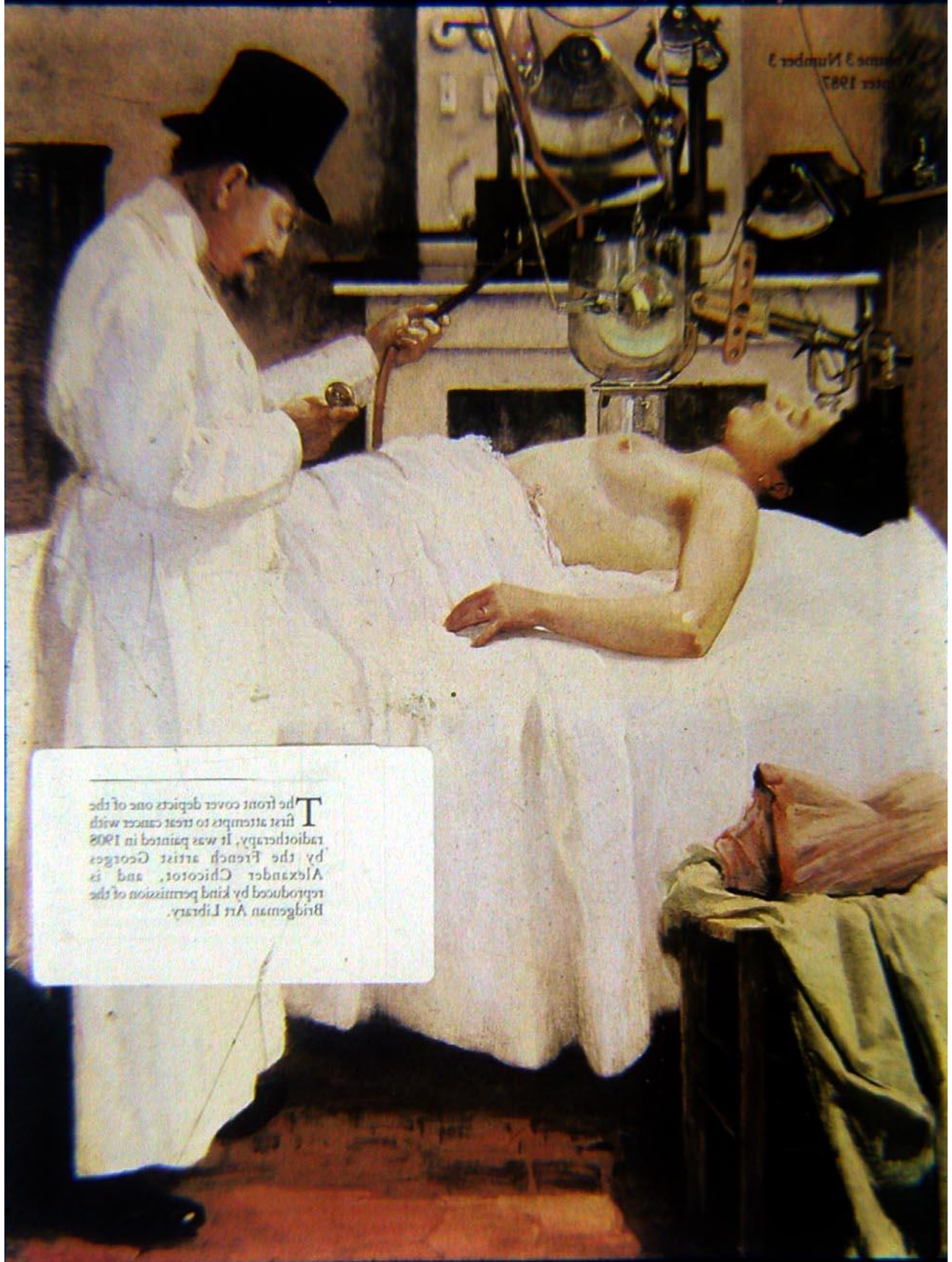
Present and Future of Radiation Therapy

ICTP School on Medical Physics
March 25 – April 5, 2019
Miramare, Trieste

Yakov Pipman, DSc

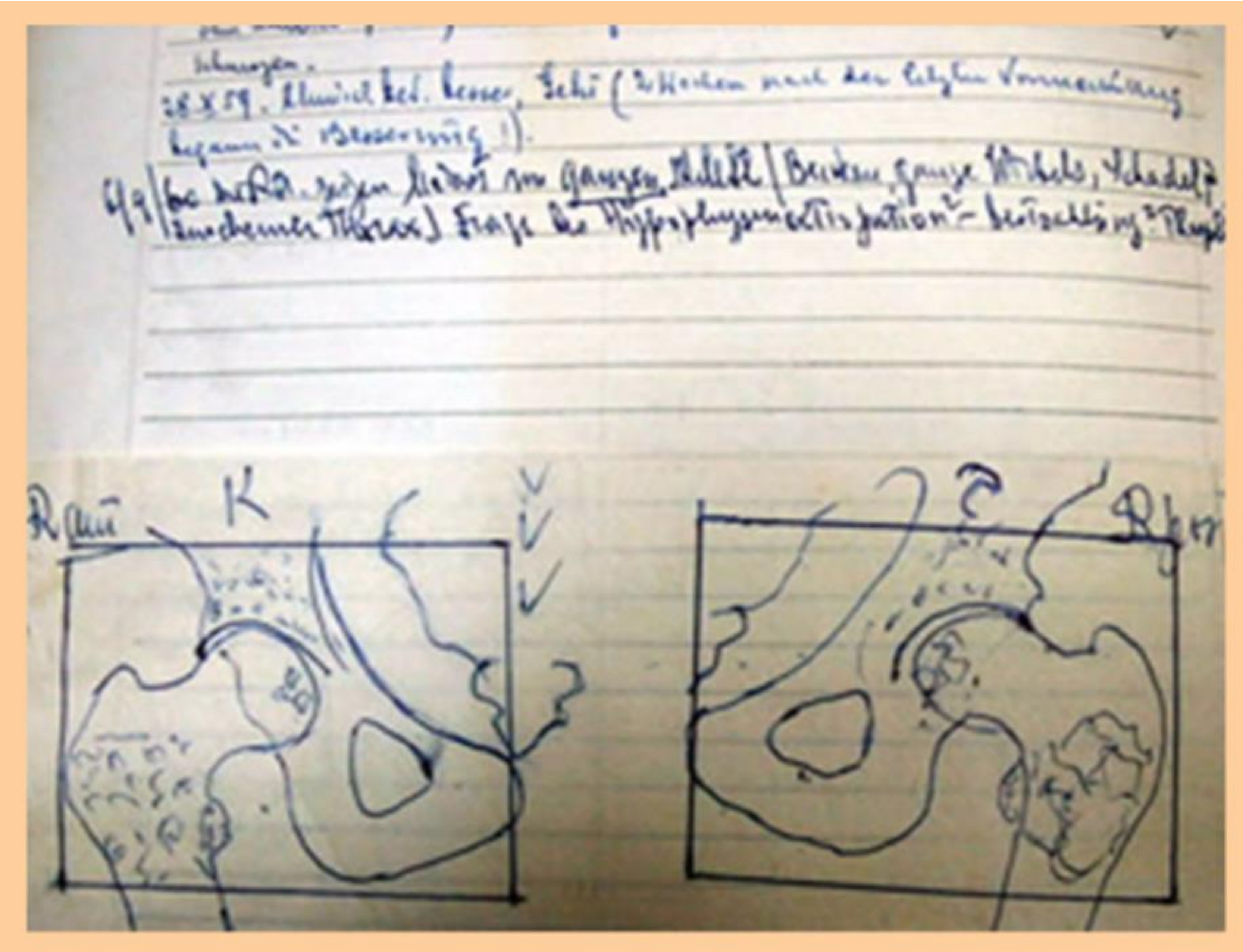
Overview

- Then
- Now
- Tomorrow
- Summary



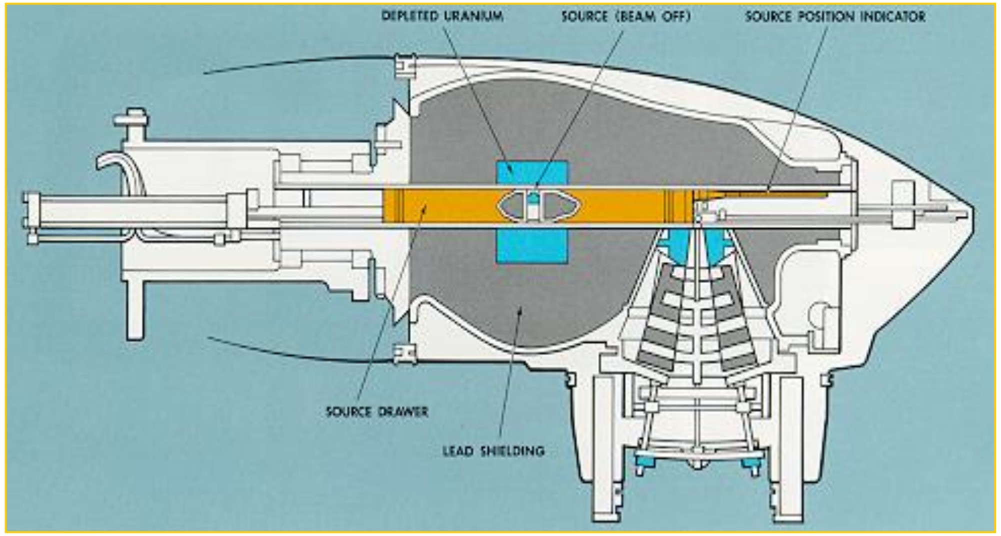
Radiotherapy 1-D

KiloVoltage therapy for breast



Radiation therapy simulation… a note and a diagram in the chart

Radiotherapy 1-D and 2-D



Typical dosimetric calculation

=

Computation of Beam- ON time for a Co-60 treatment

$BOT_i = PD_i / 100 \times T_{100,d,FS}$

April 1, 1969

Co-60 TREATMENT TIME and "SKIN" DOSAGE CHART
at
The Long Island Jewish Hospital
270-05 76th Avenue
New Hyde Park, N.Y. 11040

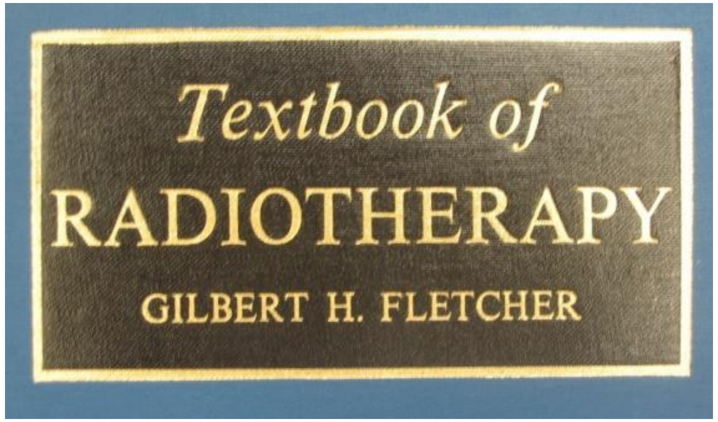
80 CM. S.S.D.

Time in Minutes to give 100 rads tumor dose at depth and Max.r "skin" dose for 100 Rads at depth
for period April 1, 1969 through June 30, 1969.

Output 104.8 r/Min. at 80 Cm. S.S.D.

Depth in CM.	AREA IN SQ. CM 25		50		100		200		400	
	Max. Rads	Min.	Max. Rads	Min.	Max. Rads	Min.	Max. Rads	Min.	Max. Rads	Min.
.5	100	.97	100	.96	100	.96	100	.94	100	.94
1.0	103	1.00	102	.98	102	.97	102	.96	102	.95
2.0	110	1.06	108	1.00	107	1.02	107	1.00	106	.99
3.0	117	1.13	115	1.10	113	1.08	112	1.05	111	1.04
4.0	125	1.22	122	1.17	120	1.14	118	1.11	117	1.10
5.0	134	1.30	130	1.25	127	1.21	125	1.18	124	1.16
6.0	145	1.40	139	1.35	136	1.30	133	1.25	131	1.23
7.0	156	1.51	150	1.44	145	1.39	141	1.33	139	1.30
8.0	169	1.63	161	1.55	156	1.49	151	1.42	147	1.38
9.0	183	1.78	174	1.68	167	1.59	161	1.52	156	1.46
10.0	198	1.92	188	1.82	180	1.72	172	1.62	165	1.55
11.0	215	2.08	202	1.90	193	1.84	184	1.74	176	1.65
12.0	233	2.25	218	2.11	207	1.98	197	1.84	188	1.76
13.0	252	2.44	236	2.29	223	2.12	210	1.98	200	1.87
14.0	273	2.64	254	2.47	239	2.28	225	2.10	212	1.99
15.0	296	2.86	275	2.66	257	2.45	239	2.25	226	2.12
16.0	319	3.08	298	2.87	276	2.63	256	2.40	240	2.25
17.0	345	3.33	320	3.08	296	2.83	274	2.57	257	2.40
18.0	371	3.59	345	3.33	318	3.03	293	2.74	272	2.55
19.0	402	3.90	373	3.68	343	3.27	313	2.93	289	2.71
20.0	436	4.23	402	3.88	368	3.51	334	3.12	306	2.87

Lillian E. Jacobson



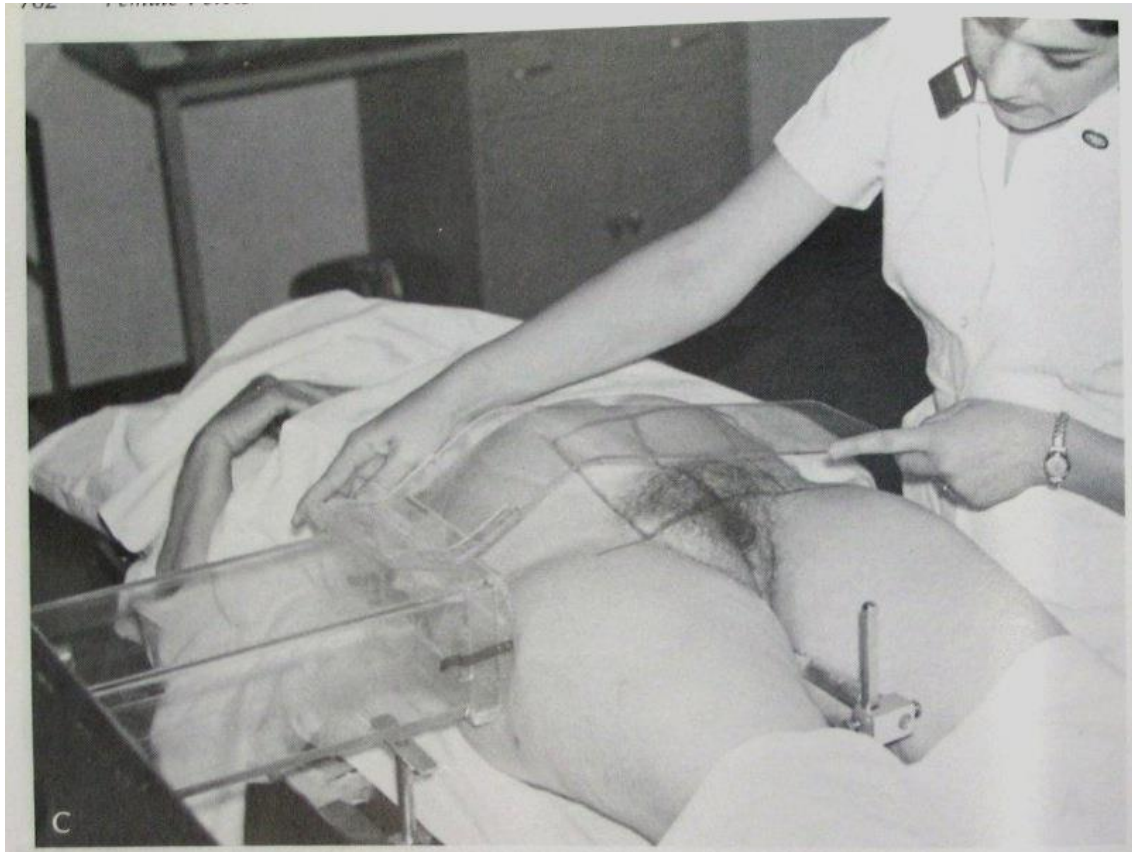


FIG. 11–37. C. The same procedure used for the localization of the lowest palpable disease is also used to determine the center of the lateral portals. A Lucite bridge used for daily treatment duplication is also shown.

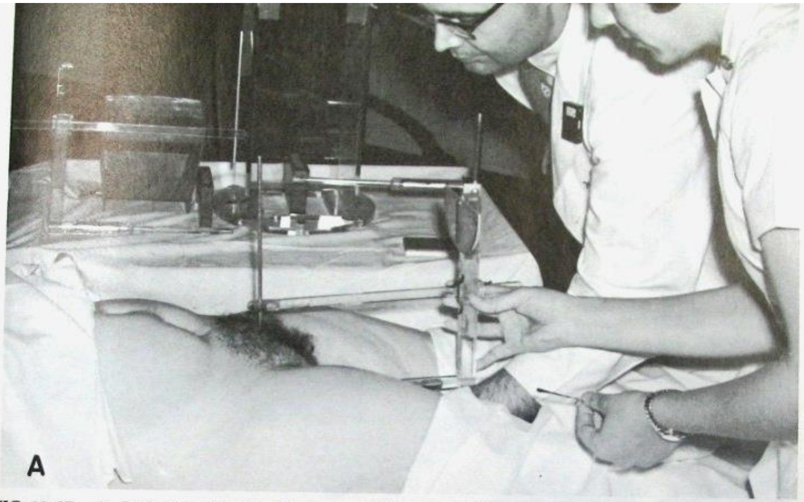
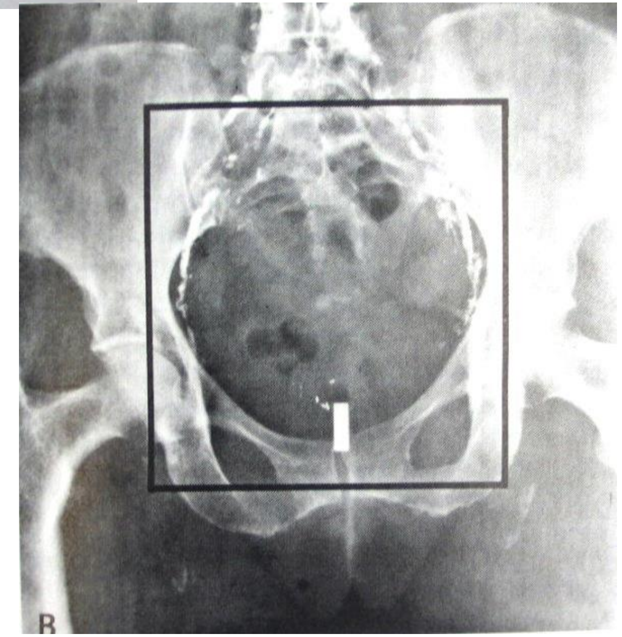
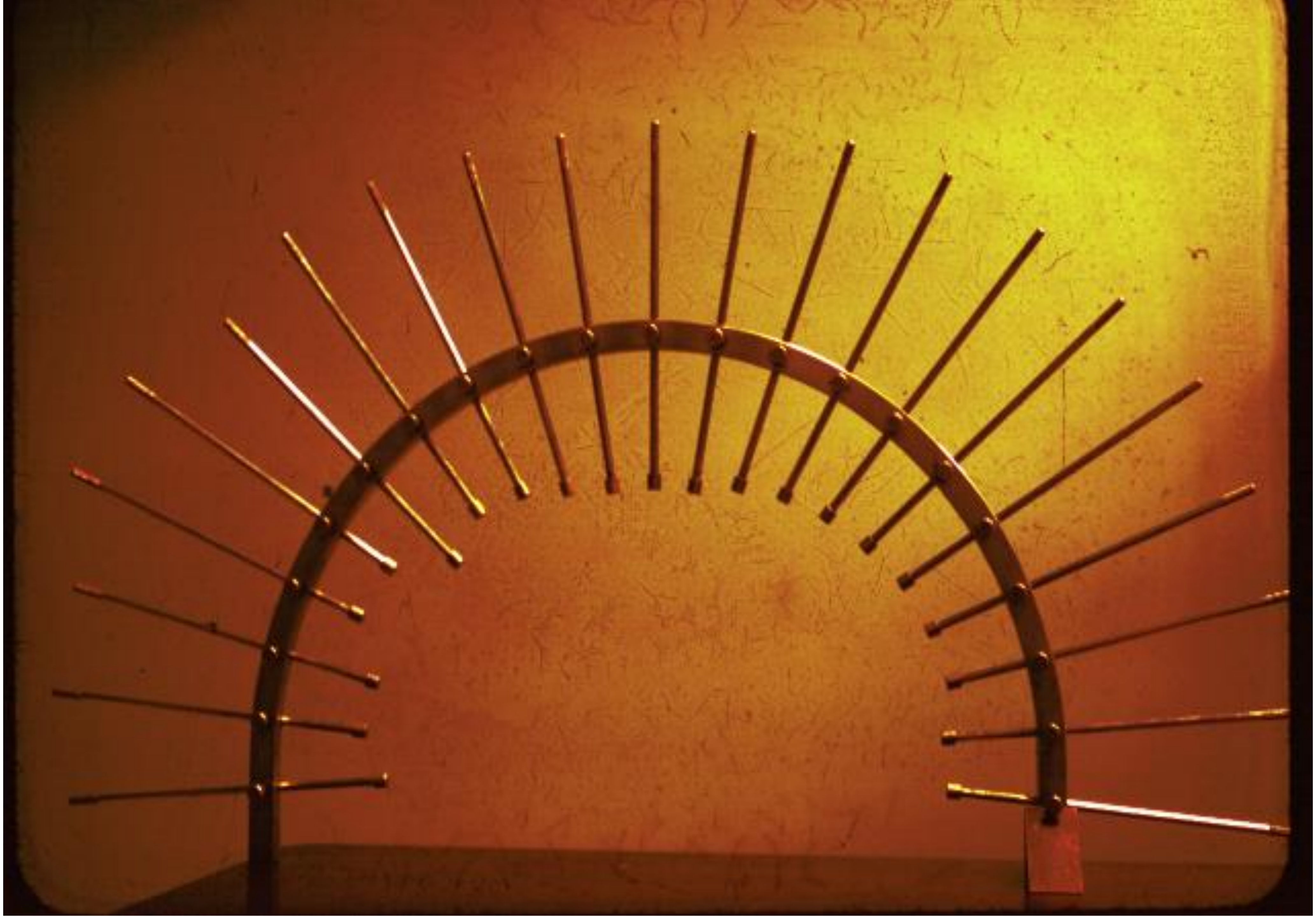
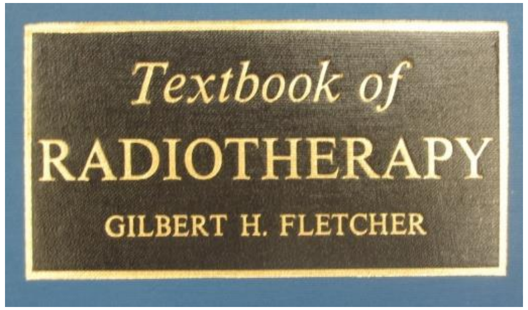


FIG. 11–37. A. Projection of vaginal disease onto the surface of the body. The cervical localizer, seen on the left side of the tray, consists of a plastic rod with a lead plug at its tip and a fluid level to assure its horizontal position. The plastic rod is introduced into the vagina, guided by the examining finger until contact is made with the lowest palpable vaginal disease. As the rod is then attached to the stand at exactly this level, the vertical pointer, which is in line with the tip of the rod, will project the location of the lowest palpable vaginal disease onto the surface of the body. The lower margin of the portal is drawn 2 cm below that projection. A verification film is taken immediately and adjustments are made until the field includes approximately 1 cm of tissue below the lead plug, which means that there will be at least 2 cm of normal vaginal tissues in the irradiated field.

