Hepatoblastoma (Brief information)

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1. General information on the disease

Hepatoblastomas are highly malignant *solid tumour*s of the liver. Since they develop directly in the liver, they are also called *primary* liver tumours in order to distinguish them from cancers of other body parts that have spread to the liver (liver metastases). Already before birth, hepatoblastomas arise from degenerated precursor cells of liver tissue. Since degeneration of these precursor cells can happen during different phases of liver development, various *histological* types of hepatoblastoma exist (for example fetal or embryonal hepatoblastoma); some hepatoblastomas can also include differently matured precursors of other tissues. The various tumour types partially also differ with regards to their growth patterns.

Hepatoblastomas preferably develop in the right lobe of the liver. They are mostly single, large, well-perfused tumours that are limited to one area of the organ (unifocal). Only about 15 % of the patients present with tumours in multiple liver areas (multifocal), thereby indicating aggressive growth behaviour. Very rarely, hepatoblastoma extends beyond the liver (extrahepatic). Tumour spread via the blood stream with development of daughter tumours (distant metastases) is mostly seen with progressive disease; the lungs are frequently affected. Hence, about 10–20 % of patients present with lung metastases at the time of diagnosis. Metastasis [see *metastasis*] into *lymph nodes* is very rare.

2. Incidence

Hepatoblastoma is the most frequent primary liver tumour in childhood and adolescence and the third most frequent abdominal tumour in this age group (following *neuroblastoma* and *nephroblastoma*). According to the German Childhood Cancer Registry (Mainz, Germany), about 2 of 1,000,000 (in total approximately 25) children and adolescents under 18 years of age are diagnosed with hepatoblastoma in Germany per year, which accounts for about 1 % of all paediatric malignancies in this age group. The incidence of hepatoblastoma has increased globally during the last few decades, assumably in the context of the increasing number of premature births and low birth weight (*see chapter "Causes"*).

As hepatoblastomas are *embryonal* tumours, the mostly occur in newborns, infants and toddlers, that is, in early childhood: The majority of patients is between six months and three years old. The average age of patients at diagnosis is 1.5 years. Children over the age of four are very rarely affected. Overall, boys are more frequently affected by the disease than girls (gender ratio: 1.4:1).

3. Causes

The underlying causes for the development of hepatoblastoma are still not completely understood. A prenatal trigger is being assumed. It is known, that premature babies and children with very low birthweight have an increased risk of developing hepatoblastoma later in life. As both of these

factors are on the rise in industrialised nations, an increased incidence of hepatoblastoma is also being recorded worldwide.

Some hepatoblastoma can also be associated with so-called *cancer predisposition syndrome*s, rare congenital diseases characterised by changes in the *genetic* material (*mutation*s) that (compared to healthy individuals) are connected with a higher risk of developing a malignancy. Cancer predisposition syndromes that play a role in the development of hepatoblastoma are, for example, *Beckwith-Wiedemann syndrome* (BWS), Edwards' syndrome (trisomy 18) and *familial adenomatous polyposis* (FAP).

Furthermore, various genetic and *chromosomal* changes have been identified in the majority of hepatoblastoma cells. These modifications are known or supposed to be at least partly responsible for tumour development, even in patients without a tumour predisposition syndrome. In these patients, the disease arises as a result of spontaneous mutations or other genomic changes in the cell's *DNA*.

4. Symptoms

Like other abdominal tumours, hepatoblastomas usually present as visible and palpable, painless abdominal tumours, for example during a routine physical exam. Aside from that, patients may show general *symptom*s such as fever, fatigue, loss of appetite and unintended weight loss as well as abdominal pain and nausea. The tumour may also cause fluid retention in the abdomen (ascites), *thrombocytosis* and/or *anaemia*.

Impaired liver function, for example presenting as a yellowing of the skin, mucous membranes and the white in the eyes (jaundice) or as an increased risk of bruising and bleeding, is less frequent. Also, tumour rupture and precocious *puberty* are rather rare presenting symptoms.

5. Diagnosis

If the doctor thinks that the young patient's history (*anamnesis*) and *physical examination* are suspicious of a kidney tumour like the Wilms tumour, he will refer the child immediately to a hospital with a childhood cancer program (paediatric oncology unit), where further diagnostics can be initiated and performed by childhood cancer experts. 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 indeed suffers from a kidney tumour and, if so, to determine the tumour type and the extent of the disease. Knowing these details is absolutely essential for optimal treatment planning and assessment of prognosis.

