

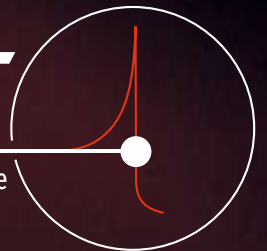


UniversitätsKlinikum Heidelberg



HIT

Heidelberg Ion-Beam Therapy Centre



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University Hospital Heidelberg

In winter 2007 / 2008 the first patients will be treated in the Heidelberg Ion-Beam Therapy Center. For the first time, patients with certain inoperable tumors are offered a realistic chance of successful treatment.

The University Hospital Heidelberg is proud to bring a worldwide unique radiation therapy facility into operation. HIT will be of great help to our patients and will lay the scientific groundwork for new cancer therapies.

The technical and scientific parts are just as innovative as the financing concept. As joint investor the University Hospital's engagement proves that major projects can be handled if they are based on firm financial grounds and scientific advancement.

Heidelberg, March 2007

The Heidelberg Ion-Beam Therapy Center HIT

Partly under ground, covering half the size of a soccer field – the Heidelberg Ion Therapy Centre (HIT) is a gigantic high tech device. HIT will start operations in winter 2007 / 2008 as the first installation of it's kind in Europe with the purpose of helping patients suffering from malignant, often otherwise incurable tumors.

Beams consist of very small particles, heavy ions like the nuclei of carbon atoms or protons, the nuclei of hydrogen atoms. They are substantially different from conventional X-rays or Gamma rays because they are effective in the depth of tissues. Furthermore, due to modern techniques they can be targeted more precisely. Therefore, patients suffering from tumors deep inside the body have the greatest benefit from heavy ion radiation – for instance tumors in the head, in the chest and hidden in the abdominal cavity. Every year about 1,300 patients will benefit from HIT.

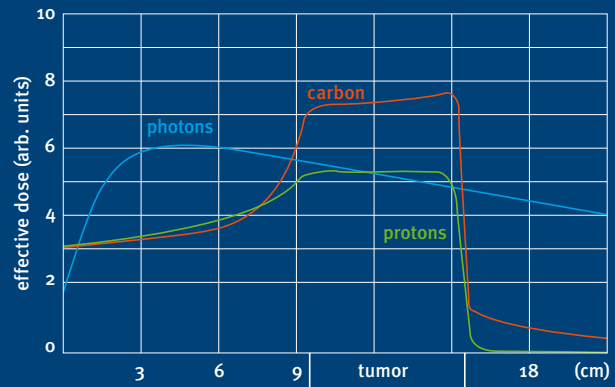
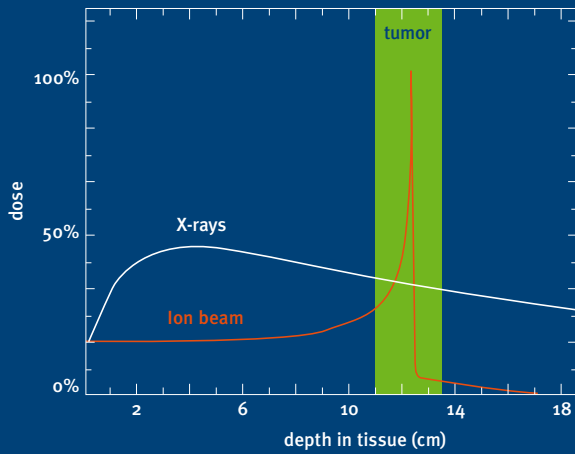
The development of HIT is a joint project of four institutions: the Universitätsklinik für Radioonkologie und Strahlentherapie, Heidelberg, the Gesellschaft für Schwerionenforschung GSI, Darmstadt, the Deutsche Krebsforschungszentrum, Heidelberg, and the Forschungszentrum Rossendorf near Dresden (see page 12), close collaborators since 1993. Their preparatory work provided the basis for the development of HIT.

Radiation devices with heavy ions or protons already exist in Europe and elsewhere abroad. However, HIT has special characteristics which make it's position in the world exceptional:

- HIT is the first combined Proton / Heavy Ion Therapy Device in Europe which is operated by a hospital and used for treating patients as well as clinical studies.
- It is the only device which uses the Intensity-Controlled Raster Scan Method and therefore provides unequalled precision in three-dimensional tumor radiation.
- It's rotatable heavy ion gantry is unique.
- The clinical and scientific environment provided by the Universitätsklinikum Heidelberg, the Nationale Centrum für Tumorerkrankungen NCT and the Deutsche Krebsforschungszentrum focusing on cancer research and treatment is unsurpassed.