Also seen on the tray are the compression cone for the 22-MeV betatron with the lead blocks to shield respectively 2 and 4 cm of tissue at 10-cm depth. The end of compression cone for the ^{60}Co unit is made of copper mesh to minimize secondary electron emission. The lead blocks can slide sideways to fit the isodose curves of the individual radium system.







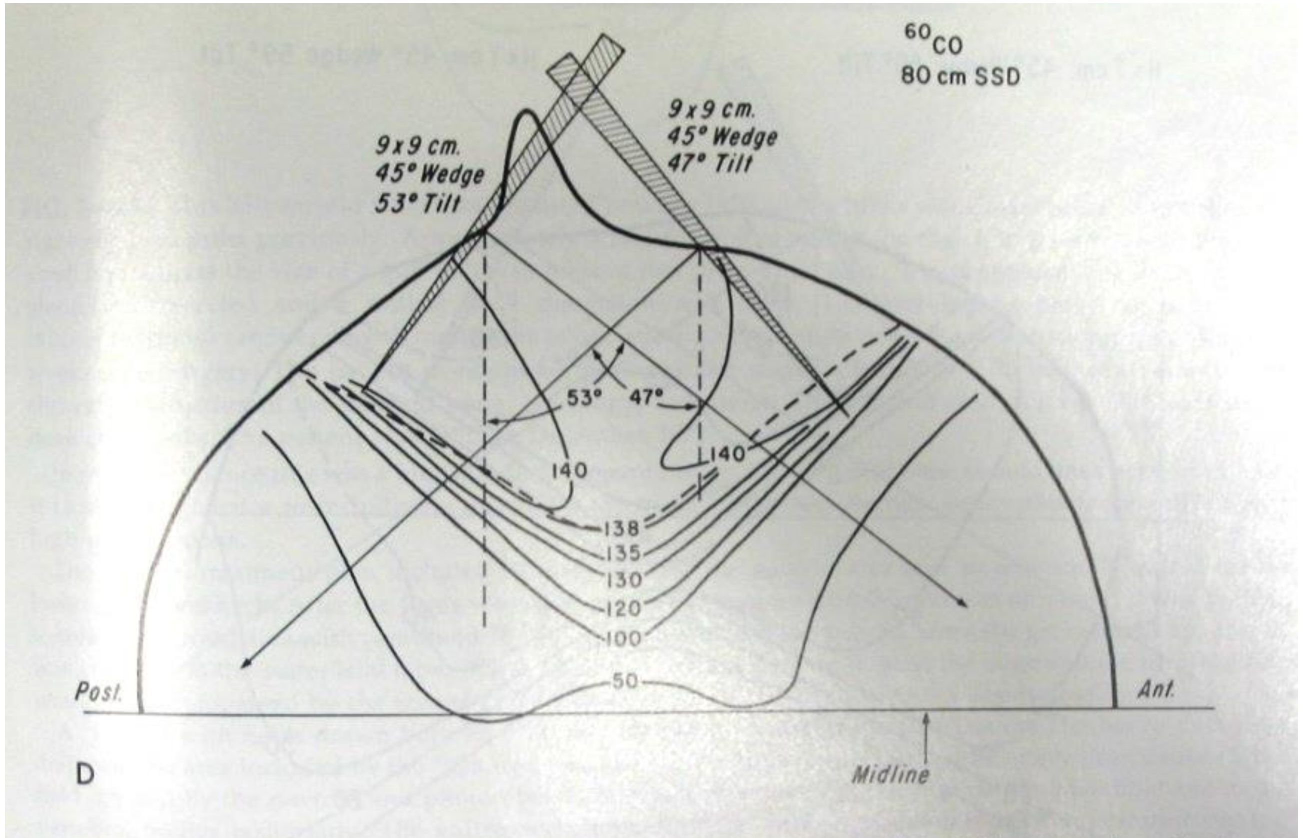


FIG. 3–124 (cont'd). C. Treatment for the ipsilateral neck. The anterior ^{60}Co field extends from the lower border of the parotid field.

D. Isodose distribution of ^{60}Co wedges. The tumor dose is taken at the 138% curve. The tissue volume included in the high dose range is not excessive.

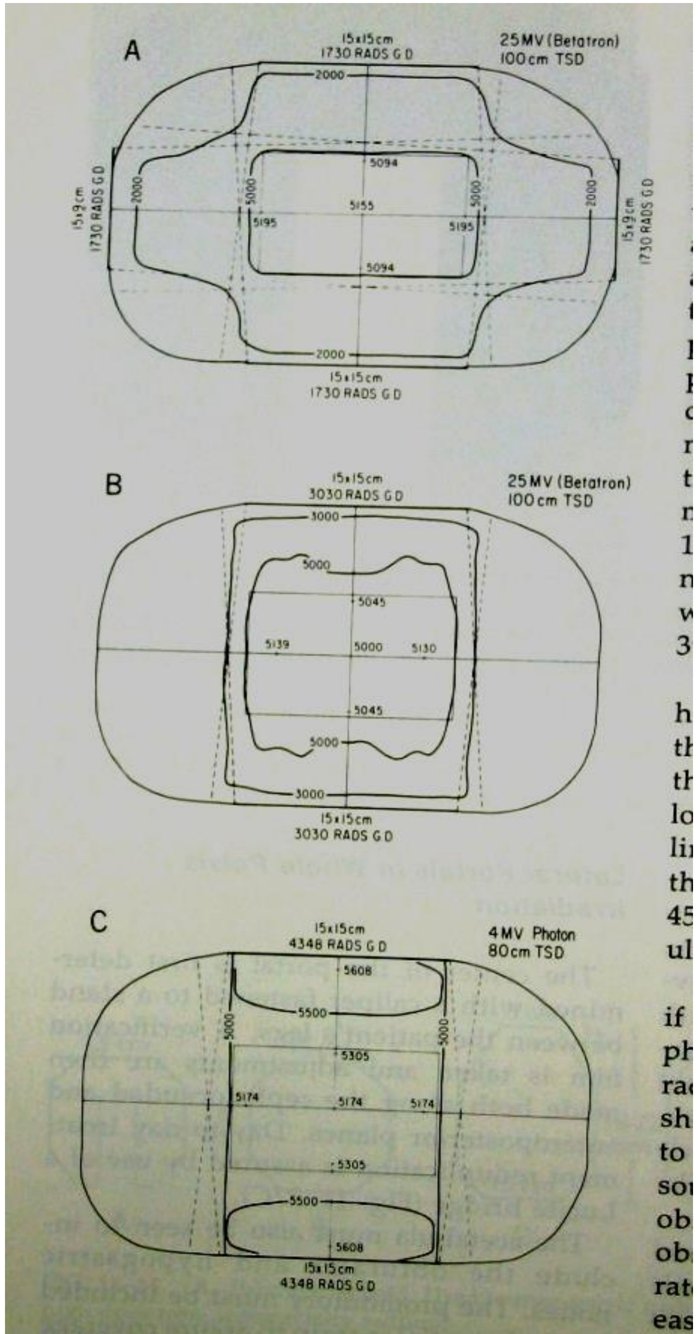
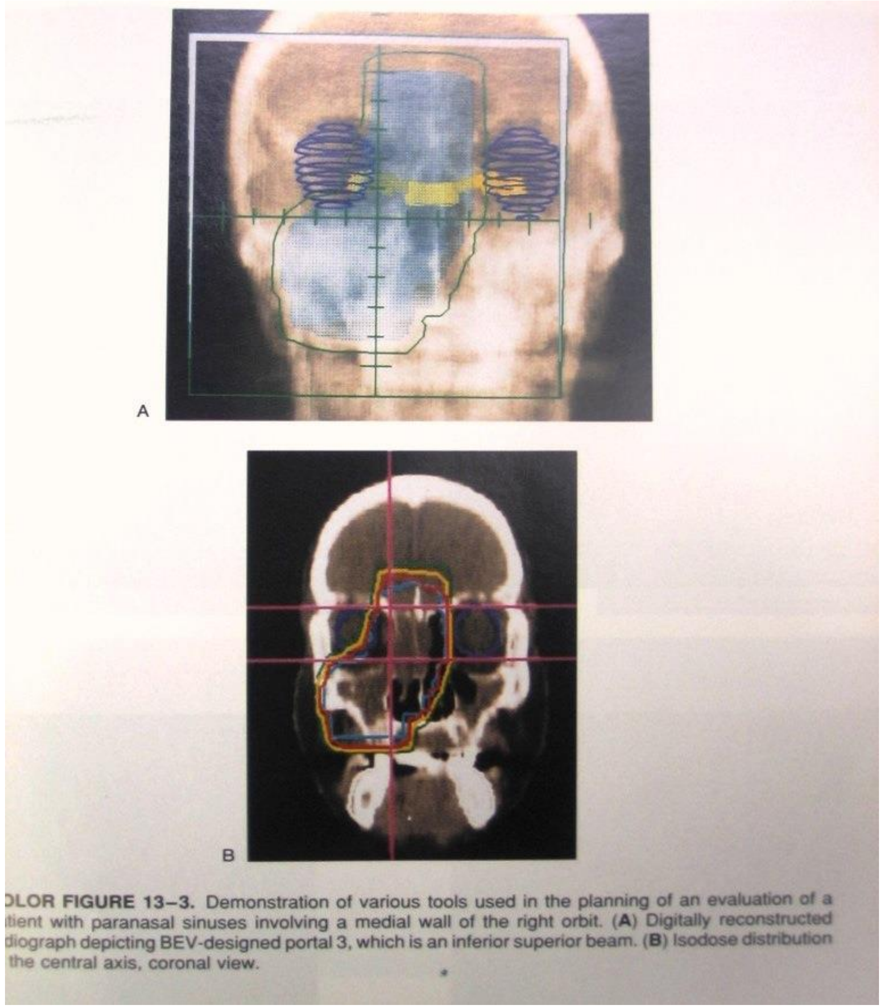
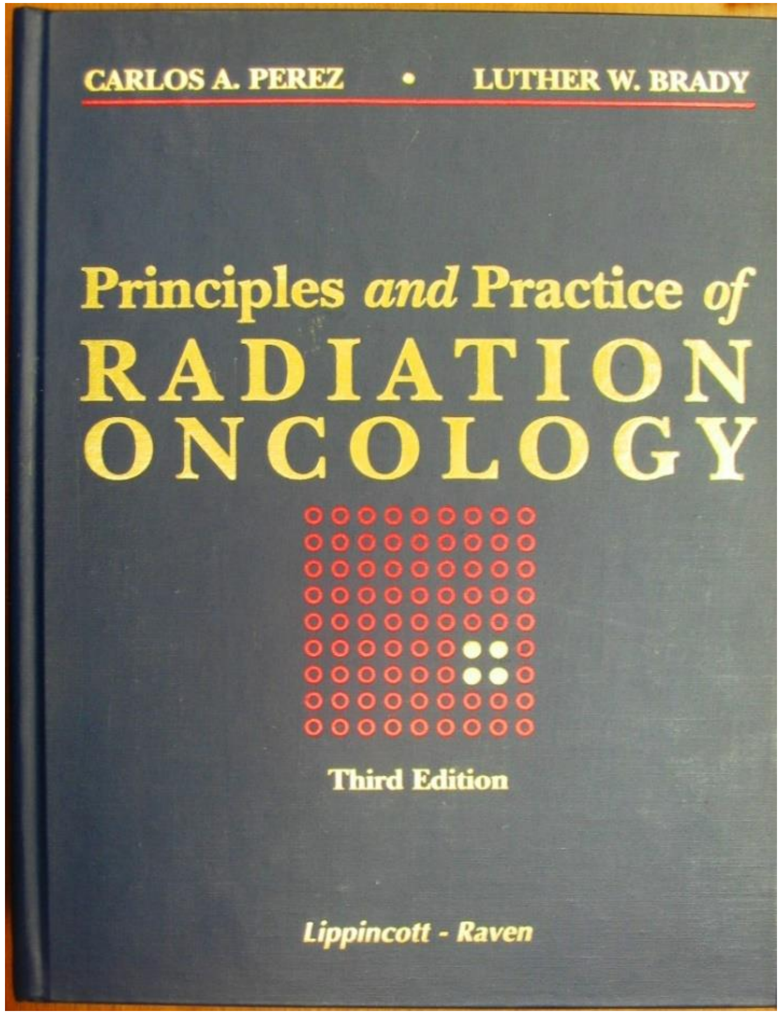
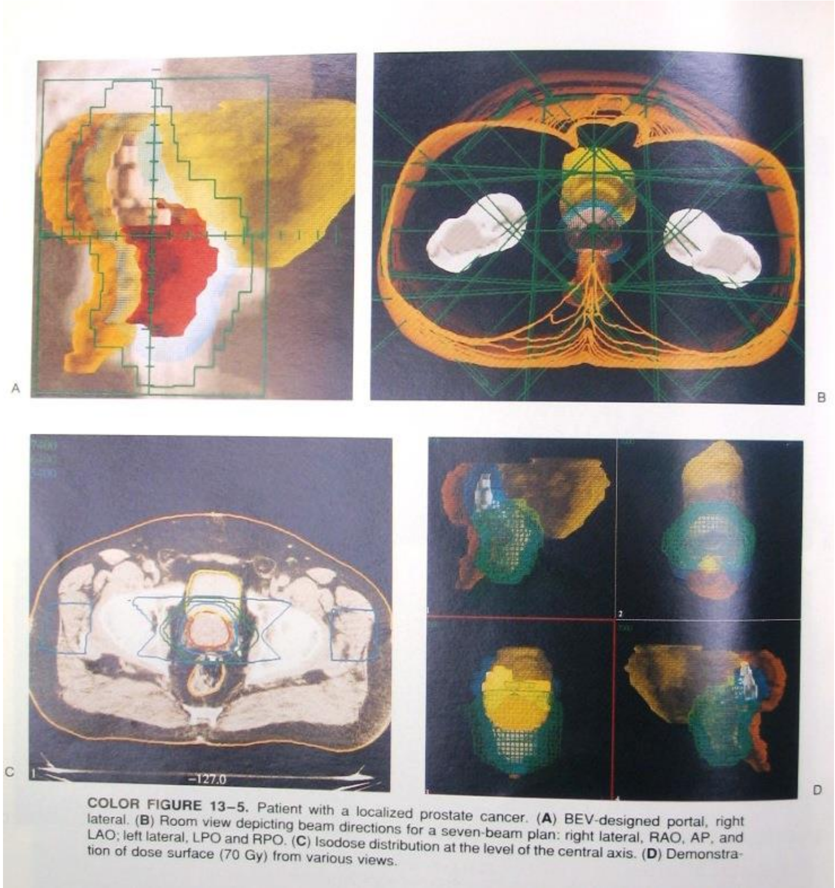


FIG. 11–36. A. Box pattern, 15 × 15 × 9 cm (approximately 2000 cm³) with 25 MeV. B. Parallel opposing 15 × 15 × 22 (AP diameter) cm (approxi-

