents under 15 years of age are newly diagnosed with one of these tumours each year. Embryonal CNS tumours are most frequent in children within their first years of life – the patients' average age at diagnosis ranges between three and four years. Boys and girls are almost equally affected. Pineoblastoma is mostly diagnosed in children and young adults.

4. Causes

Embryonal, non-rhabdoid CNS tumours and pineoblastoma are caused by a malignant transformation of *nerve tissue* cells. The reasons for tumour development have not been completely found out yet. It is well-known, though, that *radiation* of the brain, for example as received by children with certain forms of *leukaemia* or with eye cancer (*retinoblastoma*), leads to an increased risk of developing a CNS tumour later in life.

In addition, it has been shown that embryonal CNS tumours and pineoblastoma are sometimes associated with certain *genetic* and *chromosomal* abnormalities in the tumour cells. The resulting impairments of cell development and cell communication may be contributing factors promoting the transformation of a healthy into a cancer cell. However, since embryonal, non-rhabdoid CNS tumours and pineoblastoma are rare, only a few *molecular* abnormalities that might be responsible for causing the disease have been identified yet.

Good to know: rarely, pineoblastoma can be associated with hereditary retinoblastoma and thus genetic alterations of the retinoblastoma gene (so-called trilateral retinoblastoma). More information on trilateral retinoblastoma can be found in our *Retinoblastoma* chapter.

5. Symptoms

Due to the uncontrolled and aggressive growth pattern of embryonal, non-rhabdoid CNS tumours and pineoblastoma, *symptom*s typically develop and deteriorate fast. The presenting symptoms of these tumours (like other tumours of the *central nervous system*) primarily depend on the patient's

age, the site and size of the tumour as well as its pattern of spread within the CNS. The following general (nonspecific) and local (specific) symptoms can occur:

5.1. General (nonspecific) symptoms

Unspecific general symptoms occur independently of the tumour's location. They may be similar to and therefore mimic other, non-CNS diseases. General symptoms of a child or adolescent with a CNS tumour may include headaches and/or back pain, dizziness, loss of appetite, nausea and vomiting (particularly after getting up in the morning), weight loss, increasing fatigue, inability to concentrate, school problems, mood swings, and character changes as well as developmental delay, to name a few.

Major reason for these symptoms is the slowly but continuously increasing intracranial pressure (ICP). An elevated intracranial pressure may be caused by the growing, thus more and more space-occupying tumour within the bony skull. It may as well be due to the tumour blocking the regular flow of the *cerebrospinal fluid*, thereby forming *hydrocephalus*. In babies or small children with soft spots (open *fontanelle*s), elevated intracranial pressure and hydrocephalus typically present with a bulging fontanelle or a larger than expected head circumference (*macrocephalus*), respectively.

5.2. Local (specific) symptoms

Local symptoms may indicate the tumour location and, thus, which functional regions of the CNS might be affected. For example, a tumour in the hemispheres of the *cerebrum* or in the *diencephalon* can be associated with *seizures* and/or motor deficits. Also, vision impairments, speech disorders, behavioural and sleep problems, as well as moodiness and altered appetite regulation may, although to a lesser extent, be indicative of tumour location. Pineoblastoma can cause trouble with eye movements, in particular limitations of upgaze. This vision impairment results from the tumour's specific location in the diencephalon and is also known as Parinaud syndrome.

Good to know: Not all patients presenting with one or more of the symptoms mentioned above do have an embryonal CNS tumour, a pineoblastoma or another type of brain tumour. Many of these symptoms may also occur with other, harmless diseases that are not associated with a brain tumour at all. However, if certain symptoms persist or get worse (for example repetitive headaches or rapid increase of head circumference in a young child), a doctor should be seen to find the underlying reason. In case it is a brain tu-mour, treatment should be started as soon as possible.

