Intraoperative Radio Therapy

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Intraoperative Radiotherapy

- IORT is an effective therapy for a wide range of cancers.
- Delivery of radiation to the tumor bed during surgery.
- Normal tissues are displaced and protected
- Effective dose to the tumor bed is substantially increased.

Intraoperative Radiotherapy

- High dose single fraction radiation delivered to tumour bed
- Has been used in various malignancies
- This technique has shown to increase the survival rates for colorectal, gastric, Soft tissue Sarcoma

Limitations of IORT

- Limitations of existing equipment and facilities have limited its use
- Very few hospitals have operating rooms that are specially shielded for radiation
- Dedicated linear accelerator
- Reduced usability of these rooms limit their economic and practical feasibility.

TRANSPORTATION

- Transport the patient still under anesthesia
- With the surgical site open, to the radiation facility
- Radiation is given with conventional equipment
- The patient is transported back for the completion of the operation. This process is often called *"heroic transport"*

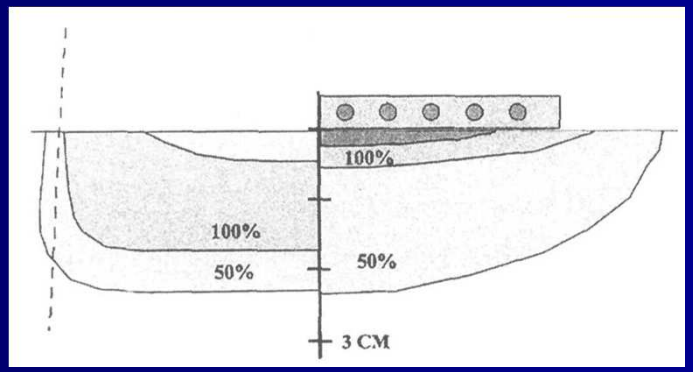
History of IORT

- IORT began with studies made by Abe and Takahashi at the University of Kyoto in the early 1960s.
- The first human IOERT treatment was given at Howard University in November 1976 and by December 1982 114 patients, with variable electron energies.
- The National Cancer Institute (NCI) began using IOERT in September 1979 (109)
- In the early 1980s, IORT programs also became active at the Mayo Clinic (April 1981)
- At Mayo Clinic, IOERT was incorporated as a component of treatment with the same general approach

Intraoperative Brachytherapy

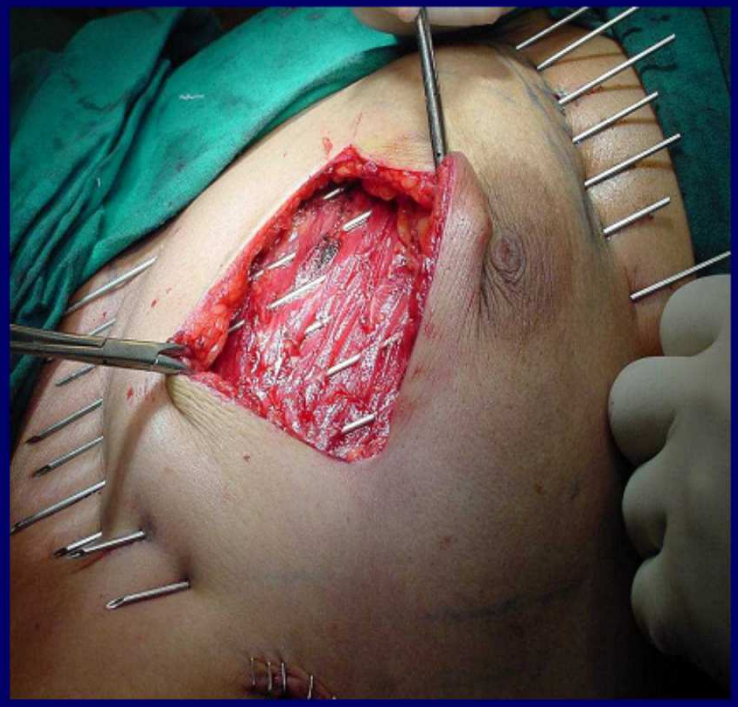
- Modern HDR IORT developed in 1980 using surface applicator
- Combined the technical and dosimetric advantage of brachytherapy
- Interstitial implantation intraoperatively has many benefits

Dose Distribution



- Dose distribution characteristic HDR IORT and IO-ERT
- Dose to the surface is higher with HDR IORT than IO-ERT
- Dose at depth higher with IO-ERT.

Intraoperative interstitial Brachytherapy



Intraoperative Radiotherapy

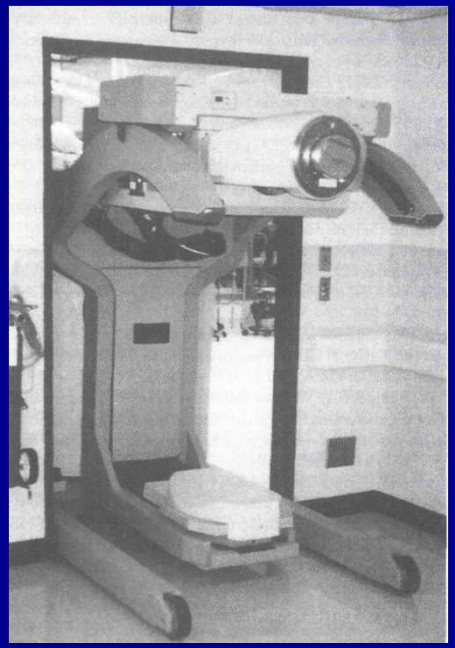
- Improved targeting of RT to tumor bed
- Improved feasibility
- Improved ability to control morbidity

