# IMRT and Cancer Risk
# Eric J. Hall

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## Suffer Little Children……
## IMRT, Second Cancers, and the Special Case of Children

Eric J. Hall, D.Phil., D.Sc., FACR
Director, Center for Radiological Research,
Higgins Professor of Radiation Biophysics,
Professor of Radiation Oncology and Radiology
College of Physicians & Surgeons of Columbia University
Radiation Biologist, Radiation Oncology and Radiology Services,
Presbyterian Hospital, New York, NY, USA

Session Chair:
Karen Goddard, Clinical Associate Professor, Active Staff,
Vancouver Cancer Centre, Vancouver, Canada

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*Suffer Little Children…*

## IMRT, Second Cancers, and the Special Case of Children

**Eric J. Hall**, D.Phil., D.Sc., FACR, FRCR
Columbia University, New York

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## Knowledge of Radiation-Induced Cancer Comes from:

- A-bomb survivors.
- Accidents.
- Individuals medically exposed.
  - Includes second cancer in RT patients.

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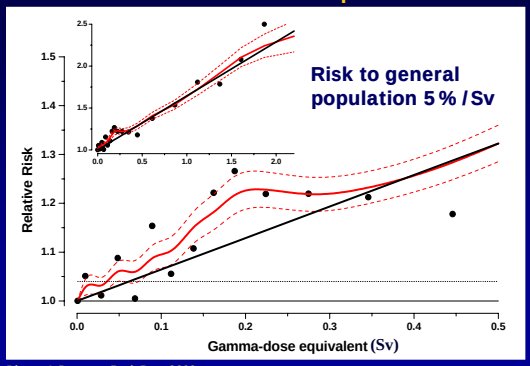
## Cancer Rates (1958–94) in A-bomb Survivors Relative to Those for an Unexposed Person




*Pierce & Preston, Rad. Res. 2000*

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## Lifetime Probabilities of Developing Fatal Secondary Malignancies by Organ Site

| Organ | Probability of Fatal Cancer (%/Sv) |
|---|---|
| Bladder | 0.30 |
| Bone marrow | 0.50 |
| Bone surface | 0.05 |
| Breast | 0.20 |
| Esophagus | 0.30 |
| Colon | 0.85 * |
| Liver | 0.15 |
| Lung | 0.85 * |
| Ovary | 0.10 |
| Skin | 0.02 |
| Stomach | 1.10 * |
| Thyroid | 0.08 |
| Remainder of body | 0.50 |
| Total | 5.00 |

From NCRP Report 116(13) for entire population

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## Radiotherapy Patients

- In most cases, difficult to assess risk of second cancers because no good control available.
- Exceptions:
  - Ca Prostate & Cervix where surgery is an option.
  - Hodgkin's disease where risk of breast cancer in young women is obvious.

# IMRT and Cancer Risk
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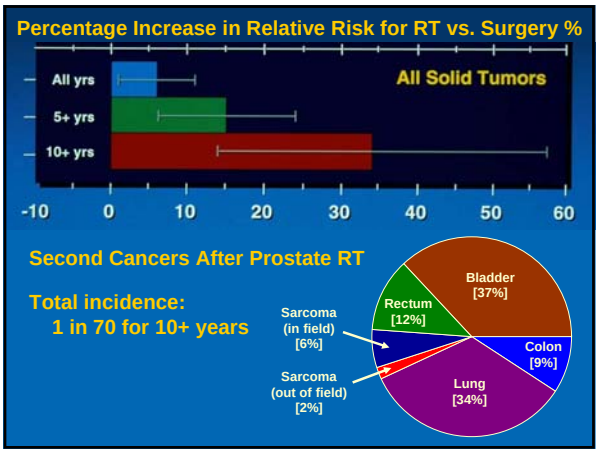



## 3D-CRT → IMRT

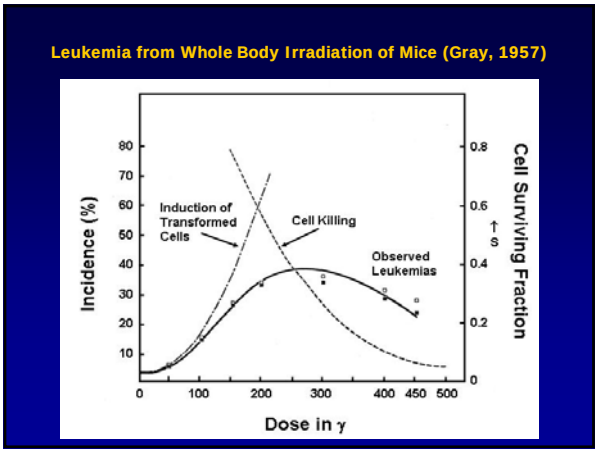
- **More monitor units** *(factor of 2-3)*
  - therefore larger total body dose.
- **More fields**
  - therefore bigger volume of normal tissue exposed to lower doses.