6. Diagnosis

If the paediatrician thinks that the young patient's history (*anamnesis*) and *physical examination* are suspicious of a tumour of the central nervous system (CNS), the child should immediately be referred to a hospital with a childhood cancer program (paediatric oncology unit), where further diagnostics can be initiated and performed by childhood cancer professionals. Very close collaboration between various specialists (such as *paediatric oncologist*s, paediatric

neurosurgeons, paediatric *radiologist*s, to name a few) is required, both to find out, whether the patient really suffers from a malignant CNS tumour and, if so, to determine the tumour type and the extension of the disease. Knowing these details is absolutely essential for optimal treatment and *prognosis*.

6.1. Tests to secure diagnosis

The initial diagnostic procedures for a young patient presenting with a suspected CNS tumour at a childhood cancer centre include another assessment of the patient's history, a thorough physical/ *neurological* exam and *imaging* diagnostics, such as *magnetic resonance imaging* (MRI) or (less often) *computed tomography* (CT). These tests help find out exactly whether the patient has a tumour of the central nervous system. Also, localisation and extent of the tumor, its demarcation regarding adjacent tissue as well as a potential *hydrocephalus* can be diagnosed by these imaging techniques very well.

In order to validate the final diagnosis, *histological* and *molecular* analysis of surgically obtained tumour tissue (*biopsy*) is required. Usually, this is done using the tissue obtained during surgical tumour removal. The extent of histological and, especially, *molecular genetic* workup has been substantially increased over the past years. Today's option of using modern lab techniques makes it possible to identify molecular tissue characteristics that do not only help finalize the diagnosis, but can also provide information on what to expect regarding the course of the disease (such as growth behaviour). Therefore, molecular diagnostics will play a major role in designing future treatment strategies.

6.2. Tests to assess spread of disease

Once the diagnosis of an embryonal CNS tumour or a pineoblastoma has been confirmed, additional tests are required to assess the extent of the disease within the central nervous system (CNS). Apart from *MRI* scans of the complete CNS (brain and spine) for macroscopic metastases, these tests also include microscopic checking of the *cerebrospinal fluid* (CSF) for tumour cells in the *spinal cord* (which are not visible by MRI scan). Cerebrospinal fluid is mostly obtained from the spine in the lower back (*lumbar puncture*), since the risk of the puncture needle damaging the spinal cord is lowest at the lower back level.

6.3. Tests before treatment begins

In preparation for the intensive treatment of the brain tumour, further investigations are performed, such as *electrocardiography* (ECG) and *echocardiography* to check cardio function. Furthermore, additional blood tests are needed to assess the patient's general health condition and to check whether the function of certain organs (such as liver and kidneys) is affected by the disease and whether there are any metabolic disorders to be considered prior or during therapy. Any changes occurring during the course of treatment can be assessed and managed better based on the results of those initial tests, which thus help to keep the risk of certain treatment-related side effects as low as possible.

Also, the patient's *blood group* needs to be determined in case a *blood transfusion* is required during treatment. In sexually mature females (which means after they have experienced their first menstruation), a pregnancy test is recommended prior to treatment as well.

Good to know: Not every patient needs the complete check-up. On the other hand, tests might be added that haven't been mentioned here, depending on the individual situation of the patient. Your caregivers will inform you and your child, which diagnostic procedures are individually required in your child's situation and why.

Psychosocial Care

A child's cancer is a stressful situation for the whole family. The psychosocial team of the clinic or later the aftercare facility provides advice and support to patients and their relatives from diagnosis to completion of treatment as well as during aftercare. Don't hesitate to take advantage of this offer. It is an integral part of the treatment concept of all paediatric oncology centres in many countries. Here you will find comprehensive information on this.

7. Treatment planning

Once the diagnosis and extent of a CNS tumour has been confirmed, treat-ment planning starts. In order to provide the patient with the best possible individual and risk-adapted therapy, the treatment team considers specific factors that are known to have an impact on the *prognosis* (so-called prognostic factors).

