INTRABEAM System from ZEISS
Targeted Radiotherapy
The moment radiotherapy can be ideally tailored to the needs of your patient.

This is the moment we work for.
The moment radiotherapy can be ideally tailored to the needs of your patient. This is the moment we work for.
Targeted intraoperative radiotherapy with the INTRABEAM® System from ZEISS – Precision simplified

The trend in oncological therapy is moving towards the targeted, risk-adapted and interdisciplinary treatment of tumors. The ZEISS INTRABEAM System*, the innovative radiotherapy system from ZEISS, is an ideal system for these requirements. It uses low-energy X-ray photons to deposit the high-dose radiation directly into the tumor or the tumor bed. The result is a localised and highly effective therapy. The ZEISS INTRABEAM System received FDA approval in the USA in 1997 and was awarded the CE certification in Europe in 1999. It provides key benefits for the intraoperative irradiation of solid tumors:

- **Localised tumor control – targeted effectiveness**
  Intraoperative radiotherapy (IORT) with the ZEISS INTRABEAM System enables high dose treatment. The INTRABEAM System from ZEISS is used to irradiate the tumor bed, the area where the risk of recurrence is highest immediately after R0 resection. It can also be used for the irradiation of incomplete tumor resections in R1 and R2 scenarios.

- **Localised irradiation with a high relative biological effectiveness**
  The relative biological effectiveness of low-energy X-rays is very high as a result of the higher ionization density of radiation in tissue compared to megavolt X-rays. At the same time, due to the steep dose falloff, a special characteristic of the low-energy radiation, the tissue of interest is irradiated avoiding collateral damage.

- **Practical mobility and fast workflow integration**
  The mobile ZEISS INTRABEAM System is a flexible instrument that can also be implemented without high investment costs for complex radiation protection measures in the building. The miniaturized mobile accelerator permits easy and safe handling and simple integration into the existing workflow. It can be deployed in multiple operating rooms and managed by a single radiation oncologist.

- **Versatility of the clinical application**
  The ZEISS INTRABEAM System has been approved for the treatment of all areas of the body. In addition to the successful treatment of breast cancer, the system opens up entirely new radiotherapy alternatives for a wide range of tumors.

- **Higher quality of life outcomes and treatment comfort for patients**
  Irradiation with the ZEISS INTRABEAM System enables localised treatment. The tumor is irradiated avoiding collateral tissue damage. In comparison to conventional radiotherapy, the shortened overall treatment regime with the ZEISS INTRABEAM System can also reduce associated side effects and is gentle on patients – a key element to increase their quality of life.
TARGIT – targeted intraoperative radiation therapy with the INTRABEAM System from ZEISS

Step 1  The position of the tumor is determined.
Step 2  The tumor is surgically removed.
Step 3  The ZEISS INTRABEAM Spherical Applicator is positioned in the tumor cavity.
Step 4  The radiation is applied for about 30 minutes. The applicator is removed and the incision closed.
TARGIT radiation therapy for breast cancer: Effective, risk-adapted and targeted

In recent years, a new approach has been gaining ground in the treatment of breast cancer: radical surgical methods are being replaced by less-invasive, breast-conserving therapy. Such a trend is now also appearing in radiotherapy. Oncologists are moving away from the current, largely standardized treatment plan to risk-adapted individualised therapy.

Targeted irradiation avoids collateral tissue damage

In traditional radiotherapy the tumor bed is frequently missed due to postoperative changes or oncoplastic reconstruction. The exact position of the tumor cavity is difficult to localize, even with modern-day imaging techniques.\(^1\)

This issue is negated with the targeted intraoperative irradiation using the INTRABEAM System from ZEISS. The 30-minute irradiation procedure is performed during the operation immediately after the tumor is excised. During this procedure, the isotropic dose distribution is applied directly into the tumor cavity using a spherical applicator in a way that ensures direct contact with the target tissue. Radiation is applied precisely to the area with the highest risk of tumor recurrence. The surrounding healthy tissue is spared.

