Advances in Radiotherapy

Thomas Rockwell Mackie
Professor
Depts. Of Medical Physics, Human Oncology, and Engineering Physics
University of Wisconsin
Madison WI 53706

trmackie@wisc.edu

Financial Disclosure

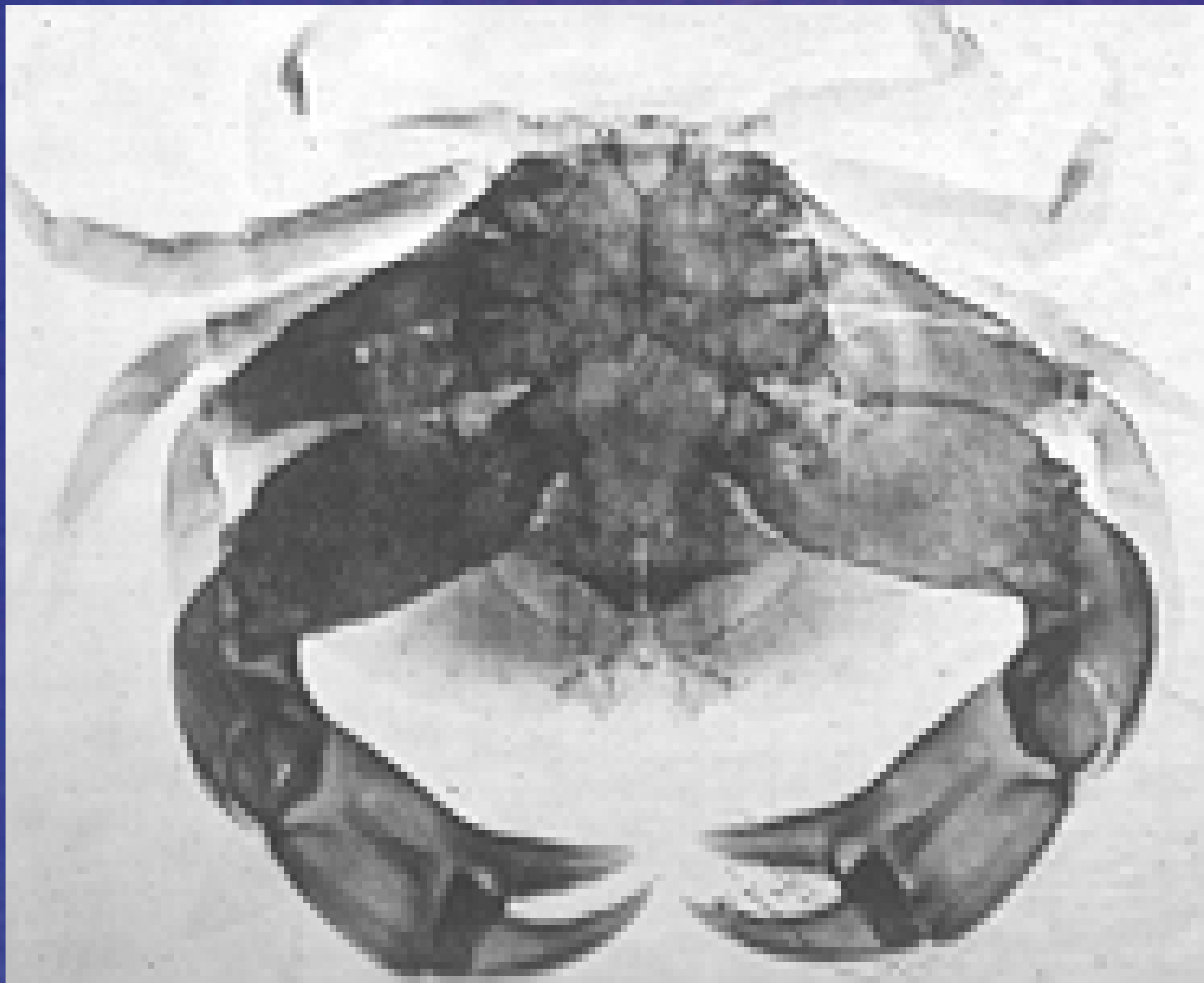
I am a founder and Chairman of TomoTherapy Inc. (Madison, WI) which is participating in the commercial development of helical tomotherapy.

TomoTherapy's 63,000 sqft. Madison WI Facility

Assembly Floor

www.tomotherapy.com

99% of Radiation Therapy Procedures are to Treat Cancer



Diagnostic Planar X-ray of a Crab

Somatic Mutations and Cancer

- Like wrinkles and other aging symptoms, cancer is usually the result of many somatic mutations.
- Reversing cancer is about as likely as reversing aging.
- There is more money spent on wrinkles than cancer, so it is likely that a cure for wrinkles will happen before a cure for cancer.

Sell betatron stop Sell Cobalt unit stop The cure for cancer will come from polyoma virus research stop

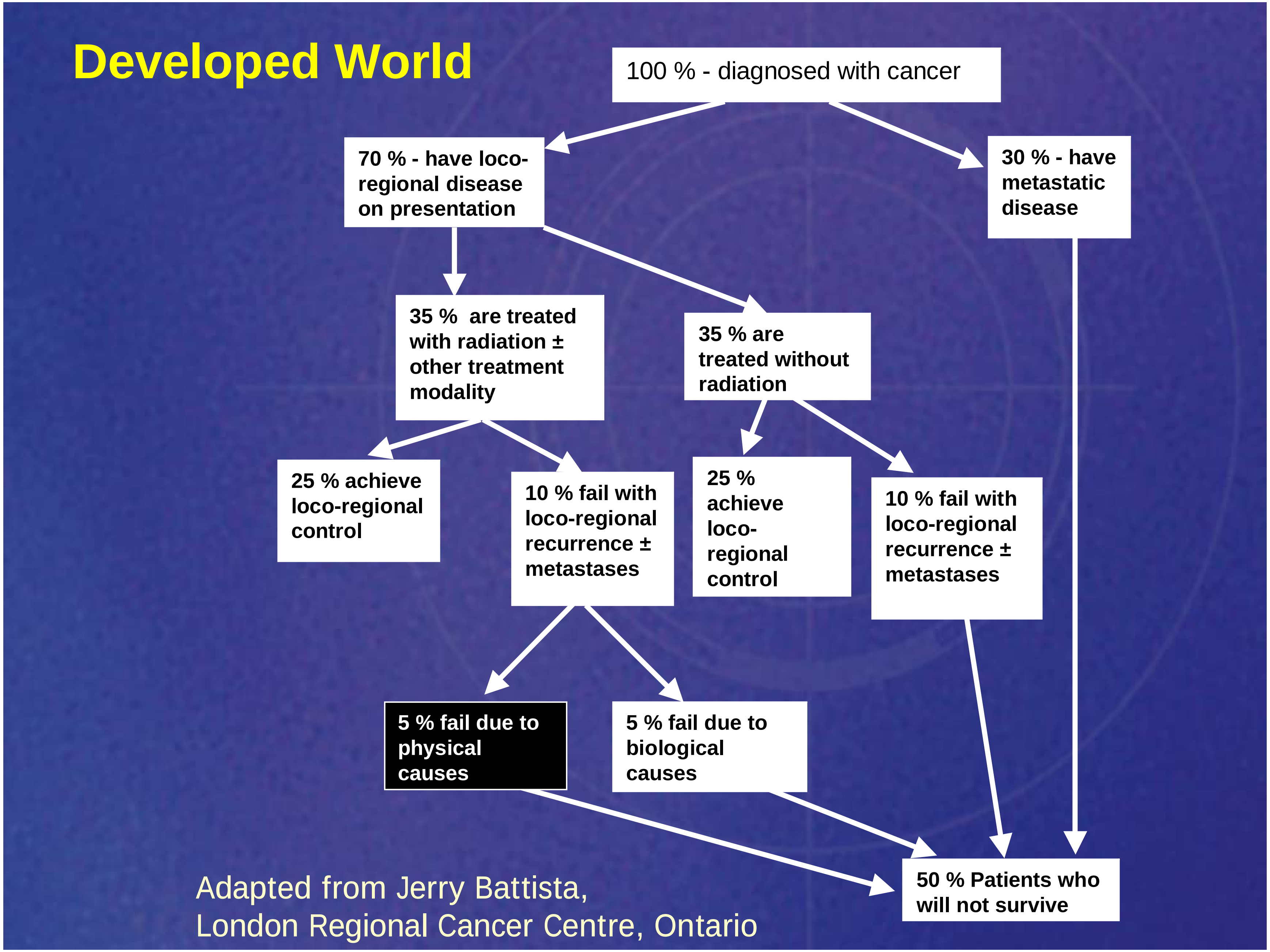
Telegraph from E.A McCulloch to H. Johns 1962

“It will take another 15 to 20 years for the new biology to revolutionize our concepts of cancer treatment”

E. Hall 1995

Imagine if Radiation Were A Drug

- It could target arbitrarily-defined anatomic sites.
- It would cause little damage to normal tissue away from the tumor.
- The site of its action could be verified precisely.
- Its side effects were well known.
- It could be non-invasively measured in small quantities.
- It would make other drugs more potent.
- Drug tolerance would not develop.
- Saving hundreds of thousands of people a year, it would surely be considered our most important anit-cancer drug.


Developed World
100 % - diagnosed with cancer
70 % - have loco-regional disease on presentation
30 % - have metastatic disease
35 % are treated with radiation ± other treatment modality
35 % are treated without radiation
25 % achieve loco-regional control
10 % fail with loco-regional recurrence ± metastases
25 % achieve loco-regional control
10 % fail with loco-regional recurrence ± metastases
5 % fail due to physical causes
5 % fail due to biological causes
50 % Patients who will not survive
Adapted from Jerry Battista,
London Regional Cancer Centre, Ontario

Societal Costs

- The direct costs of cancer in the US is about $80B annually.
- Radiotherapy costs about $10B.
- Radiotherapy equipment is about $2B.
- In addition there is over $150B in indirect costs due to disability and premature death.