5.1. Clinical exams and laboratory tests

The caregiver team at the hospital will first take a thorough history followed by a physical exam. In addition, there will be blood tests. Of particular interest are certain substances in the blood (so-called *tumour marker*s), which – if their levels are increased – can be indicative of hepatoblastoma. 80 to 90 % of patients with hepatoblastoma present with severely increased levels of a substance

called *alpha-1 fetoprotein* (α-Fetoprotein, AFP). The tumour marker β-HCG is increased in about 60 % of patients.

5.2. Imaging tests for tumour detection and the assessment of tumour spread

Using *ultrasound* (sonography) of the abdominal organs, the location, extent, structure and blood supply of a hepatoblastoma can be visualized. In order to obtain a more comprehensive and detailed diagnosis, additional diagnostic *imaging* such as *magnetic resonance imaging* (MRI) and, less frequently, *computed tomography* (CT) are required. They are done using *contrast agent* and provide better assessment of the tumour with regard to its extent within the liver and adjacent tissue as well as a possible invasion of a large *vein* or lymph node involvement, respectively. Furthermore, these methods may give hints regarding tumour type. Since the patients are young, those scans are done in sedation (*anaesthesia*). For identifying potential metastases, lung *X-ray examination* and CT, also with contrast medium and usually under *anaesthesia*, are performed.

5.3. Tissue removal (biopsy)

For final diagnosis, *histological* examination of tumour should be performed. The required sample can be obtained via abdominal surgery (*laparotomy*), which also aims at tumour removal (so-called open *biopsy*). Alternatively, percutaneous punch biopsy is an option. This approach involves the sampling of multiple tissue cylinders from the tumour, guided by ultrasound and done in sedation. A *laparoscopy* is done rarely. The choice of biopsy technique depends on multiple factors, including the size and *operability* of the tumour.

Good to know: children aged between six months and three years may be spared from biopsy, when imaging shows a liver tumour accompanied by elevated AFP-levels in the patient's blood (higher than 1.000 ng/ml), and when this level is also three times as high as the normal reference at that age. According to experience, it is well-known that these scenarios are in accordance with the diagnosis of hepatoblastoma. In the framework of research studies, however, a biopsy might be recommended for obtaining more detailed histological information as well as for *molecular genetic* testing.

5.4. Tests before treatment begins

Depending on the type of treatment being considered, further tests are needed in order to assess the condition of different organs. For example, prior to *chemotherapy*, the doctors will recommend an examination of the heart (*electrocardiography* [EKG], *echocardiography*), a hearing test (for example, *audiometry*, *BERA hearing test* or *otoacoustic emissions*), special diagnostics for determining kidney function as well as various blood tests. 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.

Good to know: Not all of the above-mentioned tests apply to every single patient. On the other hand, additional tests not mentioned here may be required individually. Ask the attending doctors which diagnostics are necessary 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.

6. Treatment planning

After the diagnosis has been confirmed, therapy is planned. In order to design a highly individual, risk-adapted treatment regimen for the patient, certain individual factors influencing the patient's *prognosis* (called risk factors or prognostic factors) are being considered before and during treatment (risk-adapted treatment strategy).

Important *prognostic factors* are the localisation and the extent of the tumour at diagnosis and, thus, its *operability* (*see chapter regarding stages of disease below*). Complete removal of the tumour and of potential *metastasis* has a big impact on the patient's prognosis, and therefore the exact evaluation of the stage of the disease is crucial for valid risk assessment and treatment planning. Since most patients receive a chemotherapy prior to surgery to shrink the tumour, the response to this *preoperative* therapy has an effect on prognosis, too.

Additional relevant prognostic factors include the patient's age at diagnosis, certain laboratory parameters (*alpha-1 fetoprotein*, AFP), and the *histological* characteristics of the tumour (in case it could be removed at diagnosis). All these factors are included in treatment planning in order to achieve the best outcome possible for each patient.