Shorter treatment duration is gentle on patients

Unlike traditional irradiation, radiotherapy with the ZEISS INTRABEAM System can be adapted to the needs of the patient. The standard approximate six weeks of post-op irradiation is reduced and can be completely eliminated for selected patients with a low risk profile. The shorter irradiation period eliminates repetitive journeys for treatment and also considerably lowers the overall physical and physiological stress on the patient.\(^2\)
TARGIT single fraction treatment for breast cancer: Radiotherapy administered in 30 minutes instead of approximately six weeks

The targeted, intraoperative single dose of radiation with the INTRABEAM System from ZEISS is on the way to becoming the new treatment standard of care for breast cancer. This risk-adapted therapeutic solution makes it possible for a patient cohort with a favorable prognosis to complete surgery and irradiation in a single session. Traditional radiotherapy, including the stress of protracted treatment regimes, is eliminated for these patients. In situations in which definitive irradiation cannot be performed, such as local recurrence, the TARGIT single dose of radiation** also provides an opportunity for a second attempt at breast-conserving therapy.

TARGIT-A Trial: The Study

Study Design
TARGIT-A is currently the largest multicenter randomized clinical trial in the field of Partial Breast Irradiation. 3451 patients aged 45 and older with invasive ductal carcinoma were randomized in 33 centers from 11 countries between 2000 and 2012. Over this time 1721 women received the study treatment (TARGIT), compared to a control group of 1730 women who received standard EBRT treatment.
Patient Characteristics
The patients selected for the TARGIT-A trial were mainly good prognosis but not elderly, and there were a substantial number of adverse prognosis patients.

<table>
<thead>
<tr>
<th>Duration</th>
<th>2000 - 2012</th>
</tr>
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<tbody>
<tr>
<td>No. of patients</td>
<td>3451 patients</td>
</tr>
<tr>
<td>Screen detected</td>
<td>~ 69 %</td>
</tr>
<tr>
<td>Tumor size</td>
<td>~ 87 % ≤ 2 cm</td>
</tr>
<tr>
<td>Tumor grade</td>
<td>~ 15 % grade 3</td>
</tr>
<tr>
<td>LN invasion</td>
<td>~ 16 % Node positive</td>
</tr>
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5-Year Results of the TARGIT-A Trial – with the INTRABEAM System from ZEISS

Efficiency of TARGIT compared to EBRT
The results of patients with no local recurrence in the ipsilateral breast at 5 years point out that there is no significant difference comparing TARGIT concurrent with lumpectomy and EBRT.

Mortality of TARGIT compared to EBRT
There were significantly less non-breast-cancer deaths with TARGIT concurrent with lumpectomy but caused by cardiovascular causes and other cancers.

Tolerability of TARGIT compared to EBRT
Wound-related complications were much the same between both groups but grade 3 or 4 radiotherapy-related skin complications were significantly reduced with TARGIT.

Study conclusion
The randomized multicenter clinical trial confirmed that Targeted Intraoperative Radiotherapy (TARGIT) using the ZEISS INTRABEAM System is non-inferior to External Beam Radiotherapy (EBRT).
Targeted irradiation allows second breast-conserving therapy
A special case is the treatment of patients in whom a tumor recurrence is found in an already treated breast. Here, thanks to the targeted irradiation of the tumor bed and the protection of the surrounding tissue, the therapy with the ZEISS INTRABEAM System can offer the patient the possibility of a second breast-conserving treatment.4, 5

Key advantages for patients with lower risk profile
- Reduction of the radiotherapy treatment duration to around 30 minutes.
- Targeted irradiation of the tissue of interest, avoiding collateral damage.
- Less physical and psychological stress on patients.
- Time and cost savings.
TARGIT boost irradiation for breast cancer:
High effectiveness through targeted irradiation

Local recurrences after breast-conserving surgery and postoperative EBRT normally occur within the original index quadrant of the primary. Additional irradiation of the tumor bed (boost) is therefore part of the standard of care in breast cancer therapy. In intraoperative radiotherapy with the ZEISS INTRABEAM System, the boost element of the EBRT regime can be replaced and be administered to the target tissue immediately after wide local excision. This boost element of the overall treatment regime is highly accurate as it is applied at the time when the tumor bed is visualised during surgery. This method shows a better treatment outcome than expected and can additionally reduce traditional radiotherapy by 5-8 days. The ZEISS INTRABEAM System is used for this purpose.