Important *prognostic factors* in case of an embryonal, non-rhabdoid CNS tumour or pineoblastoma are the type (subtype), localization, extent and spread of the tumour. Also, the biological (molecular) features of a tumour increasingly impact the choice of optimal treatment. In addition, the patient's age and overall physical condition play an important role. Age at diagnosis, above all, determines whether the patient may receive radiotherapy or not. All these factors are included in treatment planning in order to achieve the best outcome possible for each patient.

8. Treatment

Treatment of children and adolescents with an embryonal, non-rhabdoid CNS tumour or with pineoblastoma should take place in a children's hospital with a paediatric oncology program. Only in such a childhood cancer centre, highly experienced and qualified staff (doctors, nurses and many more) is guaranteed, since they are specialized and focus on the diagnostics and treatment of children and teenagers with cancer according to the most advanced treatment concepts. The doctors in these centres collaborate closely with each other. Together, they treat their patients according to treatment plans (protocols) that are continuously optimised. The goal of the treatment is to achieve higher cure rates while avoiding side effects as much as possible.

Current treatment concepts involve neurosurgical tumour removal, chemotherapy and, depending on the patient's age, radiotherapy.

8.1. Surgery

The first step in treating an embryonal CNS tumour or a pineoblastoma is *surgery*. Goal of surgery is gross (microsurgical) total tumour removal. This means that at the end of the surgical procedure, no tumour tissue can be identified through the surgical microscope. Frequently, however, total tumour resection cannot be achieved due to the localization of these tumours.

In most patients, neurosurgical intervention results in normalising the flow of *cerebrospinal fluid* (CSF). Patients initially presenting with *hydrocephalus* may need a transient hydrocephalus *drainage* **prior to** tumour removal or, sometimes, even a permanent drainage system later.

8.2. Additional, non-surgical treatment

Since embryonal CNS tumours and pineoblastomas tend to infiltrate adjacent tissue and, furthermore, often spread into other parts of the central nervous system via the cerebrovascular fluid (CSF), treating the tumour locally only is not sufficient. Therefore, surgery is followed by additional non-surgical treatment, comprising *radiation therapy* and/or *chemotherapy*.

Chemotherapy uses drugs (so-called cytostatic agents or *cytostatics*) that can kill fast-dividing cells, such as cancer cells, or inhibit their growth, respectively. Radiotherapy is done using energy-rich, *electromagnetic* radiation, given through the skin to the tumour region. Radiation causes *DNA* damage in tumour cells, thereby leading to cell death. Aside from this so-called conventional radiotherapy, particle-radiation with protons (also known as proton therapy) can be an option for some patients as well. This type of radiotherapy provides the benefits of better targeting the tumour area, thus sparing more adjacent, healthy tissue from the effects of radiation. Proton therapy is gaining an increasing importance in the treatment of children and teenagers with *solid tumour*s.

Decision upon which therapy is to be applied (treatment modalities, intensity of chemo-/ radiotherapy) is based on the patient's age, the histological and molecular subtype of the tumour, certain biological risk factors, as well as on the extent of both metastases and surgical tumour removal.

Treatment options for pineoblastoma patients

After maximal possible tumour removal, patients with non-metastasised pineoblastoma, who are older than four years of age, will receive *radiation* of the complete central nervous system (craniospinal radiotherapy), followed by an additional boost to the tumour site. Radiotherapy is followed by a so-called maintenance *chemotherapy*, which includes multiple cytostatic agents. In cases of *metastasis*, treatment will be intensified, for example by giving higher doses of radiotherapy combined with a preceding chemotherapy (induction chemotherapy).

In children under four years of age, whose brain development is not completed yet, radiotherapy should be avoided or delayed in order to minimize the risk of serious late effects. Instead of radiotherapy after surgery, patients will receive chemotherapy with multiple agents. In some patients, radiotherapy may be an option later on. Some patients are also eligible for *high-dose chemotherapy* followed by *autologous stem cell transplantation* to increase the chances of survival.

Treatment options for patients with other embryonal CNS tumours

For other embryonal tumours of the central nervous system, various subtypes have been identified according to recent reports. These require individual treatment approaches depending on the presenting subtype.