6.1. Staging of hepatoblastoma based on the extent of the disease (PRETEXT grouping system)

Assessment of the stage of the disease is based on the so-called PRETEXT grouping system ("PRETEXT" means "PRE-Treatment EXTent of disease") of the hepatoblastoma study group of the International Society of Pediatric Oncology (SIOPEL). This system considers – using diagnostic imaging – the tumour extent within the liver prior to surgery (preoperatively): depending on how many of the four (surgically relevant) liver sections of a liver lobe are affected, four stages of disease are defined (I-IV).

Assessment of tumour extent also takes under consideration whether the large liver vessels, such as the portal vein (P) or liver veins (V), are affected by the hepatoblastoma or whether the tumour has grown beyond liver tissue (E, for extrahepatic growth), whether there is multifocal extent (F), tumour rupture (R) or lymph node involvement (L) at the time of diagnosis, or whether there even

are distant metastases (M), respectively. Such findings are known as additional risk factors and documented with the assigned capital letters.

6.2. Staging of hepatoblastoma based on risk groups

The previously assessed extent of the disease as well as additional *prognostic factors* result in therapeutical consequences, for example with regard to decision-making of tumour removal (resection) versus *transplantation* or how intensive *chemotherapy* should be, respectively. In order to provide optimal individual therapy, patients are assigned to risk or treatment groups with different treatment plans. The higher the patient's risk of relapse (*recurrence*), the more intensive will usually be his treatment.

Good to know: The international therapy optimising trial PHITT, which had been open for recruitment of all patients with newly diagnosed hepatoblastoma until 31/12/2023, differentiated between a total of four risk groups. This risk group classification is also applied within the current interim recommendations. Information on risk-adapted therapy according to those interim recommendations can be found *here*.

7. Treatment

Treatment of children and adolescents with a liver tumour 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 and 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.

7.1. Treatment methods

Treatment of children and adolescents with hepatoblastoma includes **surgery**, the goal of which is to remove the liver tumour, and almost always **chemotherapy**. For some patients, **liver transplantation** may be an option. Due to the patients' young age, radiotherapy is not considered as part of the therapy. The individual treatment choice is based particularly on the type, site and extent (thus, operability) of the tumour as well as on other prognostic factors (*see chapter „Treatment planning"*). The overall treatment duration takes about three to twelve months.

Treatment of a patient with hepatoblastoma is mainly based on two columns: *chemotherapy* and surgical tumour removal. Gross complete tumour resection is the most important factor for the patient's probability of survival.

In rare situations of a small single tumour (for example PRETEXT stage I or even II), *surgery* is an immediate option to remove the tumour. However, in most patients, hepatoblastoma is

already too large for successful surgery at the time of diagnosis or presents with lung metastases, respectively. For these patients, chemotherapy prior to surgery serves to shrink the tumour volume for subsequent removal. Since most hepatoblastomas respond well to chemotherapy, this strategy has proven successful in up to 90 % of patients.

Following preoperative chemotherapy, response to treatment and surgical options are reassessed. In case the tumour has not responded sufficiently to chemotherapy, additional cycles of chemotherapy can be an option. Following surgical removal, chemotherapy will be continued (postoperative chemotherapy) with the goal to eliminate potentially remaining tumour cells, thereby minimizing the risk of relapse.

7.1.1. 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. In order to optimize treatment efficacy, multiple agents are being used in different combinations and given in blocks. Usually, chemotherapy involves two major phases: preoperative induction chemotherapy and postoperative chemotherapy (consolidation).

The most important cytostatic agent is cisplatin, which can also be given in combination with other medications (such as carboplatin, doxorubicin, vincristine, 5-fluorouracil and etoposide). The intensity of chemotherapy (total dose, number of treatment cycles) is based on the risk group the patient has been assigned to due to the individual extent of the disease. The more progressed the disease is, the more intense will treatment be.

7.1.2. Surgical tumour removal

Gross total tumour resection as well as the removal of distant metastases, if present, are crucial for the patient's probability of survival. Hence, even for large hepatoblastomas, extended removal (including sufficient surrounding safety margin within normal tissue) is attempted. This is eventually achieved by using special techniques, for example by occluding both efferent and afferent blood vessels.

Usually, complete liver segments or even a complete liver lobe are removed. The latter is called right or left resection or extended right or left resection, respectively. Also, distant metastases diagnosed by imaging require removal, if they are still detectable following preoperative chemotherapy. In general, surgery should always be followed by at least one chemotherapy cycle. It also has to be considered that lung rehabilitation is required prior to a liver transplantat.

