Commissioning and Radiobiology of the INTRABEAM System

Susha Pillai and Junan Zhang

Scheme

- INTRABEAM System.
- Physics Commissioning, QA, and Radiation Protection
- Radiobiology

Disclosure

- OHSU is an INTRABEAM user but does not receive any financial support from Carl Zeiss, Inc.

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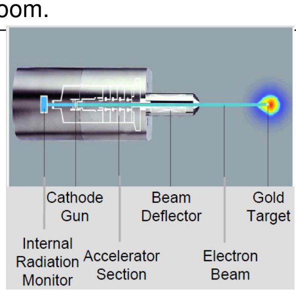
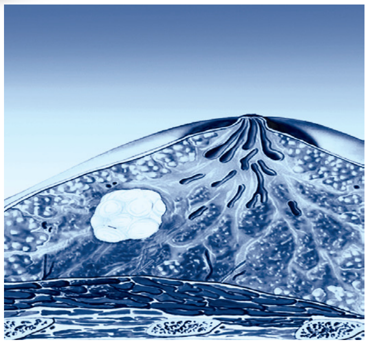
INTRABEAM: a portable kV accelerator

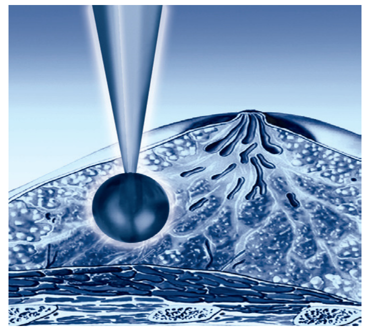
- Small accelerator that generates electrons and produces x-rays.
- The accelerator itself is quite small. (175mmx110x70 mm, 1.62 kg)
- Probe is 10 cm long with 3 mm diameter
- X-rays are 50 kV in energy;
- No additional shield is needed for OR room.



INTRABEAM: breast treatment



Surgical removal of the tumor



Applicator with X-ray probe positioned in the lumpectomy site. Treatment lasts for about 20 to 50minute to deliver 20Gy in single fraction to the applicator surface

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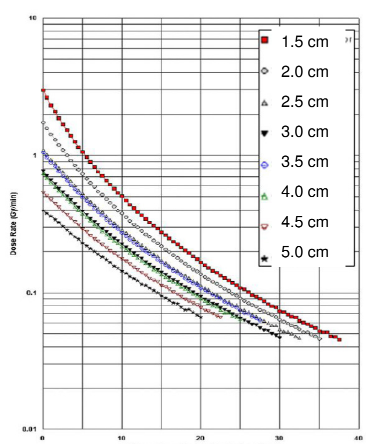
Depth Dose Curve

Sharp dose falls off (approx. r^{-3}) in tissue.