Good to know: the details of how an individual patient is treated will be discussed between the responsible physician, the patient and the family.

9. Therapy optimising trials and registries

The majority of the children and adolescents with embryonal non-rhabdoid CNS tumour or pineoblastoma or a *recurrence* of these diseases receive therapy according to the treatment plans of *therapy optimising trial*s or registries. Therapy optimising trials are standardised and controlled clinical trials that aim at steadily developing and improving treatment concepts for sick patients based on the current scientific knowledge.

Patients who cannot participate in any study, for example because none is available or open for them at that time or since they do not meet the required inclusion criteria, respectively, are often included in a so-called **registry**. One goal of a registry is to collect treatment data for research questions. Furthermore, the registry centre supports the doctors at site with (non-commital) treatment recommendations based on the most recent data on best treatment options, in order to provide the patient with optimal therapy even without the framework of a clinical study.

In Germany, a long-term therapy optimising trial (trial “HIT 2000”) for the treatment of children and adolescents with embryonal, non-rhabdoid CNS tumours (then named CNS-PNET) or pineoblastoma (also including patients with medulloblastoma and ependymoma) was closed in 2011. Many children’s cancer centres in Germany and Austria had participated in this trial. Currently, there is no open trial for patients with first diagnosis of embryonal CNS tumours or pineoblastoma. Newly diseased patients may, however, take part in the I-HIT-MED Registry (*see below*).

The following registries are available at the moment:

- **I-HIT-MED Registry**: Patients with embryonal, non-rhabdoid CNS tumours (before called CNS-PNET), who, for different reasons, cannot or do not want to participate in any currently available or open trial, can be enrolled in this registry (International HIT-MED Registry), regardless of the treatment given. These patients will receive treatment as per individually designed treatment plans. The goal of the registry is not to assess the feasibility of an ongoing trial, safety or efficacy of a certain treatment. It rather aims at collecting individual patient data for future analysis. The headquarters of the registry are located in the Children’s Cancer Centre at the University of Hamburg, Germany. The head of the study is Prof. Dr. med. Stefan Rutkowski.

- **HIT-REZ Registry:** Patients, whose disease does not respond to current treatments or with recurrent disease (relapse), respectively, can be enrolled in this registry, which has been open since January 2015. This registry does not serve to test new treatment regimens or drugs.

However, the experts running the registry are providing treatment recommendations based on the most recent results obtained from national trials (for example from the HIT-REZ 2005 trial, which was closed in 2016) as well as international relapse trials. The headquarters of the registry are located in the Children's Cancer Centre at the University of Essen, Germany. The head of the study is Prof. Dr. med. Gudrun Fleischhack.

10. Prognosis

The cure rates for children and adolescents with an embryonal, non-rhabdoid CNS tumour is, according to the German Childhood Cancer Registry, about 60% (5-year-survival rate). Overall prognosis for pineoblastoma patients is a bit more favorable.

However, in individual patience, prognosis is dependent on various factors. Since embryonal CNS tumours are a very heterogeneous group, the probability of survival can be different depending on the tumour type. Also, this stage of the disease, and the patient's age play a significant role. Hence, children and adolescents with metastasized disease have generally a more unfavourable prognosis than patients with localized disease. Also, very young patients, for whom *radiation therapy* is not an option, have a rather unfavourable prognosis; only 20 to 30% of the patients experience long-term disease-free survival.

Note: The survival rates mentioned in the text above are statistical values. Therefore, they only provide information on the total cohort of patients with childhood Medulloblastoma. They do not predict individual outcomes.

In the context of cancer, the term „cure" should rather be referred to as „free of cancer", for even if current treatment regimens may help remove the tumour, the the tumour's growth may have caused irrepairable damage to the brain or the treatment may be associated with late effects. Early detection and appropriate management of these long-term secondary effects typically require intensive *rehabilitation* and thorough long-term follow-up care.