7.1.3. Liver transplantation

For patients for whom surgical tumour removal is not possible, the option of a liver *transplantation* can be evaluated. This may affect patients whose liver, for example, is affected in all four sectors (PRETEXT IV) or who have been diagnosed with a multifocal hepatoblastoma involving different sectors. In those situations, it is rather unlikely, that all hepatoblastoma foci in the liver can be surgically removed. Also, patients with stage PRETEXT IV and blood vessel involvement, whose

tumour stage does not decrease to stage III upon chemotherapy, maybe considered for a liver transplant.

7.1.4. Further treatment methods

If the tumour does not respond to chemotherapy, or for any other reasons that do not allow tumour removal or liver transplant to be an option, other treatment strategies need to be considered. The most promising approach is the so-called chemo*embolization*. This involves the injection of certain agents bound to carry substances in the afferent blood vessels, thereby occluding (embolising) them. Aim of this local chemotherapy is to shrink the tumour volume by destroying tumour cells. For some patients, this makes subsequent surgical removal possible or bridge the time until liver transplant. This approach, however, can be associated with complications and hence, thorough assessment of the individual benefit-risk-ratio is crucial.

Other strategies as used in adults with liver tumours – such as *laser therapy*, cryoablation (freezing of tumour tissue), radiofrequency ablation (overheating of tumor tissue) – are currently of no importance in treating children and adolescents and are only considered in *palliative therapy* settings.

8. Therapy optimising trials and registries

In Germany, the majority of the children and adolescents with neuroblastoma in receive therapy according to the treatment plans of *therapy optimising trial*s. 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**. Such a registry primarily serves to acquire disease- and treatment-associated data, which are supposed to help structuring the knowledge about the disease and its management, thereby continuously optimizing treatment. The liver tumour registry also collects *molecular genetic* data on the tumour, thus expecting to gain a better understanding of tumour biology. 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.

The following trials and registries for treatment of children and adolescents with hepatoblastoma are currently active in Germany (with international participation):

- **GPOH Lebertumorregister**: liver tumour registry of the Germany Society for Paediatric Oncology and Haematology for children, adolescents and young adults (aged 0–20 years) who are diagnosed with a malignant or benign liver tumour in Germany; the registry was opened in 2011 and has been serving particularly for data acquisition since, with the aim to improve the understanding of the disease, thereby optimising future treatment options. The study group has also been involved in the development of the PHITT study (*see below*). Prinicipal investigator is

Prof. Dr. med. Irene Schmid (Dr. von Hauner Childrens‘ Hospital, Ludwig-Maximilians-University München, Munich, Germany). The study centre will provide treatment recommendations.

- **Trial PHITT:** From September 2018 until the end of 2023, children, adolescents and young adults (under 30 years of age) with a newly diagnosed hepatoblastoma or hepatocellular carcinoma were recruited into the **P**aediatric **H**epatic **I**nternational **T**umour **T**rial (PHITT). In numerous childrens‘ hospitals and treatment centres all over Germany and other European as well as non-European countries, patients were treated within this trial. The German trial centre is located at the Ludwig-Maximilians-University Munich (Dr. von Hauner Children’s Hospital), with Prof. Dr. med. Irene Schmid as the national coordinating investigator. **Note:** The trial is currently being analysed; study results may be expected within the next years. Once the study results have been published, the International Liver Cancer Study Group will design a PHITT II study.

Treatment according to current interim recommendations: For information on current treatment recommendations for hepatoblastoma patients within different risk-/therapy groups, please see *here*.

9. Prognosis

The probability of survival for children and adolescents with hepatoblastoma depend on the extent of the disease, the response to chemotherapy and the possible extent of tumour removal. Total gross tumour resection is crucial for a favourable *prognosis*.