The 90's – the era of 3D

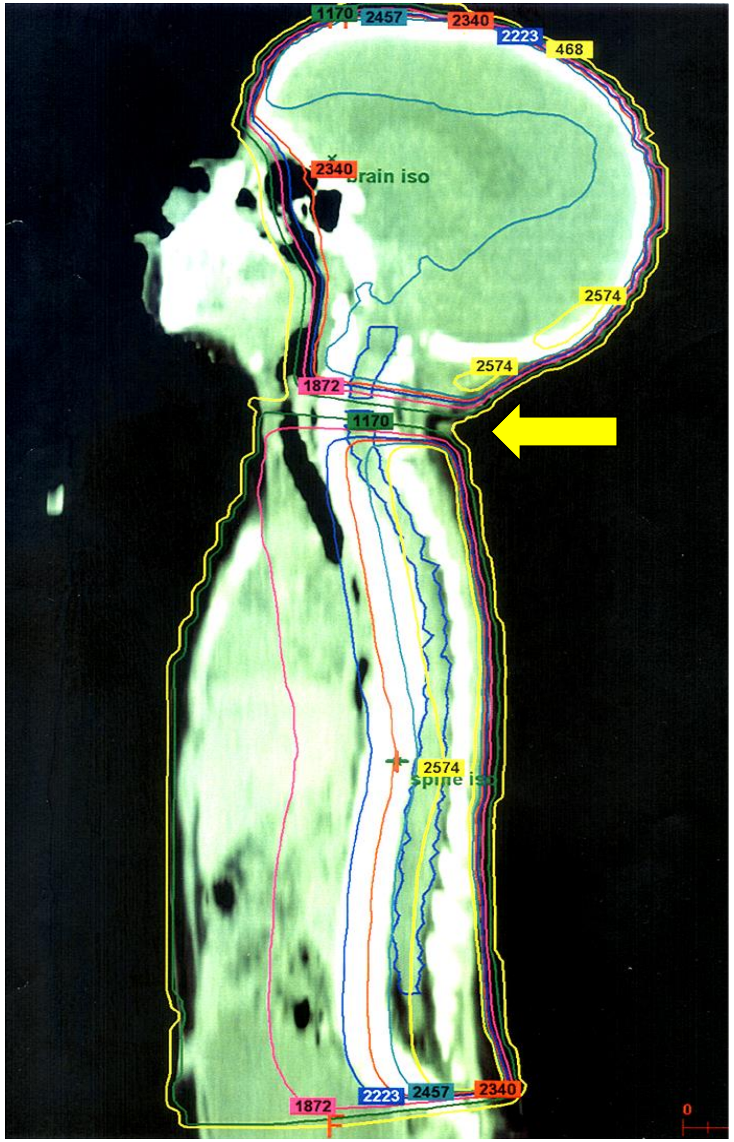


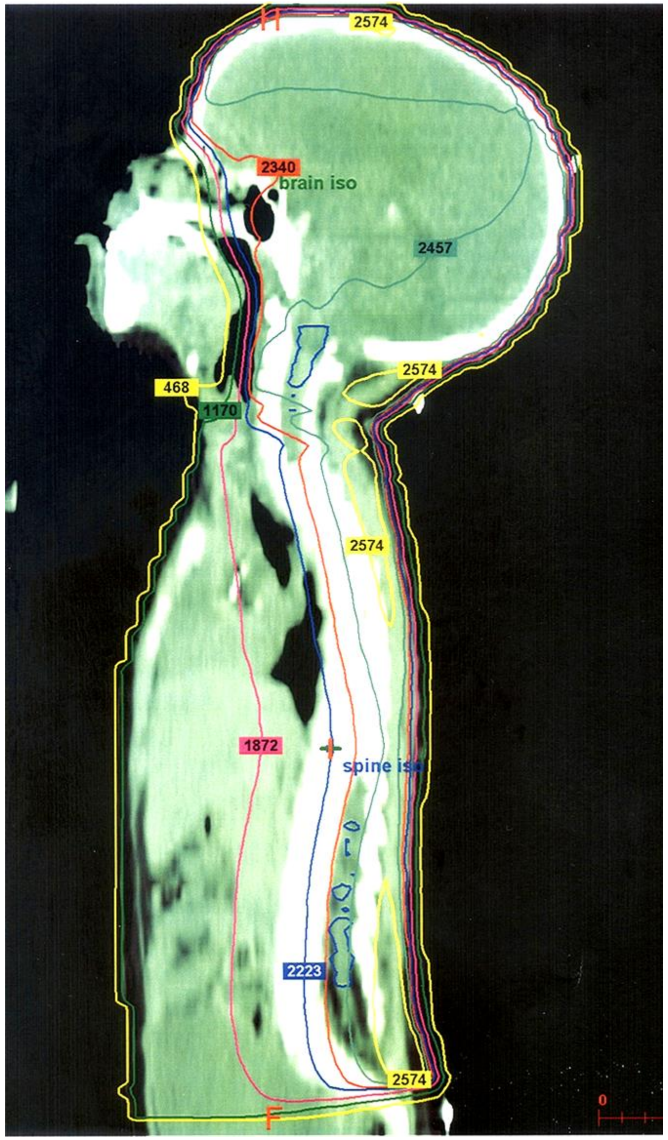




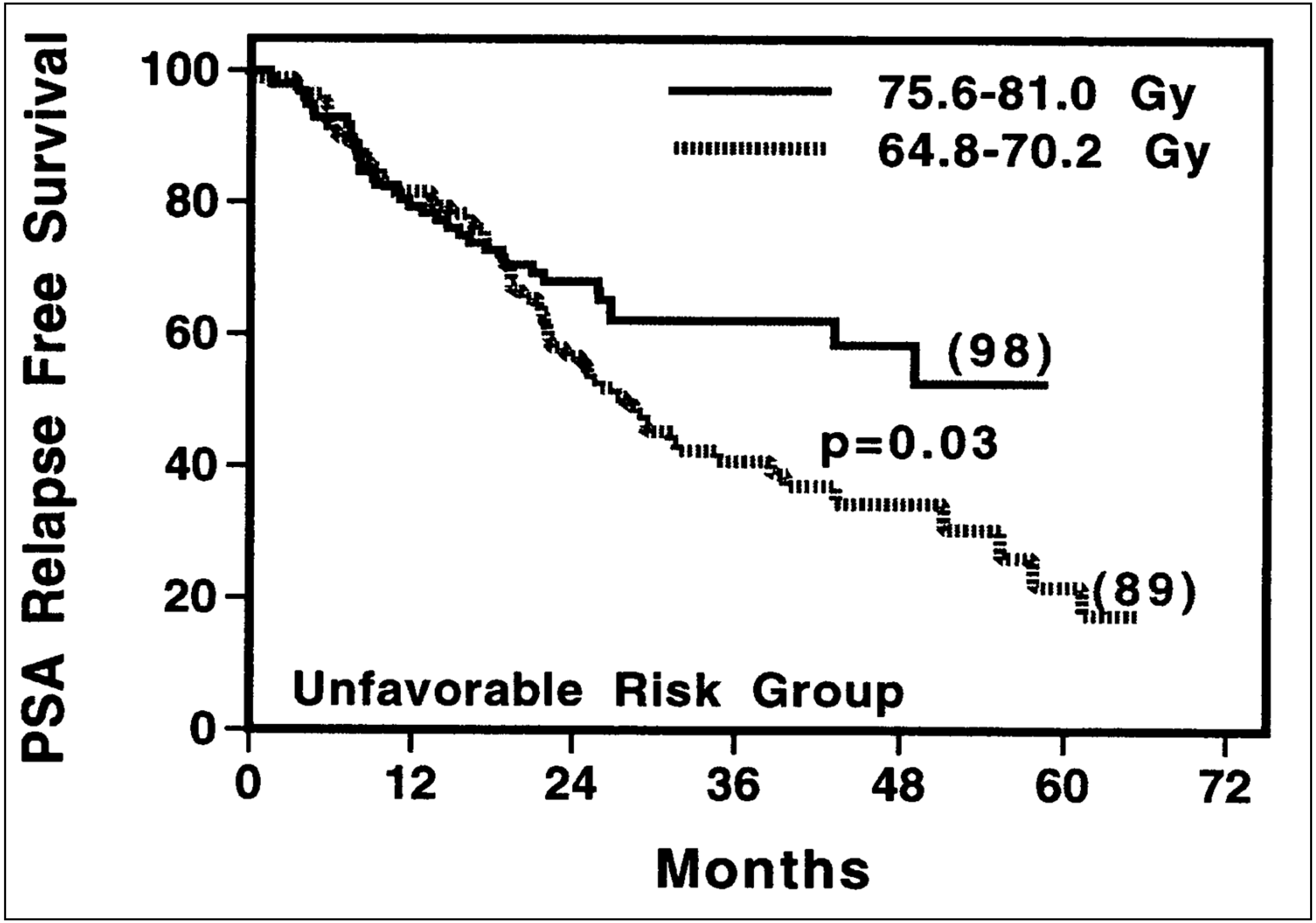
Perez and Brady - Principles and Practice of Radiation Oncology-1998, and others…

Cranio- spinal Irradiation





RFS vs. DOSE - RT alone



From: M.J.Zelefsky et. al.; IJROBP June 1998

RFS vs. DOSE - RT alone

657 patients treated in 1994-95

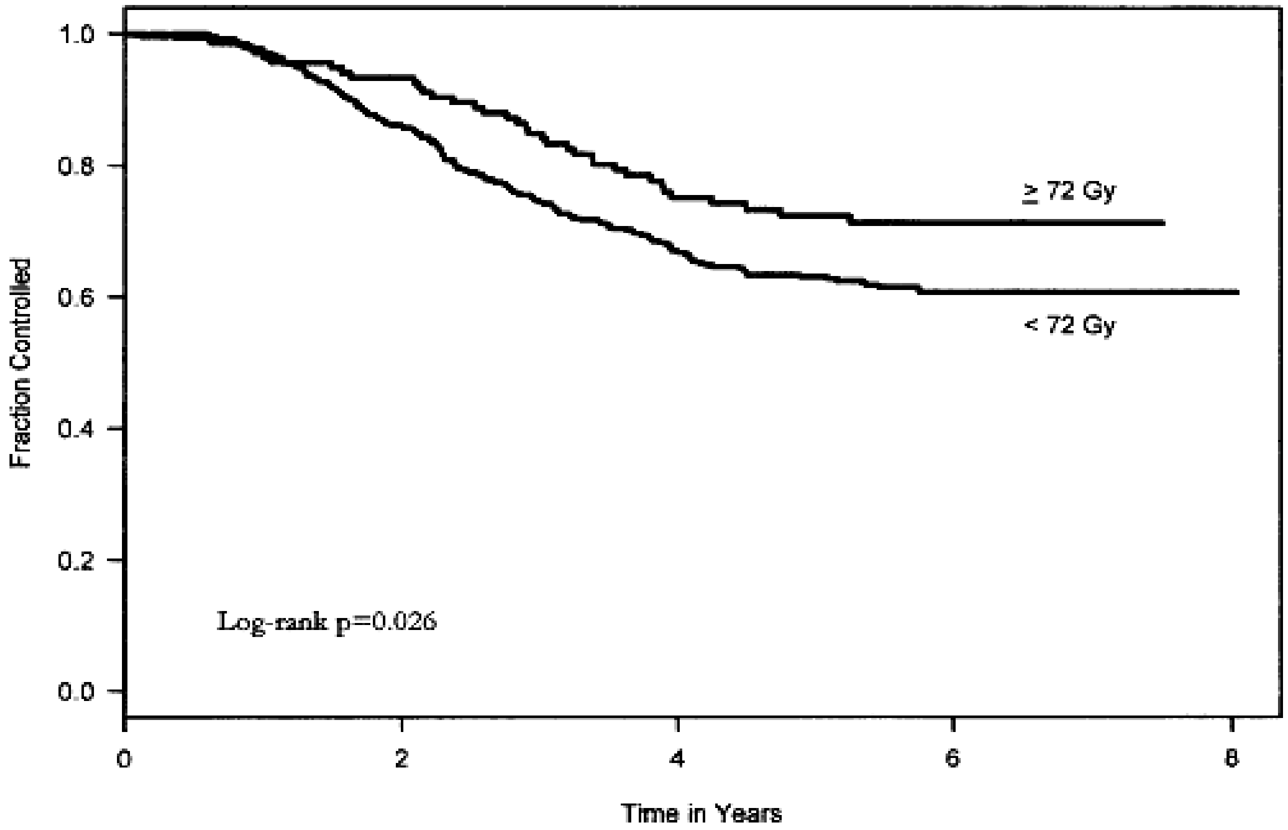


Fig. 2. Kaplan-Meier prostate-specific antigen (PSA) disease-free survival curves of patients with intermediate-risk tumors (T1b, T1c, T2a, GS ≤6 and PSA >10 ng/mL but ≤20 ng/mL or T2b, GS ≤6 and PSA ≤20 ng/mL or GS 7 and PSA ≤20 ng/mL).

From: P. Kupelian et. al.; IJROBP Feb 2005

Dose Response

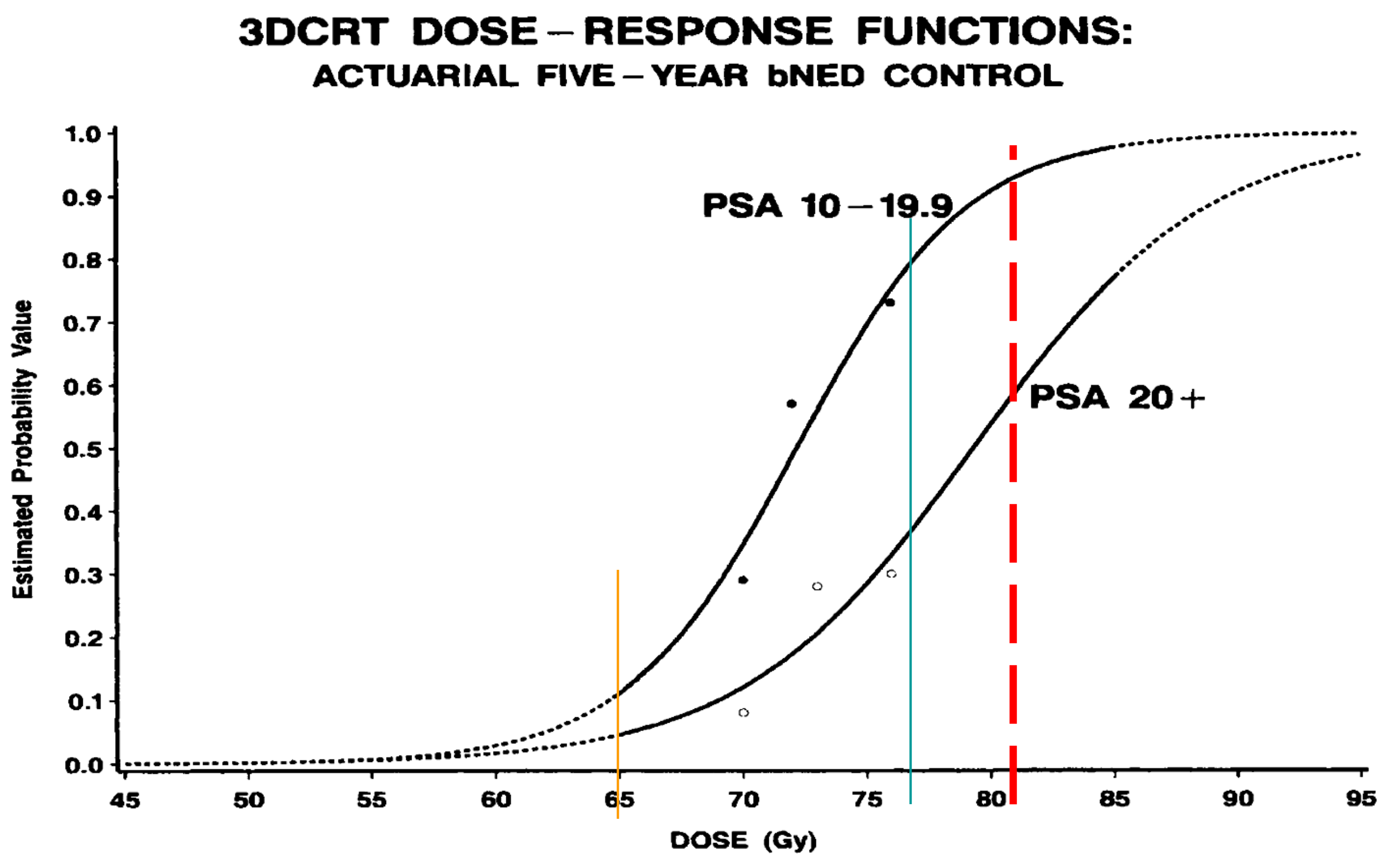


Fig. 2. Logistic response models for bNED for two pretreatment PSA groups.

- From: G.E.Hanks et. al., IJROBP, June 1998

Morbidity vs. Dose

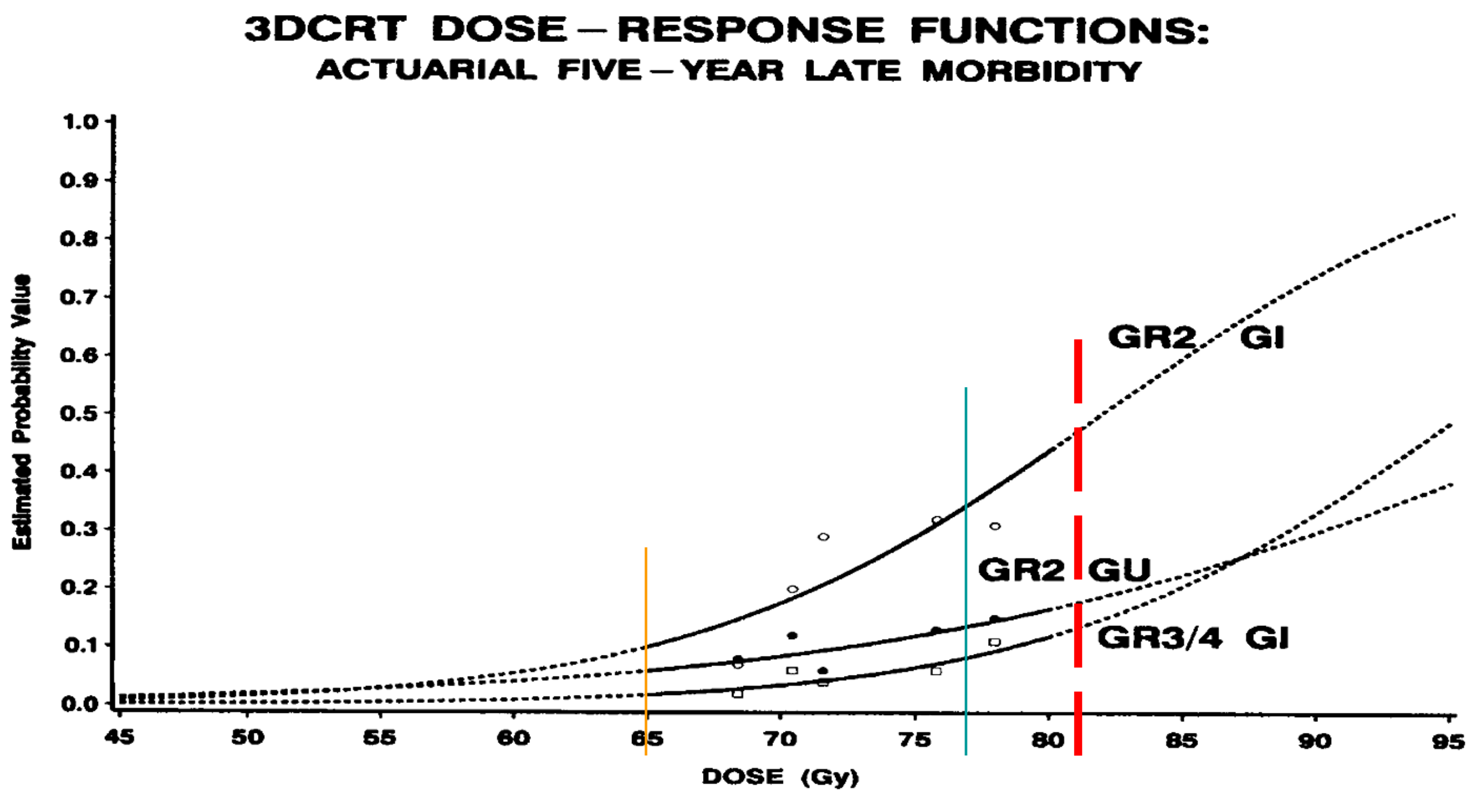


Fig. 5. Logistic response models for gastrointestinal and genito-urinary radiation sequelae.

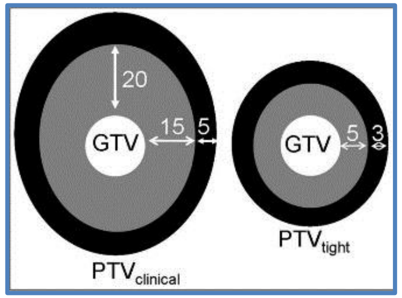
From:G.E.Hanks et. al., IJROBP, June 1998

Hypothesis … for new technologies

More accurate dose delivery & better dose distributions yield better clinical outcomes!

Basic Strategy

- Reduce treatment volume
  - Irradiate a smaller volume of normal tissue



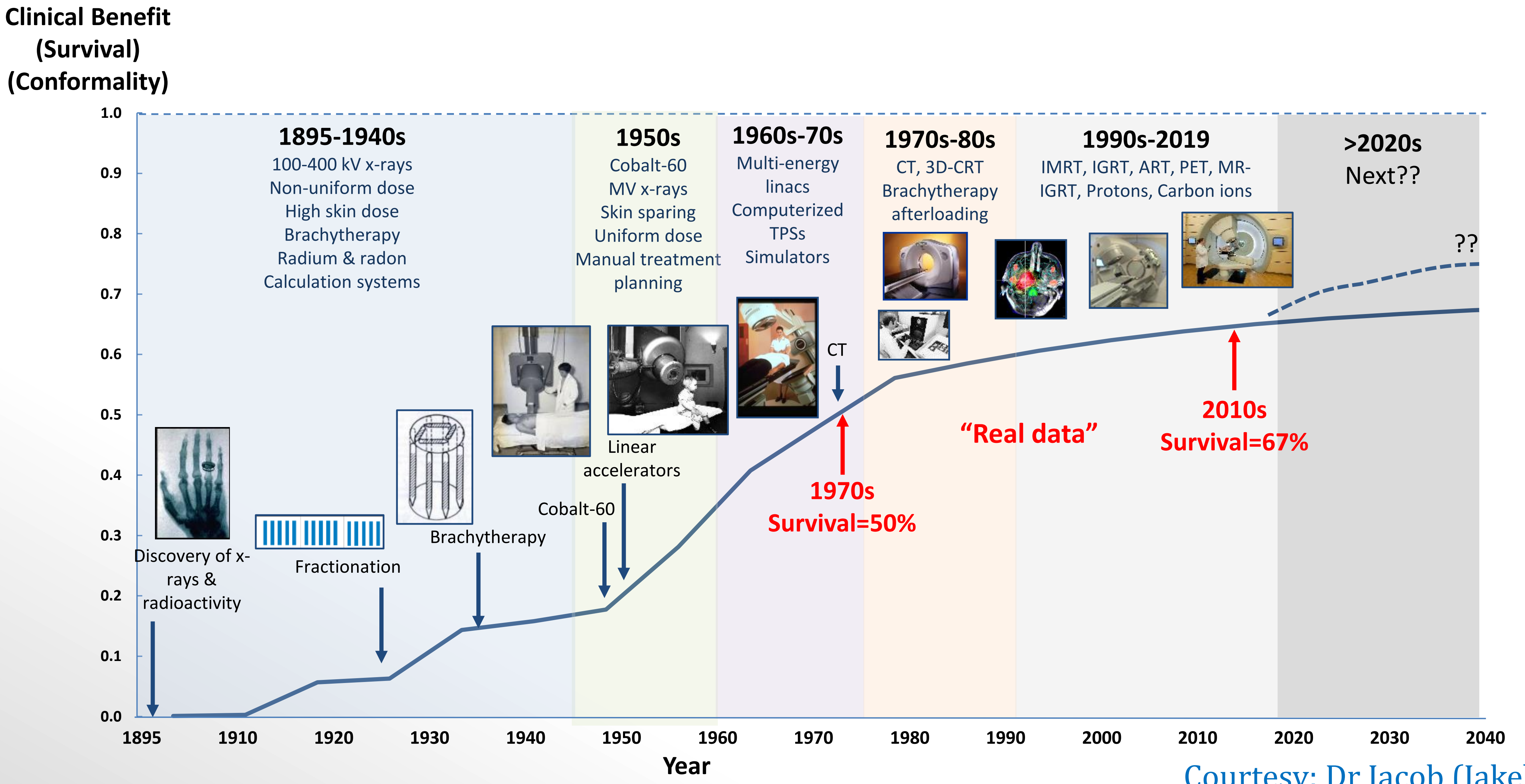
… allows dose escalation
- higher doses to tumours

Tumour Control Probability (TCP)

Normal Tissue Toxicity (NTCP)