Equivalent Dose

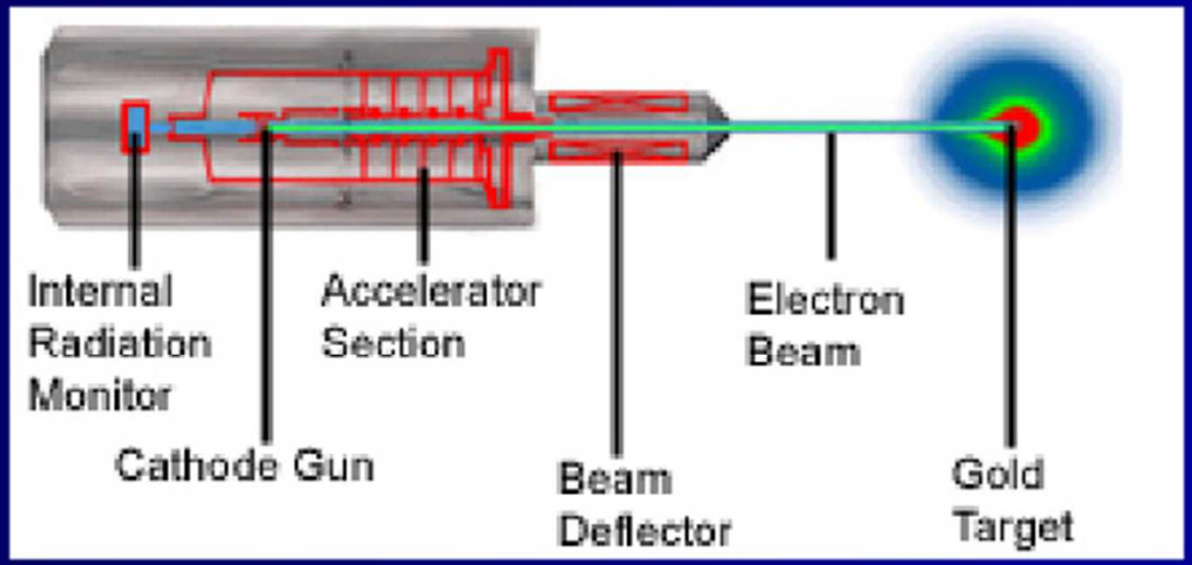
- The biologic effectiveness of a single dose of IORT is estimated to be equivalent to 1.5 to 2.5 times the same total dose of fractionated EBRT
- The effective dose in the IORT boost field, when added to the 45 to 50 Gy given EBRT, is 70 to 80 Gy with 10 Gy IORT, 75 to 87.5 Gy with 15 Gy, and 85 to 100 Gy with 20 Gy.

Modern IORT

- Modern IORT can be performed either with electron beam or photons
- Mobile linear accelerator



Intra-beam Accelerator



IORT in ca Breast

- Advantages of IORT for Early Stage Breast Cancer
- Shortens the overall treatment time
- Reduces the possibility of a geometric miss
- Starts adjuvant therapy at the time of surgery when residual tumor cells are most active
- Immediate administration of radiation solves the problem of chemotherapy sequencing

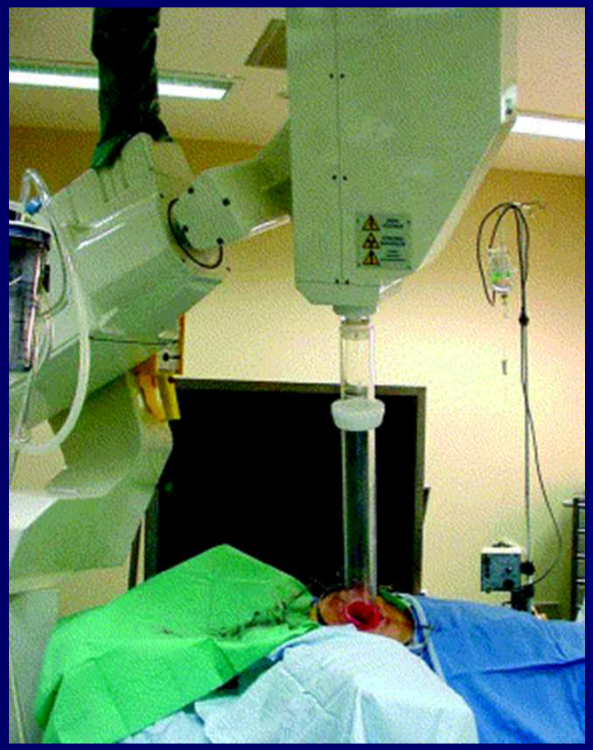
IORT in ca Breast

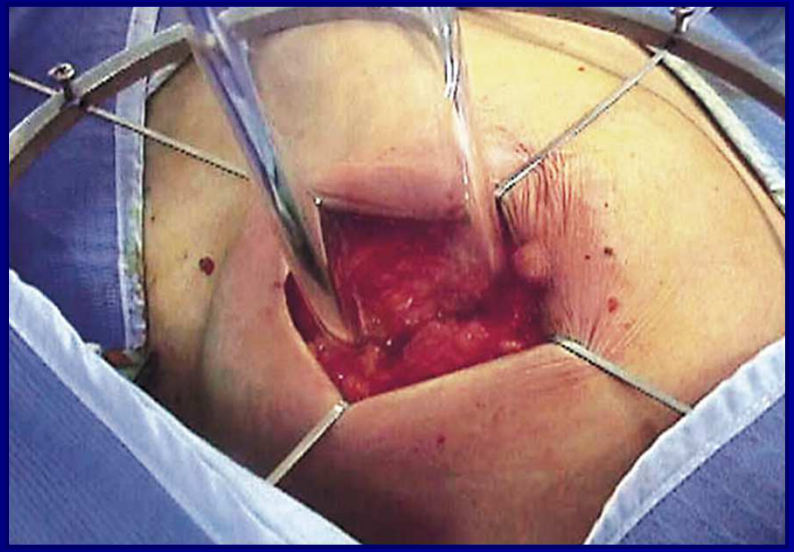
- More than 90% of local recurrences of breast cancer develop at or near the primary
- Addition of localized dose to the tumour bed reduces local recurrence
- Clinical delineation of the tumour bed carries a significant risk of missing the target