Over the past 15–20 years, the options of chemotherapy could be significantly optimised, so that improved cure rates for patients with hepatoblastoma are increasingly achieved. According to the German Childhood Cancer Registry, over 85 % of all hepatoblastoma patients achieve cure (10-year survival). Individual prognosis, however, depends primarily on the stage of the disease at the time of diagnosis and, thus, on the risk group the patient has been assigned to:

Patients in risk groups “very low” and “low” have the most favourable prognosis. Since their disease usually responds very well to chemotherapy, the probability of a total tumour resection is over 90 %, with correspondingly high survival rates (5-year-survival rate of 90 %). Patients with “medium risk” have a 5-year-survival rate of about 70 to 80 %, whereas patients with “high risk” have shown a 5-year-survival rate of 50 to 60 and thus a less favourable prognosis. The liver tumour experts are hoping for an increase in cure rates due to the PHITT study, the current interim recommendations and the trial to come.

Note: The survival rates mentioned in the text above are statistical values. Therefore, they only provide information on the total cohort of patients with osteosarcoma. They do not predict individual outcomes. Please ask the doctor, who is responsible for your child, for competent information on her individual prognosis.

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Glossary

alpha-1 fetoprotein	protein produced in the yolk sac, the liver of the fetus (fetal liver) and the digestive tract (also in adults) and detectable in serum; AFP is increased during pregnancy and in infants. However, elevated serum AFP levels are also found in liver diseases (such as cirrhosis and hepatitis) and certain tumour diseases (such as liver, germ cell and pancreatic tumours).
anaemia	„lack of blood“; reduction of the red blood pigment (haemoglobin) and/or the proportion of red blood cells (haematocrit) in the blood below the normal value typical for a given age. Signs of anaemia include palor, headache, dizziness, and fatigue.
anaesthesia	a type of anaesthesia in which the patient sleeps and reflex activity is reduced (= general anaesthesia); it leads to a complete insensitivity to pain, temperature and touch stimuli. Due to the reduced reflex activity, the patient is required to be on a ventilator during surgery.
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.
audiometry	method of studying auditory function using special tone generators that produce individual frequencies at a specific volume; it is used, among other things, to diagnose diseases of the hearing organs. A distinction is made between subjective and objective audiometric methods. An example of a subjective audiometric method is the tone audiogram. It requires the assistance of the person whose hearing is to be examined.
Beckwith-Wiedemann syndrome	congenital or acquired clinical condition, characterized in particular by a pathologically increased one-sided growth of the body (hemihypertrophy), enlargement of the liver, spleen or kidneys, considerably enlarged tongue, umbilical (cord) rupture, maldevelopment of the auricles, kidney abnormalities and an increased risk to develop certain malignant diseases (especially Wilms tumours); BWS is one of the cancer predisposition syndromes and is caused by various genetic changes (on chromosome 11).
BERA hearing test	ENT examination to determine hearing damage; it essentially measures the electrical activity of the auditory nerve and the auditory pathways to the brain stem and does not require the

	patients assistance (objective hearing test). In the BERA test, certain auditory stimuli (sounds) are emitted via headphones: with the help of an electroencephalogram (EEG), the reaction (in the form of brain waves, so-called acoustically evoked potentials) is measured. This is the brainstems response to the acoustic stimulus. The measurement of these brain waves makes it possible to detect hearing disorders or abnormalities in the cranial nerve or brainstem.
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.
cancer predisposition syndrome	genetic disorders that can include malformations and intellectual disability in addition to an increased risk of tumors; according to current knowledge, about 10% of childhood and adolescent cancers develop due to a known hereditary change or cancer predisposition syndrome. Cancer predisposition syndromes include Louis Bar syndrome (= ataxia telangiectatica), Beckwith-Wiedemann syndrome, Down syndrome, Hippel-Lindau syndrome, Li-Fraumeni syndrome, MEN syndrome, neurofibromatosis and WAGR syndrome. The familial form of retinoblastoma is also part of it.
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)
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)
contrast agent	substance that can be used to improve the visualization of structures and functions of the body in imaging techniques; contrast agents are mainly used in X-ray diagnostics (X-ray examination, computed tomography), magnetic resonance imaging (MRI) and ultrasound examinations.
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.
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.
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
embolization	injection of vascular occlusive substances into blood vessels, e.g. to cut off the blood supply to tumours, to stop life-threatening bleeding, and to close a vascular catheter;
embryonal	here: in an early stage of development, immature;
familial adenomatous polyposis	hereditary cancer syndrome (cancer predisposition syndrome), in which numerous glandular polyps develop in the colon and rectum; with their increase in size, the risk of degeneration also increases (transition into so-called adenocarcinomas).
genetic	concerning the (level of) inheritance or genes; inherited
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).
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
laparoscopy	examination of the abdominal cavity with a special endoscope, which is inserted through the abdominal wall under anesthesia by means of a minor surgical procedure
laparotomy	surgical opening of the abdominal cavity