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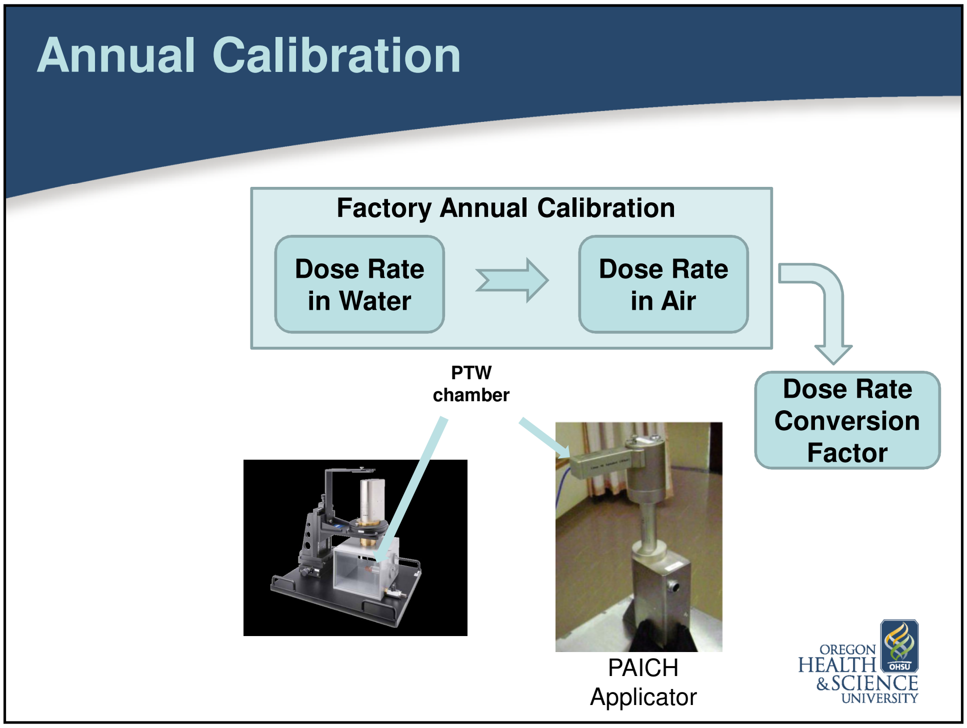
INTRABEAM Quality Assurance Tools

- Manufacturer provided full set of radiation shielded QA instruments.
- PDA(Photodiode Array)
  - Contains five photodiodes at orthogonal positions
  - Isotropy check
- PIACH (Probe adjuster/ionization chamber holder)
  - Measures and adjusts the straightness of the probe manually
  - Inbuilt thermometer for temperature/pressure correction
  - Mount for ionchamber
- High precision water phantom (optional/send back to factory to QA)
  - To perform independent verification of the depth dose and dose distribution
  - Radiation shielded with lead glass.
  - Mechanical positioning accuracy of +/- 0.1mm