ELIOT TRIAL

- A new mobile linear accelerator with a robotic arm.
- Easily moved close to the operating table to allow the full-dose irradiation during surgery
- Electron beams energies ranges from 3 to 9 MeV
- 10 to 21 Gy . a single fraction of 21 Gy is equivalent to 60 Gy delivered in 30 fractions at 2 Gy/fraction
- 10 to 15 Gy as an anticipated boost to external radiotherapy,

European Institute of Oncology "ELIOT"





ELIOT

- The ELIOT technique
- 2 dedicated, mobile linear accelerators ELIOT: a Novac7, a LIAC
- Applicators of diameter ranging from 3 to 12 cm are available

ELIOT

- The linear-quadratic surviving fraction model, known as multitarget surviving fraction model, indicated that a single dose in the range 20 to 22 Gy is equivalent to 60 Gy delivered in 2 Gy daily Fractions, 5 days a week over 6 weeks (i.e., the dose required to control microscopic residual disease after BCS)

ELIOT

- Has demonstrated its capacity for safely delivering high single doses of RT directly to the tumor bed while sparing adjacent normal surrounding tissues
- From 1999 to 2003, 590 patients (mean age, 59 years)
- As sole radiation treatment modality (574 patients) or as an anticipated boost followed by external radiotherapy (16 patients).

ELIOT

- All patients had unicentric primary carcinoma
- 2.5 cm in largest diameter
- With a mean of follow-up of 24 months

  (range, 4 to 57months), 3 local recurrences (0.5%); 3 (0.5%) patients presented with ipsilateral second breast carcinoma and (0.8%) with contralateral carcinoma

TABLE 1. Characteristics of the 590 ELIOT Patients

Characteristic	*N*	%
Age		
≤50 years	89	15.1
51–60 years	256	43.4
61–70 years	182	30.8
≥70 years	63	10.7
Tumor site		
Upper quadrants	455	77.1
Lower quadrants	123	20.8
Central quadrant	12	2.0
Tumor diameter		
≤5 mm	26	4.4
>5 ≤10 mm	144	24.4
>10 ≤15 mm	216	36.6
>15 mm ≤20 mm	130	22.0
>20 mm	62	10.5
Missing	12	2.0
Histology		
Ductal invasive carcinoma	458	77.6
Lobular invasive carcinoma	48	8.1
Ductal/lobular invasive carcinoma	24	4.1
Other histology	50	8.5
DCIS	10	1.7

TABLE 2. ELIOT Patients: July 1999 to December 2003

TABLE 2. ELIOT Patients: July 1999 to December 2003

Year	Dose (Gy)	No. of Patients
1999	10–15	13
2000	10–19	18
	21	79
2001	21	112
2002	21	127
2003	21	241
Total		590

Side Effects Among 590 Patients

TABLE 3. Side Effects Among 590 Patients

Side Effect	*N*	%
Severe fibrosis	1	0.2
Mild fibrosis	18	3.0
Lyponecrosis	15	2.5
Hematoma	2	0.3
Skin retraction	2	0.3
Total	38	6.3

Side Effects Among 590 Patients

TABLE 4. First Unfavorable Event

Event	No. (%) of Patients
Local recurrence	3 (0.5)
Ipsilateral second breast carcinoma	3 (0.5)
Contralateral carcinoma	5 (0.8)
Axillary lymph node metastases	1 (0.2)
Distant metastases	13 (2.2)
Other primary tumours	3 (0.5)
Total	28 (4.7)
Deaths	1 (0.2)

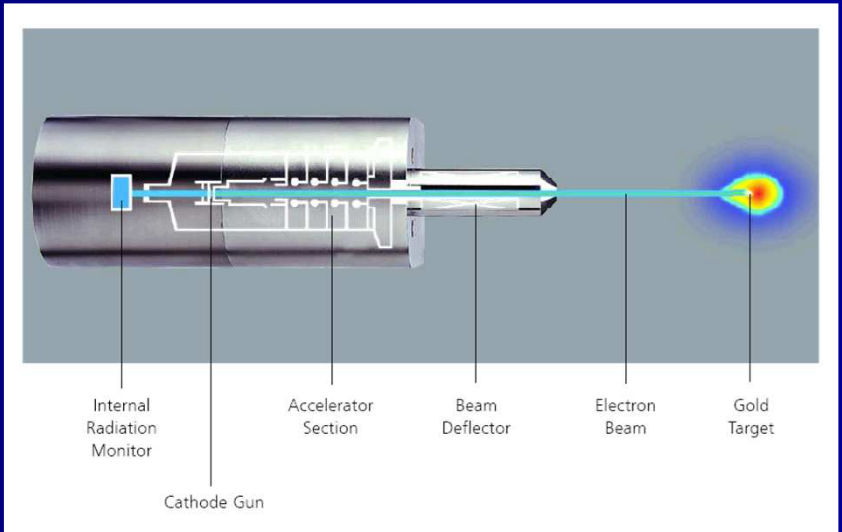
ELIOT

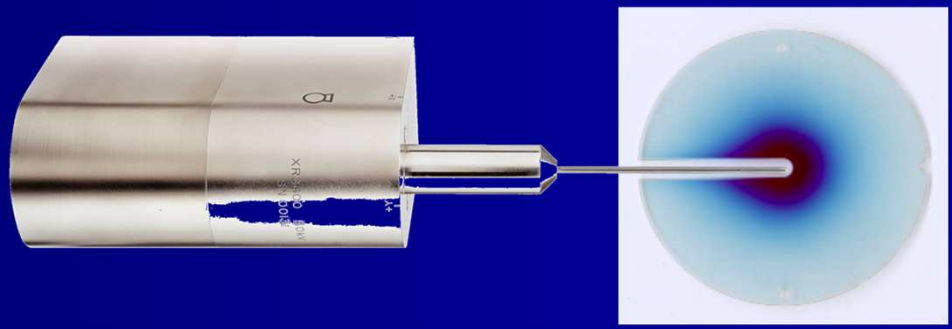
- Conclusions:
- ELIOT is a safe method for treating conservatively operated breast
- ELIOT reduces radiation to normal tissues and organs.