laser therapy	melting of tissue by the heat effect of the laser beam; is used in the removal of tissue parts and in the obliteration of vessels.
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.
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.
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 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.
mutation	alteration of genetic material; it can arise without any identifiable external cause (so-called spontaneous mutation) or be caused by external influences (induced mutation). External influences include, for example, ionizing radiation or certain chemical substances (mutagens). If somatic cells are affected, it is referred to as a somatic mutation, and if germ cells are affected, it is referred to as a generative mutation. Somatic mutations are not heritable, while germ cell mutations can lead to hereditary damage. Depending on the extent of the change (single or multiple genes, larger chromosome segments or complete chromosomes), a distinction is made between point and block mutations as well as numerical and structural chromosomal aberrations.
nephroblastoma	embryonic, malignant solid tumour of the kidney, most common in children between the ages of 1 and 5 years, especially in the presence of various syndromes or congenital abnormalities; it accounts for about 5% of all malignant diseases in childhood and adolescence.

neuroblastoma	malignant solid tumour of the sympathetic nervous system; occurs more frequently before the age of 5, mainly in infants and newborns; neuroblastoma is one of the most common solid tumours in childhood and adolescence (accounting for about 5.5% of all malignant diseases) after CNS and soft tissue tumours.
operability	feasibility of surgery as a treatment option; whether a patient is operated depends on their clinical condition and on whether the procedure is an appropriate and effective form of treatment in the respective case (indication). The operability of a tumour particularly depends on its location in the body and its growth behaviour.
otoacoustic emissions	very quiet sounds that the inner ear emits when hearing sounds (sound waves hitting the ear); these can be registered by highly sensitive microphones. The measurement of OAE is used to check the function of the inner ear; the patients assistance is not required (objective hearing test). This form of hearing test is therefore also suitable for infants and toddlers. During the examination, tiny measuring microphones are inserted into the external ear canal. The supplied sound waves cause the outer hair cells in the inner ear to vibrate, i.e. move mechanically. This generates the quiet but measurable otoacoustic emissions.
paediatric oncologist	paediatrician who is specialized on the management of children and adolescents with cancer
palliative therapy	anti-cancer therapy that is primarily aimed at maintaining or improving the quality of life; palliative therapy becomes relevant when a patient can no longer be cured. In contrast, curative therapy is primarily aimed at healing the patient.
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.
preoperative	prior to surgery
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);
puberty	the process of sexual maturation; the period during which adolescents reach sexual maturity and become capable of reproduction

radiologist	a physician specialized in diagnostic imaging and radiotherapy
recurrence	relapse, recurrence of a disease after recovery
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.
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.
thrombocytosis	abnormally increased number of platelets (thrombocytes); too many platelets can lead to certain complaints and diseases as well as an increased risk of blood clots. However, if the number of platelets exceeds a certain limit, there may also be an increased tendency to bleed.
transplantation	transfer of tissues, organs or cells
tumour marker	biological substance (e.g. protein) in the blood or other body fluids, the increased concentration of which may indicate a newly developed tumour or tumor recurrence; tumor markers play a major role in monitoring the course of the disease in patients who presented with elevated concentrations of a certain tumour marker at the time of cancer diagnosis. Tumour markers are not proof of an existing cancer, because on the one hand, they also occur naturally in the body, and on the other hand they do not necessarily rule out a tumour if they are missing (i.e. not present in conspicuously elevated concentrations).
ultrasound	an imaging technique used to examine organs, in which ultrasound waves are sent through the skin into the body; at tissue and organ boundaries, the sound waves are reflected

	back, picked up by a receiver (transducer) and converted into corresponding images with the help of a computer.
vein	blood vessel that carries the blood circulating in the body to the lungs and heart. the veins of the bodys circulation carry oxygen-depleted blood from the organs to the lungs and heart; the veins of the pulmonary circulation transports oxygen-rich blood from the lungs to the heart.
X-ray examination	imaging procedure that uses X-rays to visualize organs or parts of organs