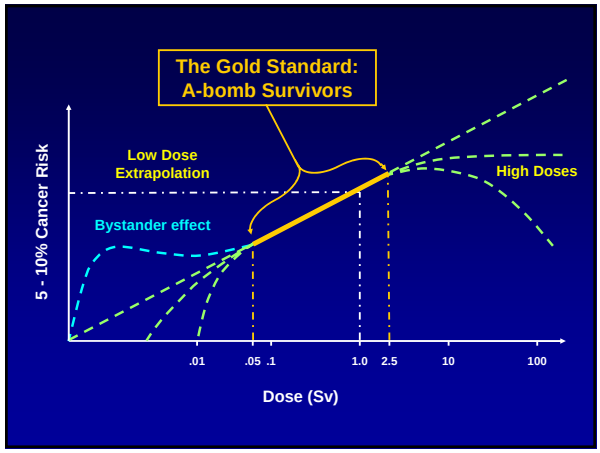
## Monitor Units

- Delivery of a specified dose to the isocentre from a modulated field, delivered by IMRT, will require the accelerator to be energized for longer (hence more monitor units).
- It therefore follows that the dose due to leakage radiation will be increased.

## More Fields

- A bigger volume of normal tissue exposed to lower radiation doses.
- The importance of this depends on the shape of the dose-response relationship for radiation-induced carcinogenesis.



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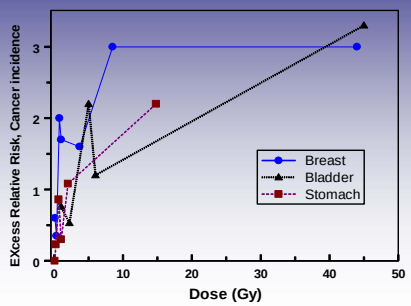
### Dose Response for Carcinogenesis at High Radiation Doses



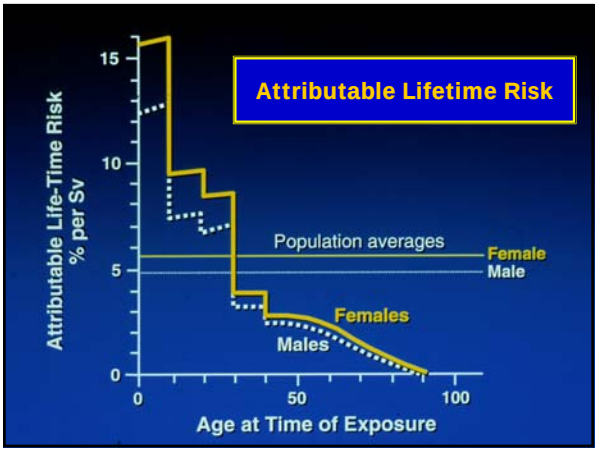

*Compiled by Dr. Elaine Ron*

### Risk of Fatal Radiation-induced Malignancy After RT for Prostate Cancer (%/Sv)

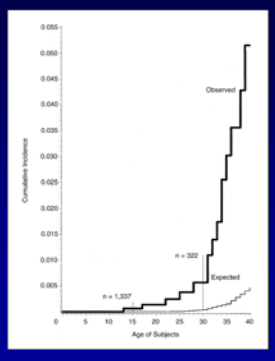
| | |
|---|---|
| ***Hall & Wu, 2003*** | |
| Conventional 6 MV | 1.5 |
| IMRT 6 MV | 3.0 |
| ***Kry et al., 2005*** | |
| Conventional 18 MV Varian | 1.7 |
| IMRT 6 MV Varian | 2.9 |
| Siemens | 3.7 |
| IMRT 10 MV Varian | 2.1 |
| IMRT 15 MV Varian | 3.4 |
| Siemens | 4.0 |
| IMRT 18 MV Varian | 5.1 |

### The Special Case of Children

- More sensitive to radiation-induced carcinogenesis by a factor of 10.
- Scatter from treatment volume is more important due patient size.
- Genetic susceptibility. Most children with cancer carry a germline mutation.

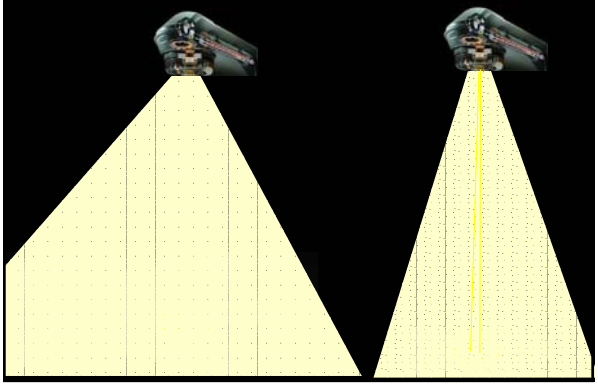



### True Cumulative Incidence of Breast Tumors According to the Patients' Attained Age




Guibout, C. et al. J Clin Oncol; 23:197-204 2005

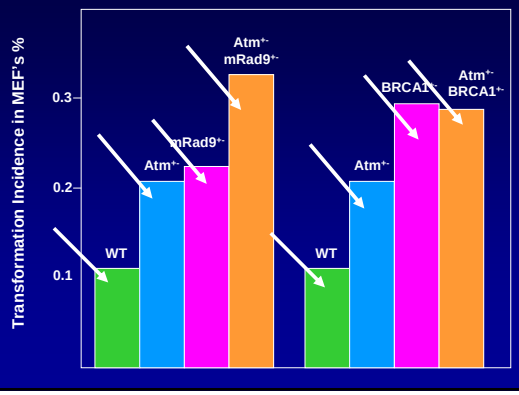
### Same leakage for adults vs. pediatric RT, but in pediatric RT scatter from the treatment volume is more important