Very good effectiveness and shorter treatment times
This method has over 10 years of clinical experience. Clinical results reveal that the recurrence rate is exceptionally low, up to one half or one third of that expected with the traditional method. This means that a tumor was found again in only 1.7 percent of the patients in the first five years after surgery.

No local recurrences after 5 years
Comparison of the breast cancer recurrence rate (Non-randomised).
With the ZEISS INTRABEAM System the recurrence rate is only half of the recurrence rate of conventional radiotherapy.
Radiotherapy with fewer side effects
The intraoperative boost therapy is tolerated very well by patients. As studies on acute and long-term toxicity following the intraoperative boost of 20 Gy have shown, there are no abnormalities. Doctors and patients also found the cosmetic result following the intraoperative boost with the ZEISS INTRABEAM System to be very good.9, 10

Benefits of boost treatment with the INTRABEAM System from ZEISS compared to merely EBRT treatment***
- Very low local recurrence rate.
- Low rate of side effects.
- Very good cosmetic result.
- Duration of conventional EBRT treatments are reduced by around 25%.
XRS 4 Miniaturized Linear Accelerator – the heart of the INTRABEAM System from ZEISS

Electrons are emitted and accelerated to a potential of 50 kV in this miniaturized linear accelerator. The electron beam is guided through a 3 mm drift tube before interacting with a 1 µm thick gold target which results in the generation of low-energy X-rays. The miniaturized linear accelerator has been designed to generate the unique spherical dose distribution emitted from the center to the tip of the tube.
The XRS 4 Miniaturized Linear Accelerator of the ZEISS INTRABEAM System – Targeted radiotherapy

The low-energy X-ray photons used by the ZEISS INTRABEAM System are known for their physical and radiobiological characteristics which can lead to superior benefits in radiotherapy. The relative biological effectiveness (RBE) increases as the photon energy decreases. The increased ionization density of the radiation in the tissue leads to the relatively high biological effectiveness of low-energy X-rays in the near range.11 At the same time, the periphery is protected through the steep physical depth dose gradient of this type of radiation. This means that the radiotherapeutic dose can be targeted at the area of interest only sparing healthy tissue.

Innovative technology that brings extra benefits to everyday hospital case loads

Safety for doctors and patients
During radiotherapy, the dose can be monitored in situ with the Control unit PRS 500 and the PRS 500 Terminal. Besides constantly recording the physical dose rate, the ZEISS INTRABEAM System automatically checks the critical parameters and indicates any deviations. A complete set of quality assurance tools ensures consistency, tolerance and aid in the daily checks.

Ease of use and precise positioning
Thanks to the perfectly balanced ZEISS NC32 INTRABEAM Floor Stand, the applicator can be effortlessly moved into any position and locked with pinpoint accuracy. During irradiation, electromagnetic couplings hold the applicator exactly in the set treatment position.

Mobility for workflow integration
The INTRABEAM System from ZEISS can be easily moved to different operating rooms and thus deployed flexibly throughout the hospital.
The INTRABEAM System from ZEISS: Targeted radiotherapy for a wide range of applications

Local control of tumors is vital in oncology. With the ZEISS INTRABEAM System, targeted radiotherapy can be performed during surgery without delay. Following the successful R0 resection of a tumor, the tumor bed, the area with the highest risk of recurrence can be irradiated directly. It can also be used for the irradiation of incomplete tumor resections in R1 and R2 scenarios. Furthermore, an in-vitro study showed that intraoperative irradiation with the INTRABEAM System from ZEISS exhibits an antitumoral effect on wound fluid within the tumor bed environment.\(^\text{14}\)

Skin cancer
The versatility of the ZEISS INTRABEAM System is also displayed in the treatment of skin cancer. Particularly in the treatment of non-melanoma skin cancer, irradiation is an important therapy option. In a prospective study, it was shown that intraoperative radiotherapy with the ZEISS INTRABEAM system was as effective in the management of non-melanoma skin cancer as conventional radiotherapy techniques.\(^\text{15}\) The well-known advantages of the ZEISS INTRABEAM System – targeted radiation delivery, low shielding requirements, and cost effectiveness – also hold true for the treatment of skin cancer.\(^\text{16, 17}\)