Water phantom


Annual Calibration
Factory Annual Calibration
Dose Rate in Water
Dose Rate in Air
Dose Rate Conversion Factor
PTW chamber
PAICH Applicator
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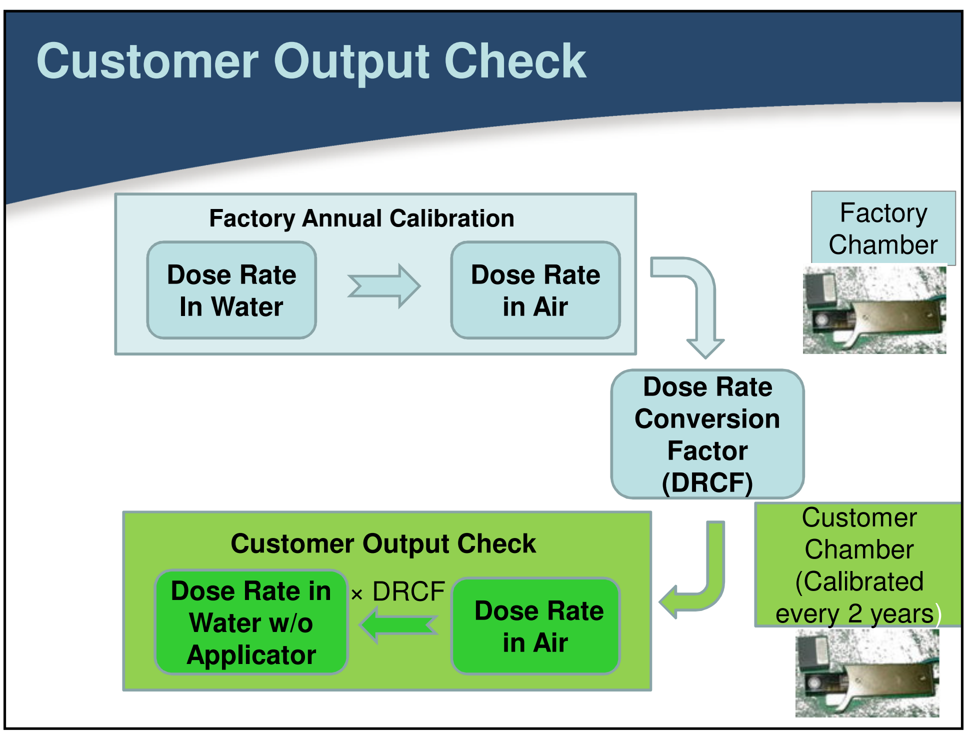
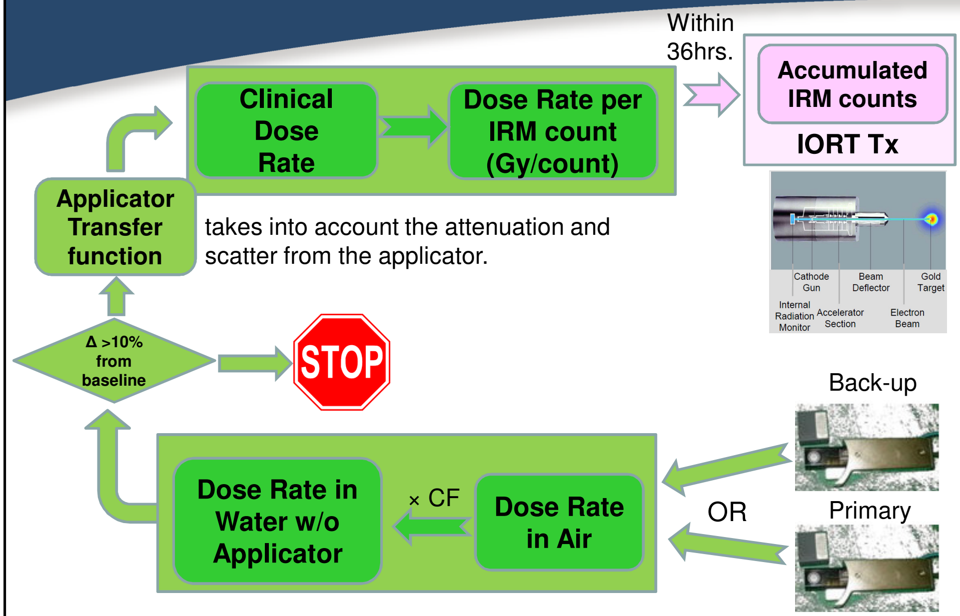

Customer Output Check
Factory Annual Calibration
Dose Rate In Water
Dose Rate in Air
Factory Chamber
Dose Rate Conversion Factor (DRCF)
Customer Output Check
Dose Rate in Water w/o Applicator
× DRCF
Dose Rate in Air
Customer Chamber (Calibrated every 2 years)

Pre-Tx Output Check: ATF & IRM



Where to calibrate the PTW parallel-plate chamber?

- ❑ Choice 1: PTW Lab
  - Pros:
    - ❑ Recommended by Carl Zeiss, Inc.
    - ❑ Factory chamber is calibrated over there
  - Cons:
    - ❑ International shipping takes a little bit time
    - ❑ Traceable to national standards of the German National Lab. No to US standards.

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Where to calibrate the PTW parallel-plate chamber?

- An ADCL Lab (UW), traceable to NIST

Calibration at UW ADCL in 2013		
Beam Quality	HVL in Al (mm)	Air Kerma (Gy/C)
UW50-L	0.760	1.151×10^9
UW40-L	0.503	1.165×10^9
50kV INTRABEAM beam quality		
Tube Voltage	HVL in Al (mm)	Interpolated Air Kerma (Gy/C)
50kV	0.64	1.165×10^9

PTW Air Kerma (Gy/C): 1.174×10^9

Δ<1%

1. TG-61: Both tube potential and HVL shall be used to specify the air-kerma calibration factor.
2. TG-61: Interpolation may only be performed within the same series (e.g. for L series. But not between L series and M series.)