Radiotherapy Costs in Perspective

PROCEDURE	COST ($/yr of life saved)
Bone Marrow Transplant	10,000 to 125,000
Treatment of Heart Disease	10,000 to 100,000
Kidney Dialysis	20,000 to 50,000
Societal Acceptance	25,000 – 100,000
Chemotherapy	4,500 to 50,000
Radiation Therapy	350* to 1,800**

ASCO 1992

*Ontario Ministry of Health, Canada

**Perez IMRT, assuming 10 years gained

Adapted from Jerry Battista,
London Regional Cancer Centre, Ontario

Radiotherapy Costs in Perspective

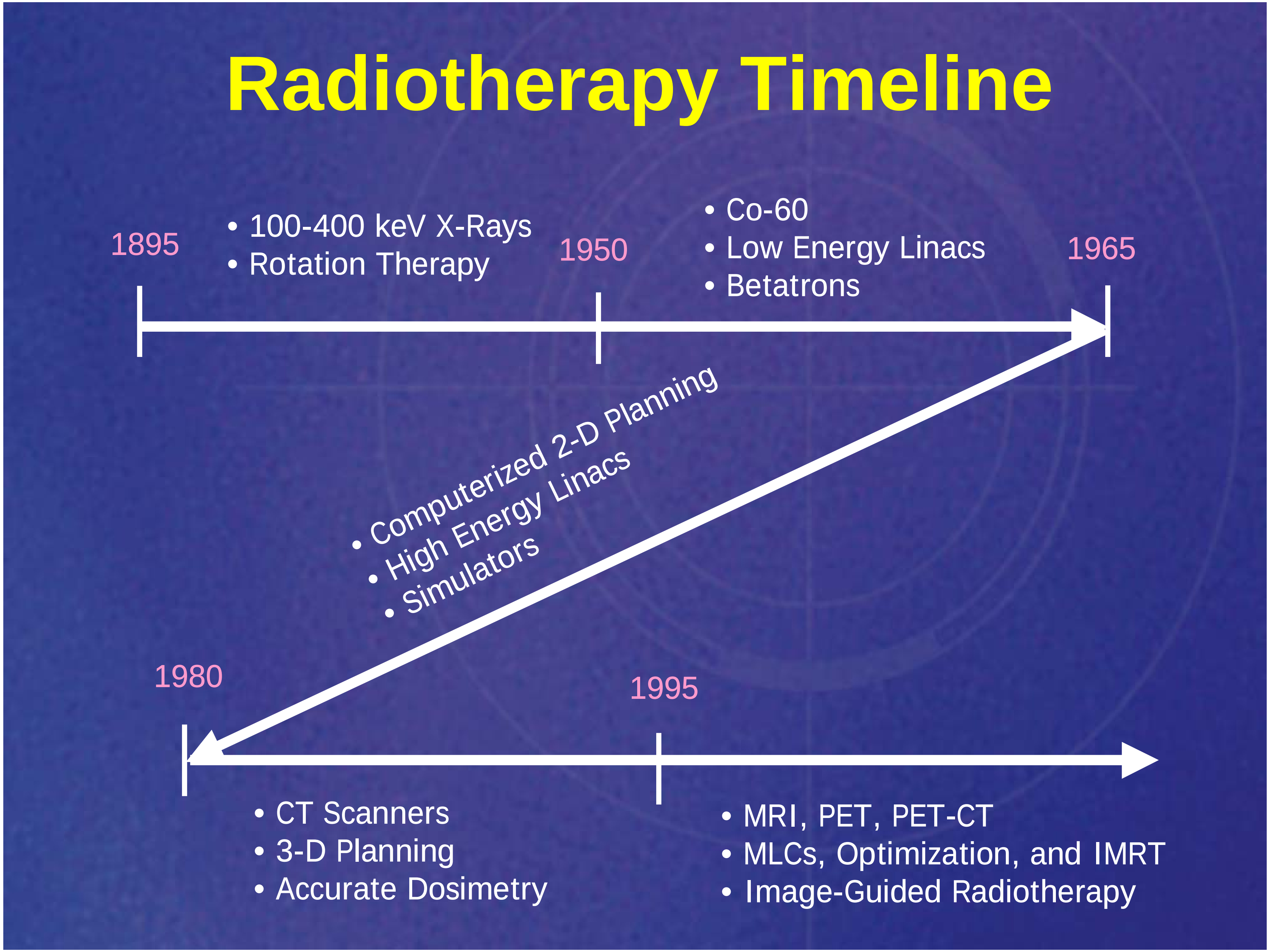
PROCEDURE	COST ($/yr of life saved)
Bone Marrow Transplant	10,000 to 125,000
Treatment of Heart Disease	10,000 to 100,000
Kidney Dialysis	20,000 to 50,000
Societal Acceptance	25,000 – 100,000
Chemotherapy	4,500 to 50,000
Radiation Therapy	500 to 3,000

ASCO 1992

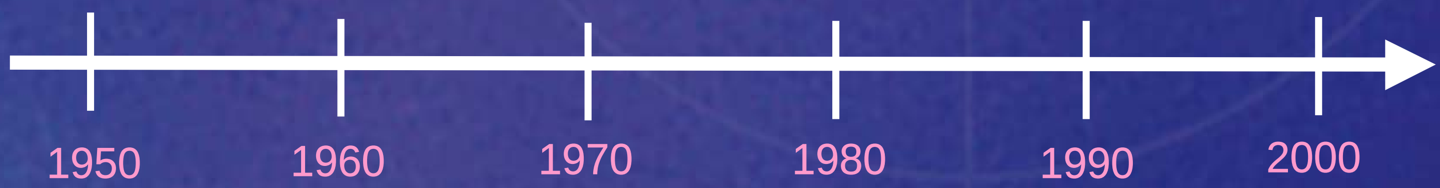
*Ontario Ministry of Health, Canada

**Perez IMRT, assuming 10 years gained

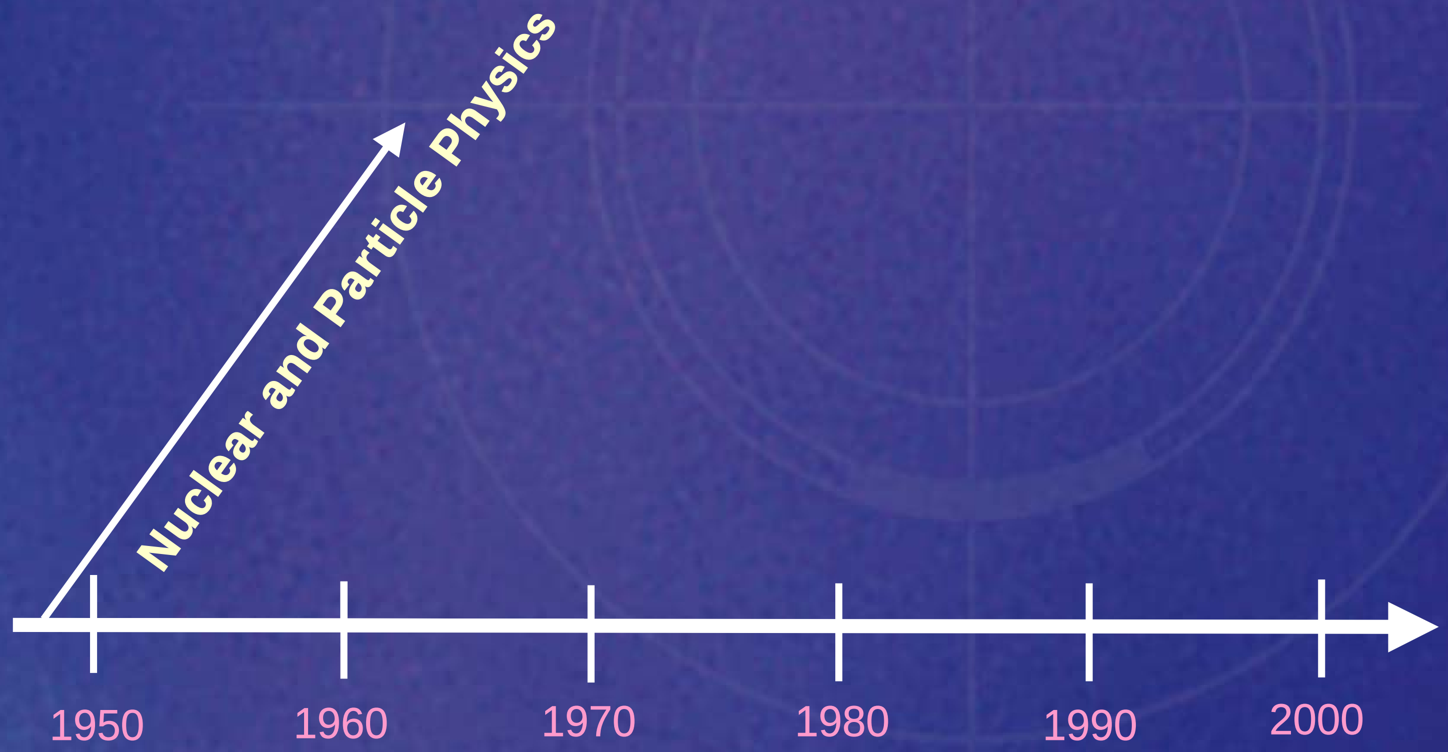
Adapted from Jerry Battista,
London Regional Cancer Centre, Ontario


Radiotherapy Timeline
1895
• 100-400 keV X-Rays
• Rotation Therapy
1950
• Co-60
• Low Energy Linacs
• Betatrons
1965
• Computerized 2-D Planning
• High Energy Linacs
• Simulators
1980
• CT Scanners
• 3-D Planning
• Accurate Dosimetry
1995
• MRI, PET, PET-CT
• MLCs, Optimization, and IMRT
• Image-Guided Radiotherapy