Results on short-term and middle-term toxicity up to 5 years of follow-up are good. Data on local control are encouraging.

INTRABEAM The X-Ray Source

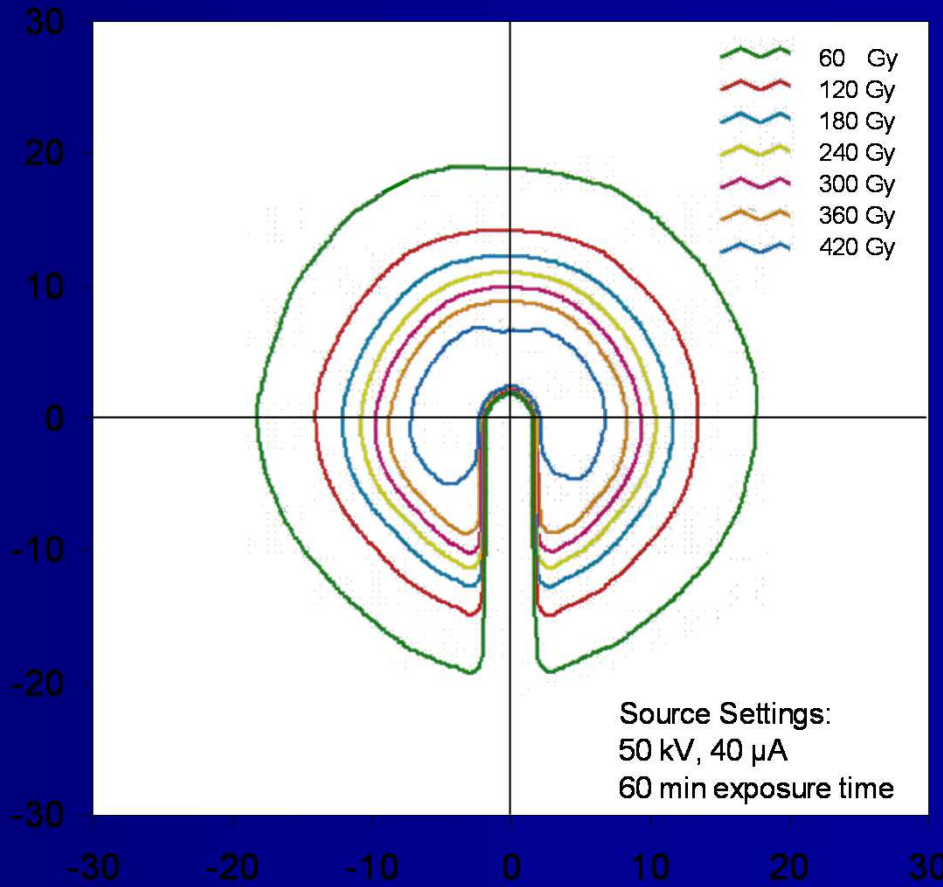
- Emits low energy X-Rays with max 50 kV
- High dose rate
- Spherical radiation field
- Only minimum shielding required
- Weighs only 1.6 kg
- Probe diameter 3.2 mm
- Probe length 10 cm





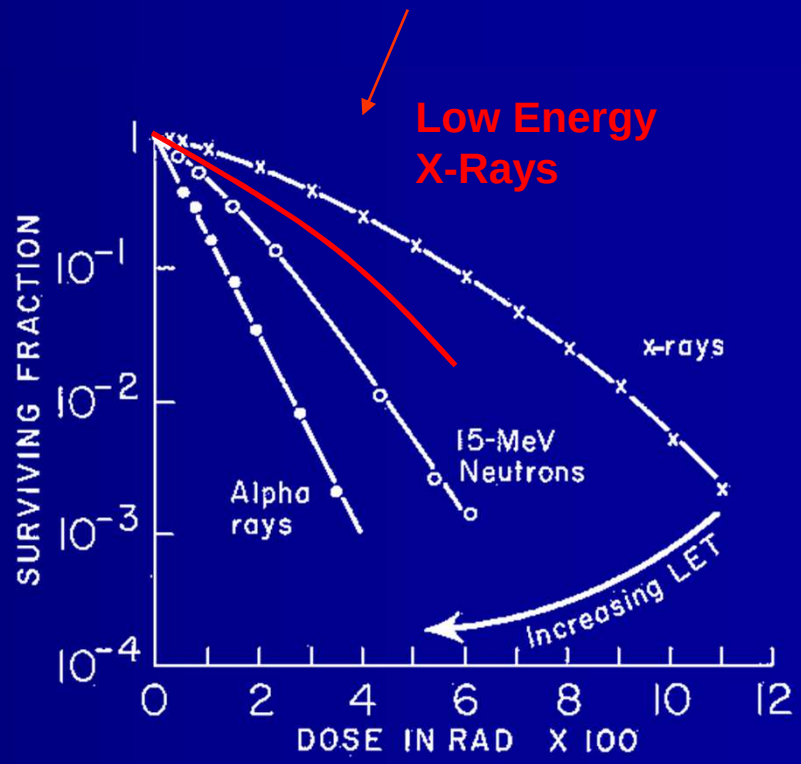
Isodose Curves

- Uniform spherical radiation field
- Steep dose gradient
- High dose rate
- Typical treatment time for interstitial application with bare probe max 10 min



Biological Aspects of Low Energy X-Rays

- 50 kV low energy X-Rays have a higher Relative Biological Effectiveness
- Typical treatment times of 15-25 min allow a certain repair of the normal tissue (Herskind et al. 2005, 2006)