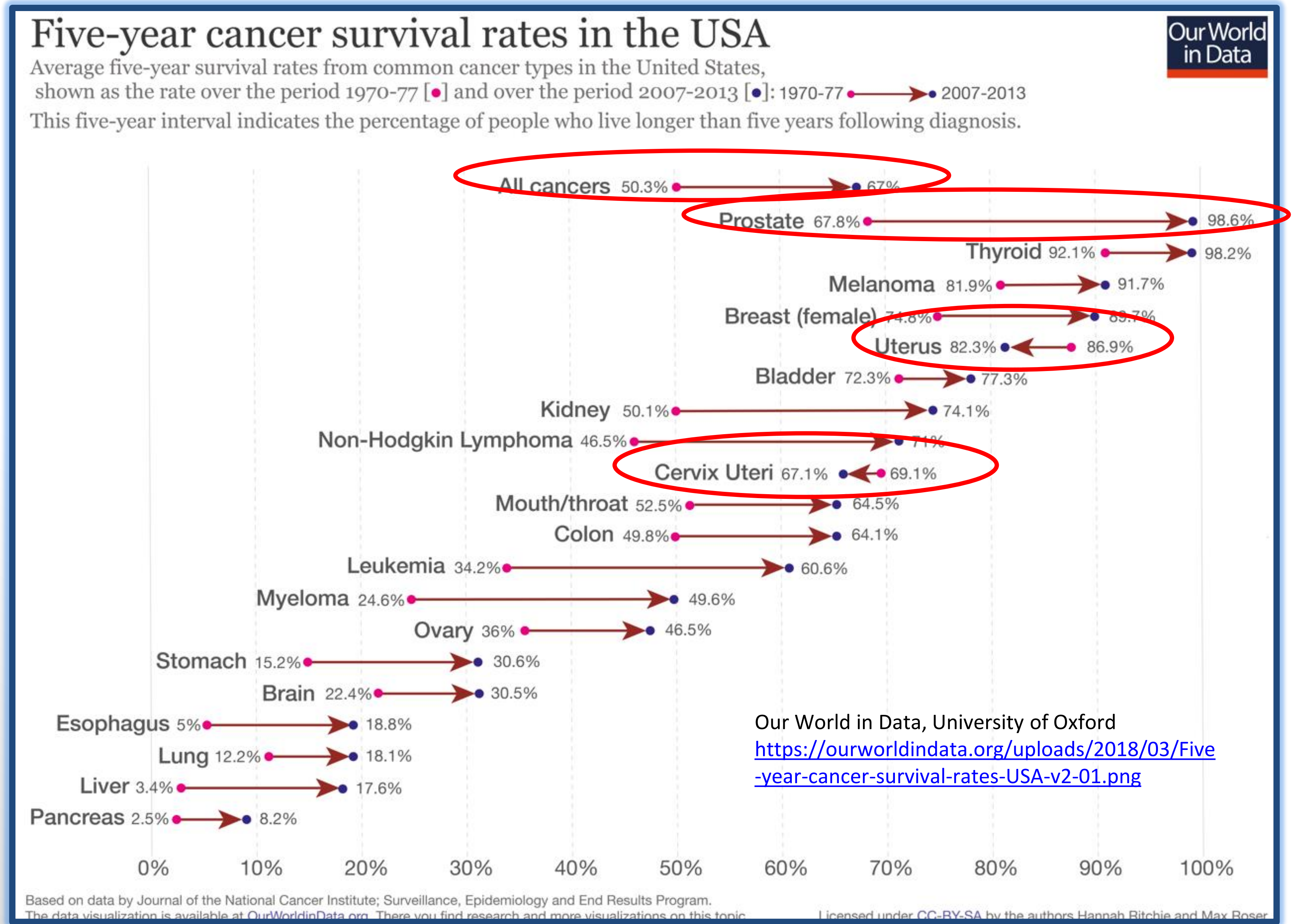
Courtesy: Dr Jacob (Jake) Van Dyk

Radiation Oncology Historical Trends



Courtesy: Dr Jacob (Jake) Van Dyk

USA 5-yr Survival: ~1970s [•] to ~2010s [•]

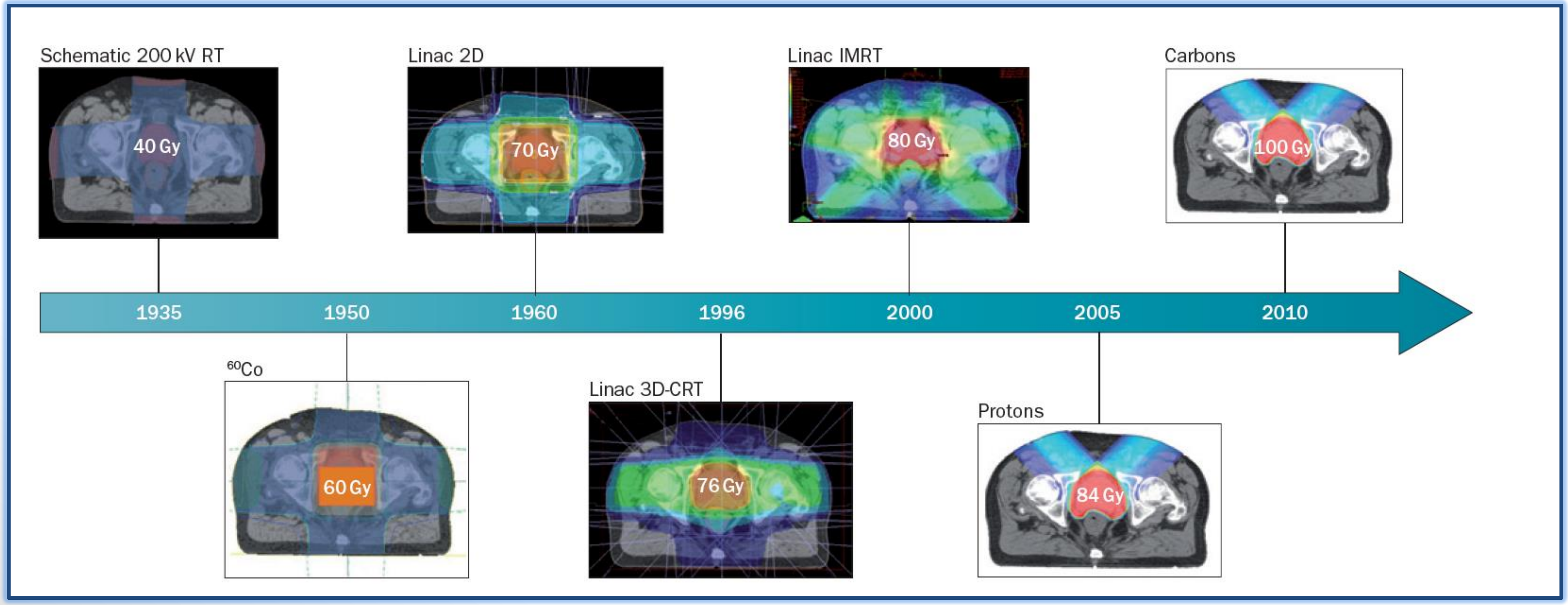


Our World in Data, University of Oxford
https://ourworldindata.org/uploads/2018/03/Five-year-cancer-survival-rates-USA-v2-01.png

- All cancers up
  - 50% → 67%
  - Except cervix & uterus
- Prostate
  - 68% → 99%
- "early detection and improved treatment"

Courtesy: Dr Jacob (Jake) Van Dyk

Prostate Cancer EBRT

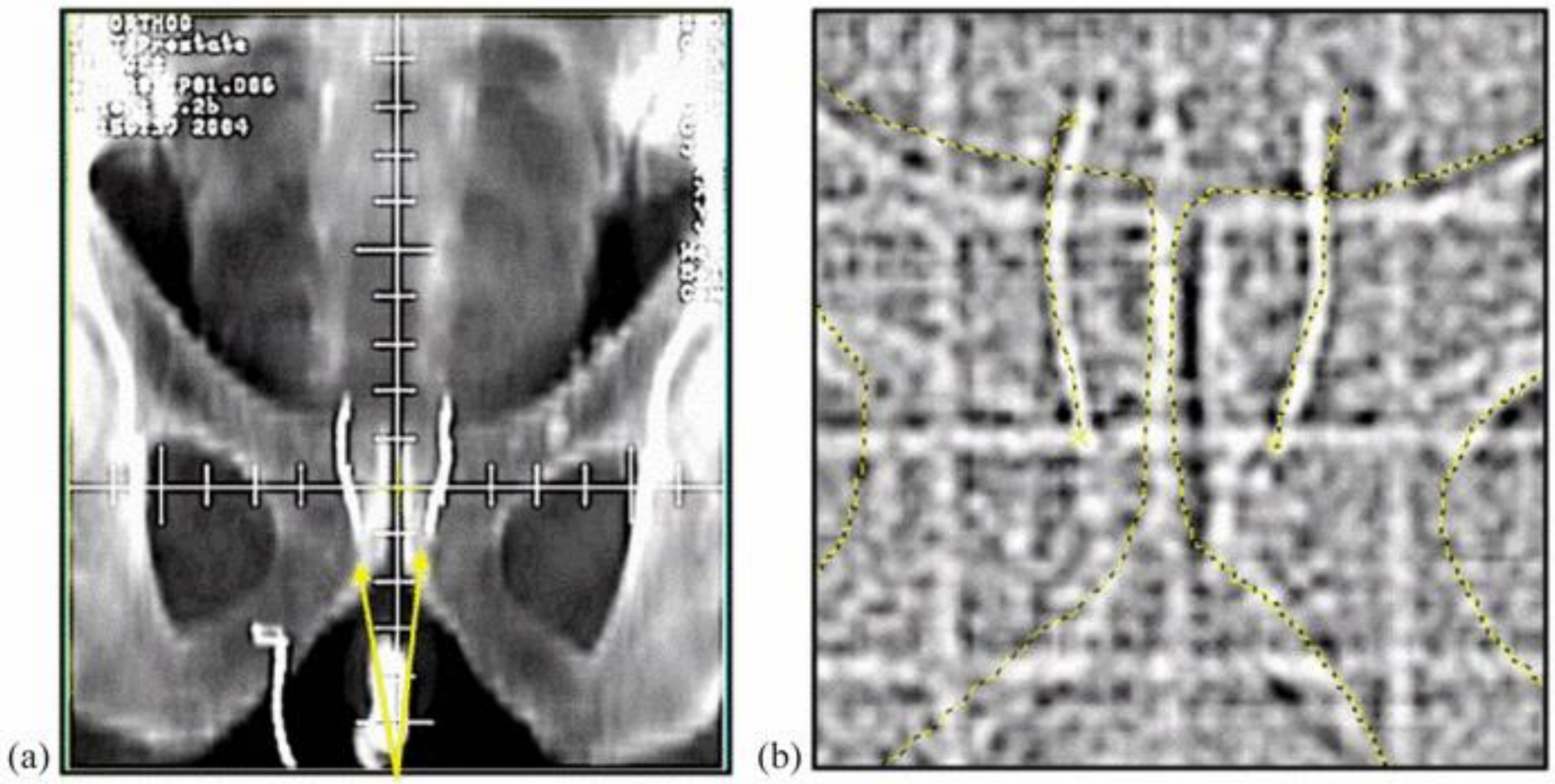


Thariat *et al.* Nat Rev Clin Oncol 10: 52–60; 2013

Image guidance over the years

- Portal Imaging (film and digital)
- Fluoroscopic tracking (range of motion)

Fiducial based 2D/2D match



Gold coils implanted in the prostate are shown on a DRR (a) and on an MV portal image (b). Image matching structures obtained from the DRR are superimposed on the EPID to target the coils, rather than the bony anatomy.

Image guidance over the years

- On Board imagers (kV and MV)

Localization and 4D RF Tracking of Implanted Markers

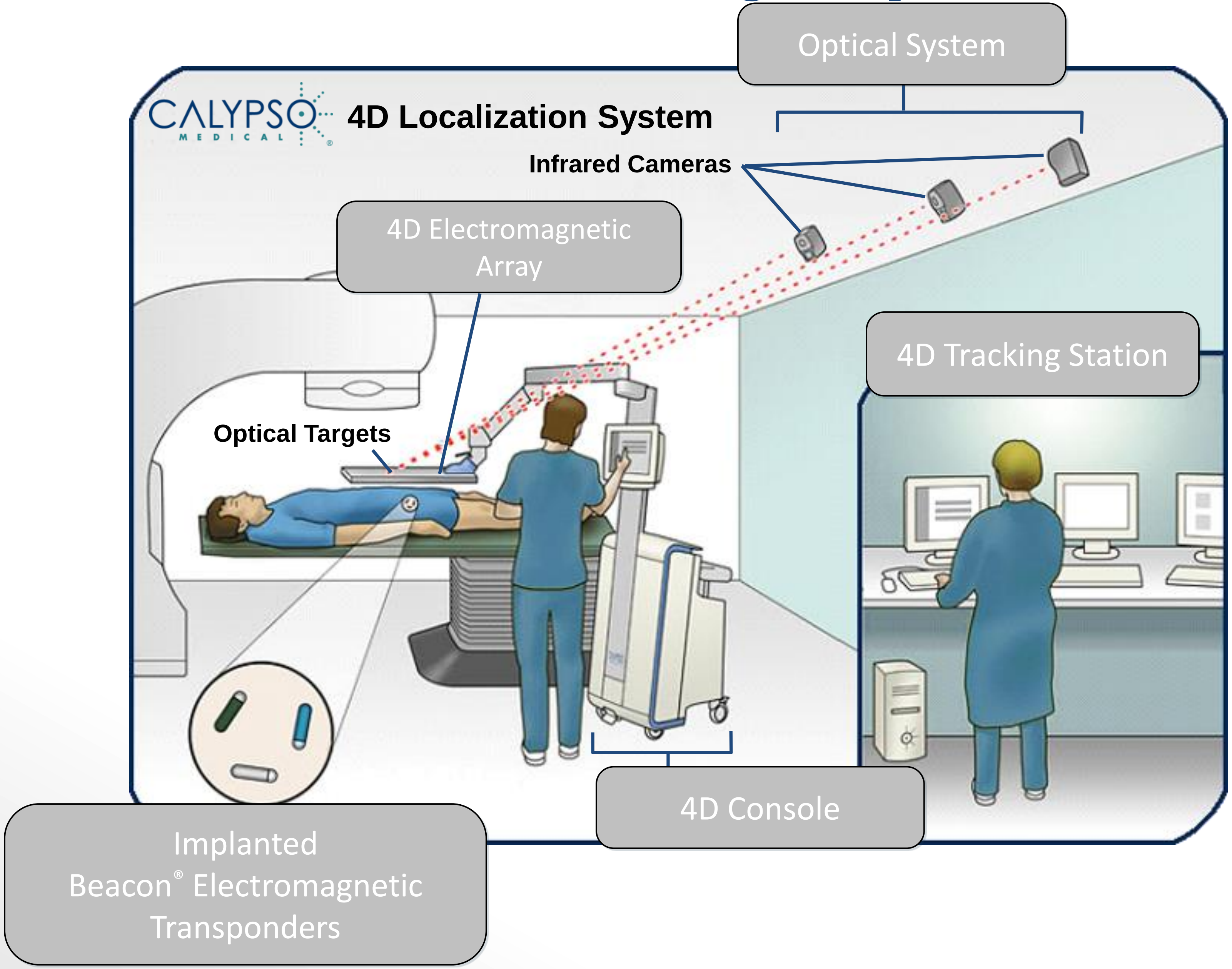


Image guidance over the years

- U-Sound targeting (mainly distance or interface)

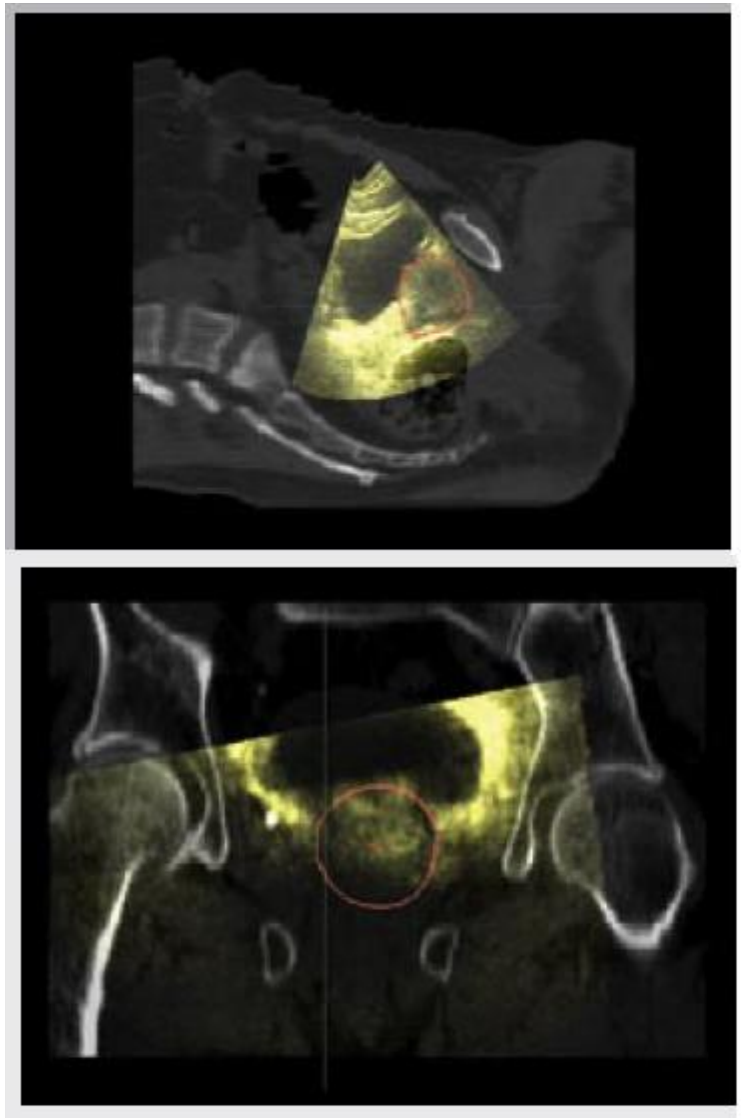
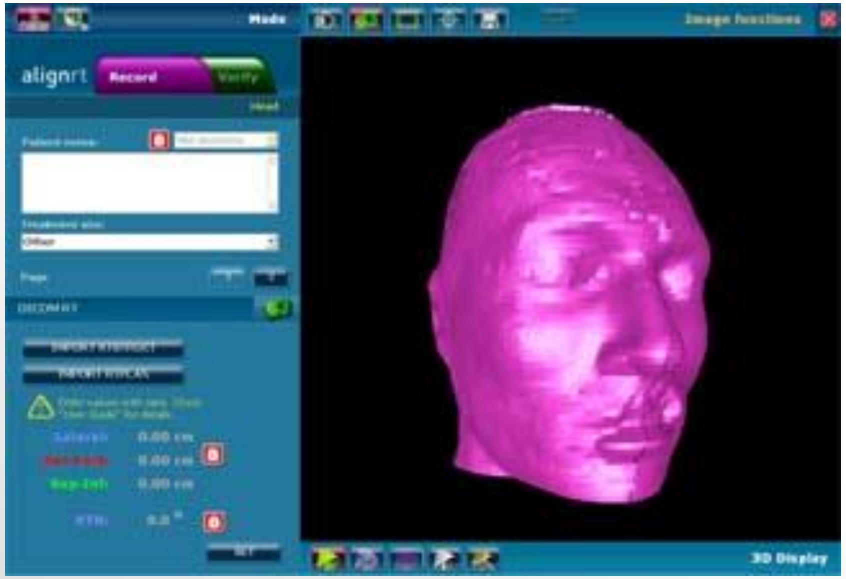
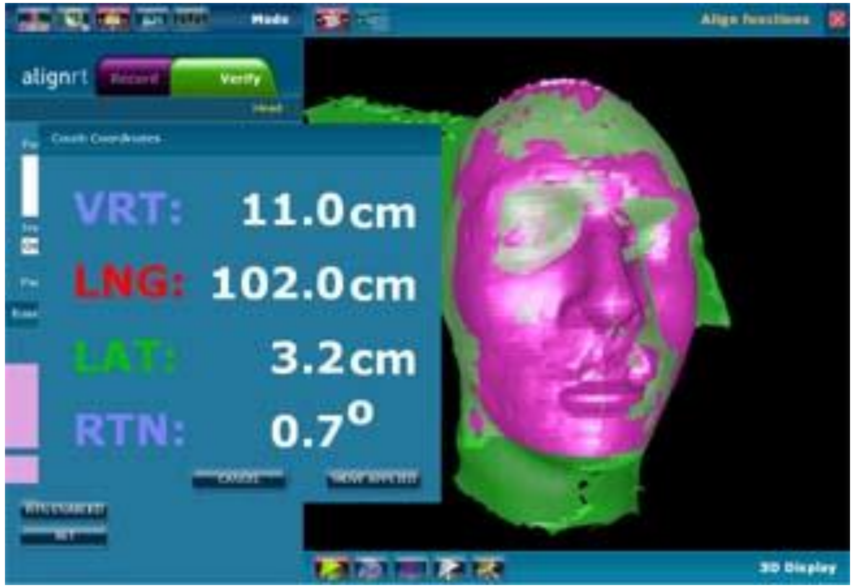


Image guidance over the years

- Optical surface matching (Visionrt)






Base Image Volume
Show Image Array
A
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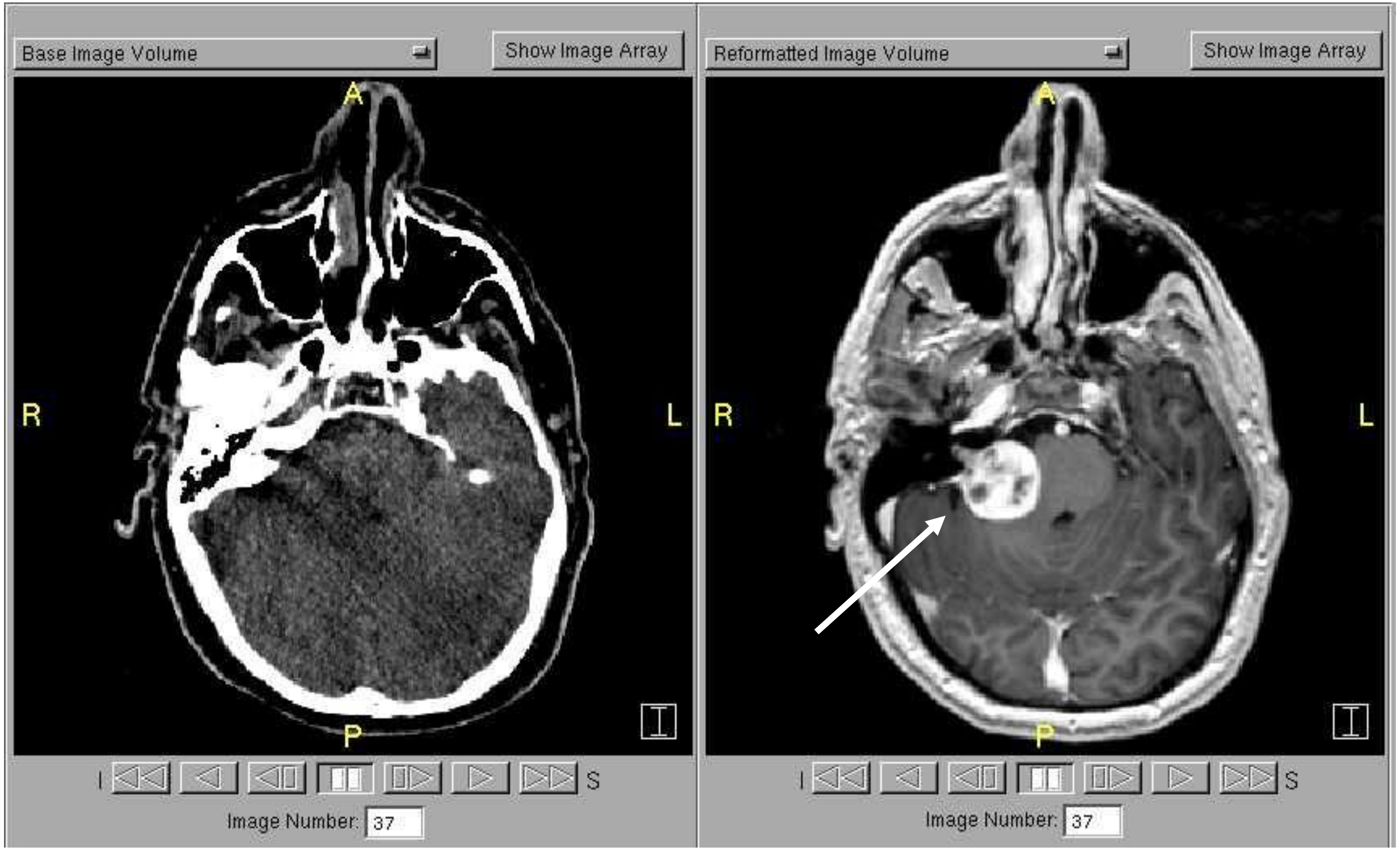
Image Number: 37