Independent verification of treatment time before beam-on

INTRABEAM:Independent Verification of Treatment Time

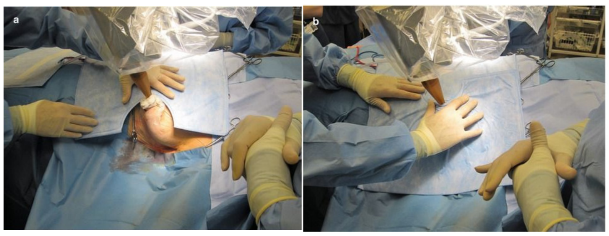
XRS SN: 507223(LOANER)		Cal Date:	11/25/2014	QA Performed by:		Susha Pillai
Date of Measurement:		6/5/2015		Treatment Date:		6/5/2015
Patient Name:				MR#:		6912757
Measured PAICH doserate in air (Gy/min)				3.845		
Temp(oC)	23.4	Pressure(kPa	99.7	Ptp	1.021	
PAICH Doserate(Gy/min)=			I(PA) * Ctp * Nk(Gy/C) * 60 s/min *E-12 A/pA			
Chamber reading I (pA)		54.28	Calculated PAICH Doserate (Gy/min)			3.85
Ionchamber:(ADCL calibration factor valid till July 2015)						
PTW TN23342 SN: 1868			Nk(Gy/C)	1.16E+09		
Electrometer:(ADCL calibration factor valid till July 2015)						
RO-20 SN: 5279			Pele	1		
Refernece doserate (Gy/min)		3.753	Cal Date: Nov 25th 2014			

Applicator(cm)	Prescription Dose(Gy)	Rx depth(cm)	Doserate(Gy/min) at the surface	Tx time(min)
2.5	20	0	1.248	15.63
3	20	0	0.841	23.19
3.5	20	0	1.111	17.55
4	20	0	0.776	25.13
4.5	20	0	0.58	33.62
5	20	0	0.421	46.32
Calculated Time (min)	Estimated Time(min)			
23'' 11''	23'20''			

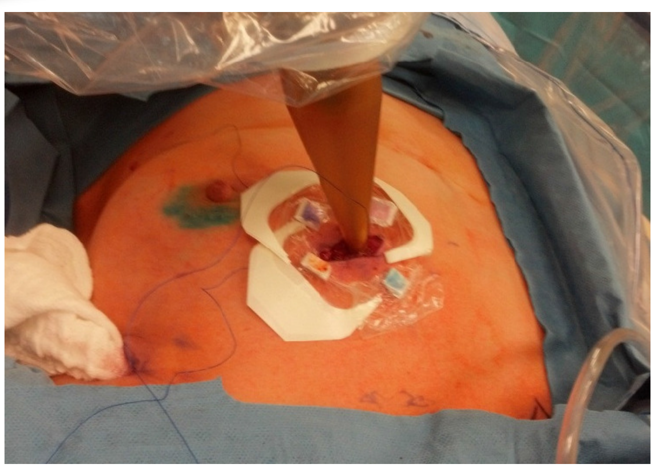
1. Actual treatment time depends on the count rate (counts/s) measured by the IRM during pre-treatment QA.
2. However, the system will stop treatment automatically, if the tx time > 110% * Calculated time