IORT with INTRABEAM
Radiation Delivery to the Tumor Bed

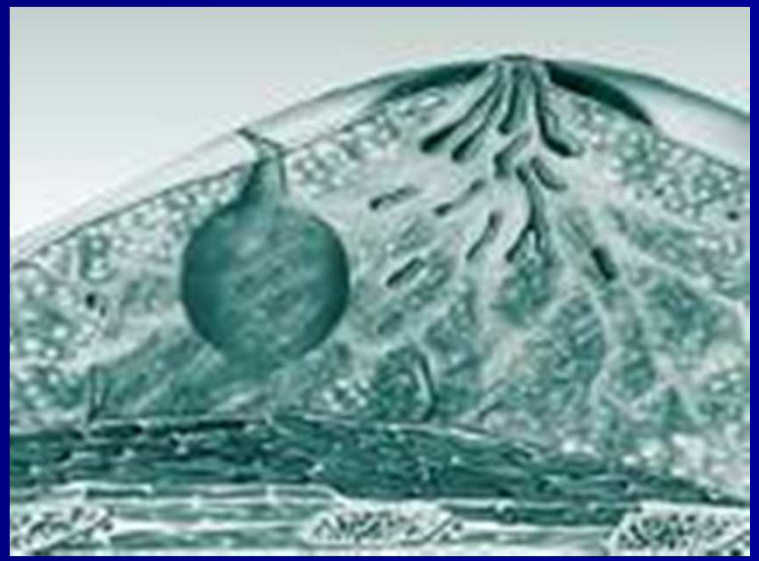
1

- Example:
  Breast tumor
  lesion

IORT with INTRABEAM
Radiation Delivery to the Tumor Bed

2

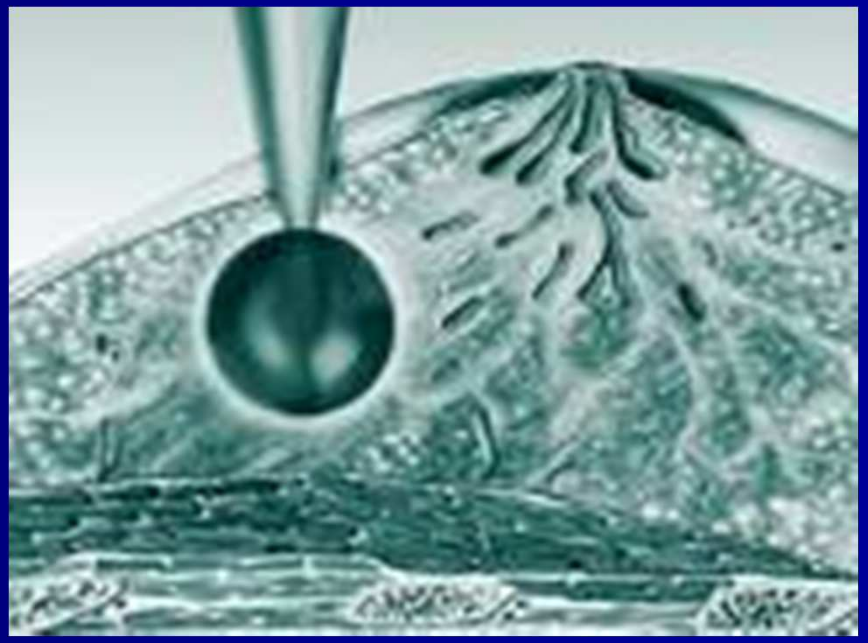
- Tumor bed after wide local excision



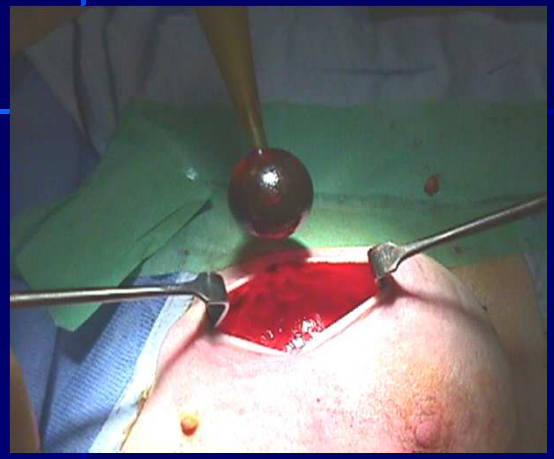
IORT with INTRABEAM
Radiation Delivery to the Tumor Bed

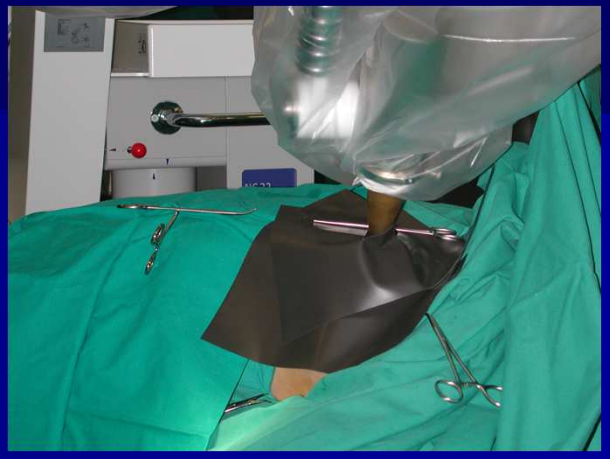
3

- X-Ray source in place for radiation



Treatment of Breast Tumors





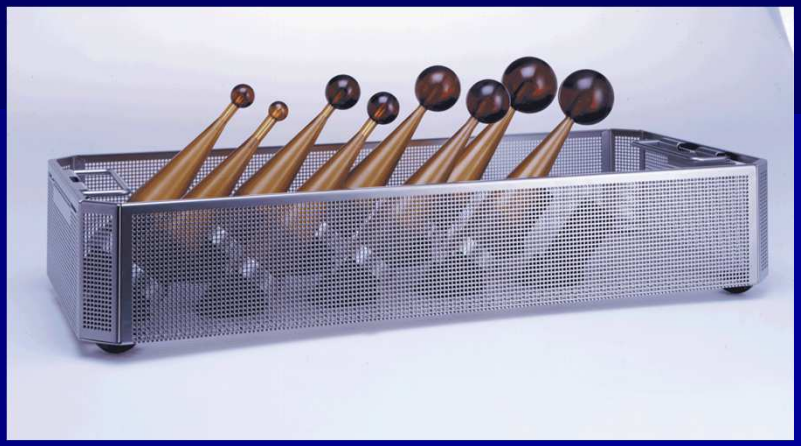
- Wide local excision
- Select applicator diameter according to size of cavity