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Glossary

anamnesis	medical interview, a patient's history, development of signs of illness; the type, onset and course of the (current) symptoms as well as any risk factors (e.g. hereditary diseases) are evaluated during a medical interview.
autologous stem cell transplantation	(re)transfer of blood stem cells, e.g. after a chemotherapy or radiotherapy; the patient receives his own cells that were previously taken from their own bone marrow or blood. Autologous stem cell transplantation may be an option, for example, for certain patients with lymphoma, neuroblastoma, soft tissue sarcoma, or a brain tumour.
biopsy	removal of a tissue sample for subsequent (mainly microscopic) examination; this can be done, for example, by puncture with a hollow needle, with the use of special instruments (such as forceps, punching instruments, probes) or surgically with a scalpel.
blood group	hereditary, usually stable, structural characteristics (blood group antigens) of blood components (e.g. AB0 blood groups) located on the cell walls of blood and other tissue cells;
blood transfusion	transfer of blood (whole blood) or blood components (e.g. red blood cells or platelets) from a donor to a recipient.
bone marrow	site of blood formation; spongy tissue with a strong blood supply that fills the cavities inside many bones (e.g., vertebrae, pelvic and thigh bones, ribs, sternum, shoulder blade, and collarbone); in the bone marrow, all forms of blood cells develop from blood progenitor cells (blood stem cells).
brain	the part of the central nervous system (CNS) located in the head; the brain is protected by the skull and the meninges and consists mainly of nerve tissue.
central nervous system	comprises the brain and spinal cord and is separated from the so-called peripheral nervous system; as a central organ of integration, coordination and regulation, it serves to process external sensory impressions as well as stimuli produced by the organism itself.
cerebellum	part of the brain that is located in the posterior fossa of the skull, between the cerebrum and the brainstem; it is mostly

	responsible for the coordination of all body movements and also for maintaining balance.
cerebrospinal fluid	fluid produced by cells of the cerebral ventricles; it floats around the brain and spinal cord to protect them from injury and provide them with nutrients.
cerebrum	largest and most highly developed section of the brain; it consists of two hemispheres connected by a thick bundle of nerves (corpus callosum). Each hemisphere of the brain is specialized on specific tasks. The outermost layer of the cerebrum, the cerebral cortex, houses the ability to learn, speak and think, as well as consciousness and memory, amongst other things. This is also where the processing centres for information from the sensory organs (e.g. eyes, ears) are located.
chemotherapy	here: use of drugs (chemotherapeutic agents, cytostatics) for the specific inhibition of tumor cells in the organism
chromosomal	referring to the chromosomes, carriers of the genetic material (see chromosomes)
chromosome	chromosomes are the carriers of the genetic material, i.e. the genetic information of a cell; chromosomes consist mainly of DNA and proteins and are components of the cell nucleus. The shape and number of chromosomes are species-specific. Humans have 46 chromosomes (23 pairs of chromosomes) per cell in the body.
CNS tumour	tumour of the central nervous system; a primary CNS tumour is a solid tumour that originates from brain or spinal cord tissue. Secondary CNS tumours are metastases of tumours located in other organs or tissues.
computed tomography	imaging, X-ray diagnostic procedure; it produces an image by computer-controlled evaluation of a large number of X-rays from different directions. This makes it possible to produce sliced images of body parts (tomograms, transverse or longitudinal sections of the human body)
cytostatics	drugs that inhibit cell growth; cytostatics can affect the metabolism of different types of cells, thereby destroying them and/or preventing them from multiplying. Cells that divide frequently are particularly affected.
diencephalon	vital part of the brain with function for numerous life processes; it connects to the brainstem towards the cerebrum and consists of functionally different sections. The "thalamus", for example, decides which sensory impressions should penetrate into