Multimodality image registration



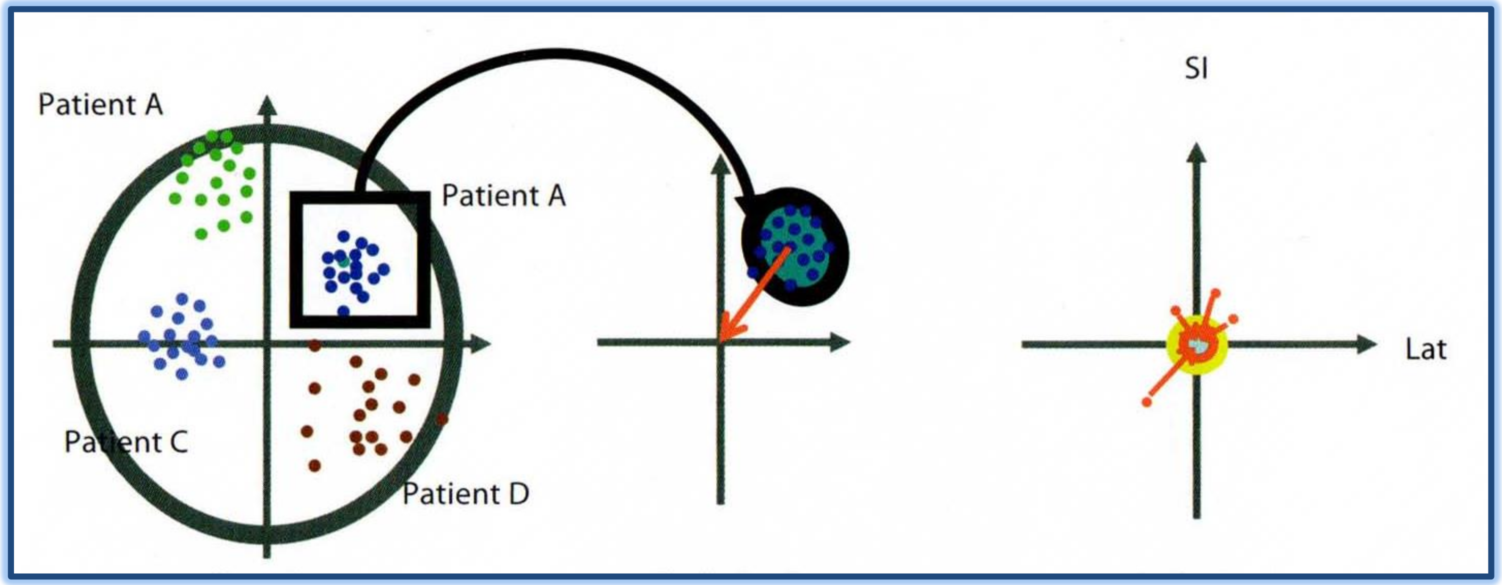
Acoustic neuroma not clearly visible on CT image

Mass clearly seen on reformatted MRI image after fusion with CT

Current

Image-Guided Radiation Therapy (IGRT)
4-D Radiation Therapy

Meyer et al 2007



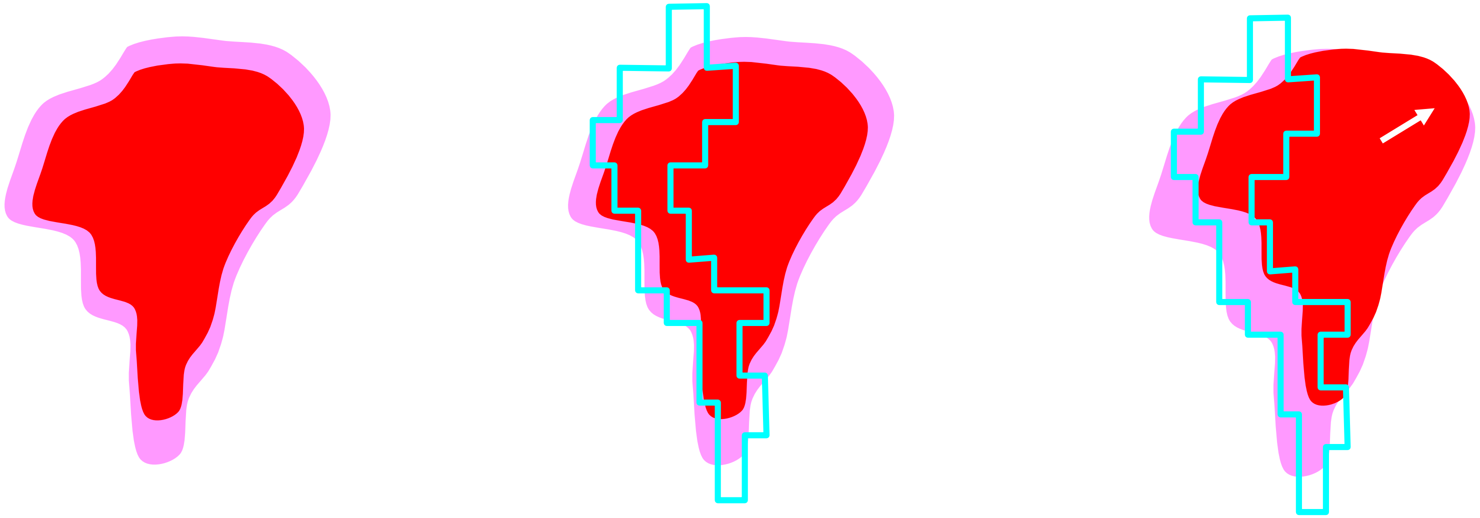
Reduction of systematic and random uncertainties

Adapted from Dr Jacob (Jake) Van Dyk

- Do We Deliver the Correct Dose Distribution for every Treatment?

  For many anatomical sites we have limited control of the internal organ motion

Effects of Intra-Fraction Organ Motion on the Delivery of IMRT with an MLC



Conventional treatment
Effect of organ motion on **GTV** is accounted for by **PTV**, which is always inside the beam aperture.