Gastrointestinal cancer
In cancer surgery, the primary goal is to completely excise the tumor. However, incomplete resection is sometimes the outcome. The ZEISS INTRABEAM System can be used to improve local control of colorectal tumors.\(^\text{18}\) Its value has also been demonstrated in the setting of laparoscopic hemicolectomy in patients with colon cancer and gastrectomy in patients with gastric cancer.\(^\text{19}\)

Oral cancer
Delivering a boost radiation intraoperatively with the ZEISS INTRABEAM System has potential advantages in the treatment of oral cancers. After resection, the margins of the tumor can be immediately treated with radiotherapy, which may have a positive impact on local recurrence rate. Additionally, the numerous sensitive structures in this anatomical region can be spared due to the steep fall-off of the low-energy radiation emitted by the system. A geographical miss is unlikely since the applicator can be positioned directly in the tumor bed. First study data have convincingly demonstrated the value of this concept.\(^\text{20}\)
Spinal metastases
For many cancer patients who develop spinal metastases in the natural course of their disease, percutaneous kyphoplasty and vertebroplasty are a valuable treatment option. By using intraoperative radiotherapy with the ZEISS INTRABEAM System during kyphoplasty or vertebroplasty, the metastases can be sterilized and if necessary simultaneously stabilized, a solution that results in reduction of the patient’s discomfort. It also restores mobility, significantly enhancing the patient’s quality of life. The first clinical trial experience of this approach has yielded very promising results.21

Glioblastoma
Post-operative irradiation of brain tumors and cerebral metastases is often delayed due to wound healing problems and long patient recovery times following the operation. Intraoperative radiotherapy with the ZEISS INTRABEAM System offers a cost-efficient and immediate treatment. A substantial number of studies have proven the value of the ZEISS INTRABEAM System in the treatment of brain and cerebral tumors in both children and adults.22,23,24
The benefits of the simple implementation of radiotherapy alternatives in your hospital

With the ZEISS INTRABEAM System, you are offering your patients one of the most innovative radiotherapy methods with considerable treatment comfort. The INTRABEAM System from Zeiss can be easily installed in your hospital. Unlike linear accelerators and radioactive preparations, this system does not require any structural radiation protection measures. This saves time and money. The very low shielding requirements also mean maximum safety for your patients and staff.

Increasing effectiveness with the INTRABEAM System from ZEISS
Intraoperative radiotherapy with the ZEISS INTRABEAM System shortens the duration of treatment, sometimes considerably compared to conventional EBRT treatments. The resulting time savings enable higher throughput in your hospital without changing personnel expenses. Fewer days of treatment also mean that patients have lower travel costs. With the INTRABEAM System from ZEISS, you can react flexibly to the fluctuating use of your linear accelerator, thus providing you with more freedom to plan your treatments.

Mobility delivers more flexibility
Furthermore, the mobile ZEISS INTRABEAM System provides the medical team with a physically flexible device. The 1.6 kg XRS 4 can be quickly removed from one ZEISS NC32 INTRABEAM Floor Stand and mounted to another one in a second or third operating room. This allows radiotherapy at multiple locations by a single radio oncologist.

Made by ZEISS
With the ZEISS INTRABEAM System, you are purchasing not only an innovative irradiation system but also the quality and precision that has been associated with the name ZEISS for more than 160 years. As a global company, we invest considerably in research and education – for the safety of our products and for the good of your patients.

The INTRABEAM System from ZEISS also stands for customized service:
- Intensive clinical training at the TARGIT Academy
- Application training during the installation
- Supervised training in hospitals
- More than 40 sales companies and more than 100 representatives around the world ensure fast, on-site service
System overview
General technical information

**ZEISS INTRABEAM Core System**
The Control unit PRS 500, the PRS 500 Terminal and the XRS 4 Miniaturized Linear Accelerator are part of the ZEISS INTRABEAM Core System. The Control unit PRS 500 is controlling and monitoring the XRS 4 during the treatment. The PRS 500 Terminal is the interface between the user and the machine and it is directly linked to the Control Unit PRS 500 via bidirectional communication. The XRS 4 emits low-energy X-rays (max. 50kV) with isotropic dispersion. The target tissue is evenly irradiated.