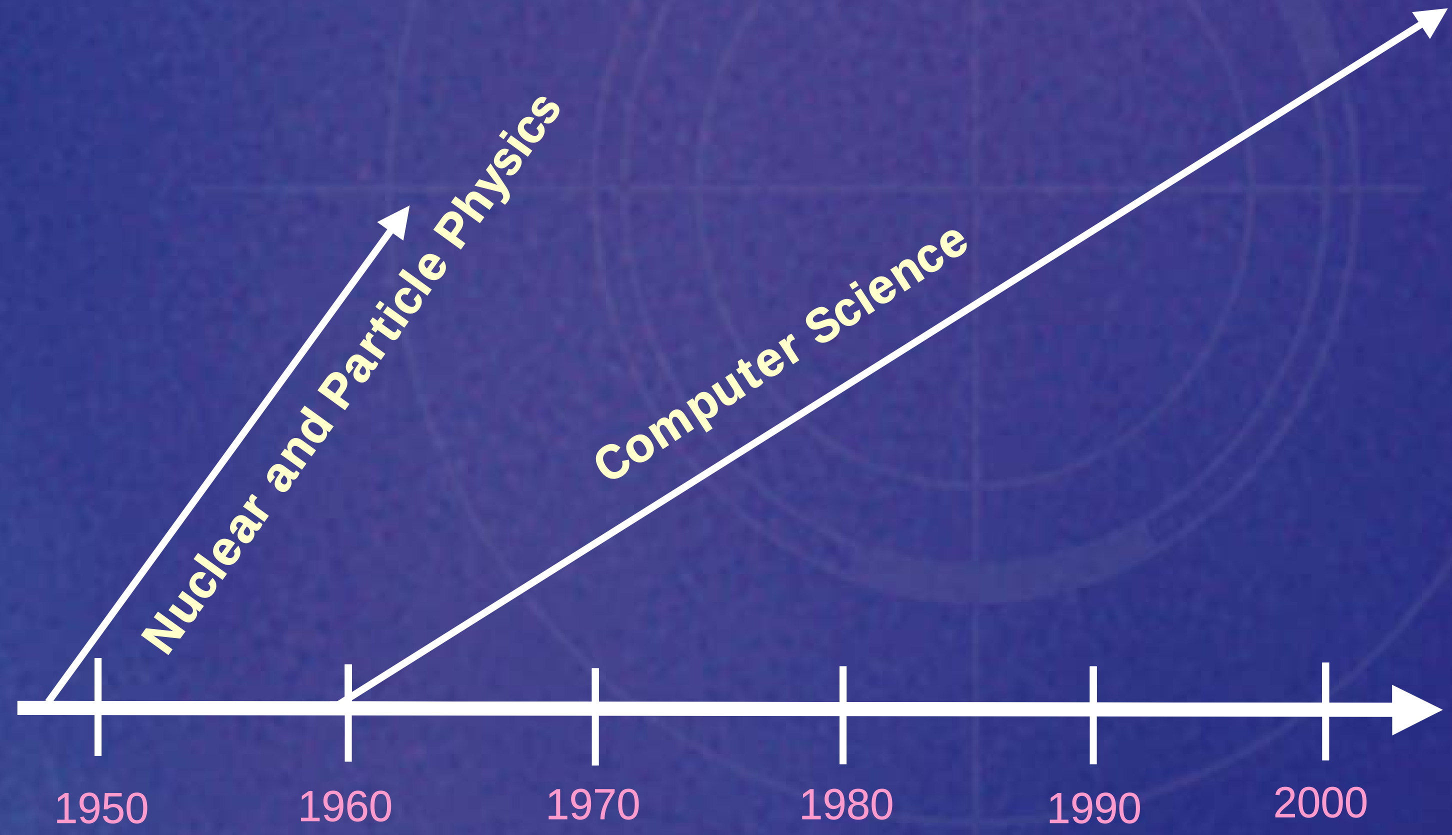
Scientific Forces Behind Our Field



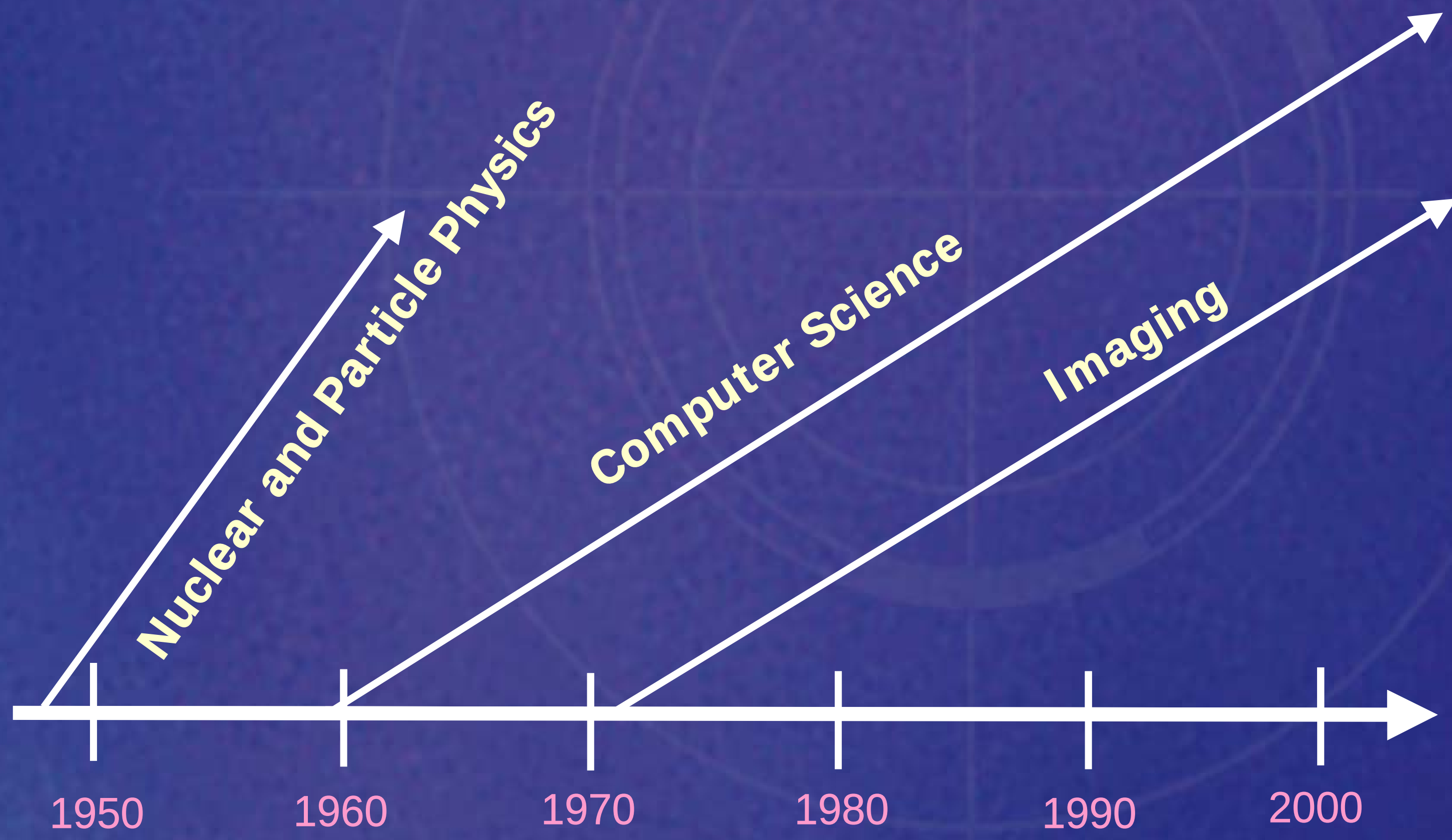
Scientific Forces Behind Our Field



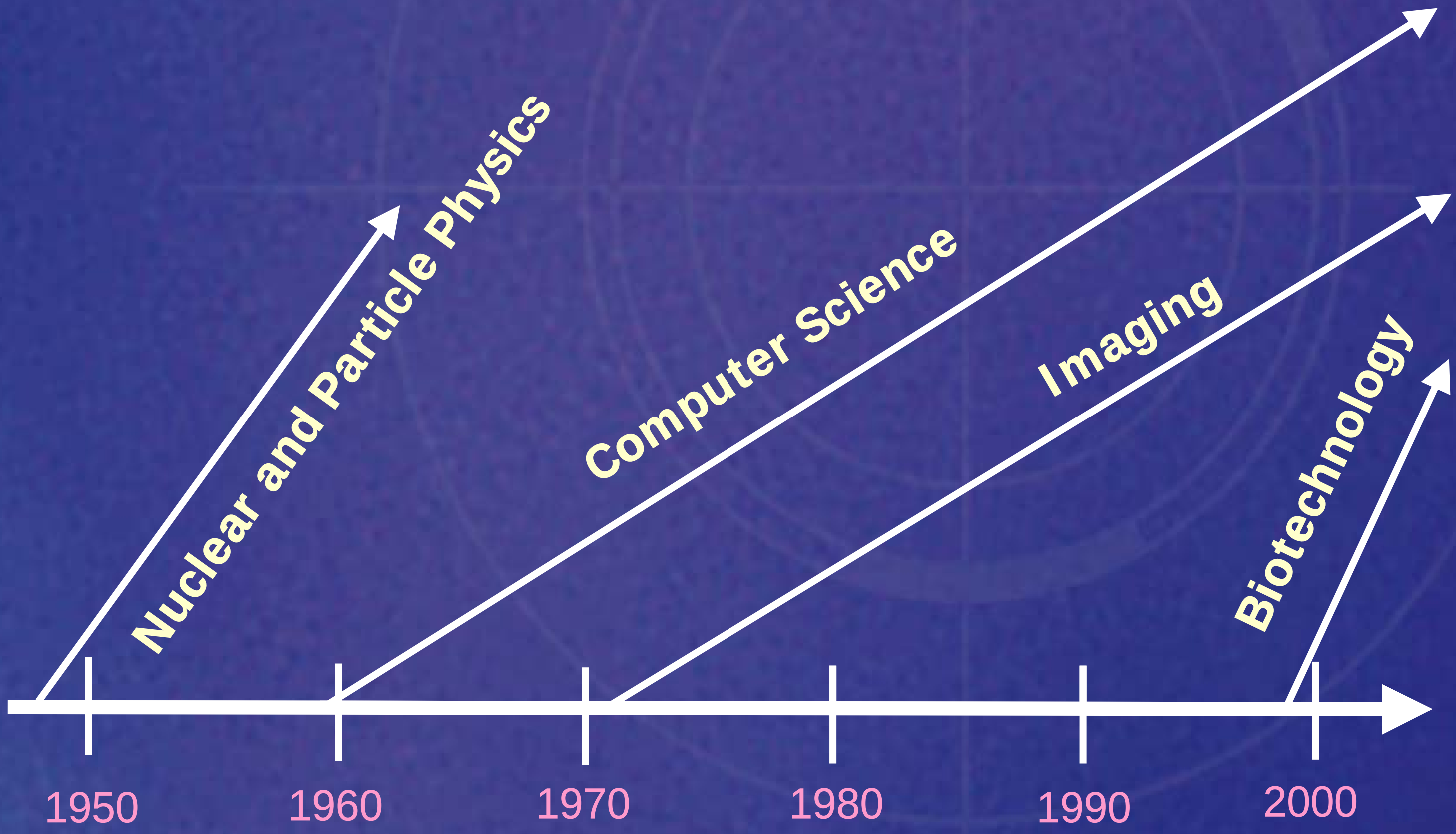
Scientific Forces Behind Our Field



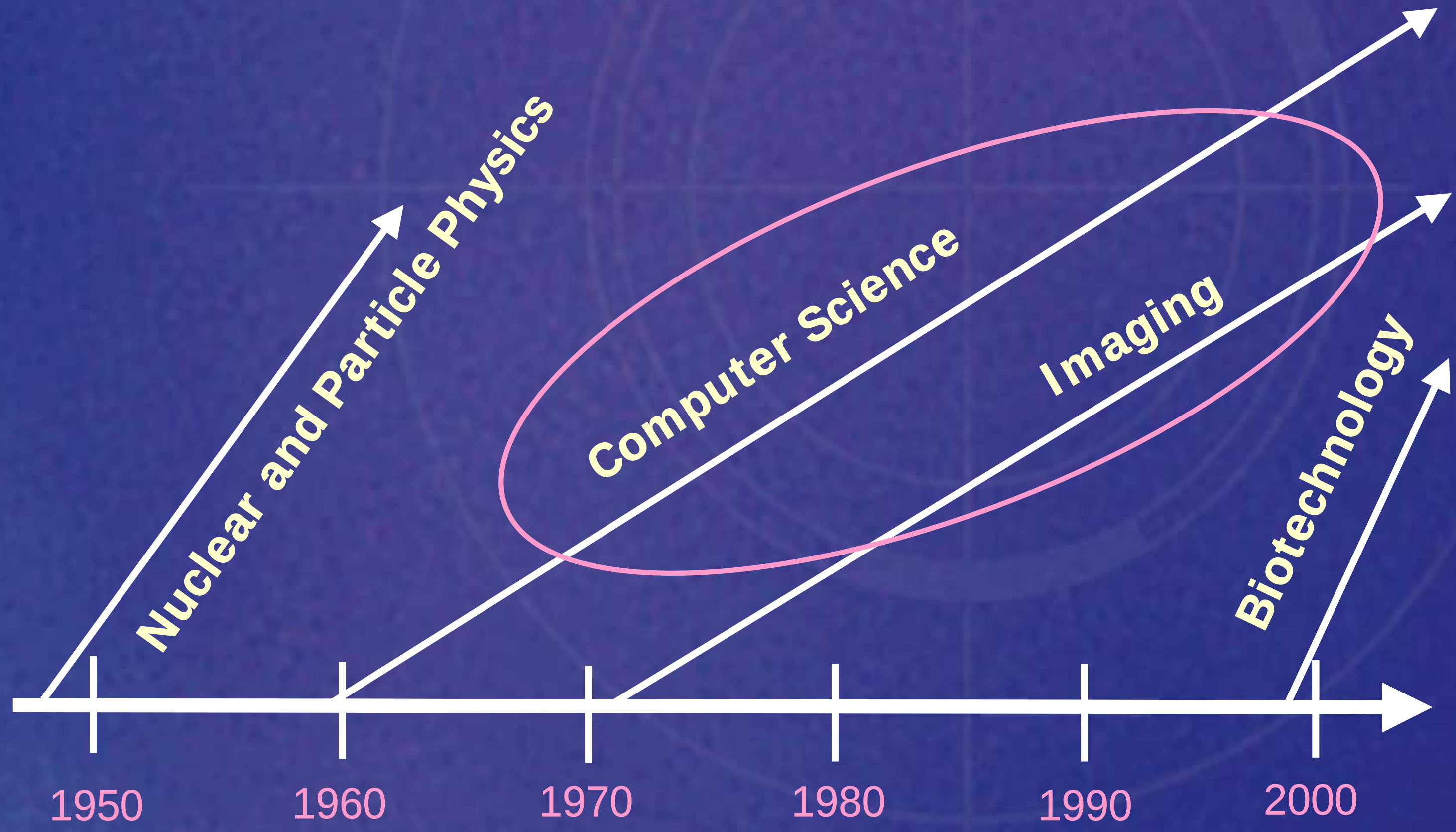
Scientific Forces Behind Our Field



Scientific Forces Behind Our Field

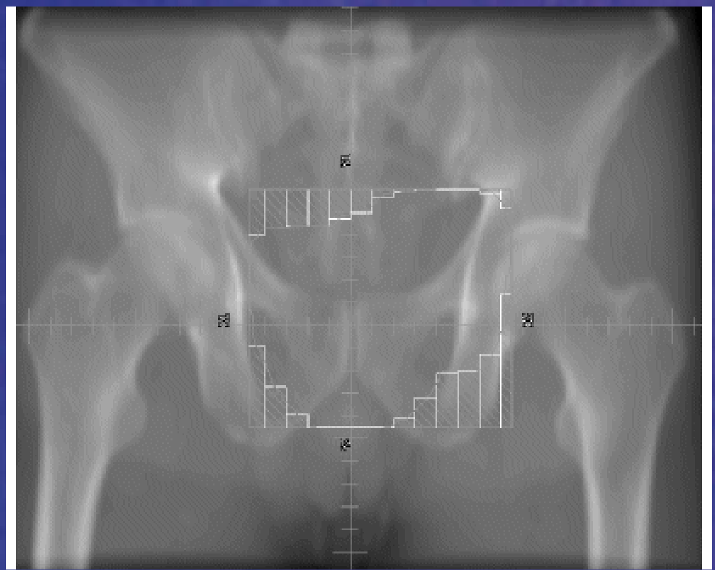


Scientific Forces Behind Our Field