HIT Building



Variations in Radiation Therapy

For many years, radiation therapy has been an indispensable part of cancer therapy. Especially, X-rays and Gamma rays, consisting of small particles called photons, have been used for attacking the tumor. They remove electrons out of tumor cell atoms and destroy larger molecules within the cells by destroying smaller chemical compounds before. Radiation beams also damage the genetic code, the DNA of the cells and thereby the construction plans for essential proteins. Furthermore, cells cannot replicate any more. Consequently, they die. However, the energy is only partly transferred to the tumor.

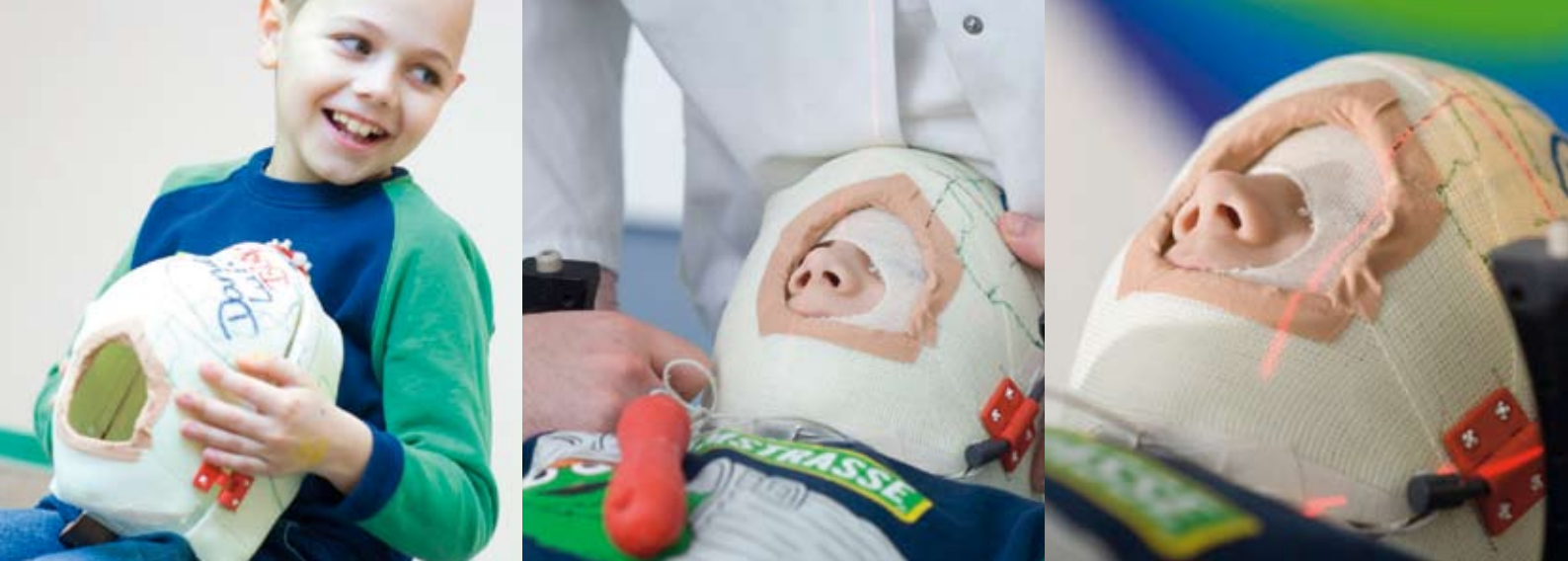
This problem has been partly solved by modern technique:

Photon beams hit the tumor from multiple directions and meet at a defined target where they discharge a maximum of energy. At the same time mobile apertures screen the sensitive healthy tissue from radiation. The so called Intensity Modified Radiation Therapy (IMRT) improves the treatment results of conventional radiotherapy considerably.

Ion radiation does not use photons, but positively charged ions, atomic nuclei which have lost their electrons from the atom shell. The particles mainly used are Hydrogen atomic nuclei (protons) and Carbon atomic nuclei, which are very heavy. This particular type of ions is therefore called heavy ion. Atomic nuclei are accelerated in large devices to about three quarters of the speed of light and shot into the tumor. The depth of penetration can be enhanced by speeding up the ions.