- **Attach applicator to X-Ray Source and engage into tumor bed**
- **Evert skin edges away from applicator to avoid necrosis**

- **X-Ray Source in place for radiation delivery**
- **Place radiation shields to prevent scattering**

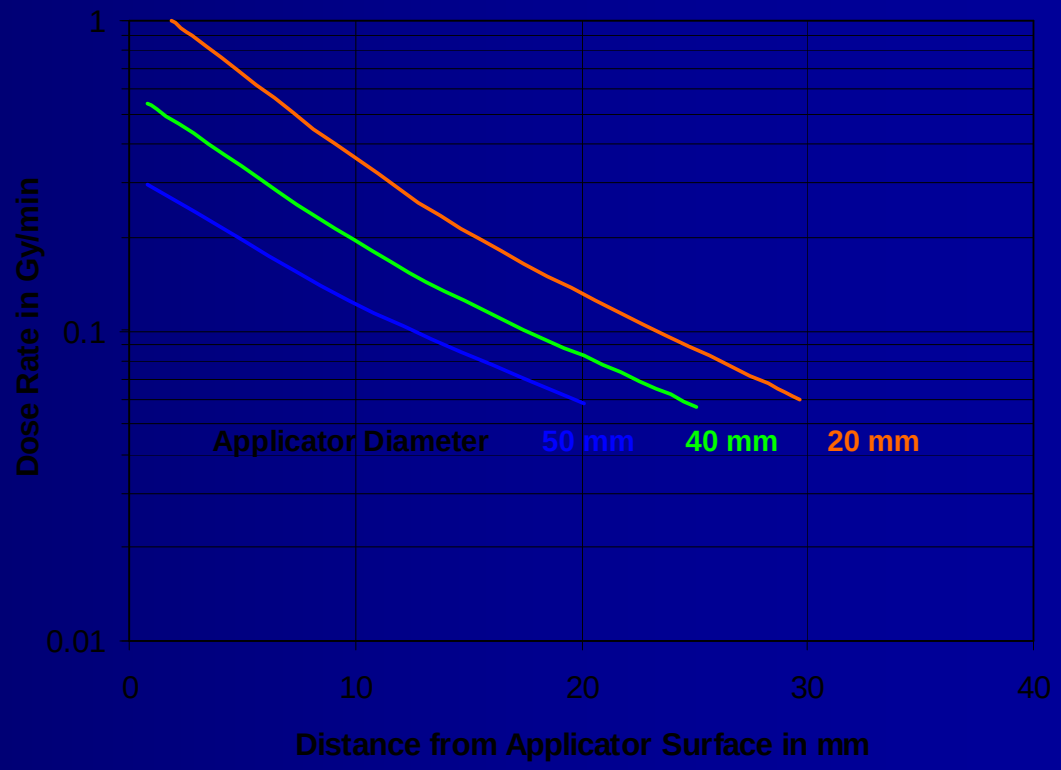
INTRABEAM Spherical Applicators

- For tumor bed irradiation
- Tissue is adapted to the surface to ensure uniform dose delivery
- Medical grade polymer material, biocompatible
- Diameter: 1.5 – 5.0 cm in steps of 0.5 cm
- Provided in a tray for conventional autoclaving
- May be re-sterilized 100 times



Depth Dose Curves with Spherical Applicators

- Steep dose gradient
- Curve is individual for each applicator diameter
- Dose is prescribed relative to applicator surface
- Treatment time for tumor bed irradiation 10 - 25 min



The INTRABEAM Floor Stand

- Precise positioning of the X-Ray Source in the tumor bed
- Free-floating system with 6 axes
- Long arm allows flexible position in the OR
- Can be moved easily from OR to OR

INTRABEAM Shielding Material

- Flexible foil adapts easily,
  can be customized
- Biocompatible silicone rubber material
  filled with Tungsten
- To protects critical structures or to
  cover
  the surgical field (95% radiation
  shielding)
- Flat shape (20 cm x 20 cm) or curved
  (Ø 2 - 5 cm) for applicators

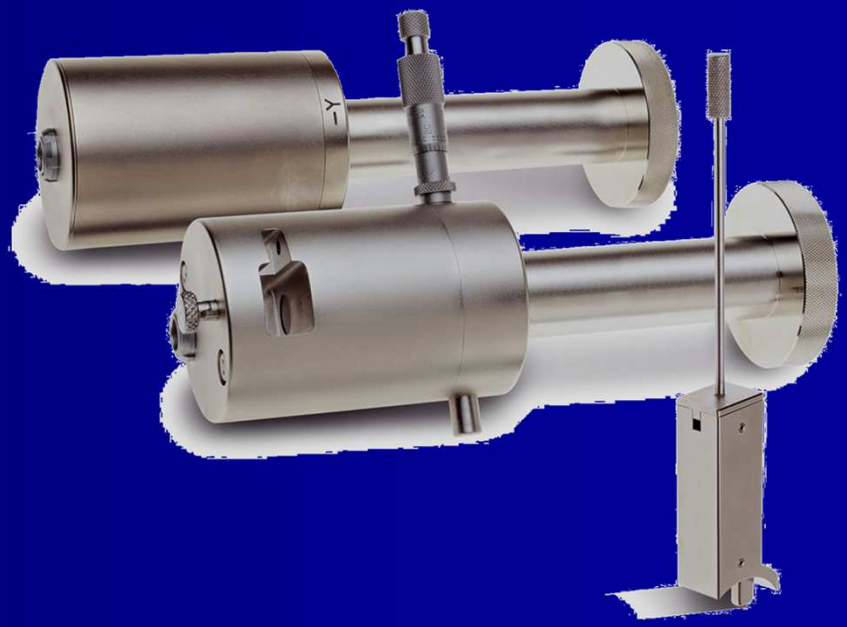
The INTRABEAM PRS 500 Control Unit

- Controls the output of the X-Ray Source
- Treatment parameters are uploaded from a computer terminal
- Works independently from the terminal once parameters are set