2D Treatment Planning

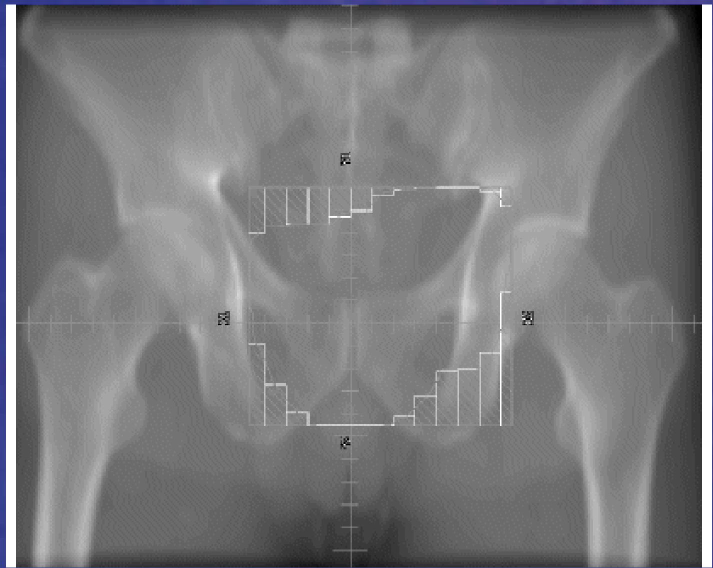
2D Treatment Planning



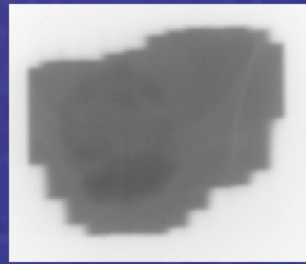
2D **simulation films** or
computer-generated **“DRRs”**

2D Treatment Planning

Tumors are hard to see in 2D images, especially port films, and you must rely on “landmarks.”

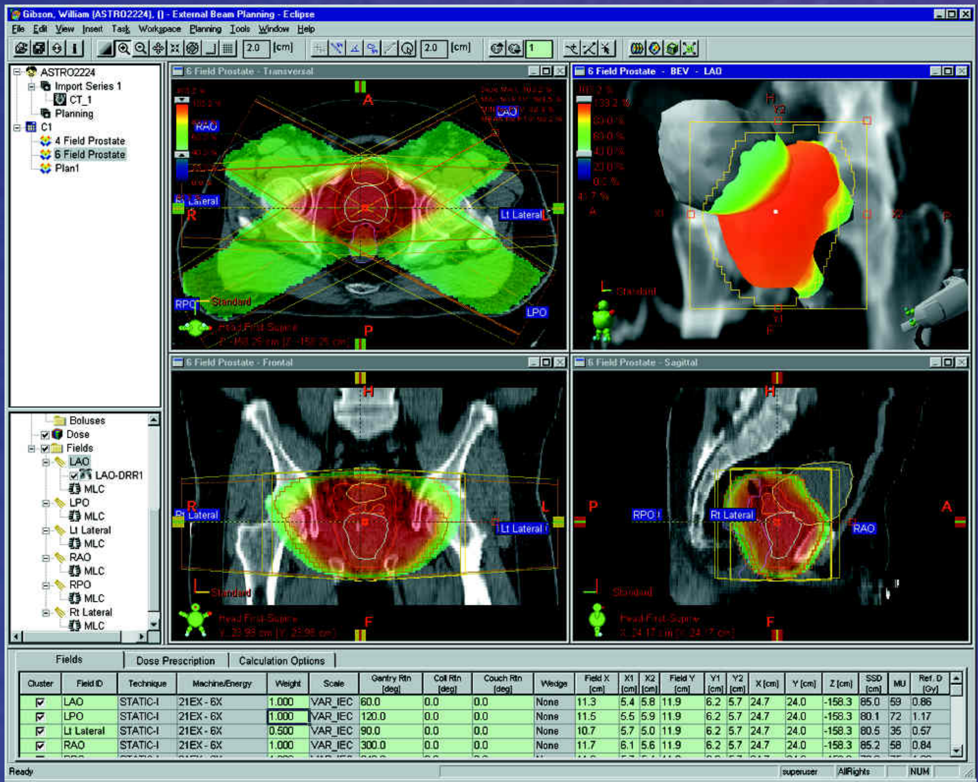


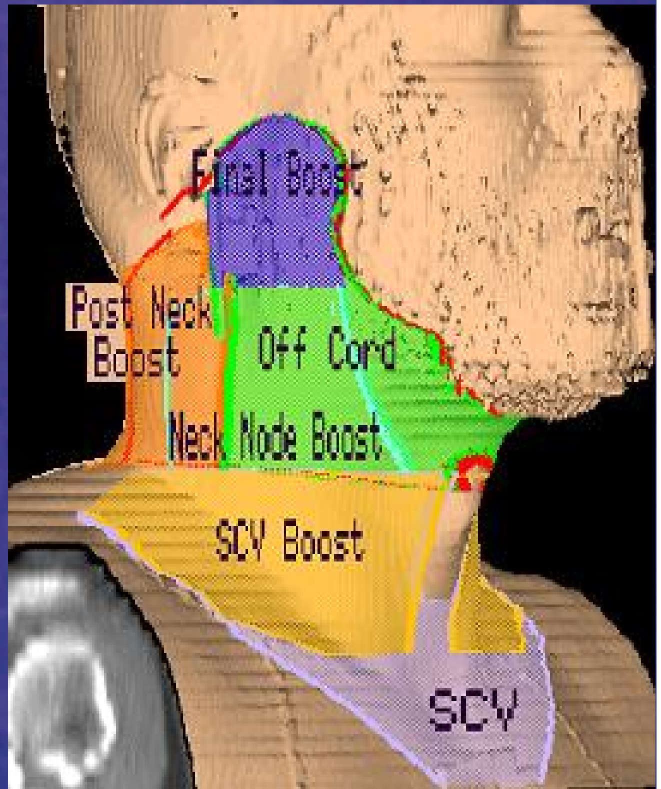
2D **simulation films** or computer-generated **“DRRs”**