IMRT treatment: summation of small beams

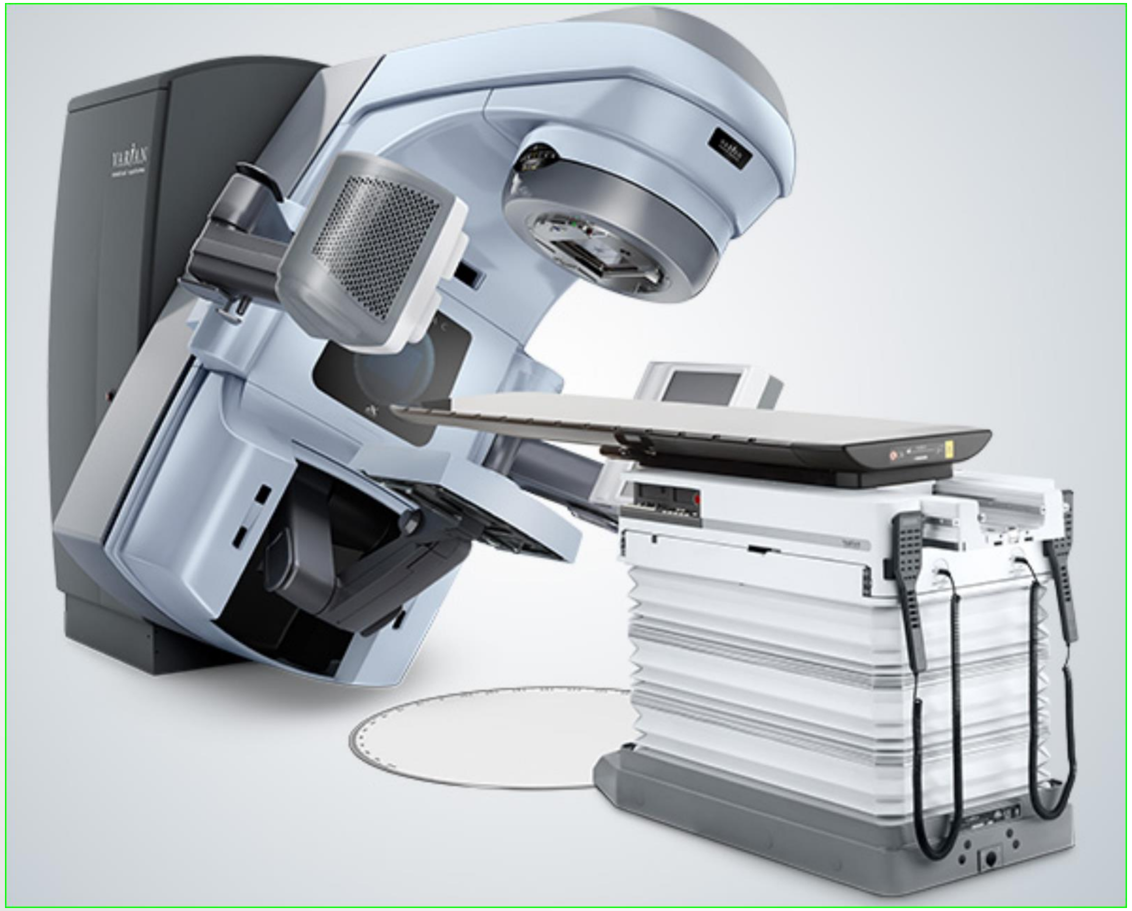
No organ motion
delivered = planned

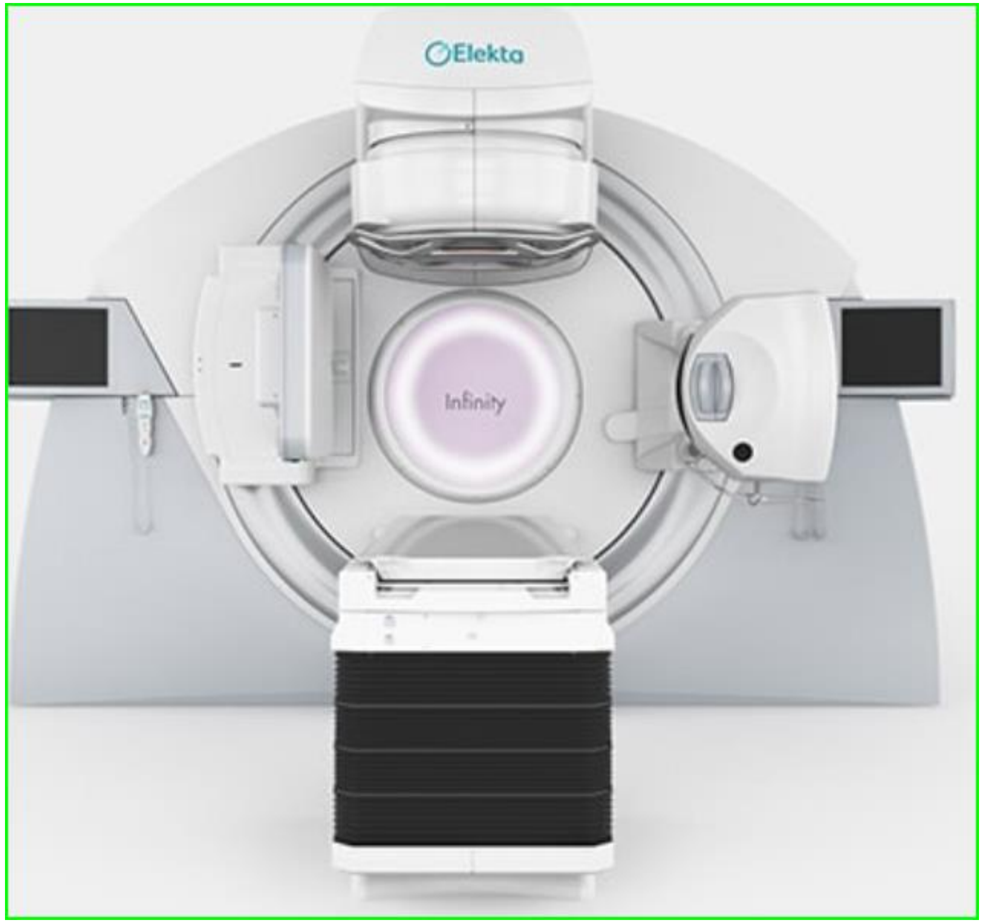
with organ motion
delivered ≠ planned

Courtesy of Dr C. S. Chui

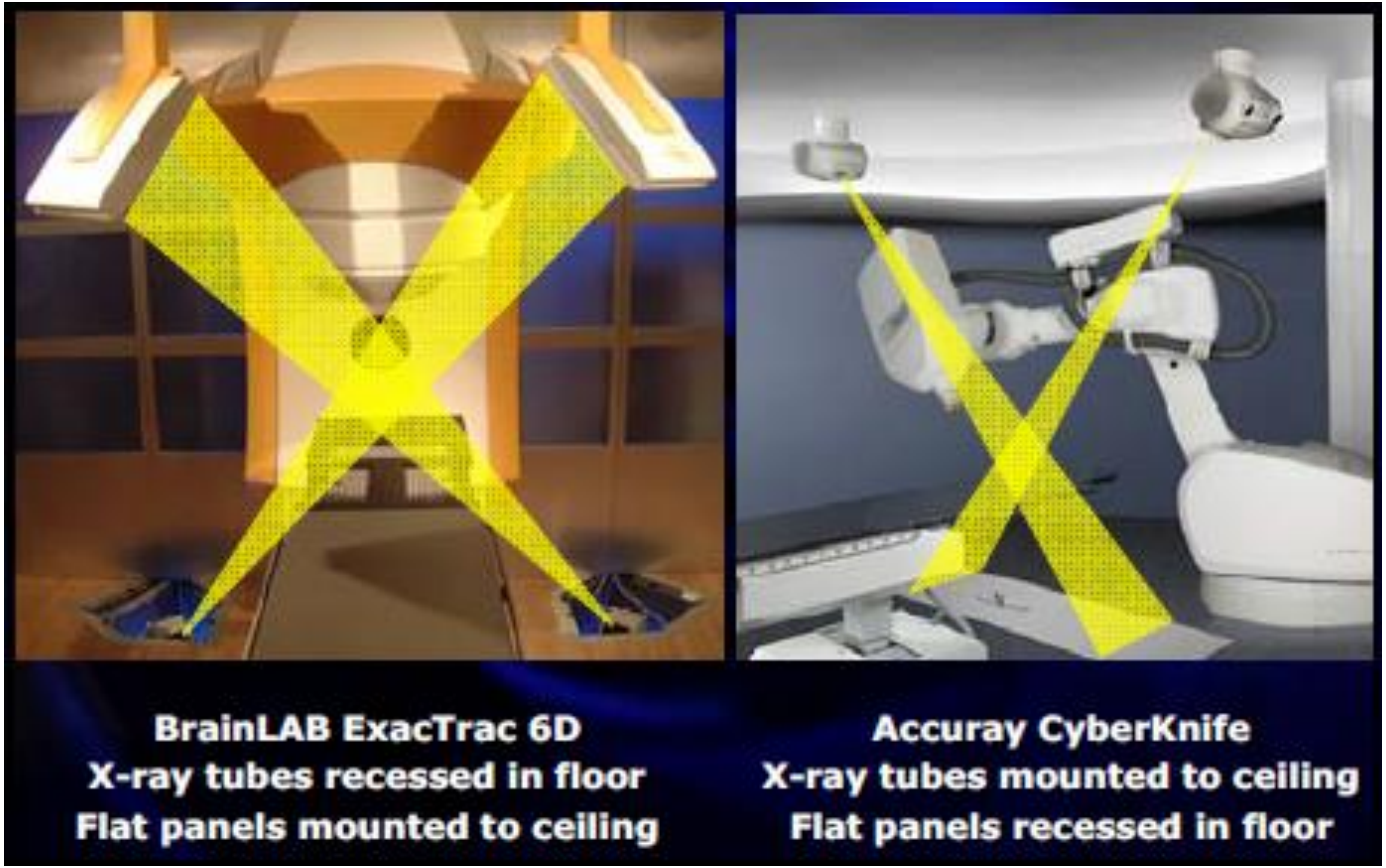
Hybrid Technologies-Imaging and Therapy

- Linac/CBCT



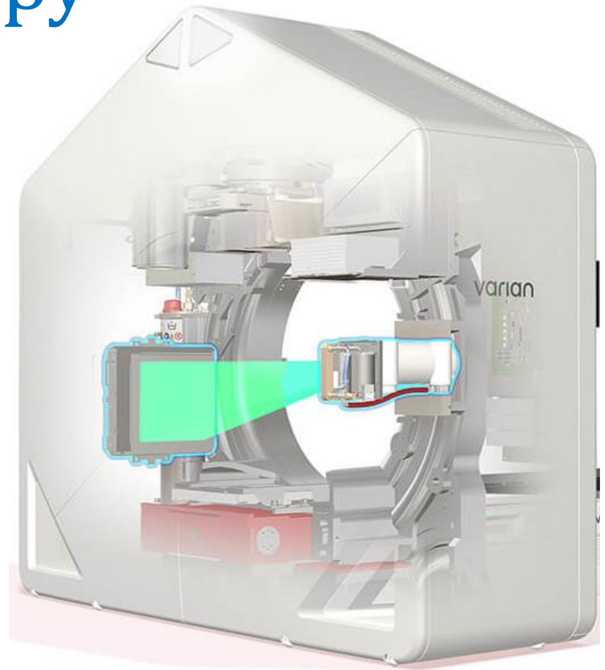


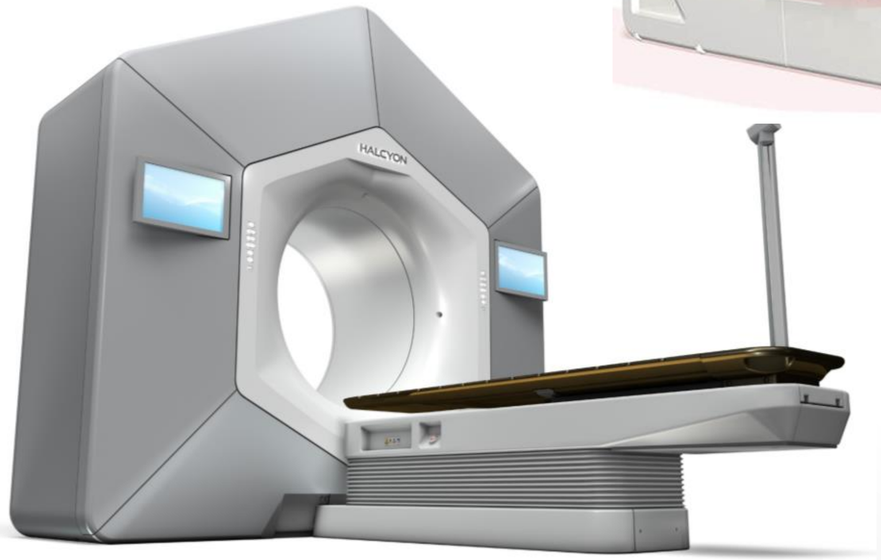
In Room Radiographic guidance

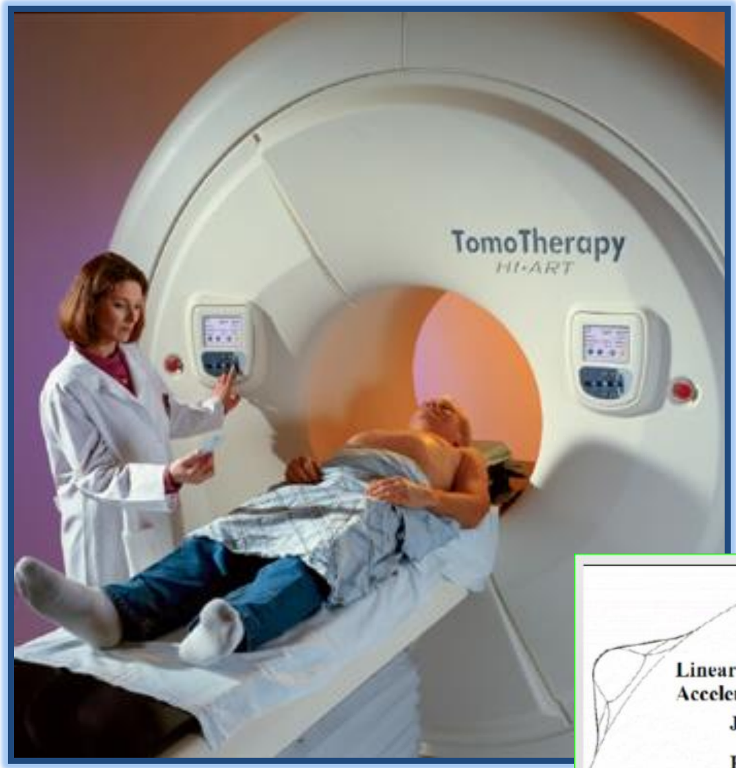


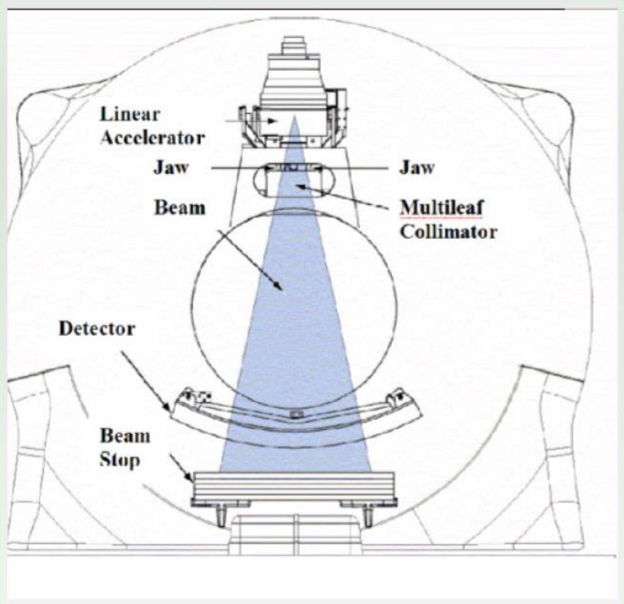
Hybrid Technologies-Imaging and Therapy

- Tomotherapy
- Halcyon







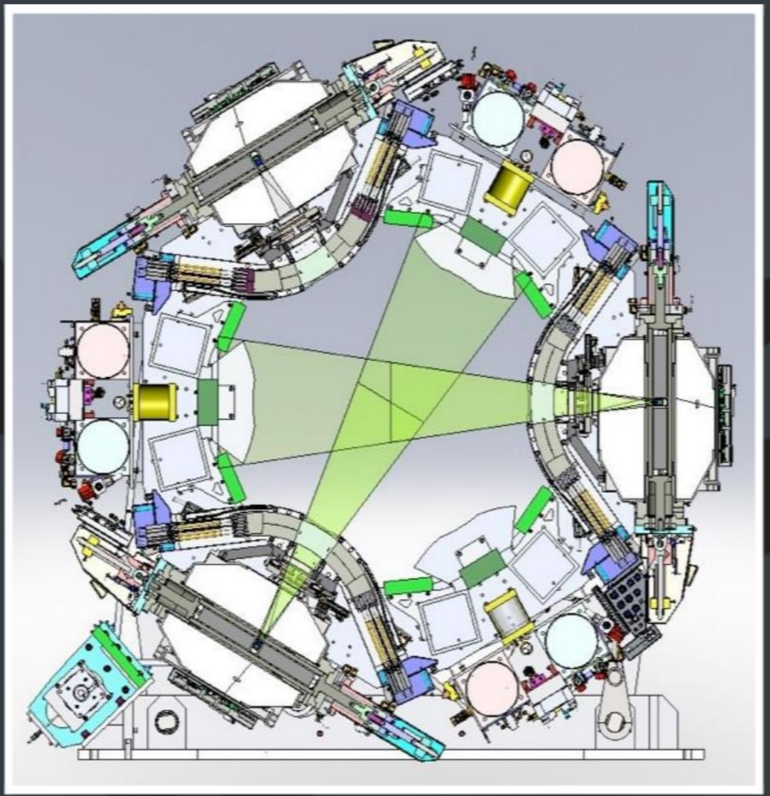


Jeswani S, Mackie TR, Aoyama H. Overview of the HI-ART TM Helical Tomotherapy System.

Hybrid Technologies-Imaging and Therapy

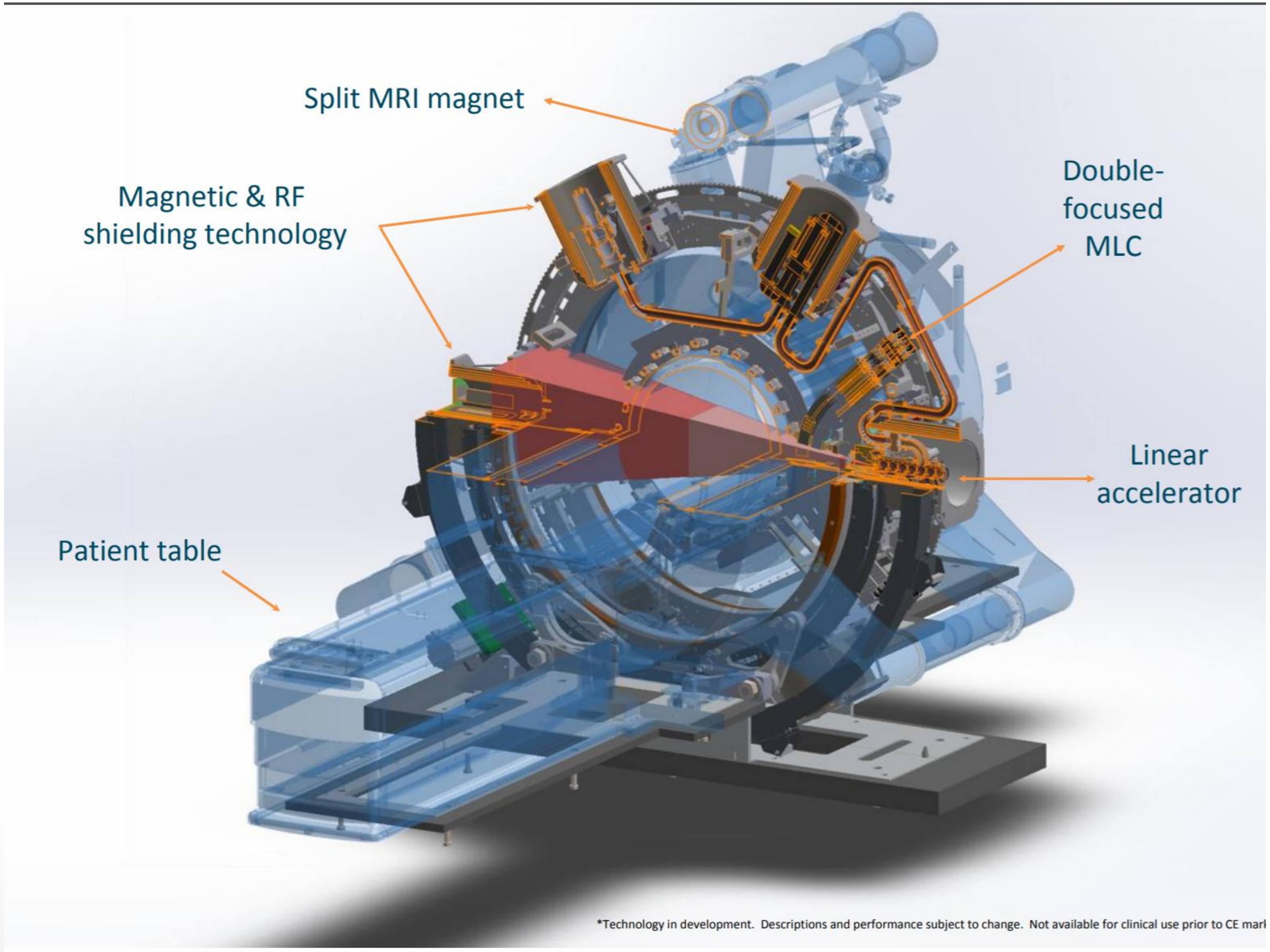
Cobalt/MR

- Rotating Gantry Assembly
- 3 Independent Co60 Headed Design
  - Asynchronous Delivery
  - Mounted with 120 degree separation
  - 15,000 Ci per source
  - +-240 degree Rotation for 2 or 3 Head Operation for Maximum Reliability.
- 3 Doubly Focused MLC Systems
  - 180 MLC Leaves. 60 per Head
  - Best-in-class MLC for Reduced Penumbra & Interleaf Leakage



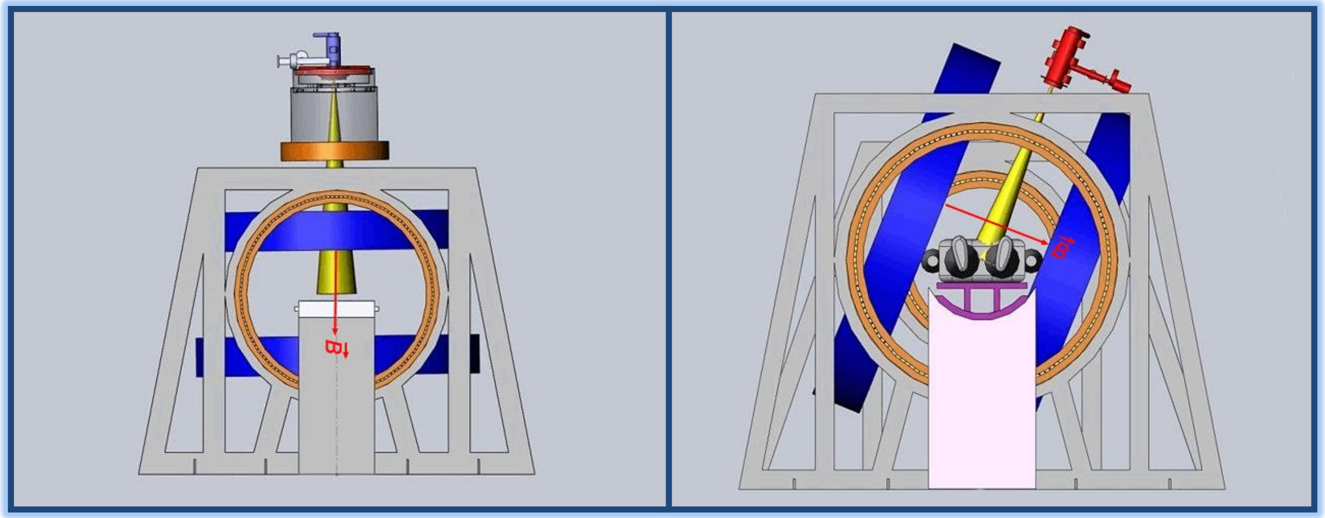
Hybrid Technologies-Imaging and Therapy

- →Linac/MR

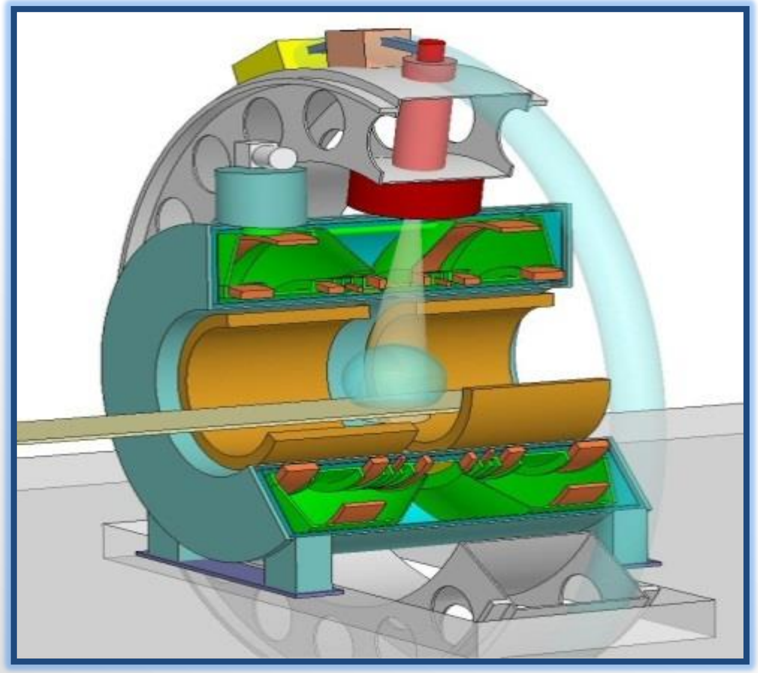


Hybrid Technologies-Imaging and Therapy

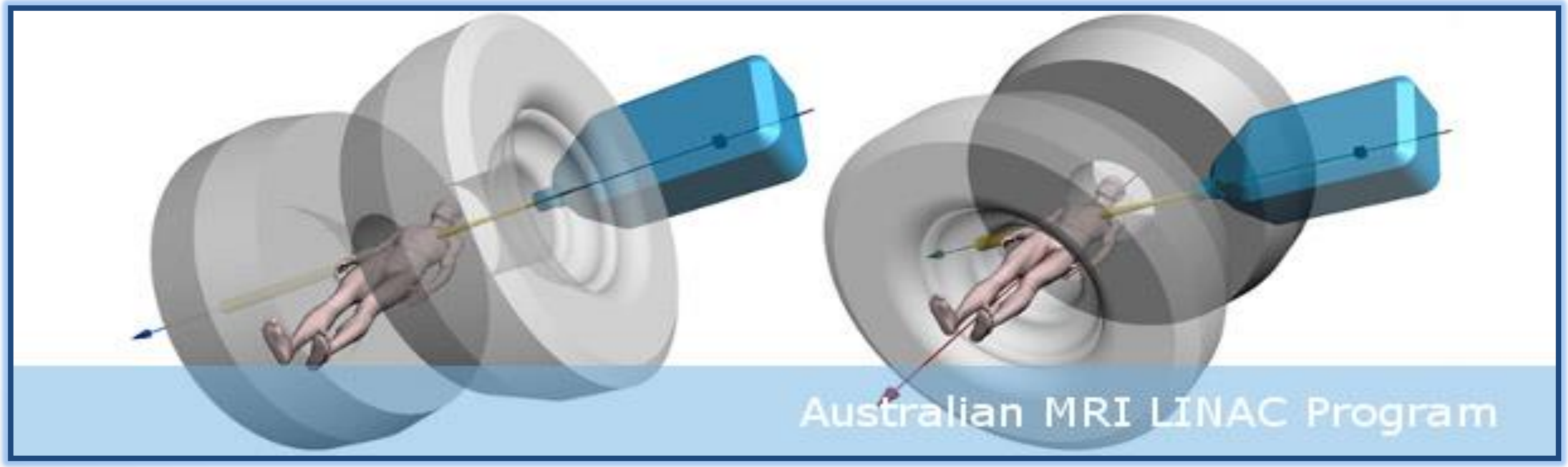
- Linac/MR



Alberta, Canada (G. Fallone)



UMC Utrecht ELEKTA/Philips



Figures from: Uwe Oelfke, Paul Keall

Hybrid Technologies- Anatomy and Function

- PET/CT
- PET/MR

- Other advances

Autocontouring

Adaptive Radiation Therapy (ART)

Computing advances

Computer hardware (Moore's "law"):

Size ↓, Density ↑ (Doubling time < 2y)

Processor Speed ↑

Software:

Parallel processing

Optimization

Processing capability ↑↑↑

- Real-time adaptive RT
  - 4-D
  - Real-time replanning
  - Dose accumulation


RADIATION THERAPY NEWS

ME ABOUT RT RT CLINICAL TRIALS CONTACT US

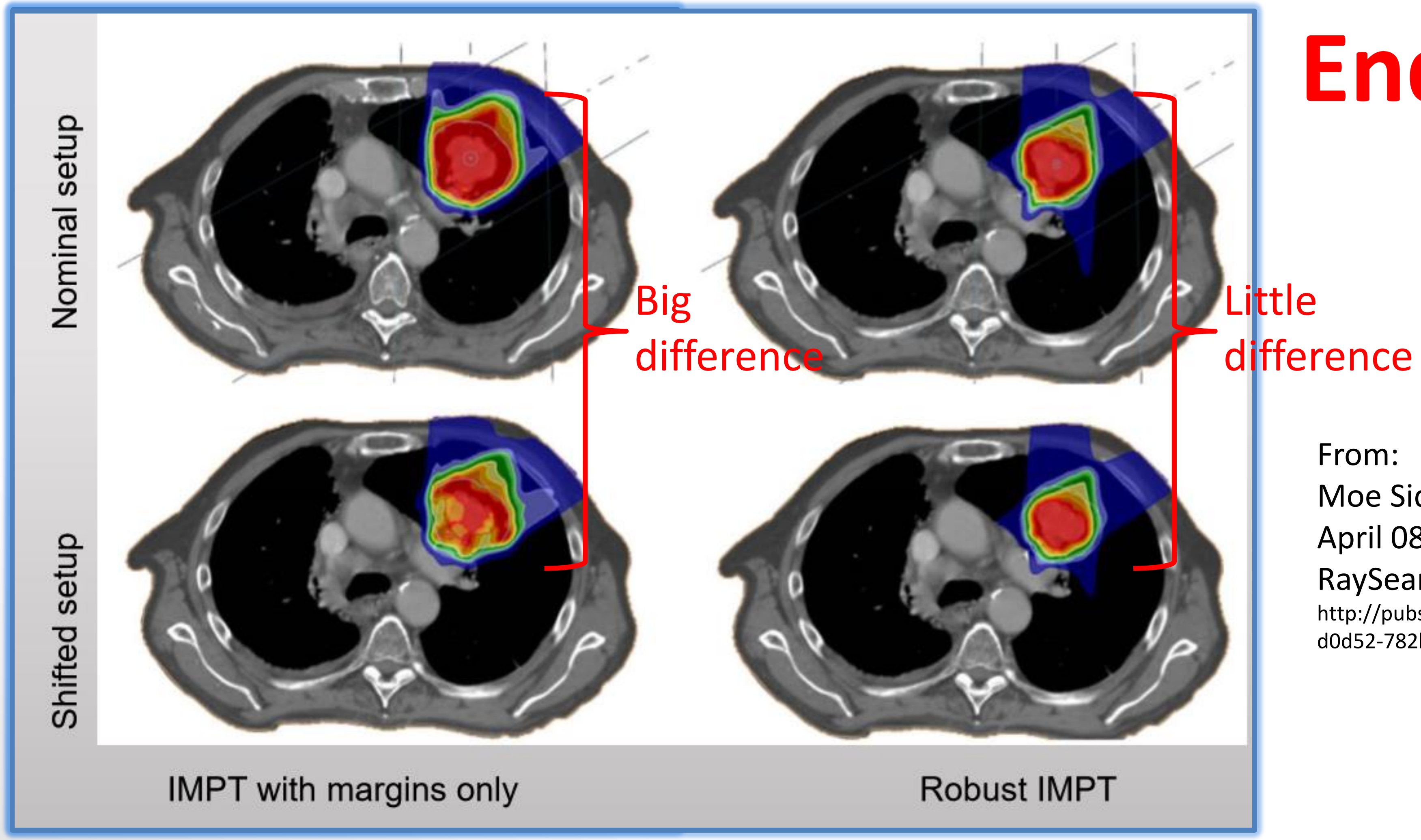
Real-Time Adaptive Radiation Possible With MRIdian System

SEPTEMBER 11, 2014 BY ANNA TAN, RN IN NEWS.

Advanced algorithms

- Monte Carlo planning calculations, but much faster!
- Boltzmann transport
- Radiobiological models
- Accounting for Uncertainties (Robust Optimization)

Example of Robust Optimization



End of PTV?