INTRABEAM Tools for Quality Assurance

Provide full physics service

- Verify source output
  with calibrated ion chamber
- Calibrate the Internal
  Radiation
  Monitor of the X-Ray Source
- Verify dose isotropy
- Check probe alignment,
  correct if required
- Takes typically 5 – 10 min



Practical Aspects

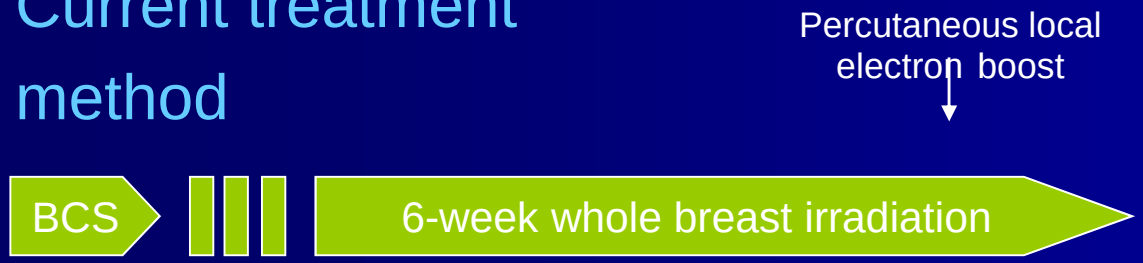
- No room shielding required, can be used in regular OR
- In general, easy to get local operating license
- Can be shared between several ORs
- Establishing IORT requires to adapt hospital logistics and workflow

IORT is Team work

- Surgeon
  - Surgical procedure
  - Tumor removal
  - Select appropriate applicator size
- Radiation Oncologist
  - Prescribe radiation dose
- Physicist
  - Quality assurance
  - Calculate exposure time
  - Program the control console
  - Monitor dose delivery

Treatment Options in Breast Conserving Surgery (BCS)

Current treatment method

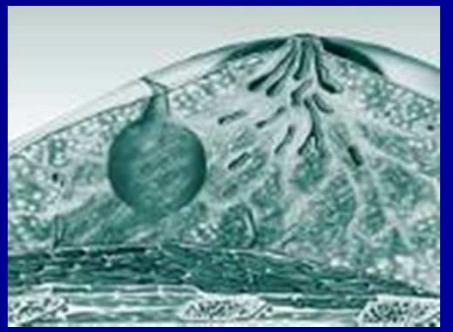


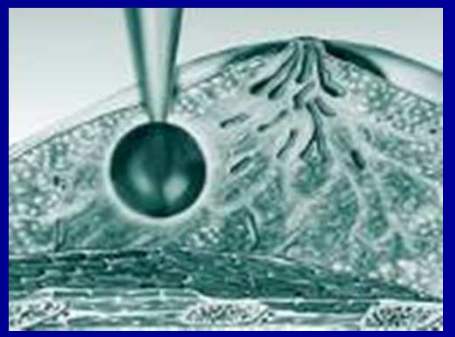
percutaneous electron boost

- Reduces tte risk for recurrence from 7.3 % to 4.3 % after 5 years
- often initiated with a delay of several months after surgery causing higher recurrence rate
- It fails to hit the exact former location of the tumor in 50 - 80% of patients
  (e.g. Benda RK et al., Cancer 2003; 97:905)