Treatment machine **port films**

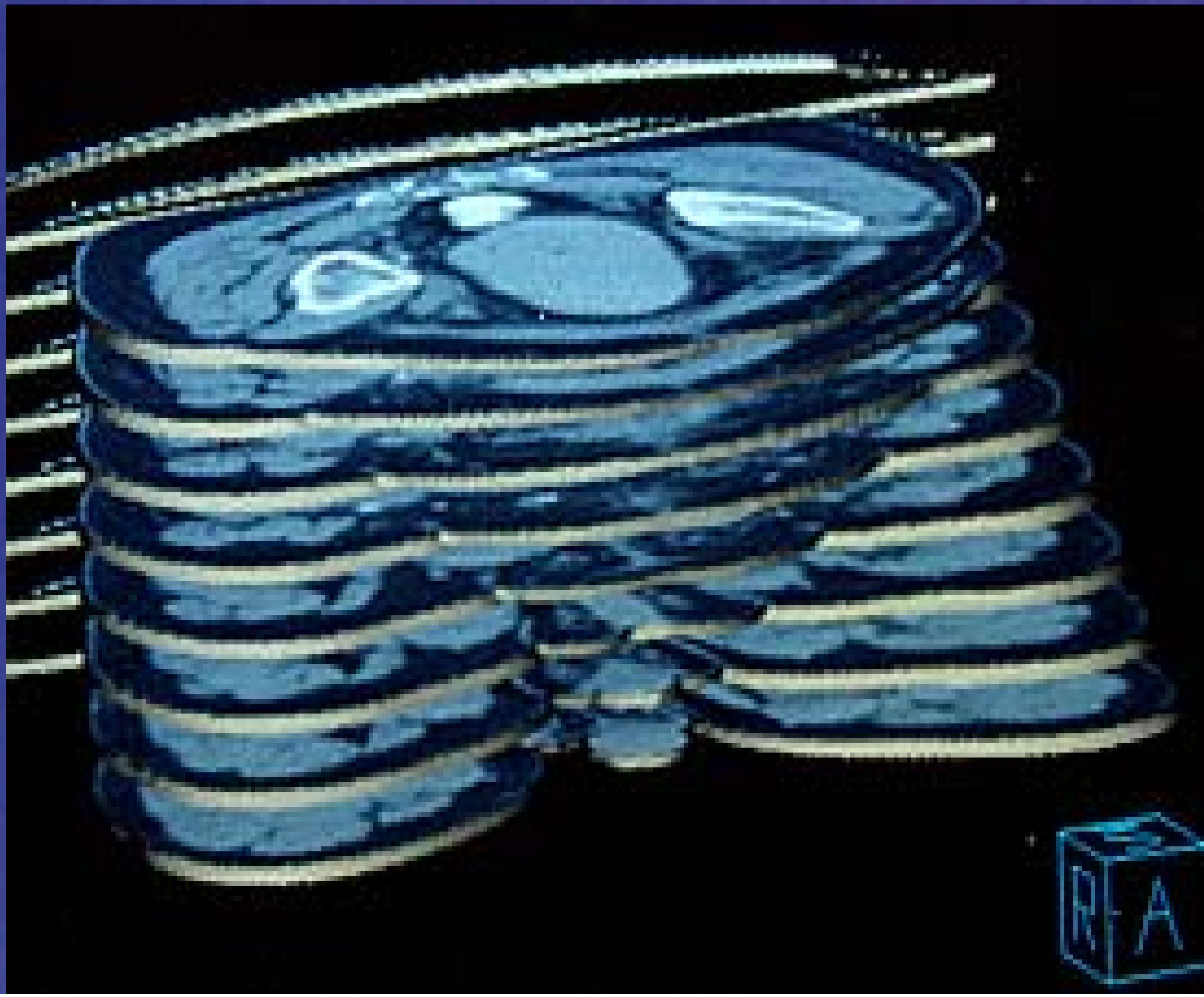
3-D Treatment Planning



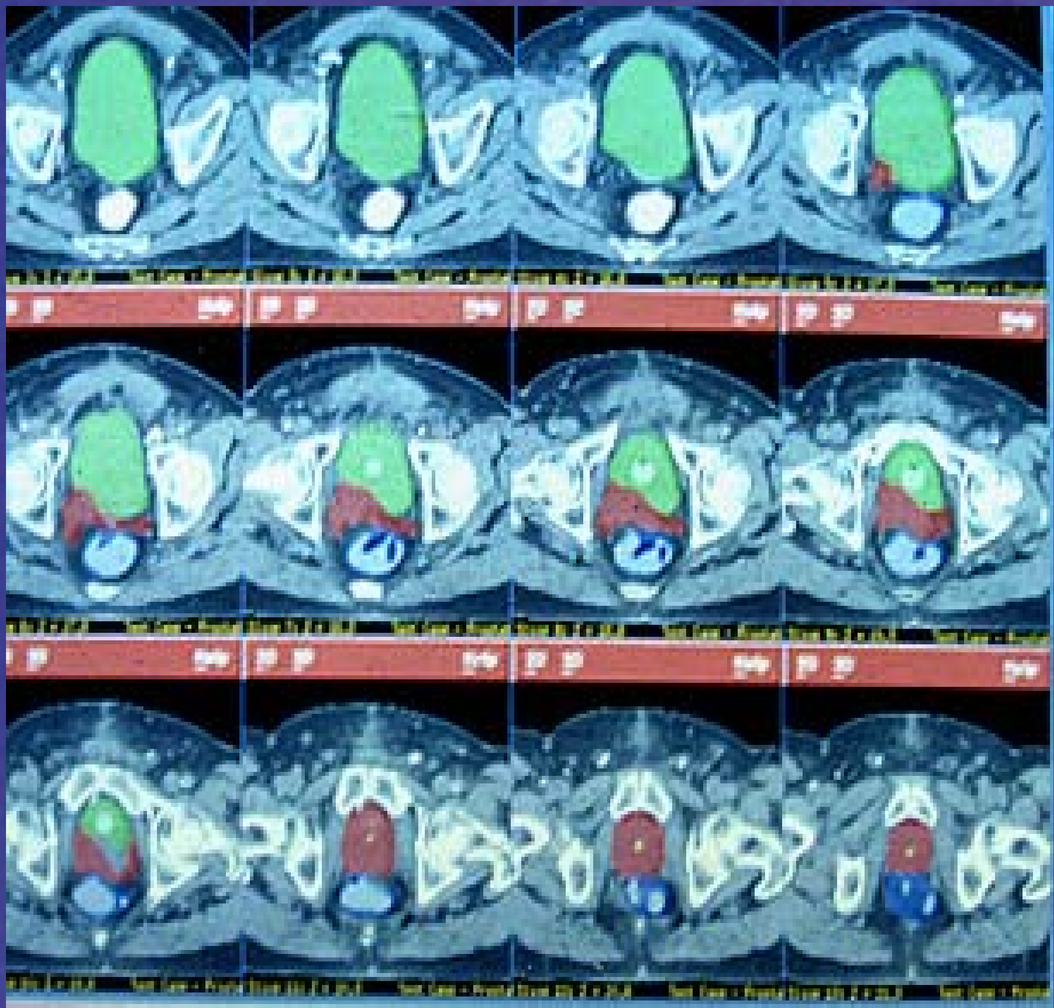


Planning workstations use 3D imaging and accurate dose calculations to allow highly “conformal” treatment planning.

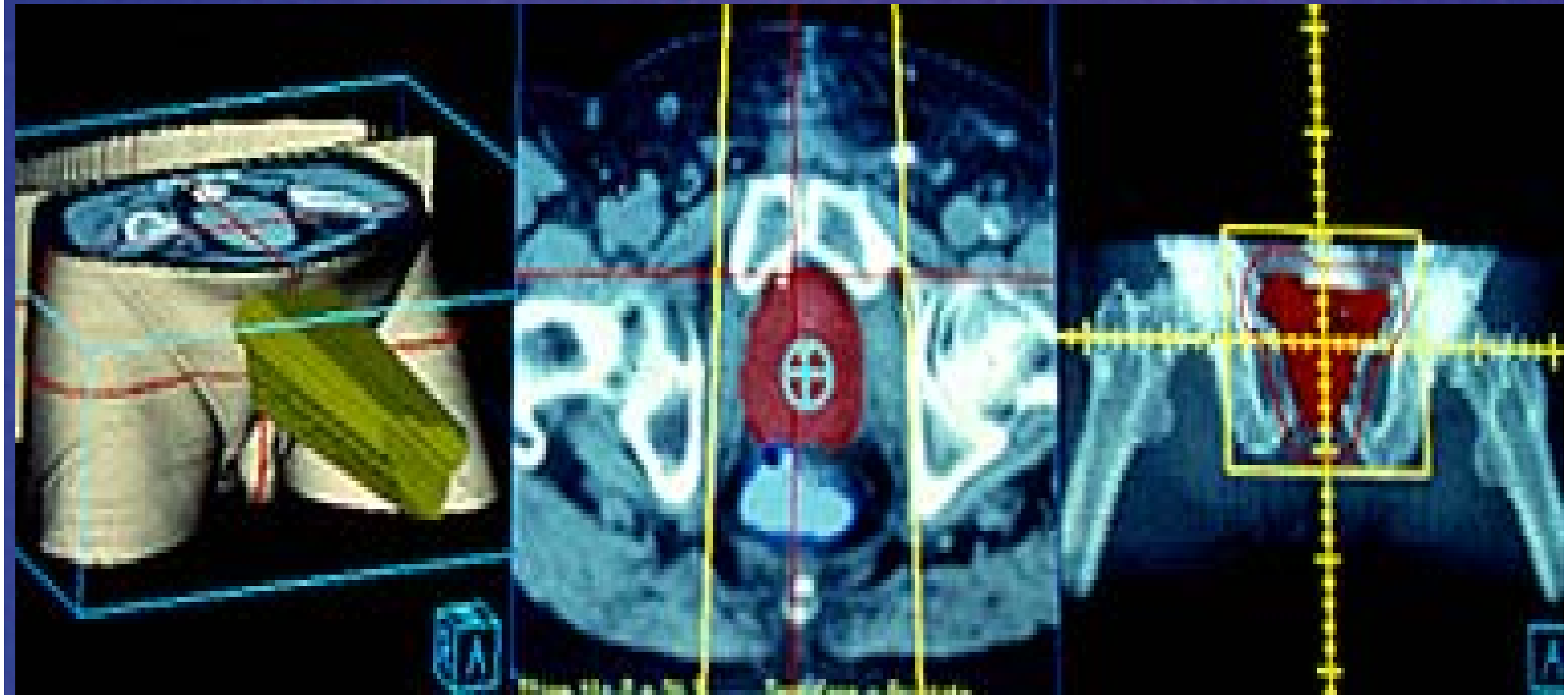
CT Slices Forming a Patient Representation is the Modern Basis for Radiotherapy



The Tumor and Sensitive Structures are Outlined



The Beam Directions are Chosen



Preconditions for 3D Conformal Radiotherapy

- Early detection of cancer.
  - Blood testing (e.g., PSA test).
  - Mammography.
  - Imaging screening of selected patients.
- CT to produce accurate representations of the patient.
- Well trained radiation oncologist and physicists.
- Much of the developing world does not have the preconditions for modern radiotherapy.

The Gamma Knife


Gamma Knife Model C (Elekta)

201 Co-60 Sources Collimated by a “Helmet”

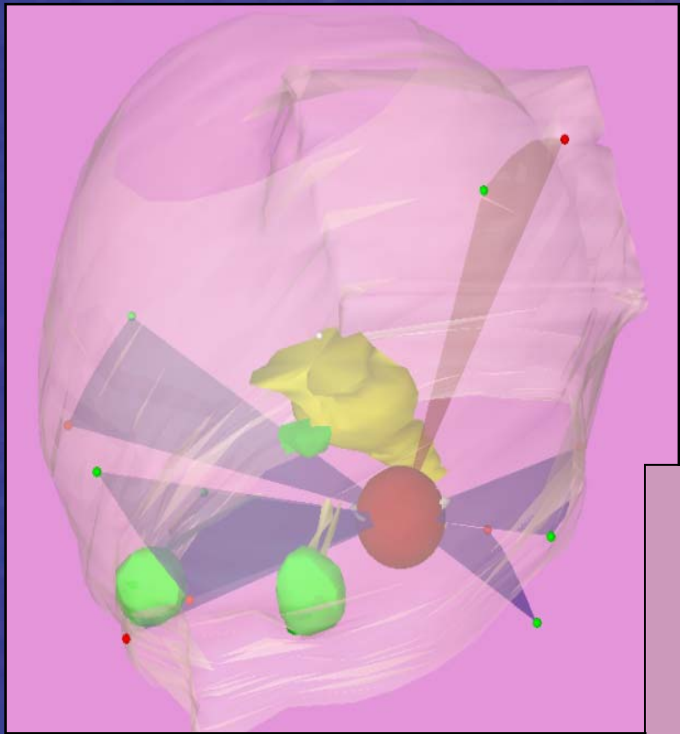
Traditional Linac Stereotactic Radiosurgery Equipment