Radiation Protection

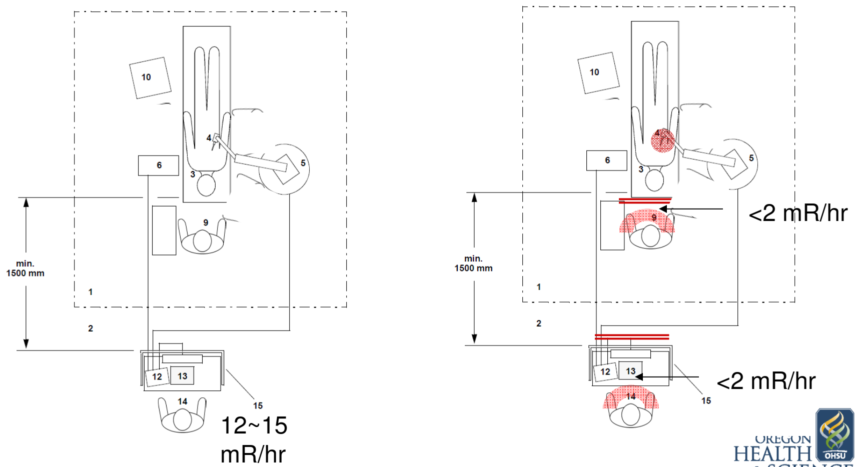
- No additional shield is needed for OR room.
- Two tungsten-rubber shields (0.1mm lead equivalent. 95% reduction) to put over the breast.
- Two lead mobile barriers (>0.5mm lead equivalent). One for anesthesiologist and one for physicist, therapist and radiation oncologist, all wearing lead aprons.
- All other OR people have to leave the room.



Calibrated OSLDs used to monitor skin doses



Radiation Survey



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- Radiobiology

References

- Book: Keshtgar, Mohammed, Katharine Pigott, and Frederik Wenz. *Targeted Intraoperative Radiotherapy in Oncology*. Springer, 2014.
- Book: Hall, Eric J., and Amato J. Giaccia. *Radiobiology for the Radiologist*. Lippincott Williams & Wilkins, 2006.
- Brenner, David J., et al. "Clinical relative biological effectiveness of low-energy x-rays emitted by miniature x-ray devices." *Physics in medicine and biology* 44.2 (1999): 323.
- Herskind, Carsten, et al. "Radiobiological aspects of intraoperative radiotherapy (IORT) with isotropic low-energy X rays for early-stage breast cancer." *Radiation research* 163.2 (2005): 208-215.
- Liu, Qi, et al. "Relative Biologic Effectiveness (RBE) of 50 kV X-rays measured in a phantom for intraoperative tumor-bed irradiation." *International Journal of Radiation Oncology* Biology* Physics* 85.4 (2013): 1127-1133

Single Fraction, High dose

- INTRABEAM delivers high single dose (typical 20Gy) to tumor bed. Similar to SRS.
- Linear-quadratic model has limitations in predicting the effects of single dose in the range of 15 Gy and higher.

(Kirkpatrick, John P., Jeffrey J. Meyer, and Lawrence B. Marks. "The linear-quadratic model is inappropriate to model high dose per fraction effects in radiosurgery." *Seminars in radiation oncology*. Vol. 18. No. 4. WB Saunders, 2008.)

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~~Proliferation~~

- No proliferation of tumor cells between surgery and initiation of radiotherapy
  - Delaying the beginning of radiotherapy was estimated to be responsible for a loss in local control of about one-third (local recurrence rate of about 6 % vs. 9 %) when the delay exceeded 8 weeks. (Huang et al. 2003).

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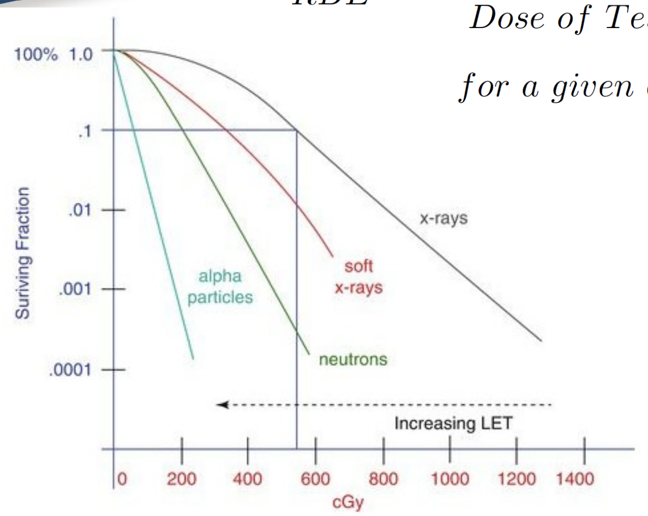
Relative Biological Effectiveness (RBE)