Ion beams have always been interesting candidates for radiation therapy, since they have special physical characteristics: When they hit the body they travel very fast through the outer layers and lose hardly any energy before they decelerate in the depth and eventually get stuck and transfer their entire deleterious energy to the surrounding tissue.

Scientists call this moment the Bragg peak after its discoverer, the English physicist William Henry Bragg. Therefore, ion beams are tailor made for treating tumors located deeply inside the body. Also, tumors with irregular edges can be scanned accurately to the millimeter with the Intensity-Controlled Raster Scan Method (see page 8 / 9).



Which Patients benefit most from HIT?

Ion beams hit their targets precisely and transfer an exact dosage of energy to the tumor. Is heavy ion or proton radiation therefore the panacea for all radiosensitive tumors?

“About 5 to ten percent of all cancer patients will benefit from ion radiation” says Professor Dr. Dr. Jürgen Debus, Medical Director of the Universitätsklinik für RadioOnkologie und Strahlentherapie and HIT. “These patients suffer from tumors which are deeply situated in the body and are therefore hardly attainable for conventional radiation treatment.”

Doctors and scientists in Heidelberg diligently prepare the wider implementation of ion radiation by conducting clinical studies comparing the treatment results from HIT with conventional radiotherapy. So far, the effectiveness of heavy ion radiotherapy is solely documented for a small number of tumors. These are malignant soft tissue tumors on the spine (Chordoma) and cartilage at the base of the skull (Chondrosarcoma). Furthermore, rare tumors of the salivary glands (Adenocarcinoma) can be successfully treated with heavy ion radiation. It is likely that the treatment results for other tumors can also be improved, for instance for certain types of lung cancer and prostate cancer.

Ion beam treatment is especially beneficial for children suffering from malignant tumors, because it avoids long-term side effects. It is possible to treat gently and with greatest care and at the same time prevent further cancer growth and occurrence of new tumors.

The German Health insurance companies have already agreed to bear the expenses if the treatment in HIT. The costs for one treatment cycle of approximately 19,500 Euro are three times as high as for conventional radiation, but are in the same dimension as extensive medication or operation of patients.



HIT treatment room
with rotating X-ray systems

What happens before und during the Treatment?

Before treatment starts, tumor specifications and dimensions will be determined accurately with modern imaging techniques like Computer Tomography (CT) and Magnetic Resonance Imaging (MRI). The HIT physicists adjust the ion beam to the coordinates. In order to ensure maximum precision the patient is fixated in an individually manufactured suspension device. Patients with brain or skull tumors wear individually manufactured masks out of plastic material. Similar splints are available for other parts of the body, for instance when tumors of the spine are treated.

The patient is fixated in his suspension device and placed by technical assistants with the help of a robot arm on a high tech table which is used for the first time ever in HIT. Thereby, the calculated position of the patient is reached with a precision of less than a millimeter. An X-ray picture ensures that that the patient has been positioned correctly and the ion beam will be targeted at the tumor: Doctors compare the bone structures of the X-ray pictures with the previous CT and MRI images.

Then radiation commences. The patient does not notice anything when the ion beam hits his tumor with very high speed. Radiation lasts between one and five minutes. During the entire radiation sensors monitor 20,000 times per second whether the beam hits precisely the target. The therapeutic beam also scans the tumor for any deviation. This Intensity-Controlled Raster Scan Method was especially developed for Ion Beam radiation by scientists from the GSI.

The entire procedure – putting on the mask, positioning the patient and the radiation – takes about 20 minutes. Likewise conventional radiotherapy, one treatment is not enough to destroy the tumor and avoid harm to the surrounding tissue. Therefore, treatment has to be repeated in the following days. An average treatment cycle lasts about 15 days.

Several weeks after the treatment cycle, with the help of CT and MRI images doctors check up whether the tumor has shrunk or has even vanished altogether.

The intensity-controlled raster scan method →

The tumor volume is subdivided into layers of equal depth. By varying the energy of the ions, the penetration depth of the beam is adjusted. The individual layers are scanned line by line, similar to the image on a TV screen. The lateral deflection of the beam is achieved by means of rapidly controllable dipole magnets. To control the intensity, each line is subdivided into pixels. The beam remains in a given pixel until the calculated target dose has been reached. As a result, this method of intensity-controlled raster scans allows a precise three-dimensional scanning of the target volume defined by the physician.

This approach represents a significant improvement over conventional treatment methods with photons, as well as over passive beam application techniques previously used in proton and ion beam therapy.

