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# A Novel Mobile Device for Intraoperative Radiotherapy (IORT)

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## Introduction

In many clinical situations, the radiation dose which can be safely delivered to the tumour is limited by normal tissues in close proximity to the tumour volume. On the other hand, the likelihood of obtaining local control improves with increasing irradiation doses. If microscopical residual disease persists after gross tumour resection, the external beam radiotherapy doses necessary to achieve local control are higher than 60 Gy in 1.8–2 Gy fractions. Dose requirements would even be higher if gross residual disease remains after maximal resection, but with dose requirements >60 Gy the radiation tolerance of numerous organs and structures would be exceeded.

Single high radiation doses can also be given by intraoperative radiotherapy (IORT). First experiences with IORT before or after combined external beam radiotherapy were gained during the 1960ies in Japan and the 1970ies in the United States, as a preferred treatment alternative for patients with locally advanced malignancies. This treatment method is now used in specialised centres for gastrointestinal tumour entities and sarcomas [1–3]. By direct visualisation, the tumour bed can be treated by a high single dose, while sparing the normal tissue as a result of mobilization or shielding.

IORT, as a multidisciplinary therapy, requires a well-coordinated cooperation between the involved anaesthesia, surgery and radiotherapy staff. Most of the technical problems can be overcome with dedicated or semi-dedicated IORT facilities, which can be built as specialized operating rooms with integrated accelerators in order to avoid patient transportation and sterility problems. However, the dedicated IORT facility in an operating room (OR) is quite expensive and the OR has to be fitted for proper shielding.

New technologies try to improve the availability of IORT not only from the perspective of cost-effective alternatives. By using mobile machines, IORT can even be given in different ORs by moving the mobile accelerators to the OR table, instead of transporting the patient to the accelerator. New technologies include mobile intraoperative brachytherapy (HDR-) units, mobile electron facilities, e.g. Mobetron (Siemens AG, Munich, Germany) and Novac-7 (Hitesys SPA, Aprilia, Italy), and the miniature x-ray source Intrabeam™ (Carl Zeiss, Oberkochen, Germany). Since the beginning of 2002, this novel mobile x-ray system has been used for IORT in our institution.

This report includes our first experiences using the system and describes 6 cases of patients with in-breast tumour recurrences after breast-conserving surgery and radiotherapy, who were treated with local excision and IORT.

## Patients and Methods

The miniature x-ray source (PRS-400, Photoelectron Corporation, Massachusetts, USA and Carl Zeiss), which is small and light-weight (1.8 kg), is combined with a balanced floor stand with 6 degrees of freedom to gain access to target sites throughout the body. This flexibility enables radiation therapy in any operating theatre in any direction. Due to low-energy x-rays no special shielding is required, and the treatment can be carried out in unmodified operating rooms.

Before each use of the Intrabeam system, a standardized quality assurance program has to be used to ensure the homogenous dose distribution and dose rate. Intrabeam has a miniature x-ray source with a probe with 10 cm in length and 3.2 mm in diameter. At its end the accelerated electrons strike a gold target resulting in an isotropic x-ray distribution around the tip (fig. 1). Specialized spherical applicators ranging from 1.5 to 5.0 cm in diameter are available. On the applicator surface a homogeneous dose distribution isotropic to all surfaces of the tumour cavity can be precisely applied. After surgical tumour removal the tumour bed is assessed and the appropriate applicator is placed inside the tumour cavity. Intrabeam is then completey wrapped up in a sterile plastic cover with a hole for the sterile applicator to pass through. A purse-string suture is made within the mobilized breast tissue, in order to bring the target tissue in close contact to the applicators surface. With this technique, the mobilized pliable tissue around the tumour cavity can be conformed to the x-

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ray-source. If the tumour is on the left side, a sterilized 0.5 cm perspex plate is put on the chest wall to protect the heart and the coronary vessels. After the purse string is tightened around the applicator, the skin is everted by one or two distractors to avoid that skin tissue is less than 1 cm from the applicators surface. Before starting the therapy the treatment field is covered with a tungsten sheet for radiation shielding.

The x-ray system produces low-energy photons (30–50 keV) that are attenuated rapidly within the tissue. Because of their low energy, the x-rays' depth-dose falls off rapidly with minimal exposure of surrounding tissue (e.g. lung tissue) in breast irradiation. The treatment times depend on the chosen applicator size and dose (10–20 Gy), and varies between 2 and 50 min (table 1). After the treatment the applicator is removed and the wound is closed as usual.