	consciousness and are to be sent to the appropriate processing centers. The "hypothalamus" serves as a mediator between the hormonal and nervous systems and controls, among other things, important metabolic processes (e.g. heat and water balance, carbohydrate, fat, protein metabolism, blood pressure). Together with the pituitary gland, it regulates the activity of subordinate glands. Other parts of the diencephalon are responsible for muscle activities and for controlling the day-night rhythm.
DNA	abbreviation for deoxyribonucleic acid; it carries the genetic information and is found in all living beings. DNA contains the genes that provide the information for the production of ribonucleic acids (RNA) or proteins. It is a large molecule consisting of two nucleic acid chains twisted into a double helix. The individual chains consist of a sequence of four different building blocks (bases), the order (sequence) of which determines the genetic code.
drainage	here: drainage of pathological or increased natural body fluids to the outside, for example drainage of cerebrospinal fluid from the cerebral ventricles or of pathological fluid accumulation from the pleura (pleural drainage);
echocardiography	ultrasound examination of the heart to check its performance (cardiac function); the position or structure of the heart valves and walls, the wall thickness of the heart muscle, the size of the heart and the ejected blood volume (pumping function of the heart) are examined and assessed, among other things.
electrocardiography	method of measuring the electrical activity of the heart
electromagnetic	electromagnetic rays (also known as electromagnetic waves) consist of coupled electric and magnetic fields; examples of electromagnetic radiation are X-rays and gamma rays as well as radio waves, thermal radiation and light.
embryonal	in an early stage of development, immature;
fontanelle	soft spot on an infant’s head, due to the bony plates not having connected yet; the final closure usually occurs before the age of two.
genetic	concerning the (level of) inheritance or genes; inherited
high-dose chemotherapy	the use of a particularly high dose of cell growth-inhibiting drugs (cytostatics); in the case of cancer, it aims to destroy all malignant cells. Since the haematopoietic system in the bone marrow is also destroyed, the patients own or foreign blood stem cells

	must then be transferred (autologous or allogeneic stem cell transplantation).
histological	concerning the tissues of the body; in a histological (fine tissue) examination, tissue samples are examined under the microscope after special preparation (preparation of tissue sections and use of certain staining techniques).
hydrocephalus	medical term for abnormal buildup of cerebrospinal fluid in the cavities (ventricles) in the brain; it is caused by a dilation of the brain's ventricles due to various causes.
imaging	diagnostic procedures generating images of the inside of the body, such as ultrasound and X-ray examination, computed tomography, magnetic resonance imaging, and scintigraphy
leukaemia	malignant disease of the blood forming (haematopoietic) system and the most common cancer in children and adolescents (about 33%); depending on the origin of the malignant cells, a distinction is made between lymphoblastic and myeloid leukaemias. Depending on the course of the disease (fast or slow), a distinction is made between acute and chronic leukaemias.
lumbar puncture	puncture of the spinal canal in the lumbar spine, e.g. to remove cerebrospinal fluid (CSF) or for the purpose of administering medication (so-called intrathecal treatment); in the case of cancer, a sample and examination of cerebrospinal fluid can be used to detect malignant cells; in the case of increased intracranial pressure due to a CNS tumour, cerebrospinal fluid removal (CSF) is also used to relieve pressure.
lymph nodes	small lenticular to bean-shaped organs that are part of the bodys immune system and are located in many parts of the body; they serve as filter stations for the tissue water (lymph) of a region of the body and contain cells of the immune system.
macrocephalus	large head, which can be caused by a hydrocephalus (hydrocephalus) in a child with unclosed fontanelles, but also by a large tumour or both
magnetic resonance imaging	diagnostic imaging method; very precise, radiation-free examination method for the visualization of structures inside the body; with the help of magnetic fields, cross-sectional images of the body are generated, which usually allow a very good assessment of the organs and many organ changes.