$$RBE = \frac{Dose\ of\ Reference\ Radiation}{Dose\ of\ Test\ Radiation}$$

$$for\ a\ given\ effect$$



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Relative Biological Effectiveness (RBE)

- Depends on LET and beam hardening
  - RBE(kV)>RBE(MV)
  - Deeper depth => Beam Hardening => Lower RBE
- Depends on radiation dose and survival level
  - Deeper depth => Lower dose => Higher Survival => Higher RBE (based on LQ model)
- Depends on dose rate and treatment time

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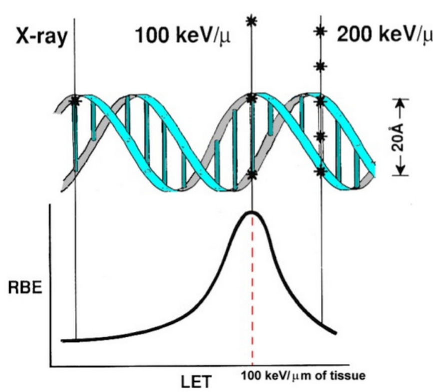
RBE varies with LET



Radiation	**LET of secondary electrons. (keV/μm)**
6-18 MV X-ray	0.2
Intrabeam (Avr. E=20 kV)	2

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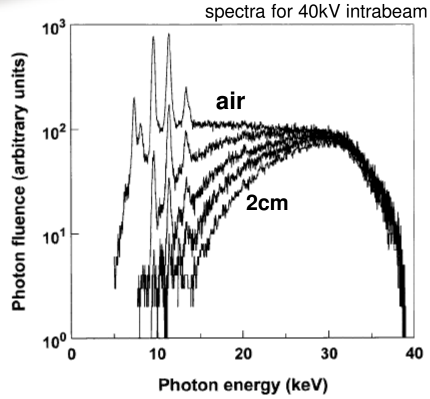
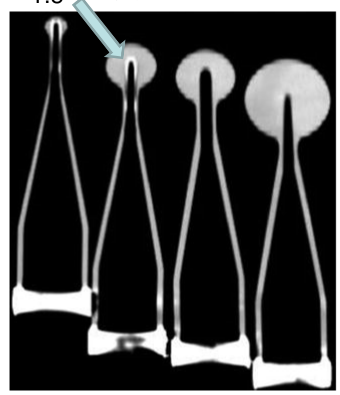
Beam hardening

Beatty et al, measured X-ray spectra for 40kV intrabeam





Spherical breast applicator absorbs lower energy photons and harden the beam. .

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RBE decreases with beam hardening

Table 1. Estimated low-dose RBEs (α_H/α_L; see equation (1)) and clinically relevant RBEs (23 min irradiation, 12.5 Gy) for low-energy x-rays as shown in figure 2, for a miniature photon radiosurgery system (Dinsmore *et al* 1996, Cosgrove *et al* 1997), operated at 40 kV.

	versus ^{60}Co		versus ^{192}Ir		versus ^{125}I	
Depth (mm)	Low dose	Clinical	Low dose	Clinical	Low dose	Clinical
0	3.05	1.53	2.11	1.38	1.23	1.12
5	2.67	1.44	1.85	1.29		
10	2.54	1.41	1.76	1.27		
15	2.48	1.40	1.72	1.25		
20	2.44	1.40	1.69	1.24		

Estimated based on LQ model, for a fixed 20Gy

Brenner, David J., et al. "Clinical relative biological effectiveness of low-energy x-rays emitted by miniature x-ray devices." *Physics in medicine and biology* 44.2 (1999): 323.