Hightech and complex Technology

Questions and Answers on HIT

How large is the Heidelberg Ionenstrahl Therapiezentrum HIT?

It is the size of half a soccer field and contains three floors. Two floors are underground, one is above ground level.

What does the building contain?

It contains two buildings in one. The first is a long glass building with offices for doctors, assistants, nurses, physicists, engineers and technicians. Adjacent to it is a copper block which houses the accelerator and the three treatment rooms. Walls, ceilings and floors are additionally protected by two meter thick concrete blocks. The building is set in a mound.

How much did HIT cost?

HIT costed about 100 Million Euro and is jointly financed by the German government and the Universitätsklinikum Heidelberg.

What are Protons?

Protons are the positively charged nuclei of hydrogen atoms.

What are Heavy Ions?

Heavy ions are atomic nuclei heavier than hydrogen nuclei which have lost their electrons. HIT uses a variety of ions which are heavier than protons, for instance helium, carbon and oxygen nuclei. Carbon and oxygen nuclei are more effective in the treatment of cancer than protons and helium nuclei.

Are protons as effective in the treatment of cancer as heavy ions?

Heavy ions are three times as effective in comparison to protons and helium ions. In body tissue, heavy ions can be directed with millimetric precision and are therefore superior to protons in the treatment of certain tumors.

How are the particles accelerated?

A very large and sophisticated device is needed (pages 10, 11). Firstly, ions are accelerated in a five meter long straight tube which leads into a “roundabout”, the so called synchrotron. There, the circulating particles are accelerated to about three quarters of light velocity.

How deep do the particles penetrate into body tissue?

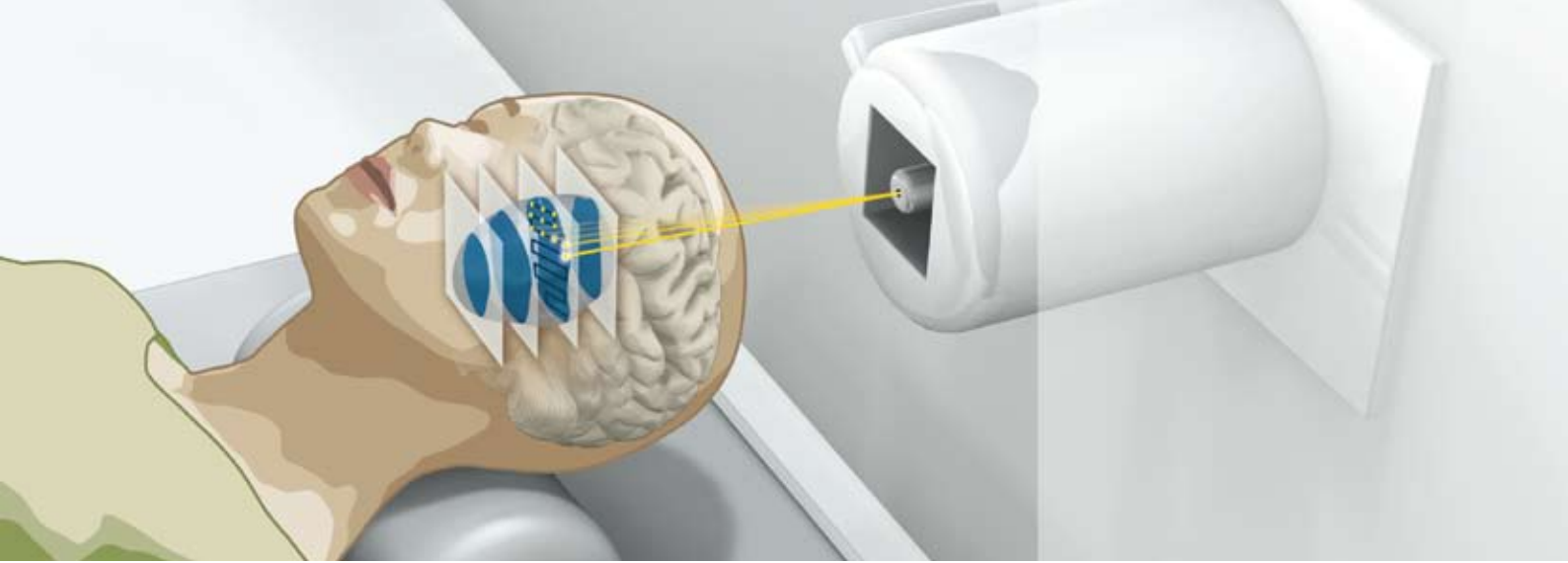
The beam can penetrate 30 cm (12 inches) into the body, depth increasing with velocity.