meninges	layers of connective tissue that protectively envelop the brain; the three meninges are joined to the outside by the skull bones. In the area of the spinal cord, the meninges merge into the three-layered spinal cord membrane, which surrounds the rest of the central nervous system.
metastasis	1. tumour spread from the primary site of tumour to other parts of the body; characteristic feature of malignant tumours (cancer). 2. collective term for a disease process characterized by malignant cells spreading from their primary site to other areas of the body via the bloodstream and/or the lymphatic system.
molecular	at the level of molecules
molecular genetic	referring to structure, formation, development, function and interactions of cells and cell building blocks (e.g. nucleic acids, proteins) at the molecular level; the focus is on the analysis of the genetic information stored in the nucleic acids (DNA and RNA) and its processing in the context of protein synthesis as well as gene regulation.
MRI	abbreviation for magnetic resonance imaging, a very precise, radiation-free examination method for imaging structures inside the body
nerve tissue	tissue of the nervous system; it consists of nerve cells (neurons) and its own special connective tissue, the glial cells.
neurological	referring to the function of the nervous system / nerve tissue
paediatric oncologist	paediatrician who is specialized on the management of children and adolescents with cancer
physical examination	an important part of diagnostic examinations; includes palpation and listening to certain body organs as well as testing reflexes to obtain indications of the nature or course of a disease.
pineal gland	hormone gland attached to the diencephalon between the two cerebral hemispheres; its function is the production of melatonin, a hormone that makes the body respond to changes in light conditions.
prognosis	prediction of the course and outcome of a disease / prospect of recovery
prognostic factors	factors that allow an approximate assessment of the further course of the disease (i.e. the prognosis);

radiation	controlled use of ionizing (high-energy) radiation for the treatment of malignant diseases
radiation therapy	controlled use of ionizing (high-energy) radiation for the treatment of malignant diseases
radiologist	a physician specialized in diagnostic imaging and radiotherapy
recurrence	relapse, recurrence of a disease after recovery
rehabilitation	medical, social, psychosocial and occupational measures after an illness for reintegration into society, work and private life, which may include, among other things, the restoration of abilities through exercise treatment, protheses and other measures
retinoblastoma	a rare malignant tumour of the retina that occurs almost exclusively in children; there are hereditary and non-hereditary forms of the disease. Either one or both eyes can be affected (unilateral or bilateral retinoblastoma). In very rare cases, hereditary retinoblastoma can also occur together with a brain tumour (e.g., pineoblastoma); in this case, it is called trilateral retinoblastoma.
seizures	uncontrolled electrical activity between nerve cells in the brain; a distinction is made between focal and generalized seizures. Focal seizures are limited to a specific area of the brain; depending on the area of the brain, the symptoms vary: e.g. twitching of one side of the body, an arm or a leg. Generalized seizures spread over large areas of the brain and lead, for example, to twitching of the limbs, sudden absence and loss of consciousness.
solid tumour	solid, localized increase of the bodys own tissue; solid tumours can originate from various tissues and can be benign or malignant; only the malignant ones are considered as cancers. Solid tumours include all cancers that do not affect the haematopoietic or lymphatic system. The latter are systemic malignancies. The most common solid tumours in childhood and adolescence are brain tumours, followed by neuroblastoma and soft tissue sarcomas.
spinal cord	part of the central nervous system; its main function is to transmit messages between the brain and other organs of the body. The spinal cord is protectively enveloped by the three spinal cord membranes and the bony spinal canal.
supratentorial	located above the cerebellar tentorium, i.e. in the middle or anterior cranial fossa

surgery	surgical intervention on or in the body of a patient for the purpose of treatment, less often also in the context of diagnostics; the surgical intervention is carried out with the help of special instruments, generally with the patient under anesthesia.
symptom	sign of illness
therapy optimising trial	a controlled clinical trial (study) that aims to provide the best possible treatment for patients and at the same time to improve and develop treatment options; therapy optimisation is aimed not only at improving the chances of recovery, but also at limiting treatment-related side effects and long-term effects.
undifferentiated	here: immature, not yet functional and usually capable of unlimited division (e.g. stem cells); the development from undifferentiated to differentiated cells and tissues (differentiation) takes place in stages. Accordingly, there are many different degrees of differentiation.
WHO	abbreviation for World Health Organization; international federation for cooperation in the field of public health
WHO classification	international guideline developed by the World Health Organization (WHO) for classification, diagnosis and differentiation/grading of (malignant) diseases