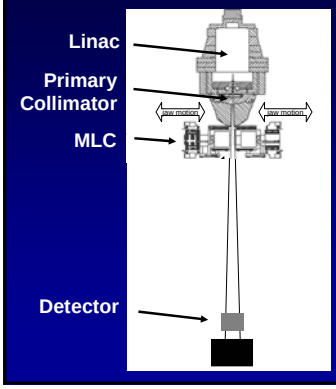
## Genetic Susceptibility

- Haploinsufficiency for ATM, BRCA1, and RAD9 result in increased radiosensitivity to oncogenic transformation in MEF's
- Many children with cancer carry a germline mutation -- ? Radiosensitive
- Hodgkin's patients are more sensitive to radiation induced breast cancer than WT or neuroblastoma patients

## ATM, BRCA1, and mRad9 in Knockout Mice




## Sources of Leakage Radiation

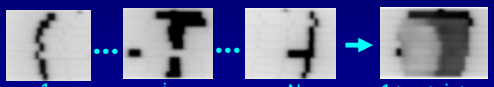



Leakage from head 0.1%

Leakage from MLC 1.5-3%

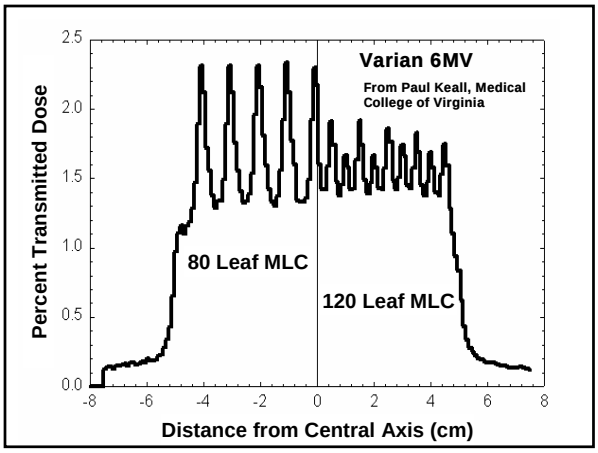
## Delivery of IMRT with *continuous leaf motion*

- Each leaf pair forms a window which slides across the field.
- Dose given through the window as function of MU.




- Leakage through MLC is about 1.5% at 6 MV.

*Courtesy of Dr. Cheng-Shie Wuu*



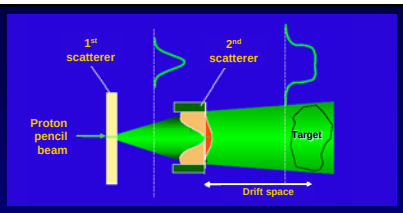

## Protons

- **Reduced vol. of normal tissue exposed.**
- **Reduce second cancer incidence.**

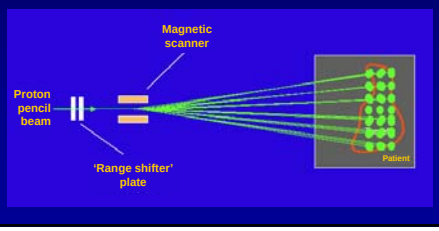
***However –***

- **Passive modulation results in total body neutron dose – offsets gains.**
- **Scanning beam allows full advantage of protons to be realized.**

Passive Scattering




Active Scanning




## The Bottom Line: Radiotherapy in Older Patients

- Induced cancers increase with time after radiotherapy.
- 1½% by ten years.
- May be doubled by new techniques (IMRT).

## Bottom Line (continued)

- In older patients (e.g., prostate Ca) doubling the second cancer incidence from 1.5 to 3% may be acceptable if balanced by a big improvement in local tumor control and reduced acute toxicity.

## Bottom Line (continued)

- Children are special case. Second cancer incidence is much higher; doubling it may not be acceptable.
- Genetic susceptibility may be a more important factor for children.
- Present levels of leakage radiation are not inevitable; they can be reduced.

## Mitigating the Problem

- Increased shielding in treatment head. 20 cm tungsten reduces leakage by 90%.
- Secondary beam blocking. Allow backup jaws to track MLC.
- Flattening filter not needed for IMRT.
  - Removes source of scatter.
  - Doubles dose-rate at center.
- Protons in place of x-rays.

## End

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More medical education materials are available at:

www.Cure4Kids.org