How much energy is needed for running HIT?

Three megawatts, as much as a small size town with 10,000 inhabitants.

How many people are working in the HIT building?

More than 70 doctors, nurses, technical assistants, physicists, engineers and technicians co-operating closely. The accelerator is continuously operated. Patients are treated in a two shift operation from Monday to Saturday.

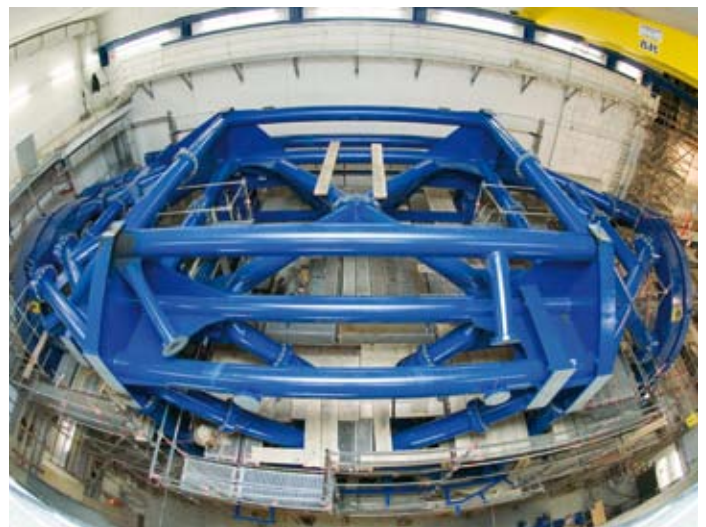


How many treatment rooms are available?

Three. Two for horizontal radiation: The beam travels through a vacuum tube out of the wall. The patient is placed on a mobile table adjusted by a high tech robot. The tumor is hit by a precisely directed beam. The third treatment room contains a rotatable, worldwide unique gantry which allows radiation treatment from all directions.

How does the Gantry work?

This gigantic device is three levels high and weighs 600 tons. Because the gantry can be rotated around the patient, the tumor can be radiated from all directions with high accuracy: the beam deviates only half a millimeter from the target. The beam transport system is placed in a complicated structure, similar to a radio telescope. The gantry room has to be climatized in order to avoid differences in temperature which deform the construction.



1. Ion Sources

Ions are positively charged atoms. In order to obtain ions, atoms must lose their negatively charged electrons. For that purpose, carbon dioxide gas flows into the ion chamber. Free electrons in the gas are accelerated by magnetic fields and microwaves. While traveling through the ion chamber, the electrons hit carbon dioxide molecules. After this collision the molecules dissociate and 4 of the 6 electrons that are part of any carbon atom are separated. Electrical fields extract the carbon ions out of the chamber; special magnets transport them further on in a regular flow in the vacuum.

2. Linear accelerator

The five metre long tubes consist of two sections: The first part converts the regular flow into a pulsating flow with 217 million micropulses per second. In this procedure the beam is collimated and the ions are accelerated. Subsequently, in the second part of the tube, electromagnetic fields accelerate the ions up to more than 10 percent of the speed of light. Exiting the accelerator through a carbon foil, the carbon atoms lose their last two electrons, such that only the 6-fold positively charged nucleus remains.

3. Synchrotron

The ions merge in a circular flow. Huge magnets deflect the beam at six turns of 60° each, until the circle is completed. Now the ions are accelerated up to 73% of the speed of light. They race through the ring 3.4 million times per second. According to their growing speed, the technicians must increase the magnetic force. This explains the term 'synchrotron' for this part of the installation.

4. High Energy Beam Transport

Vacuum tubes and magnets lead the beam further on. Shortly before entering the treatment rooms the beam passes through two scanners. These scanners are magnets which can shift the beam horizontally and vertically. With their help the ion beam can be precisely guided by raster scan method.

5. Horizontal treatment

The ion beam enters these treatment rooms through a window. In order to achieve a precise irradiation, the patient is fixed in lying position on a robotically positioned treatment couch. A plastic mask keeps head, body and extremities in a defined position. The irradiation takes up to 5 minutes.