Relative Biological Effectiveness (RBE)

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RBE changes with cell survival level

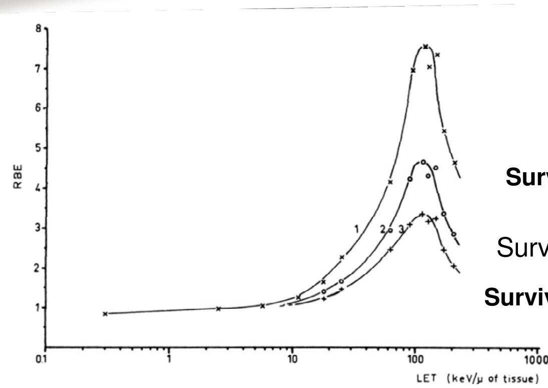

Figure 8–7. Variation of RBE with LET for survival of mammalian cells of human origin. The RBE rises to a maximum at an LET of about 100 keV/μm, and subsequently falls for higher values of LET. *Curves 1, 2,* and *3* refer to cell survival levels of 0.8, 0.1, and 0.01, respectively, illustrating that the absolute value of the RBE is not unique but depends on the level of biological damage and, therefore, on the dose level. (From Barendsen GW: Curr Top Radiat Res Q 4:293–356, 1968)

E. Hall, Radiobiology for the Radiologist

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Relative Biological Effectiveness (RBE)

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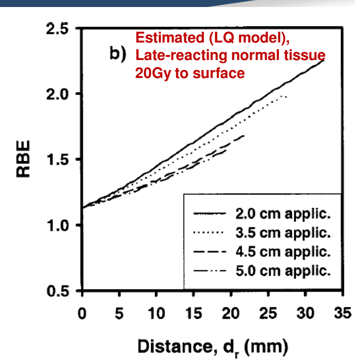
LQ model predicts that RBE increases with depth



"The decrease in RBE with depth due to beam hardening is more than compensated for by the increase in RBE with depth due to the decreasing dose."

Brenner, David J., et al. "Clinical relative biological effectiveness of low-energy x-rays emitted by miniature x-ray devices." *Physics in medicine and biology* 44.2 (1999): 323.

Herskind, Carsten, et al. "Radiobiological aspects of intraoperative radiotherapy (IORT) with isotropic low-energy X rays for early-stage breast cancer." *Radiation research* 163.2 (2005): 208-215.

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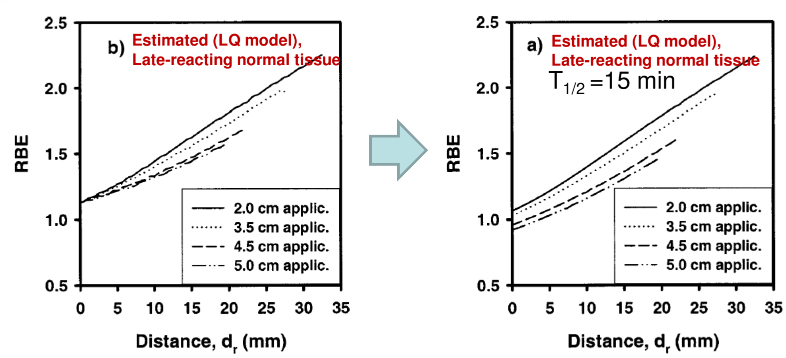
Repair of normal tissue cell during treatment



Herskind, Carsten, et al. "Radiobiological aspects of intraoperative radiotherapy (IORT) with isotropic low-energy X rays for early-stage breast cancer." *Radiation research* 163.2 (2005): 208-215.