Based on clinical experience (stereotactic radiosurgery of brain, liver and/or lung metastases) and radiobiologic modelling, the physical IORT dose can be multiplied with a factor 2.5 to approximate biologic effects. Furthermore, it is well established that the relative biological effectiveness (RBE) of low-energy photons is larger compared with higher-energy x-rays, due to the photoelectric absorption at low energies [4]. In addition, radiobiological experiments, studying cell survival after treatment with the x-ray source of the Intrabeam device, showed RBEs between 1.2 and 2.5 [5].

Between February and October of 2002, 6 out of 40 patients treated by IORT at our institution with the Intrabeam system were suffering from locally relapsed breast carcinoma. The recurrent disease was diagnosed 3–13 years after prior breast-conserving surgery (BCS), 5 out of 6 had previous external beam radiotherapy with a median dose of 56 Gy (45–56 Gy). Median age of the patients was 65 (52–80), localisation and histology was the same as the reference tumour: there were 3 ductal-invasive, 2 lobular-invasive carcinomas and one adenoid-cystic carcinoma. For additional patient data see table 2.

All 6 patients could be treated again by BCS in combination with IORT to the tumour bed. All local relapses were completely resected microscopically. Applicators were chosen depending on the size of the re-excised tumour cavity: 2 patients were treated with the 3.5 cm applicator, 1 with the 4 cm applicator, 2 with the 4.5 cm applicator and 1 with the 5 cm applicator. Median dose to the applicator surface was 17.4 Gy (14.7–20.0 Gy). Median treament time was 27.8 min (18.6–35.9 min). One patient, who had no whole-breast radiotherapy for the primary tumour, was additionally treated by 46 Gy external beam radiotherapy after complete wound healing.

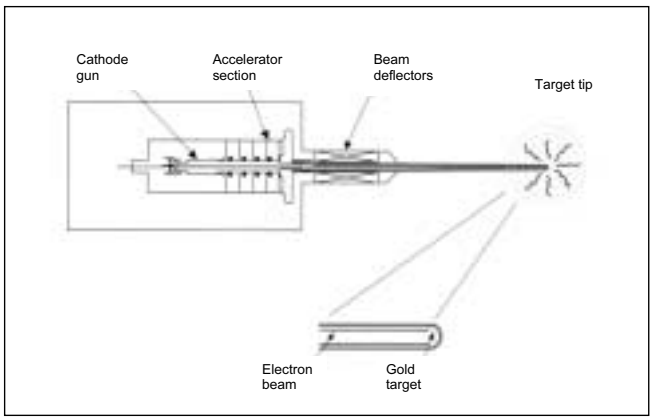


**Fig. 1.** The miniature x-ray source PRS400 consists of an electron accelerator with a gold target at the end of the probe. The probe is designed to provide an intense source of x-rays at the tip. The electrons are accelerated to the desired energy level and focused down the probe to strike the gold target resulting in an isotropic distribution of radiation around the tip of the probe.

**Table 1.** Treatment time for 20 Gy at the applicator surface according to applicator sizes at the Mannheim University hospital

| Applicator, mm | Treatment time, min |
|---|---|
| 15 | 7.07 |
| 20 | 11.53 |
| 25 | 17.43 |
| 30 | 24.98 |
| 35 | 18.57 |
| 40 | 26.8 |
| 45 | 36.58 |
| 50 | 48.82 |

## Results

IORT with the mobile Intrabeam device was feasible in all 6 cases without any technical problems. Due to the highly flexible floor stand, the fixation of the applicator was a very easy and quick procedure and took only about 5–10 min. Including treatment time the whole IORT procedure took about 25–45 min. No clinically relevant fibrosis could be detected. Neither skin necrosis nor vessel/nerve injuries could be observed after treatment. The skin reaction during additional external beam radiotherapy was within the normal range. In all 6 relapsed breast cancer patients the cosmetic outcome was excellent after treatment. After a follow-up of 8 months no further local relapse was observed.

**Table 2.** Patient data for 6 patients treated by IORT for locally relapsed carcinoma of the breast.

| Age | Date of PT | pTNM of PT | Localisation | Size of relapse, cm | Histology | Dose of prior EBRT, Gy |
|---|---|---|---|---|---|---|
| 53 | 1999 | pT2N0(0/22)G2 | left u/i | 1.2 | lobular-invasive | 56 |
| 67 | 1999 | pT1b(m)N2(6/25)G2 | right u/o | 0.8 | ductal-invasive | no EBRT |
| 52 | 1995 | pT1a(m)N0(0/13)G2 | left u/o | 0.2 | adenoid-cystic | 56 |
| 63 | 1993 | pT1b(m)N0(0/16)G2 | right u/o | 0.8 | ductal-invasive | 56 |
| 80 | 1991 | pT1cN0(0/28)G2 | left u/o | 1.2 | lobular-invasive | 50 |
| 71 | 1989 | pT1N0(0/10)G1 | right u/o | 1.2 | ductal-invasive | 45 |

PT = Primary tumour, EBRT = external beam radiotherapy, u/i = upper/inner quadrant, u/o = upper/outer quadrant.