6. Digital X-ray (radiology)

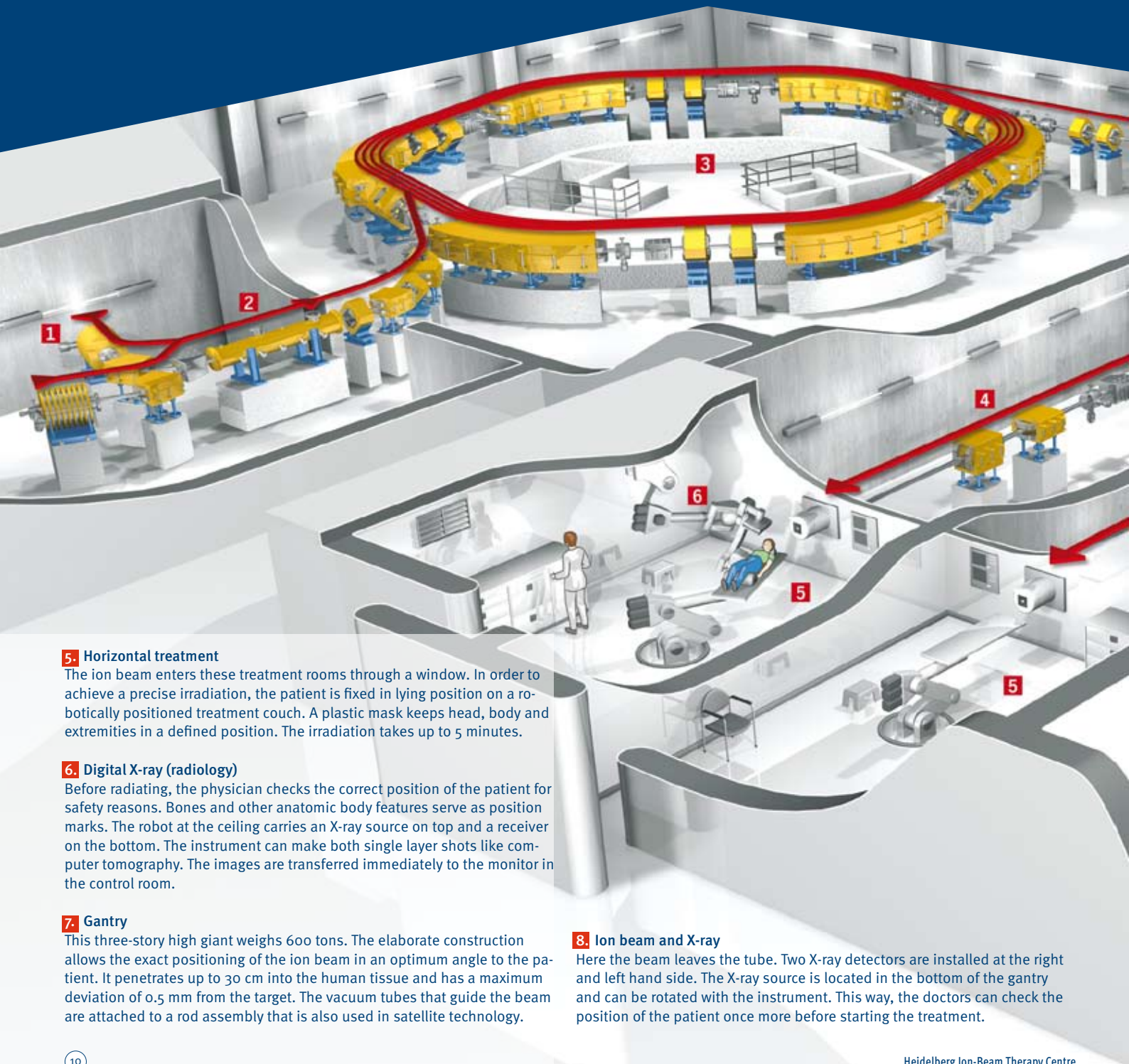
Before radiating, the physician checks the correct position of the patient for safety reasons. Bones and other anatomic body features serve as position marks. The robot at the ceiling carries an X-ray source on top and a receiver on the bottom. The instrument can make both single layer shots like computer tomography. The images are transferred immediately to the monitor in the control room.

7. Gantry

This three-story high giant weighs 600 tons. The elaborate construction allows the exact positioning of the ion beam in an optimum angle to the patient. It penetrates up to 30 cm into the human tissue and has a maximum deviation of 0.5 mm from the target. The vacuum tubes that guide the beam are attached to a rod assembly that is also used in satellite technology.