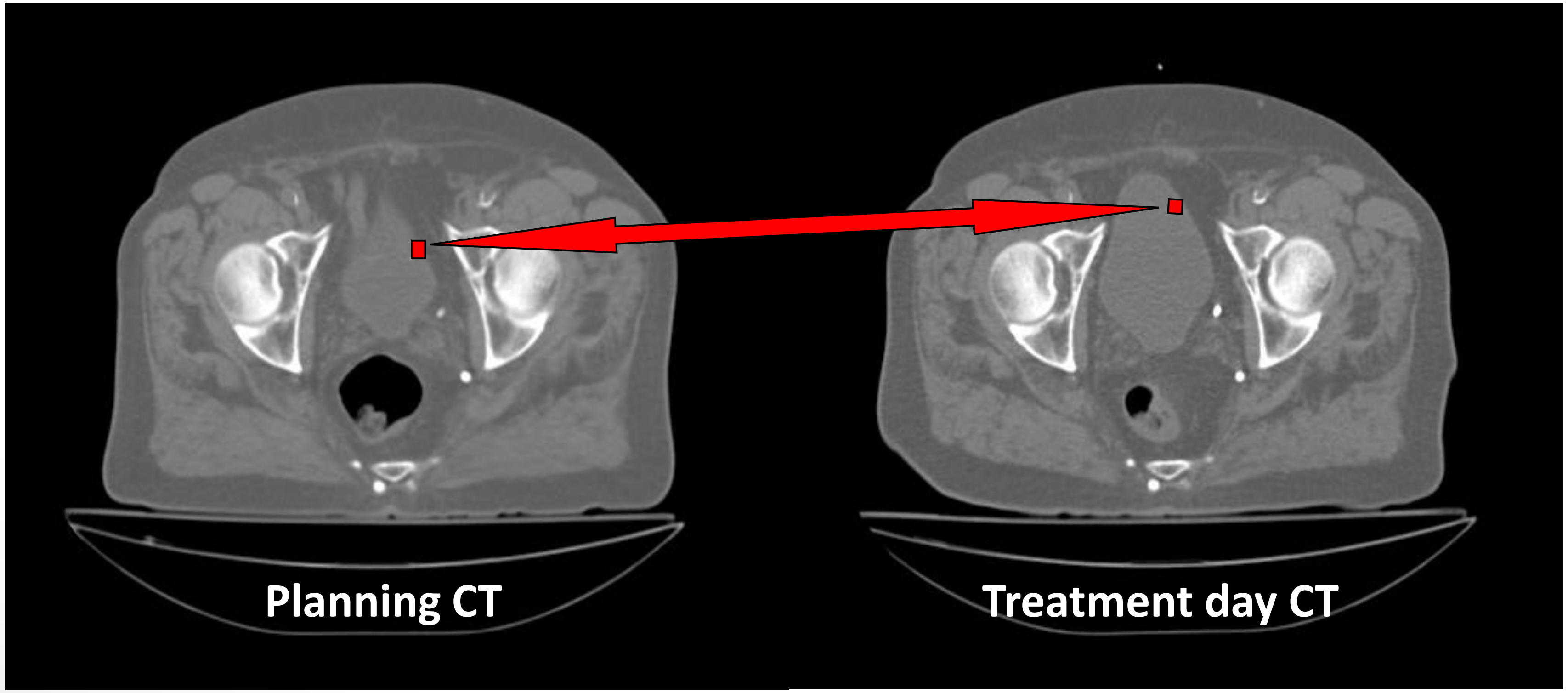
From:
Moe Siddiqui
April 08, 2017
RaySearch Labs
http://pubs.medicaldosimetry.org/pub/e5ad0d52-782b-cb6e-2763-e6a918540f5c

Adaptive technologies

- Image warping
- Daily-re-optimization
- Daily dose accumulation
- Real-time tracking of tumor markers
- Real-time tracking and correction of MLC apertures

More Adaptation … example

- Tissue voxels move/change from day to day



Schaly et al, PMB 49: 791-805, 2004

Deformable Image Registration

Thin-Plate Spline Image Warping

Source

Target

Courtesy: Jeff Kempe

Deformable Image Registration

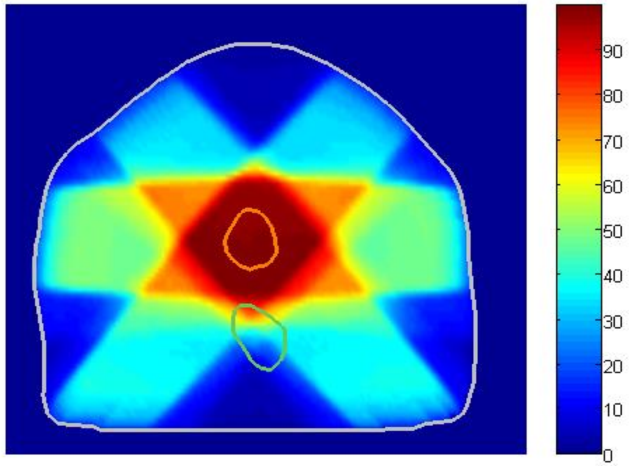
Thin-Plate Spline Image Warping

Result

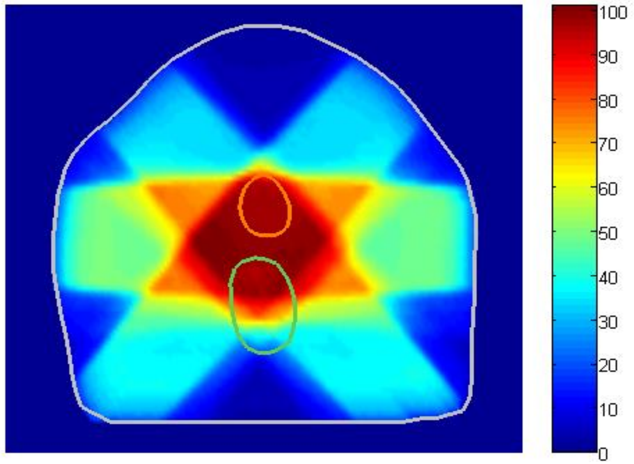
Target

Courtesy: Jeff Kempe

Warping Example: 6-Field Prostate

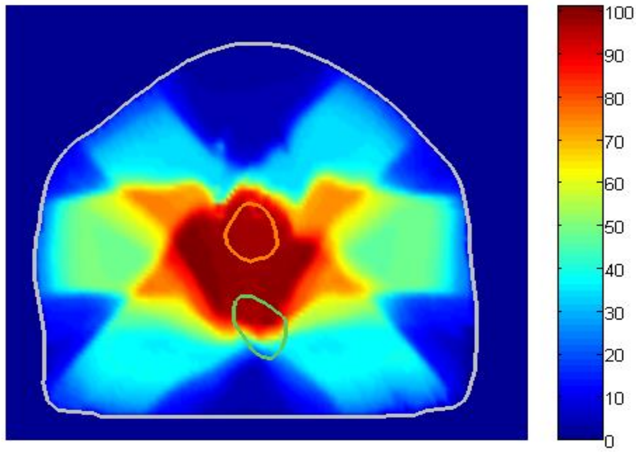


Planned

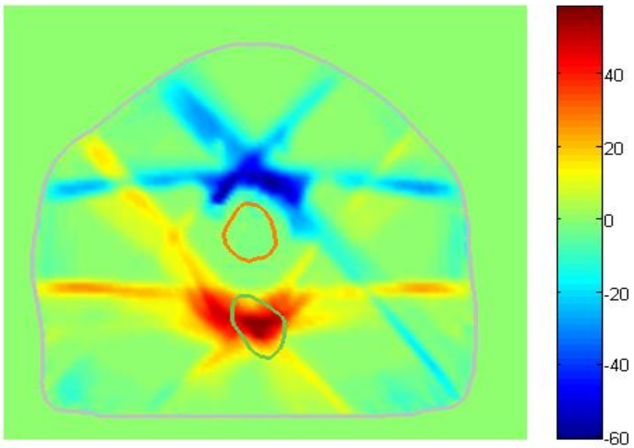


Treatment fraction 1

Note rectal distention … pushes prostate up



Warped fraction 1



Difference: warped – planned

Schaly et al, PMB 49: 791-805, 2004

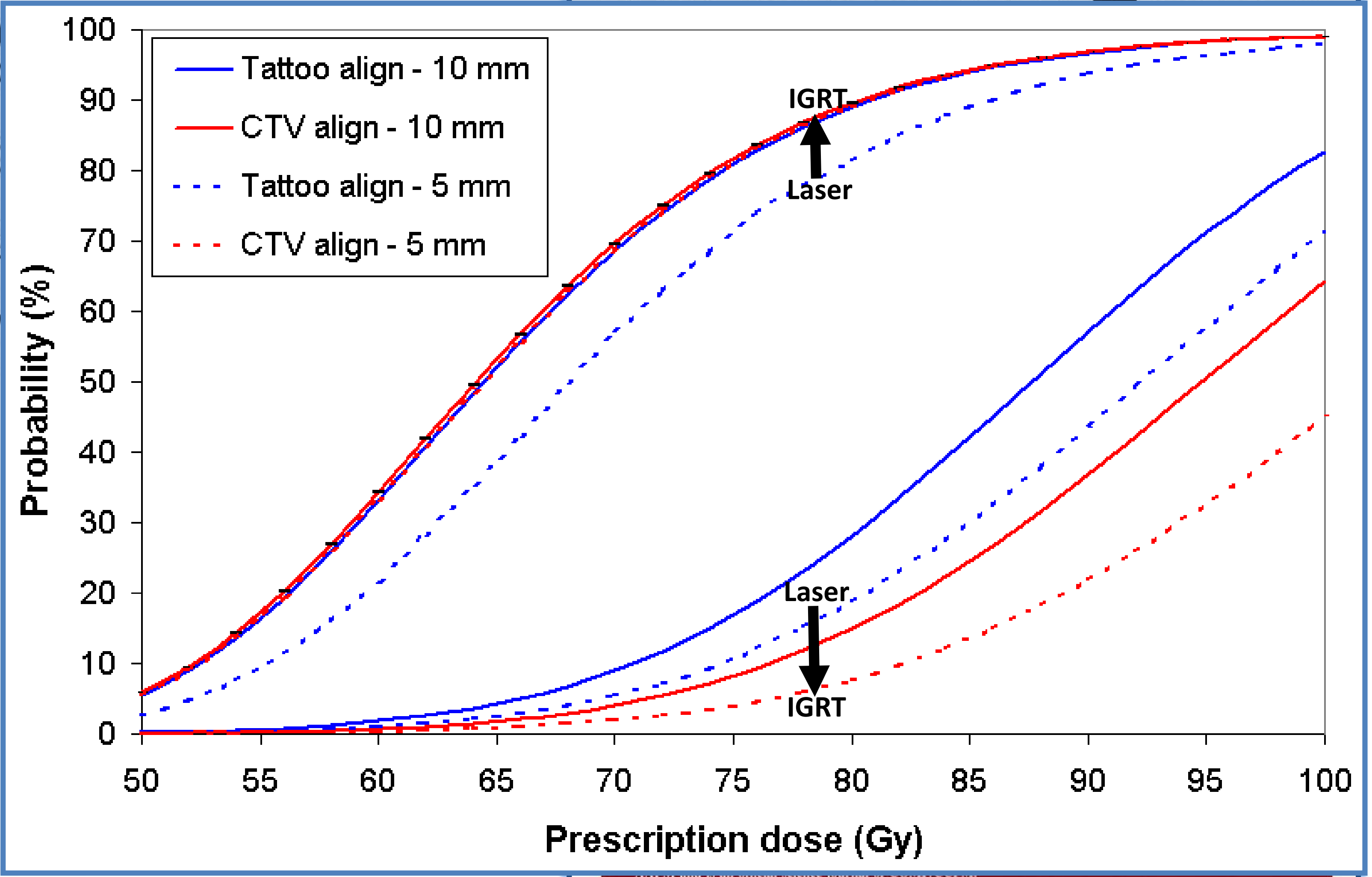
Will image guidance & dose warping improve treatment outcome?

Image-guided adaptive radiation therapy (IGART) dose escalation considerations for localized car

William Song[a] and Bryan Schaly
Department of Medical Biophysics, University of Western Ontario, and Radiati
London Regional Cancer Program, London Health Sciences Centre, London, O

Glenn Bauman
Department of Oncology, University of Western Ontario, and Radiation Treatm
London Regional Cancer Program, London Health Sciences Centre, London, O

Jerry Battista and Jake Van Dyk
Departments of Medical Biophysics and Oncology, University of Western Ontar
and Radiation Treatment Program, London Regional Cancer Program,
London Health Sciences Centre, London, Ontario, Canada



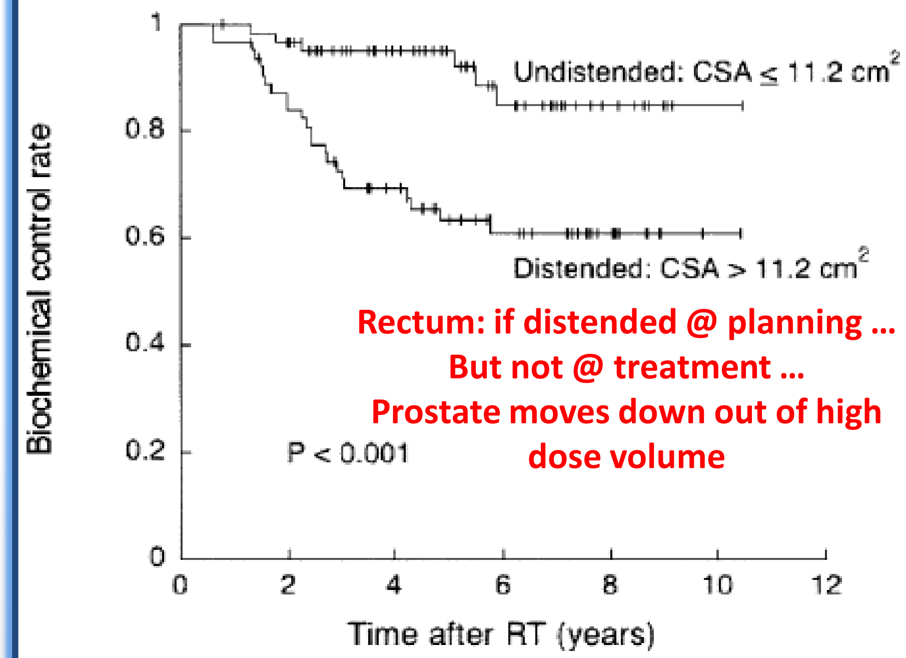
Best dose escalation strategy: Combine margin reduction (low NTCP) with daily IGRT technique (high TCP) to localize the daily moving/deforming target volume.

Song et al: Med Phys 32: 2193-203, 2005

IGRT Impact on Clinical Outcomes

NO IGRT

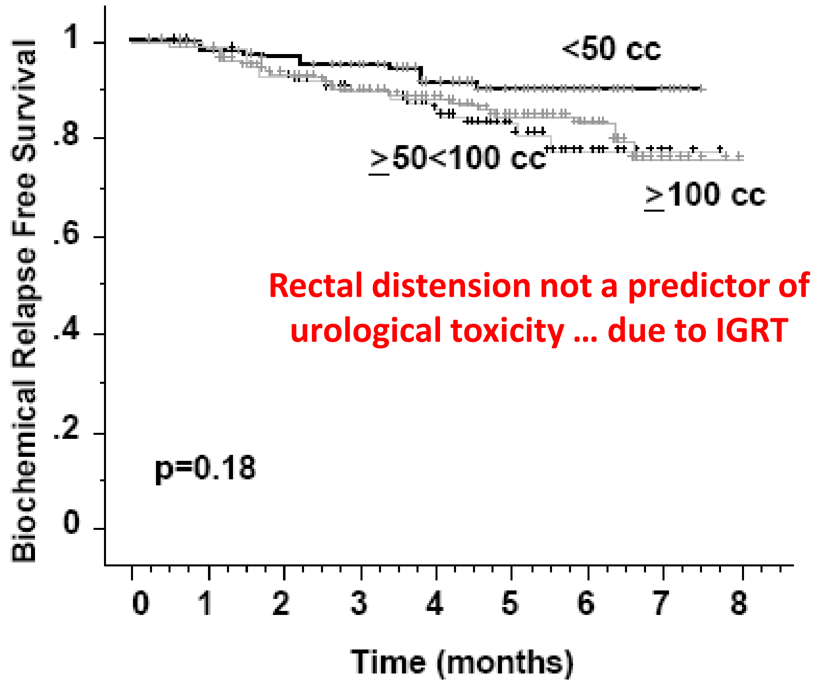
MORE ERROR



de Crevoisier, IJROBP, 62, 965, 2005

IGRT

LESS ERROR



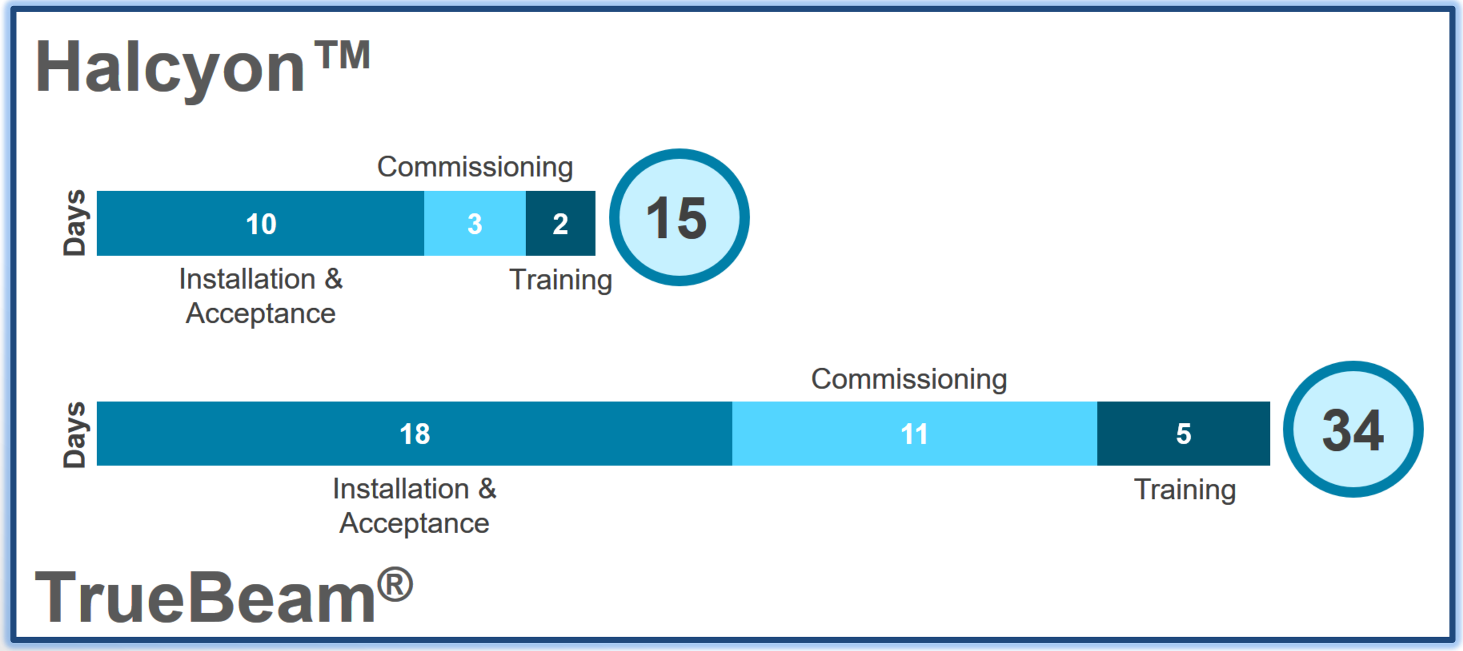
Kupelian, IJROBP (70), 1146, 2008

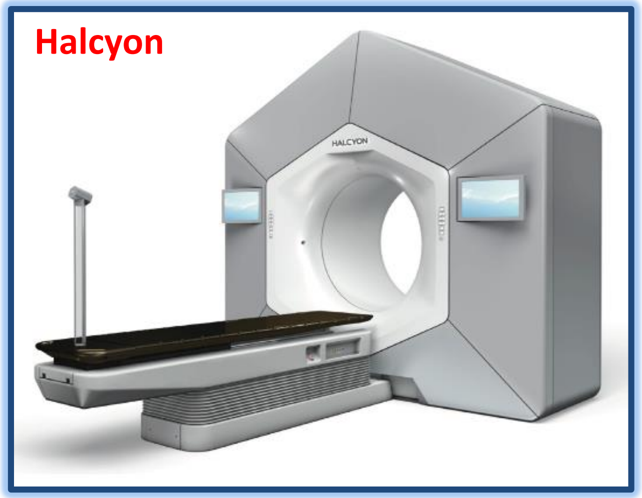
From Dr Jacob (Jake) Van Dyk

Technology advantages

- More efficient
  - VMAT, TomoTherapy, Halcyon

Example: Installation, commissioning, training



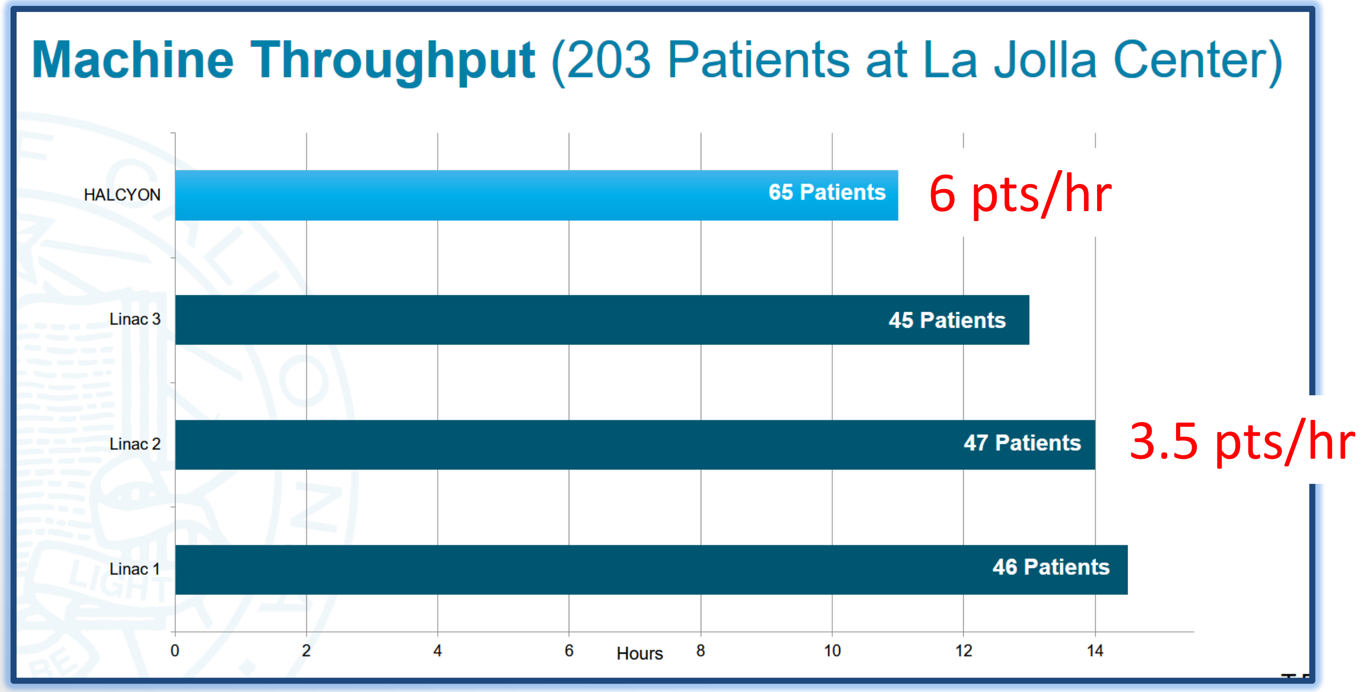


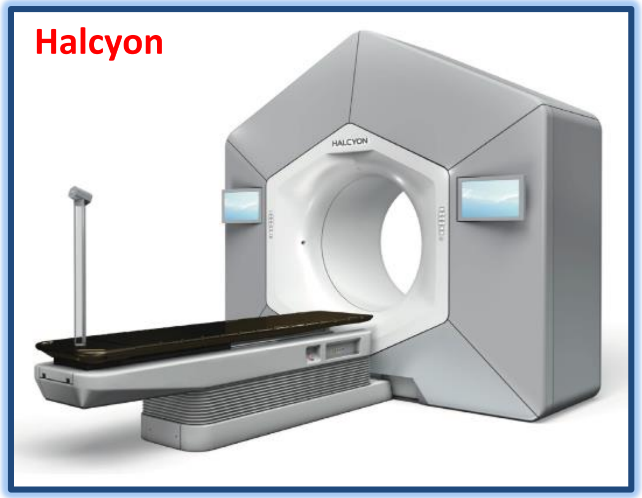
Courtesy
T.F. Atwood, UCSF
Sept 2018

Technology advantages

- More efficient
  - IMAT, TomoTherapy, Halcyon

Example: Patient throughput





Courtesy
T.F. Atwood, UCSF
Sept 2018

Trends Over the Next 10 Years

- More particles
  - Protons, carbon ions, …
  - Proton therapy
    - 92 operational (Feb 2019)
    - 45 under construction (Jan 2019)
      - Source Physics World, 25 Feb 2019
  - Carbon ion therapy
    - ~11 carbon ion facilities (2017)
      - 6 in Japan