## Discussion

IORT is a treatment modality used only in specialized departments with dedicated facilities. So far the operating rooms (ORs) had to have special shielding due to radiation exposure. Another disadvantage of IORT devices was that the anesthetised patient had to be moved for treatment on the operating table to the accelerator. Within the last few years industry has developed several mobile devices for IORT. Novac-7 and Mobetron are mobile electron devices. They have electron catchers on the bottom side and therefore need reduced radiation shielding compared to conventional linear accelerators in the OR. Treatment can be given with electrons with energies between 3 and 9 MeV resulting in treatment depths up to 3 cm. Field sizes range from 5 to 7 cm in diameter. Because of their weight and the need of radiation shielding, the mobile IORT electron devices are usually restricted for treatment in a dedicated OR.

The Intrabeam device uses soft x-rays, therefore minimal radiation shielding is required. The setting can be used in any OR and is easily moved from one room to another. Currently there are different spherical applicators available ranging from 1.5 to 5 cm in diameter making the IORT with Intrabeam useful for smaller tumour regions. Maximal treatment depth with the 50 kV X-rays is 1–2 cm. The Intrabeam device is an optimal IORT option for patients suffering from early breast cancer either as a boost [6] or, in selected cases, even as single treatment modality [7, 8] as well as for patients suffering from locally relapsed breast cancer, who have received previous whole-breast radiotherapy.

In this report we describe IORT in 6 relapsed breast cancer patients, who could be treated in combination with the IORT option with a second breast-conserving surgery. Otherwise radical mastectomy would have been the preferred surgical option.


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## References


1 Abe M: History of intraoperative radiation therapy; in Dobelbower RR Jr., Abe M (eds): Intraoperative Radiation Therapy. Boca-Raton, CRC Press, 1989, pp 2–9.

2 Dubois JB: Intraoperative radiation therapy in the treatment of gastrointestinal cancer; in Ahlgren JD, MacDonald JS (eds): Gastrointestinal Oncology. Philadelphia, Lippincott, 1992, pp 607–614.

3 Sindelar WF, Johnstone PA, Hoekstra HJ, Kinsella TJ: Normal tissue tolerance to intraoperative irradiation; in Gunderson LL, Willett CG, Harrison LB, Calvo FA (eds): Current Clinical Oncology: Intraoperative Irradiation: Techniques and Results. Totowa, NJ, Humana Press, 1999, pp 131–145.

4 Brenner DJ, Leu CS, Beatty JF, Shefer R: Clinical relative biological effectiveness of low-energy x-rays emitted by miniature x-ray devices. Phys Med Biol 1999;44:323–333.

5 Astor MB, Hilaris BS, Gruerio A, Varicchione T, Smith D: Preclinical studies with the photon radiosurgery system (PRS). Int J Radiat Oncol Biol Phys 2000;47:809–813.

6 Reitsamer R, Peintinger F, Sedlmayer F, Kopp M, Menzel C, Cimpoca W, Glueck S, Rahim H, Kopp P, Deutschmann H, Merz F, Brandis M, Kogelnik H: Intraoperative radiotherapy given as a boost after breast-conserving surgery in breast cancer patients. Eur J Cancer 2002;38:1607–1610.

7 Gatzemeier W, Oreccia R, Gatti G, Intra M and Veronesi U: Intraoperative Strahlentherapie (IORT) in der Behandlung des Mammakarzinoms – eine neue therapeutische Alternative im Rahmen der brusterhaltenden Therapie? Stellenwert und Zukunftperspektiven aus dem European Institute of Oncology (EIO), Mailand. Strahlenther Onkol 2001;7:330–337.

8 Veronesi U, Orecchia R, Luini A, Gatti G, Intra M, Zurrida S, Ivaldi G, Tosi G, Ciocca M, Tosoni A, De Lucia F: A preliminary report of intraoperative radiotherapy (IORT) in limited-stage breast cancers that are conservatively treated. Eur J Cancer 2001; 37:2178–2183.