8. Ion beam and X-ray

Here the beam leaves the tube. Two X-ray detectors are installed at the right and left hand side. The X-ray source is located in the bottom of the gantry and can be rotated with the instrument. This way, the doctors can check the position of the patient once more before starting the treatment.

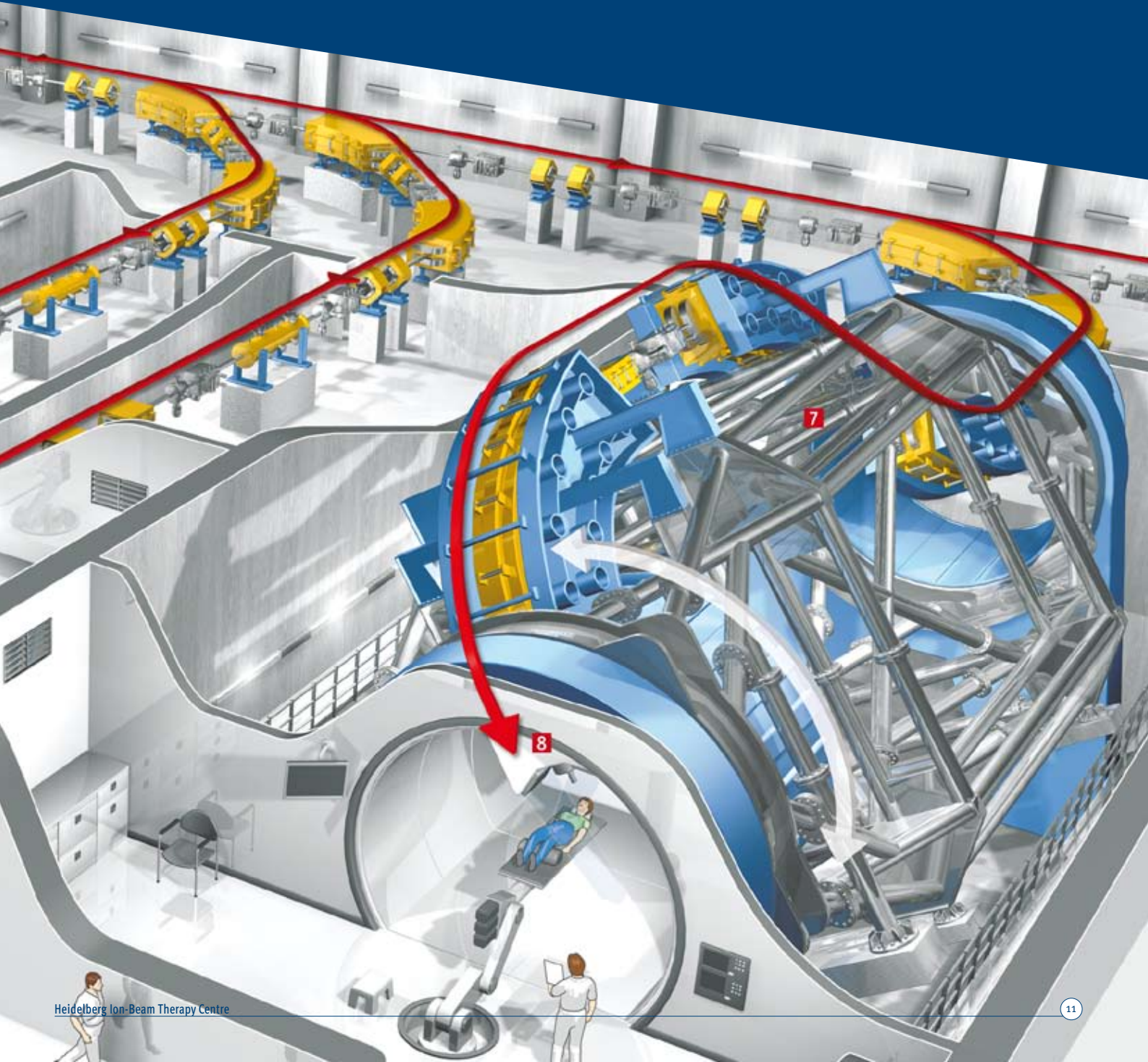
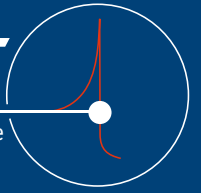




UniversitätsKlinikum Heidelberg

HIT

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Gantry Raum
Before Gantry assembly

The Pilot Project Partners

Within of the pilot project, the project partners have developed new, trendsetting methods that represent key technologies for HIT as well as future projects. This ground-work—in combination with the expertise of the participating institutes in various areas of particle therapy—represents an ideal basis for a successful completion of the new project, jointly with industrial partners.