<table>
<thead>
<tr>
<th>Component</th>
<th>Weight</th>
<th>Dimensions</th>
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<tbody>
<tr>
<td>XRS X-ray Source (XRS 4)</td>
<td>1.6 kg</td>
<td>70 x 175 x 110 mm</td>
</tr>
<tr>
<td>Control Unit PRS 500</td>
<td>4.5 kg</td>
<td>305 x 89 x 381 mm</td>
</tr>
<tr>
<td>PRS 500 Terminal</td>
<td>12.0 kg</td>
<td>400 x 341 x 100 mm</td>
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**ZEISS NC32 INTRABEAM Floor Stand**
The ZEISS NC32 INTRABEAM Floor Stand combines performance with maximum reliability and flexibility. Electromagnetic couplings lock the miniaturized accelerator in the treatment position with millimeter accuracy. Usable in any OR.

Weight: 275 kg | Transport position: 740 x 1940 x 1500 mm (width x height x length)
ZEISS INTRABEAM Cart
The ZEISS INTRABEAM Cart provides an easy means of transport in and out of the OR. The generously designed workstation of the ZEISS INTRABEAM Cart enables quality inspections directly on the ZEISS INTRABEAM Cart. The PRS 500 Terminal, the Control Unit PRS 500 and the Dosimeter, as well as all components required for quality inspection and treatment are ergonomically arranged on the cart.
Weight: 105.0 kg | Dimensions: 900 x 1690 x 600 mm (width x height x length)

ZEISS INTRABEAM Spherical Applicator
The ZEISS INTRABEAM Spherical Applicator is used to irradiate the tumor bed, e.g. in breast-conserving treatment for breast cancer patients. A complete set of spherical applicators with diameters from 15 to 50 mm enables exact adaptation to the size of the tumor bed. The spherical applicators are sterilizable and can be re-used.
The ZEISS INTRABEAM Spherical Applicators are available in diameters of 15, 20, 25, 30, 35, 40, 45 and 50 mm.

ZEISS INTRABEAM Needle Applicator
The ZEISS INTRABEAM Needle Applicator can be used for the interstitial irradiation of tumors, e.g. in the treatment of spinal metastases. The single-use ZEISS INTRABEAM Needle Applicator has a diameter of 4.4 mm.
The ZEISS INTRABEAM Needle Applicator has a diameter of 4.4 mm.

ZEISS INTRABEAM Flat Applicator Set
The ZEISS INTRABEAM Flat Applicator Set is used in the treatment on surgically exposed surfaces such as the gastrointestinal tract. The ZEISS INTRABEAM Flat Applicator Set has an optimized flat radiation field of 5 mm to the applicator surface. The flat applicators are sterilizable and can be re-used.
The applicators of the ZEISS INTRABEAM Flat Applicator Set are available in diameters of 10, 20, 30, 40, 50 and 60 mm.

ZEISS INTRABEAM Surface Applicator Set
The ZEISS INTRABEAM Surface Applicator Set is developed to treat tumors on the surface of the body e.g. non-melanoma skin cancer. The ZEISS INTRABEAM Surface Applicator Set generates an optimized flat radiation field on the surface. The surface applicators are sterilizable and can be re-used.
The applicators of the ZEISS INTRABEAM Surface Applicator Set are available in diameters of 10, 20, 30 and 40 mm.
* The ZEISS INTRABEAM System consists of: INTRABEAM System PRS 500 with XRS 4, INTRABEAM Cart and NC32 INTRABEAM Floor Stand

** The use of the TARGIT single dose of radiation should comply with local/national clinical directives. In some countries, the single dose of radiation is only permitted within the scope of clinical studies.

*** The use of the TARGIT boost treatment should comply with local/national clinical directives. In some countries, the boost treatment is only permitted within the scope of clinical studies.