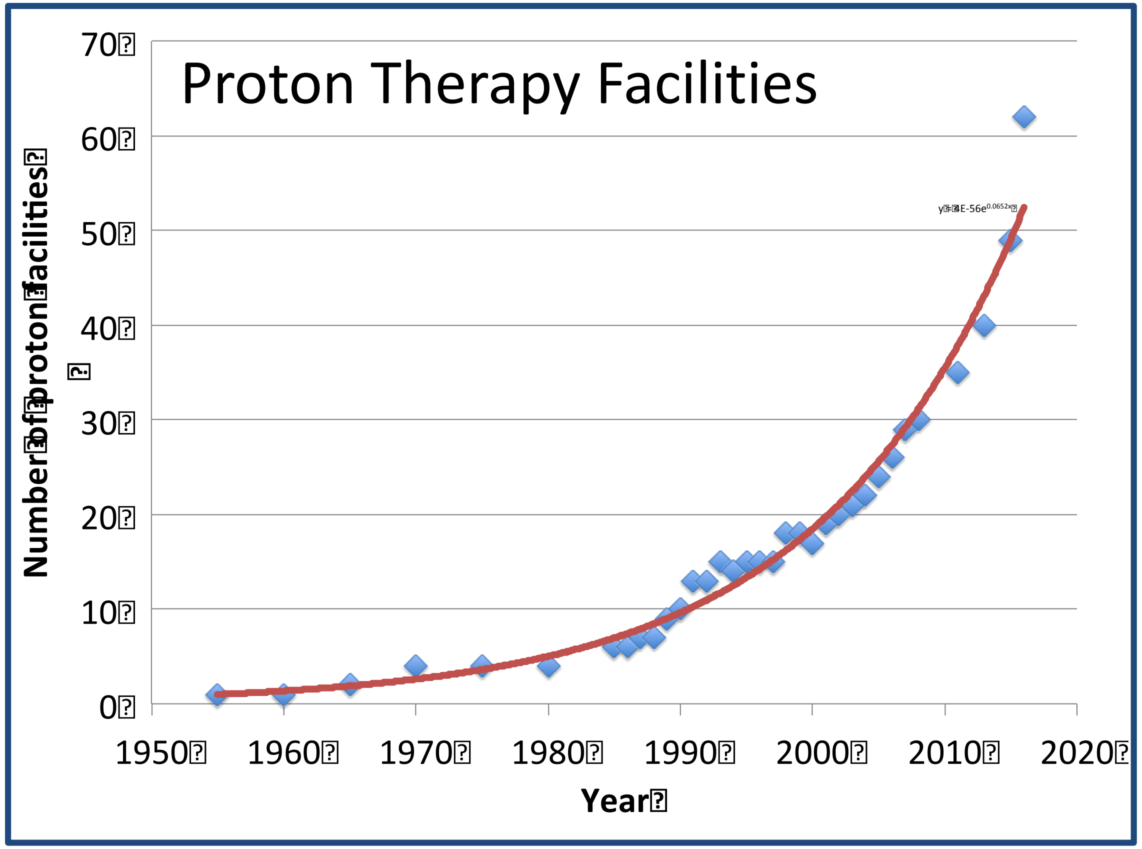
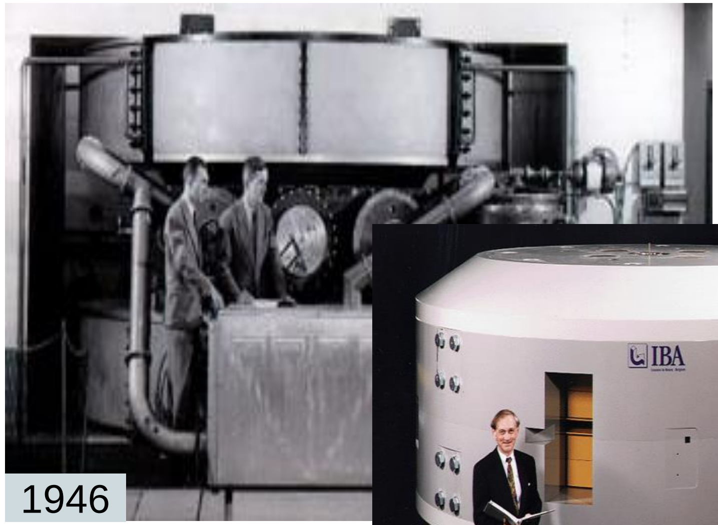


Figure courtesy Thomas Bortfeld … source: PTCOG

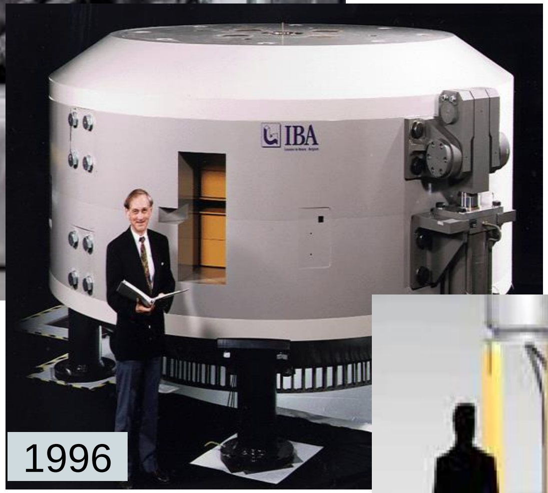
“Conservative Estimate”

- 10% of the patients who require radiation would benefit from proton therapy
  - From Thomas Bortfeld, MGH (2018)
- “… 10-20% of patients receiving radiotherapy might benefit from charged particle beams.”
  - From Jones & Burnet, BMJ 330: 979-980; 2005

More Compact … Shrinking Proton Accelerators



Harvard
(700 tons)



IBA/Sumitomo
(220 tons)

Varian/Accel
(90 tons)

Mevion Medical
Systems (<20 tons)

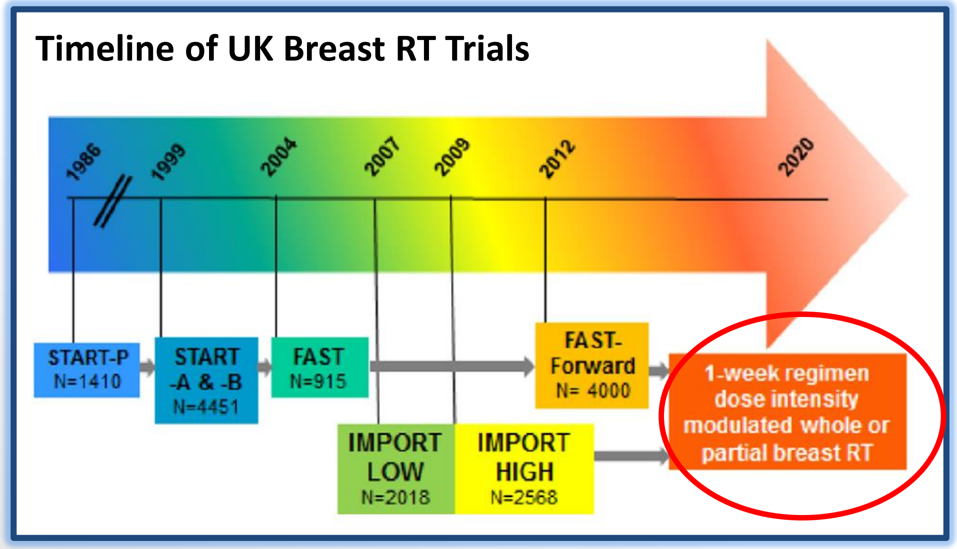
US FDA Cleared Proton Therapy Systems

Courtesy: Mevion

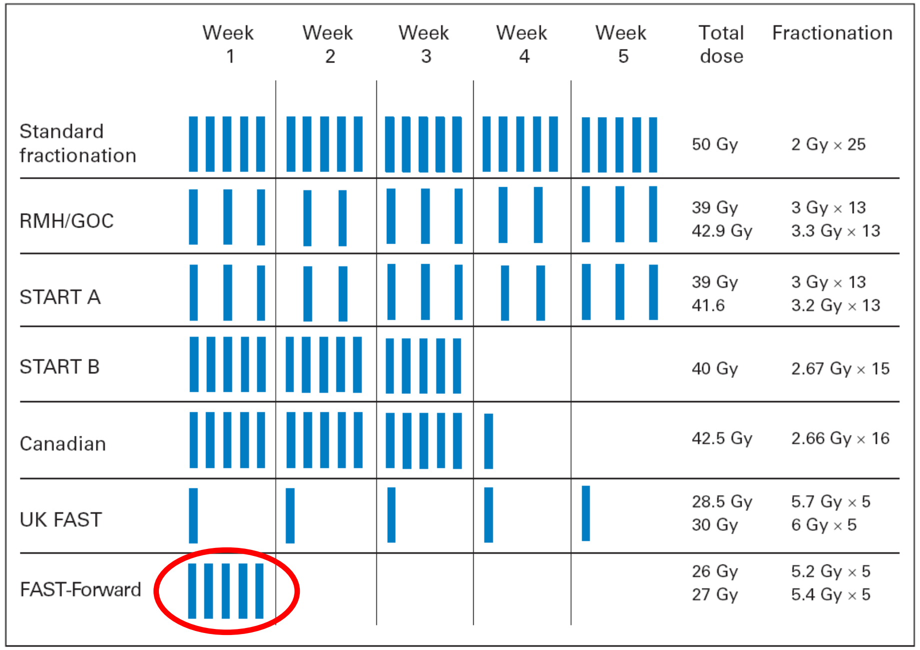
Slide courtesy Thomas Bortfeld

Trends Over the Next 10 Years

- More hypofractionation (higher doses/fraction, SBRT)
- Breast cancer



Yarnold BJR 92: 20170849; 2019



Fisher JCO 32:2894-2901; 2014

From Dr Jacob (Jake) Van Dyk

Brachytherapy

LDR

Iodine-125 seeds

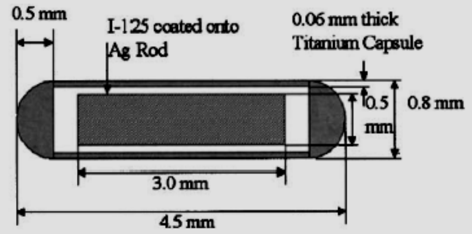


Figure 1b. Model 6711. [Reprinted from Heintz, B. H., R. E. Wallace, and J. M. Hevezi, "Comparison of I-125 sources used for permanent interstitial implants," *Med Phys* 28:671–682. © 2001, with permission from AAPM.]

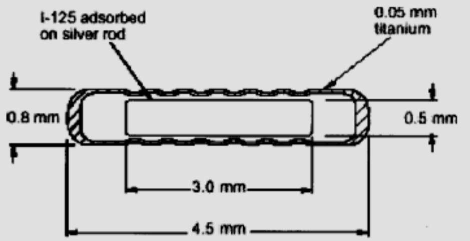


Figure 1c. Model 6733. [Reprinted from Meigooni, A. S., S. A. Dini, K. Sowards, J. L. Hayes, and A. Al-Otoom, "Experimental determination of the TG-43 dosimetric characteristics of EchoSeed™ model 6733 ^{125}I brachytherapy source," *Med Phys* 29:939–942. © 2002, with permission from AAPM.]

Palladium-103

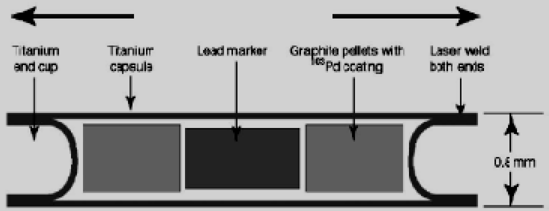
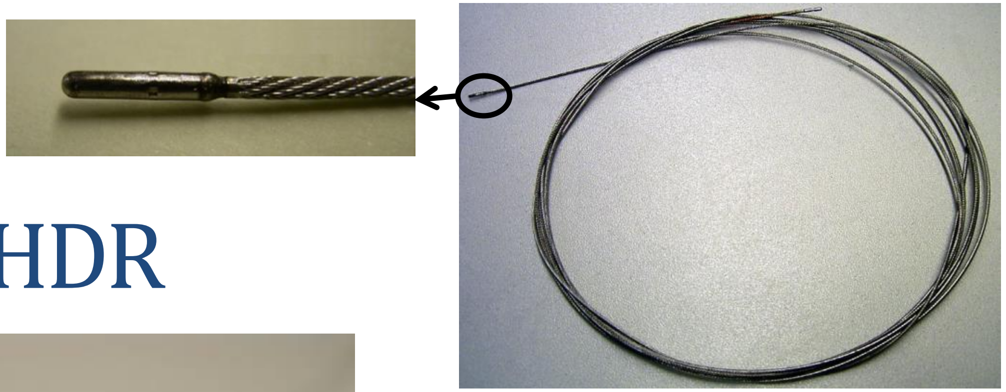
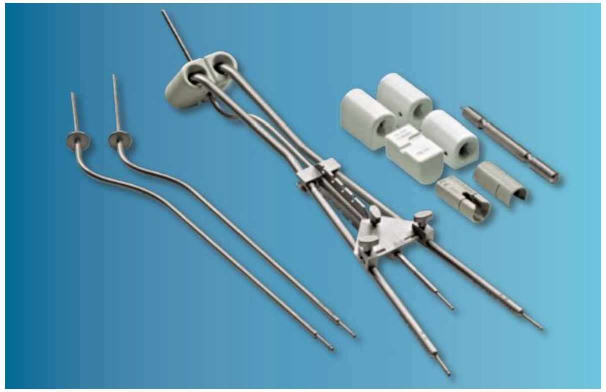
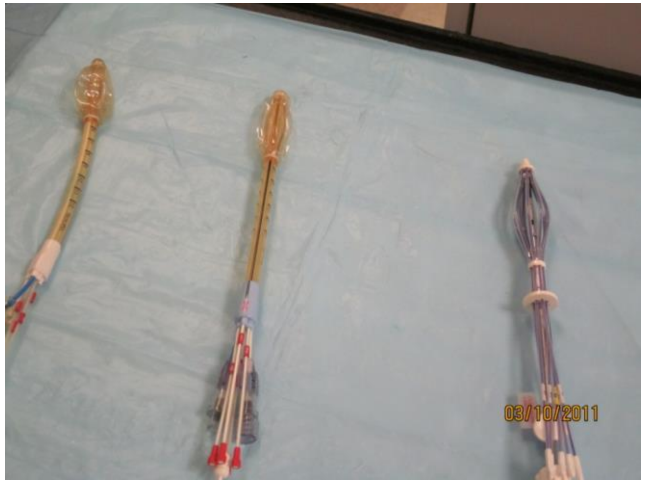


Figure 2. Model 200. [Reprinted from Rivard, M. J., B. M. Coursey, L. A. DeWerd, W. F. Hanson, M. S. Huq, G. S. Ibbott, M. G. Mitch, R. Nath, and J. F. Williamson, "Update of AAPM Task Group No. 43 Report: A revised AAPM protocol for brachytherapy dose calculations," *Med Phys* 31:633–674. © 2004, with permission from AAPM.]

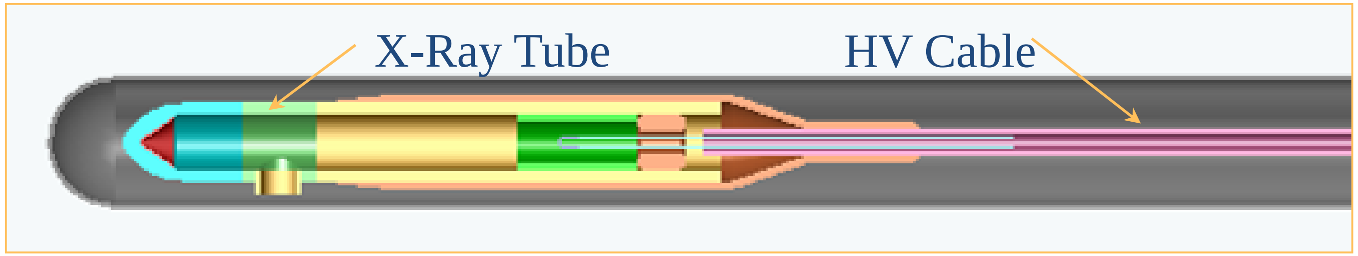
HDR

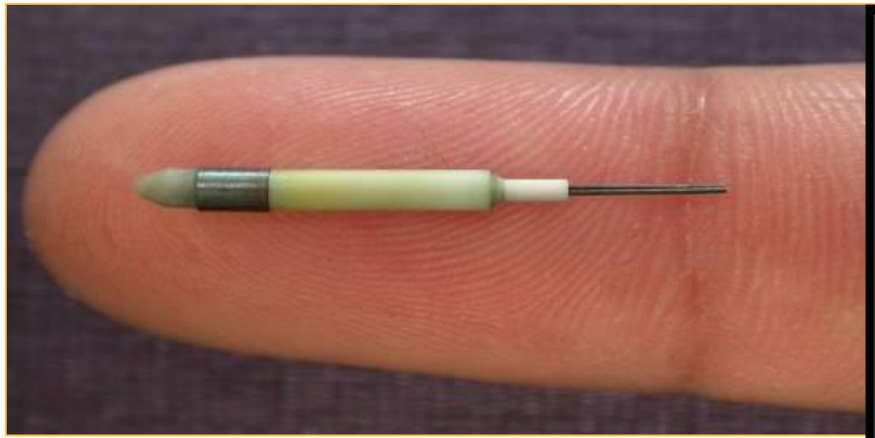


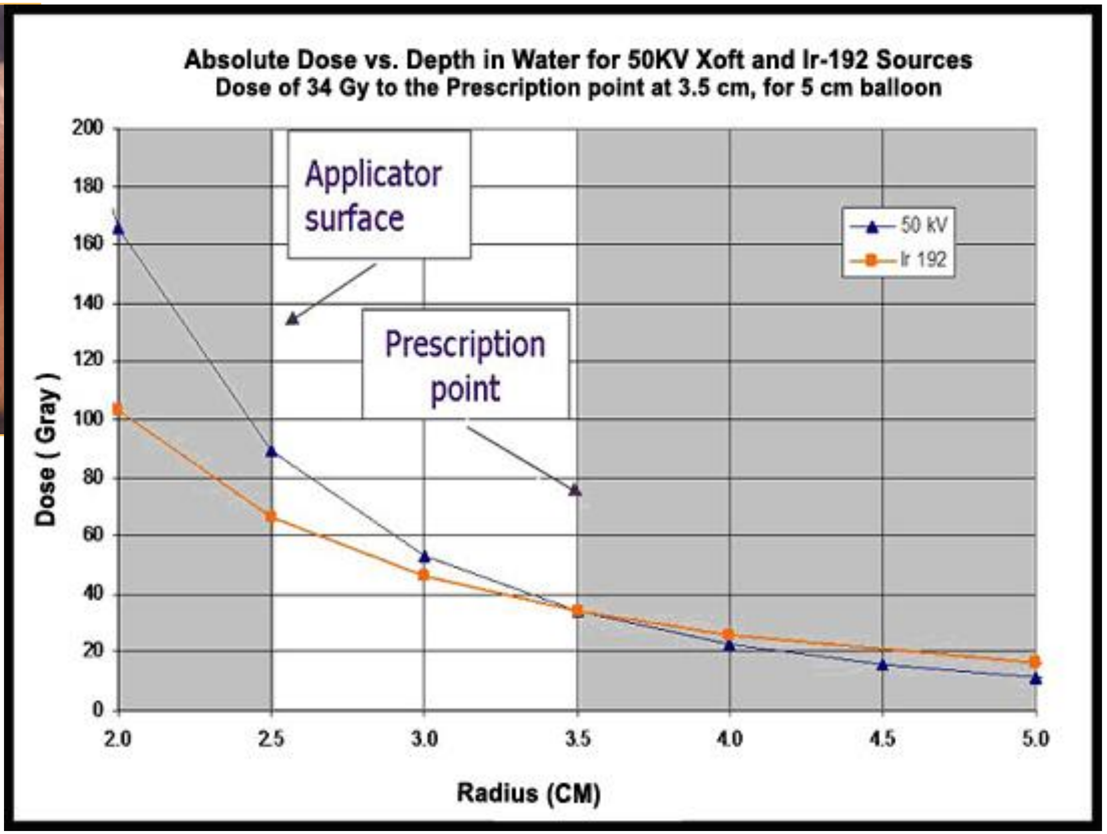




e-Brachytherapy







Professional Communication

- Radiation Oncologists and Radiation Therapists
- Radiologists
- Interventional Radiologists (Cardiology, ENT, Gynecologists)
- Surgeons (Breast, Gynecology, H&N, s
- Neurosurgeons
- Administration
- Engineers
- Computer Scientists

Thank you for listening!