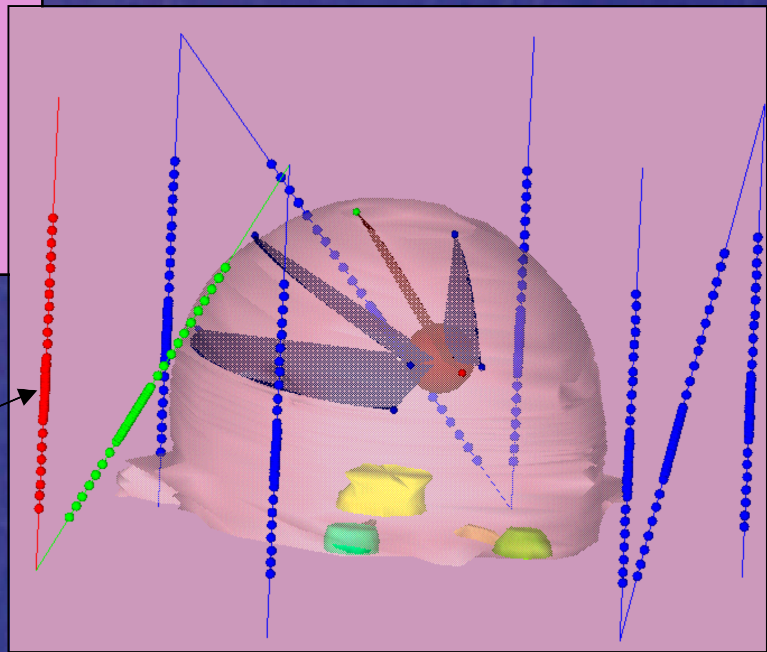
Collimator set

Typically ~10-40mm diameter

Cranial Stereotactic Localizer

Stereotactic Arc Plans

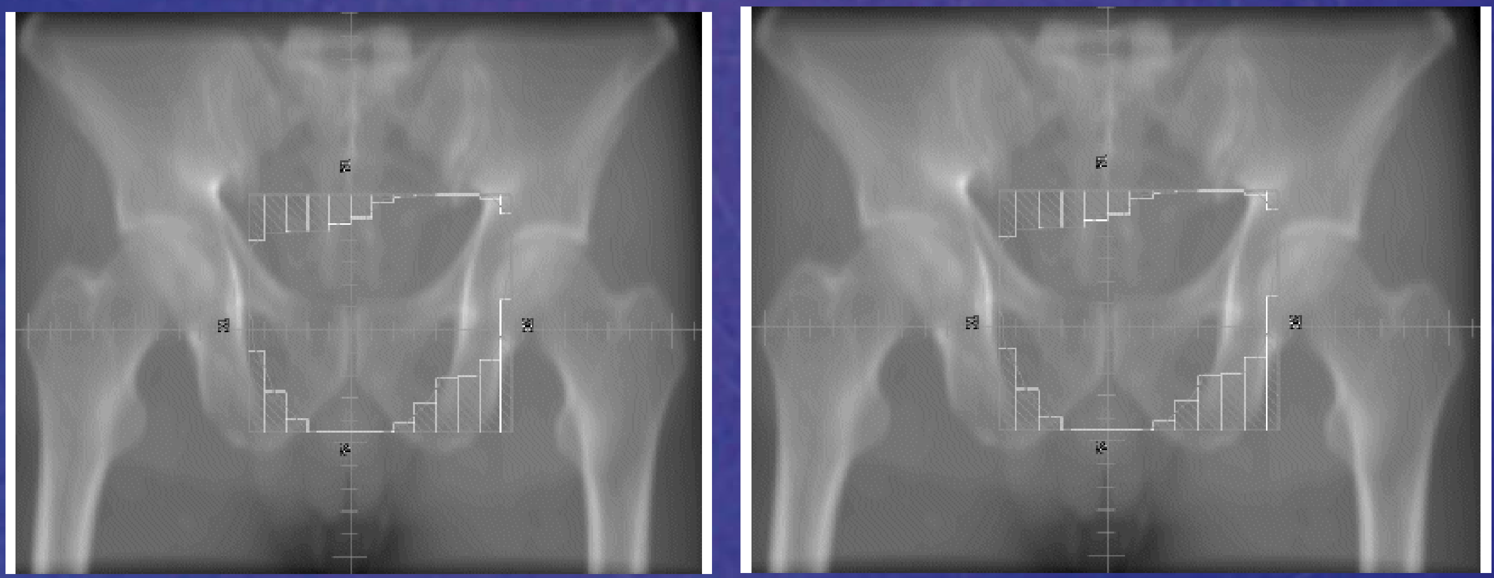




Localizer
Rods on
3D image

Optimization and Intensity-Modulated Radiotherapy (IMRT)

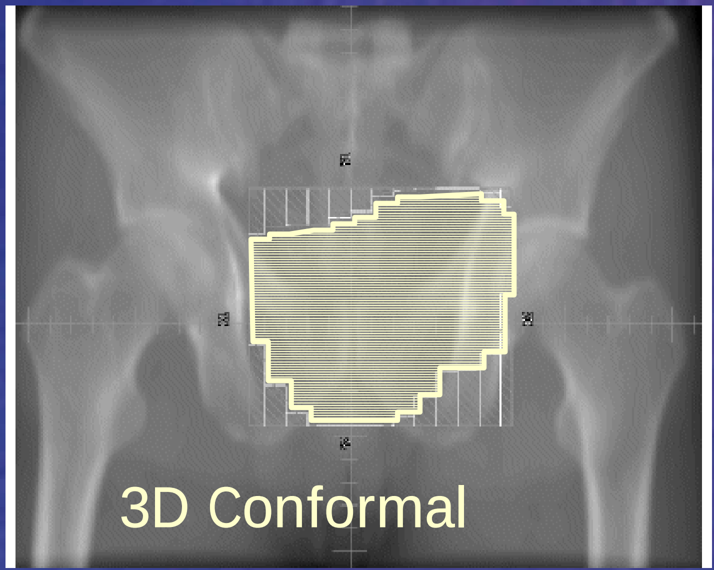
- *Let the computer do the work…*

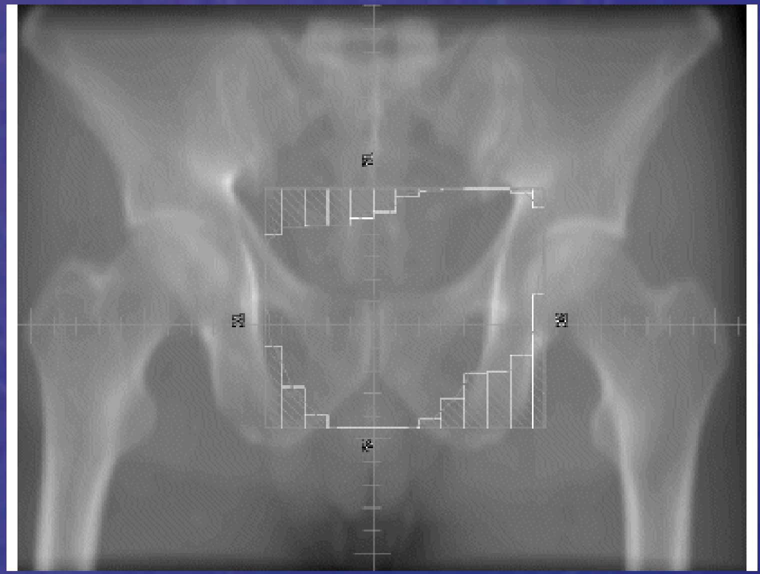


Let the computer optimize the plan, varying the intensity within each beam, to “conform” and “spare” even more.

Optimization and Intensity-Modulated Radiotherapy (IMRT)

- *Let the computer do the work…*

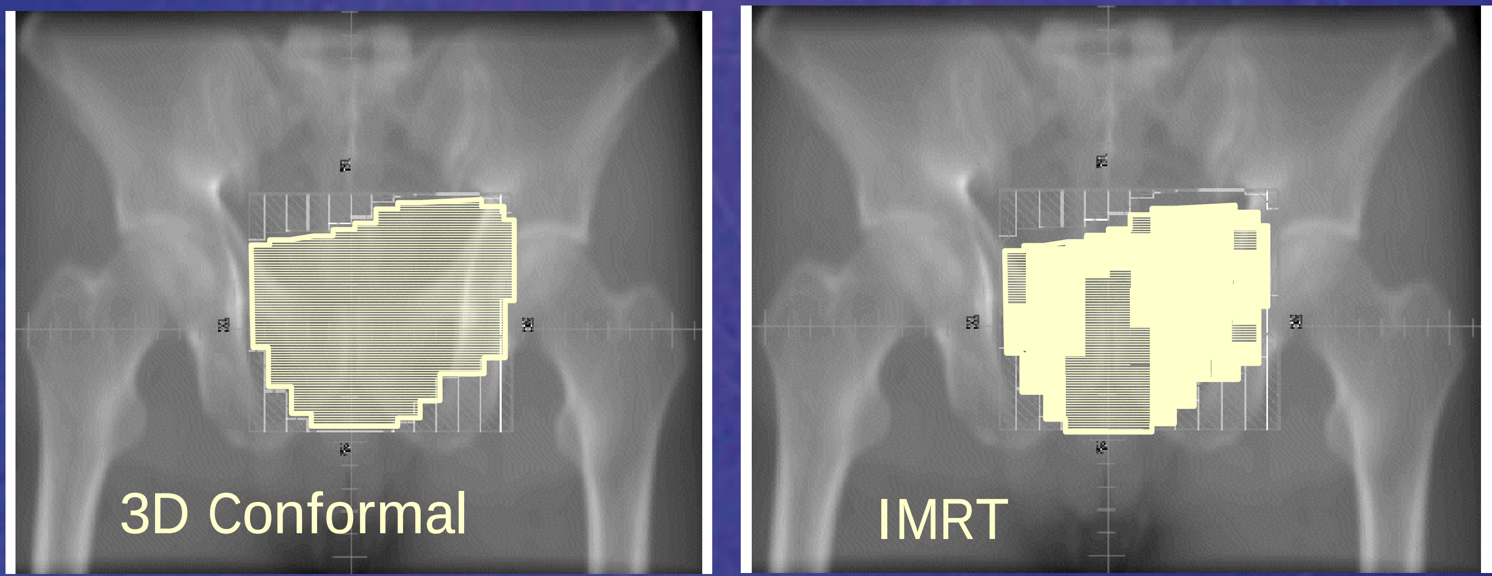




Let the computer optimize the plan, varying the intensity within each beam, to "conform" and "spare" even more.

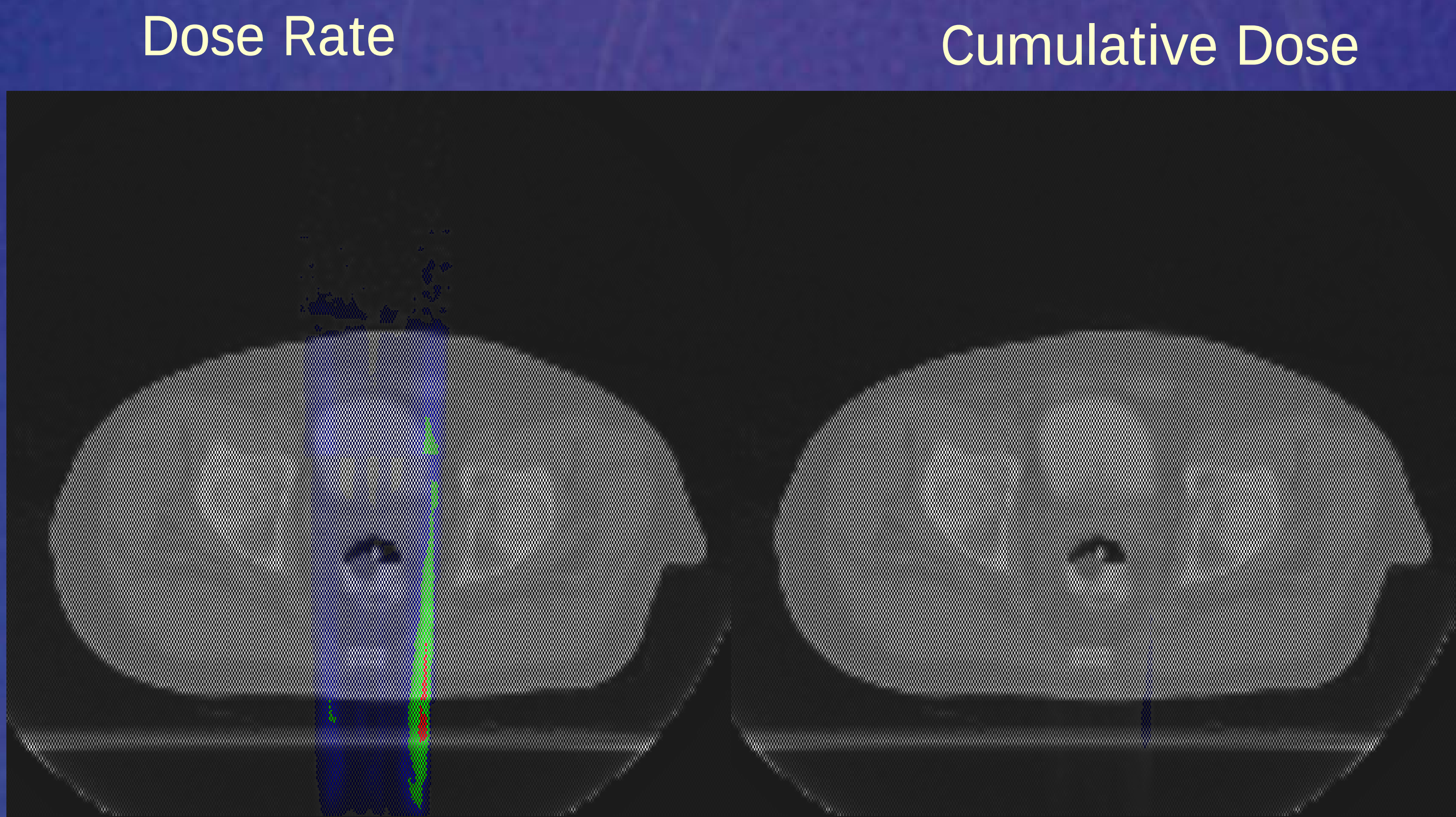
Optimization and Intensity-Modulated Radiotherapy (IMRT)