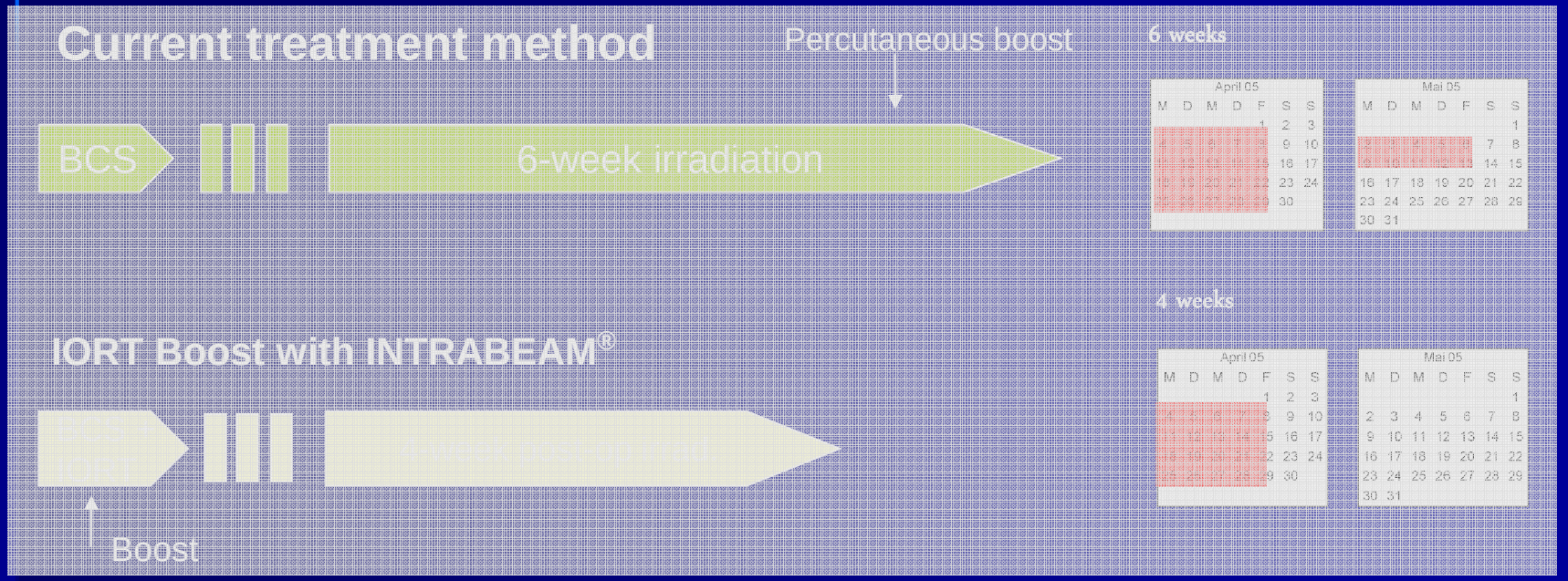
Clinical Evidence for IORT Boost

- Vaidya et al. (2006/2007):
  - 301 patients including risk factors (e.g. age, positive nodes) w/ up to 5 year follow-up
  - Statistical estimate of recurrence rate = 1.9% at 5 years versus 4.3% in literature although trial included larger numumber of risk patients
- Kraus-Tiefenbacher et al. (2006):
  - 73 patients w/ up to 4 year follow-up
  - No unexpected toxicity rates, 90% good to excellent cosmesis





Treatment Options in Breast Conserving Surgery (BCS) with INTRABEAM IORT



One time treatment with INTRABEAM® (TARGIT trial)

BCS + IORT

1 day

April 05

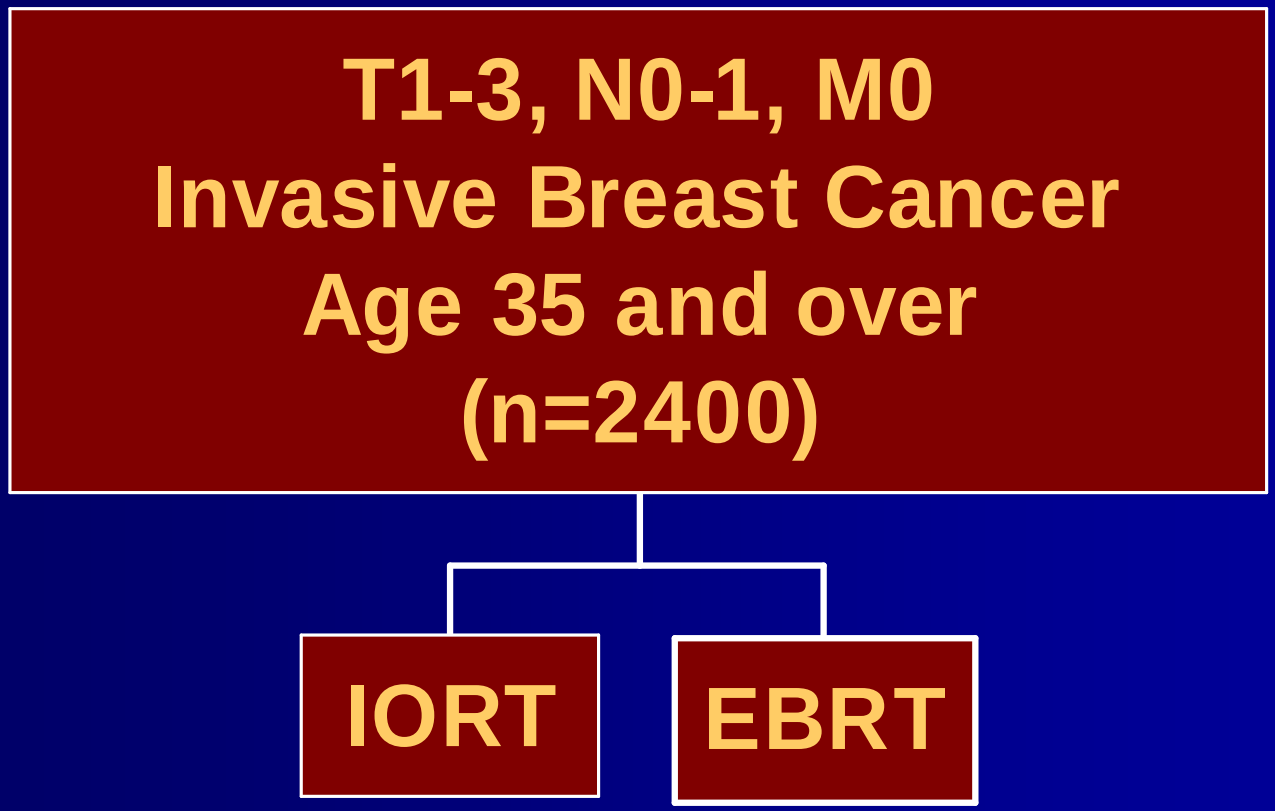
M	D	M	D	F	S	S
				1	2	3
4	5	6	7	8	9	10
11	12	13	14	15	16	17
18	19	20	21	22	23	24
25	26	27	28	29	30	

TARGIT – Aim and Study Layout

Proving equivalence of one-time IORT with INTRABEAM® in breast cancer treatment with fractionated irradiation with the linear accelerator

- Open international multi center study
- Participation criteria:
  - Hospitals with a INTRABEAM – System
  - Hospitals willing to follow the study protocol
- Criteria for patient selection:
  - Breast Cancer (T1, T2)
  - Not multi focal

Targit Trial



Targit Trial

- Endpoints
  - Site of Relapse within the breast
  - Relapse-free and overall survival
  - Local toxicity/morbidity
  - Cosmesis
  - Patient Satisfaction and quality of life

THANK YOU