The main research field oncology of the medical faculty (University Heidelberg) and the Radiology Clinic are important pilot project partners. The Universitätsklinik für RadioOnkologie und Strahlentherapie is one of Germany's largest radiation therapy centers, with about 3,000 new patients per year. In addition to patient care, a broad research program in the area of radiation oncology is pursued at Heidelberg. The clinical studies of ion beam therapy in the context of the pilot project are also being conducted under its management.

The Deutsche Krebsforschungszentrum in Heidelberg, with a focused program on radiological diagnostics and therapy, is the center of internationally renowned research and development in the field of leading edge techniques in radiation therapy. Here, major scientific achievements have been made in the field of three-dimensional treatment planning and precision radiotherapy, including dosimetry and quality assurance. New therapeutic methods are developed and clinically tested in the Clinical Cooperative Unit for Radiotherapeutic Oncology, in conjunction with the Universitätsklinik für RadioOnkologie und Strahlentherapie.

The Gesellschaft für Schwerionenforschung GSI in Darmstadt is among the internationally leading centers of heavy-ion research. More than 1,000 scientists from over 30 countries currently conduct research at its accelerator facility. Since its establishment, GSI has also been conducting studies in radiation biology, especially concerning the radiobiologic effects of ions. In addition, there is abundant expertise in the areas of accelerator technology and the development of highly precise irradiation methods. With the SIS heavy-ion synchrotron, GSI currently has at its disposal the only accelerator system in Europe where patients with deep-seated tumors can be treated with ions.

The Forschungszentrum Rossendorf near Dresden conducts basic and applied research in the fields of materials research, biomedicine and biochemistry, environmental research, as well as nuclear, hadron and radiation physics. The planned clinical facility will especially benefit from this institute's in-depth expertise in the biomedical application of positron emission tomography (PET).



Universitätsklinikum Heidelberg



RadioOnkologie
Universitätsklinikum Heidelberg



DEUTSCHES
KREBSFORSCHUNGSZENTRUM
IN DER HELMHOLTZ-GEMEINSCHAFT



Gesellschaft für Schwerionenforschung Darmstadt



Forschungszentrum
Dresden Rossendorf

Milestones of the HIT Project

| | |
|--------------------|--|
| 1991 | Scientists in Darmstadt develop the Intensity-Controlled Raster Scan Method. |
| 1992 - 1995 | Technicians in Darmstadt develop special software for a biologically based radiation planning system. |
| 1993 | Four partners initiate the pilot project on ion beam therapy: Gesellschaft für Schwerionenforschung, GSI, Darmstadt, die Radiologische Universitätsklinik Heidelberg, das Deutsche Krebsforschungszentrum, Heidelberg, das Forschungszentrum Rossendorf near Dresden. |
| 1997 | For the first time in Europe, patients are treated in Darmstadt with ion beams (Carbon). |
| September 2000 | GSI presents the feasibility study for the Heidelberg Heavy Ion-Beam Therapy Centre HIT. |
| May 2003 | The German Science Council gives permission to the commissioning of accelerator parts. |
| October 2003 | Commissioning of the Arge SIT (Strabag, M+W Zander) as main contractor for the building site. |
| 12th May 2004 | The foundation of HIT is laid. |
| 20th June 2005 | Topping-out Ceremony of the HIT building |
| 5th October 2005 | Installation of the accelerator is started. |
| 1st September 2006 | The HIT building is taken over by the Universitätsklinikum. |
| January 2007 | Assembly of the gantry. |
| Nov / Dec. 2006 | First beam after the linear accelerator (LINAC). |
| February 2007 | Maximum speed in Synchrotron reached. Installation of medical devices for horizontal radiation places finished. |
| March 2007 | First beam reaches horizontal radiation places. |
| Winter 2007 / 2008 | First patient will be treated in HIT. |

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Treatment Questions

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page 10/11: HIT facility: source and © Stern
photos: Universitätsklinikum Heidelberg, Medienzentrum

Main involved companies

Gesellschaft für Schwerionenforschung
accelerator systems (different suppliers)

MT Mechatronics GmbH
heavy ion Gantry

Siemens AG Medical Solutions
medical technology

Arge SIT (Strabag AG, M+W Zander)
building general contractor