- *Let the computer do the work…*

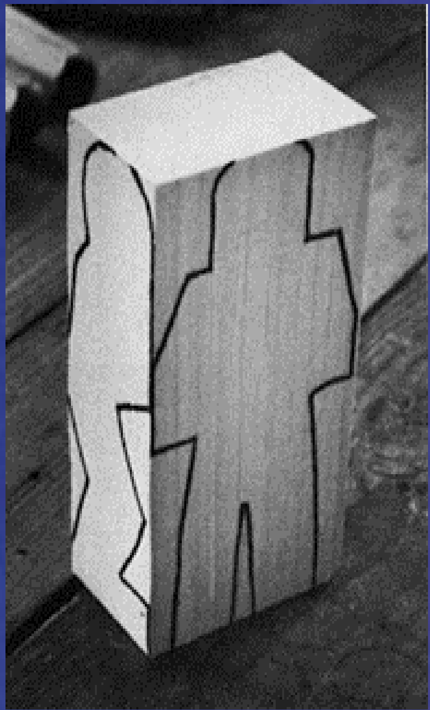


Let the computer optimize the plan, varying the intensity within each beam, to “conform” and “spare” even more.

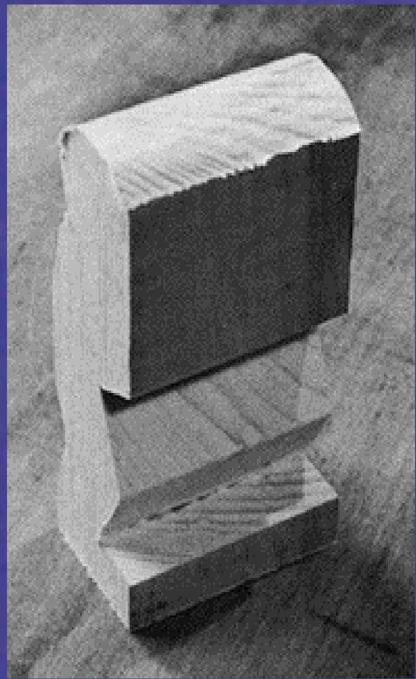
Prostate IMRT (Tomotherapy)