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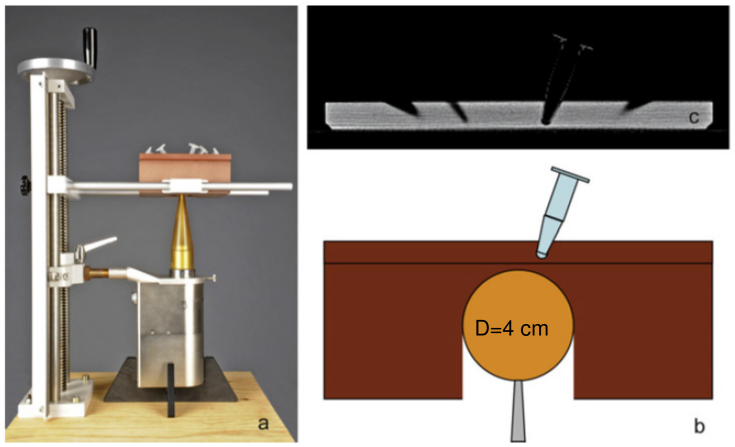
Cell survival curves with INTRABEAM. (Liu et al. 2013

Liu, Qi, et al. "Relative Biologic Effectiveness (RBE) of 50 kV X-rays measured in a phantom for intraoperative tumor-bed irradiation." *International Journal of Radiation Oncology* Biology* Physics* 85.4 (2013): 1127-1133.



Experiment showed that RBE may decreae with depth

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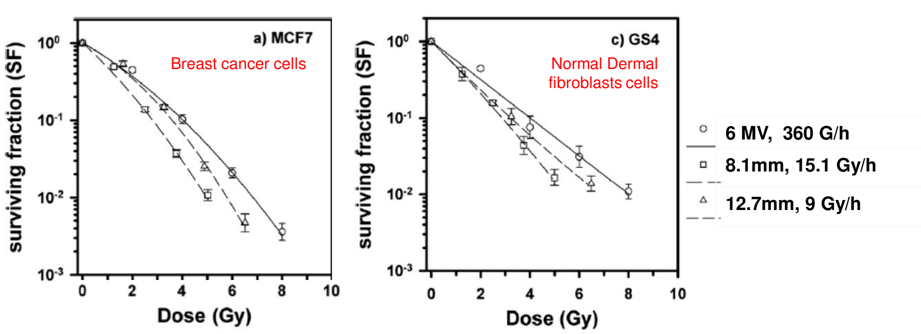


RBE(INTRABEAM,8.1mm,15.1Gy/h)

Probably due to different tx time and beam hardening

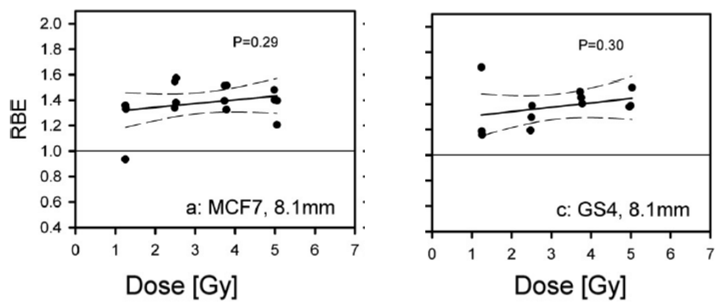
> RBE(INTRABEAM,12.7mm,9.8Gy/h)

kV X-ray has higher RBE

> RBE(6MV, 360Gy/h)

Correlation between RBE and dose level is not statistically significant.

Liu, Qi, et al. "Relative Biologic Effectiveness (RBE) of 50 kV X-rays measured in a phantom for intraoperative tumor-bed irradiation." *International Journal of Radiation Oncology* Biology* Physics* 85.4 (2013): 1127-1133.



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Acknowledgements and Future Directions

- OHSU INTRABAM team
  - Surgeons, Nurses, Radiation Oncologists, Medical Physicists, Therapists, Dosimetrists
- Upcoming Task Group Report: No. 182 - AAPM Recommendations on Electronic Brachytherapy Quality Management

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