Dose Sculpting

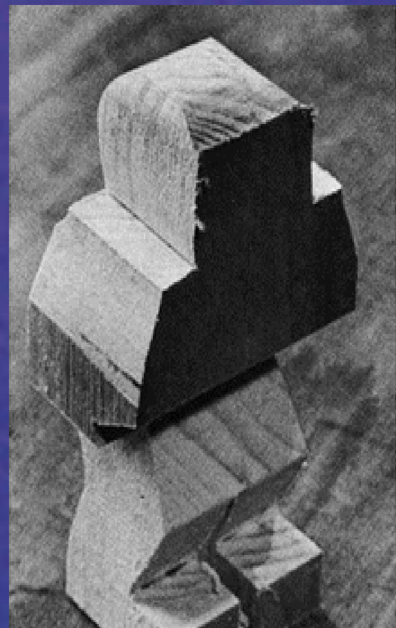


2-D Planning

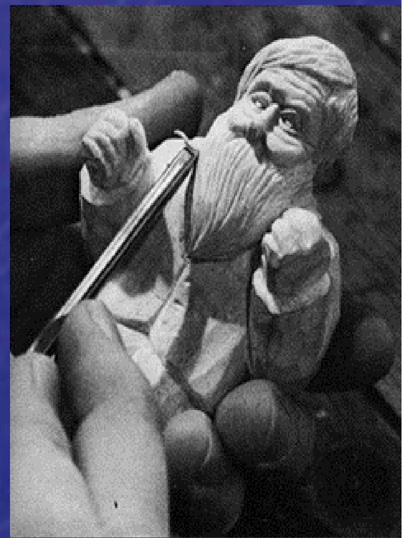


3-D

Conformal

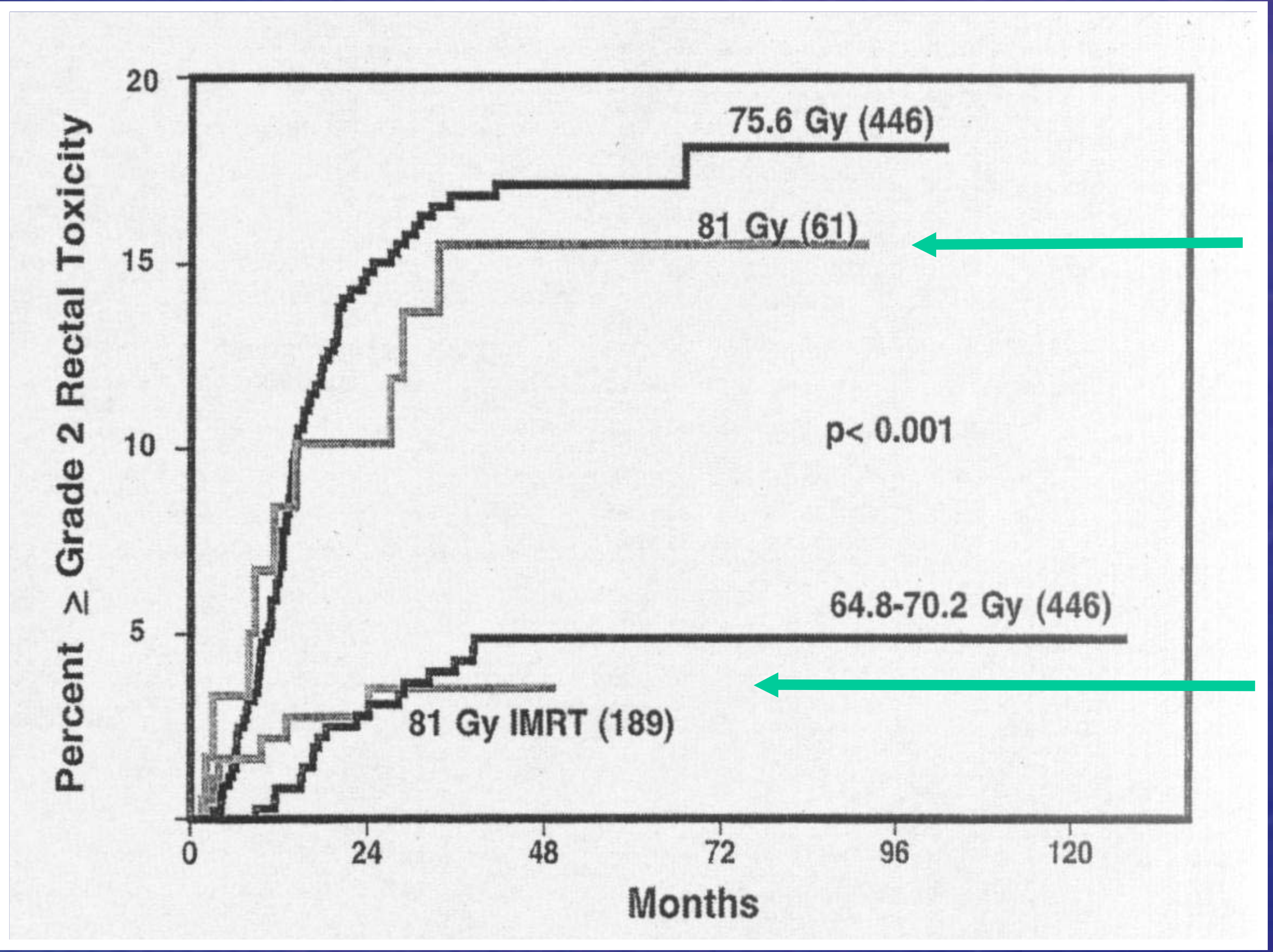


IMRT



Courtesy of J. Schreiner Kingston Regional Cancer Centre, Ontario

IMRT Significantly Reduces Rectal Complications

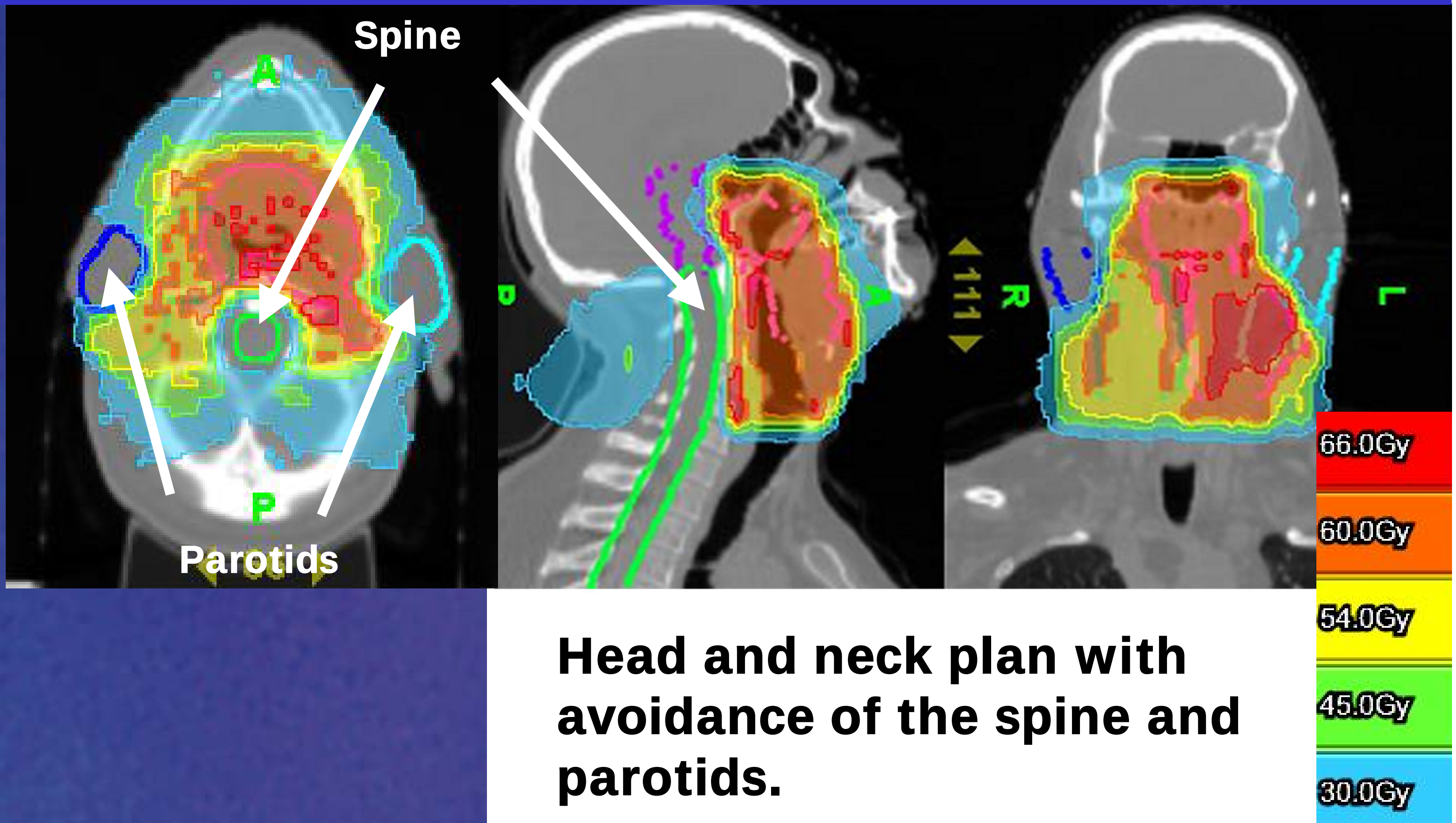


3D Conformal

IMRT

Zelefsky et al, J Urol, 2001

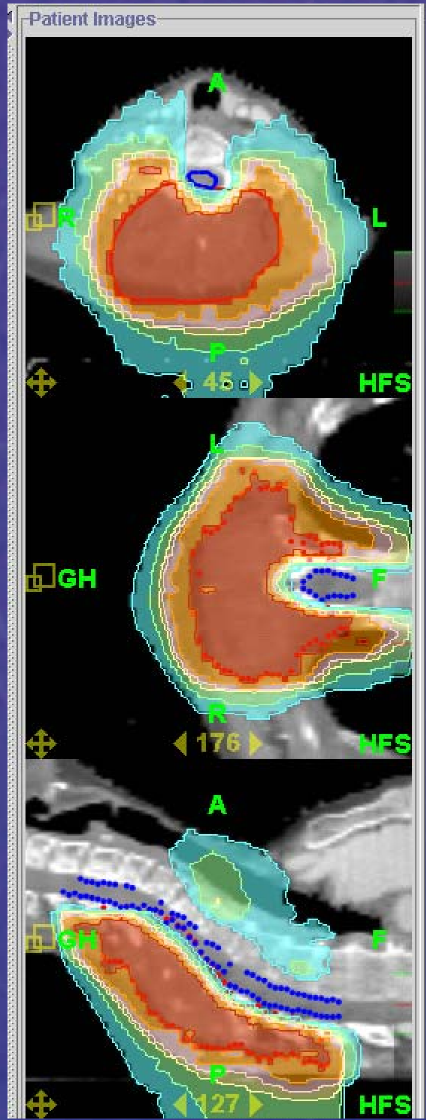
Tomotherapy IMRT Plan

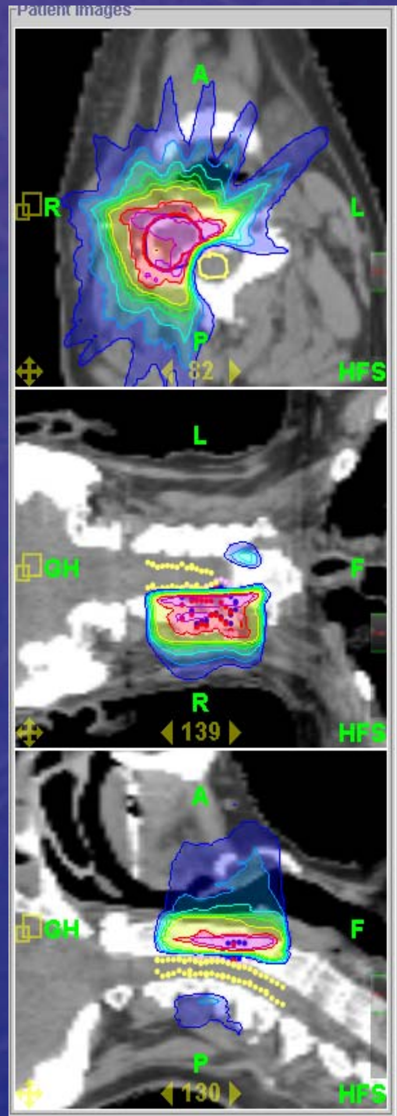


Head and neck plan with avoidance of the spine and parotids.

Re-Treatments

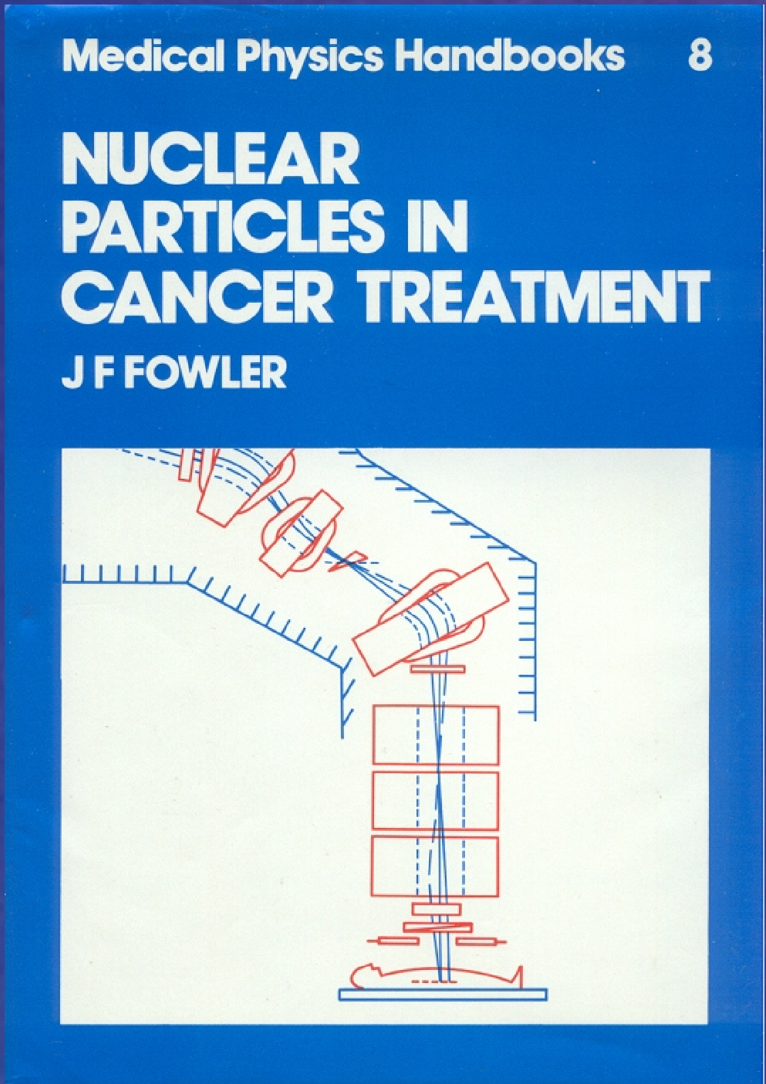
Re-treatments, using tomotherapy for patients not eligible for conventional photon radiation therapy due to cord tolerance.

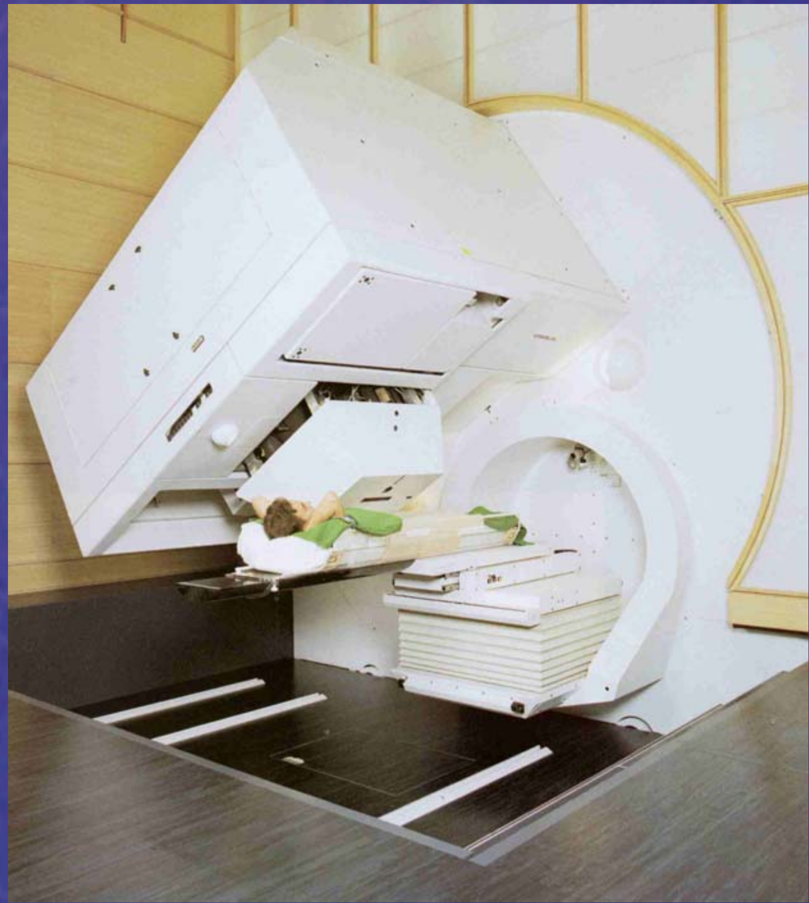




Patients courtesy of UAB

Protons and Heavy ("Light") Ions

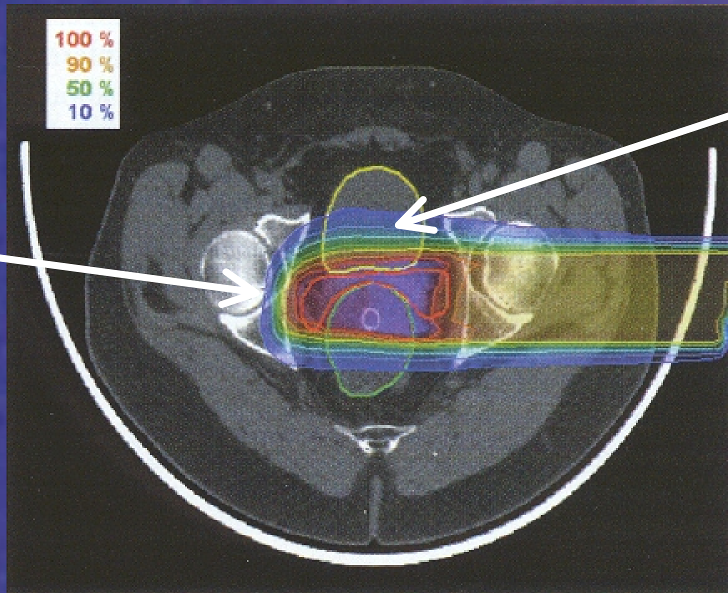




PSI Switzerland

Will the Long Term Future Be Protons?

Protons stop so integral dose is less.



Not so great lateral penumbra.

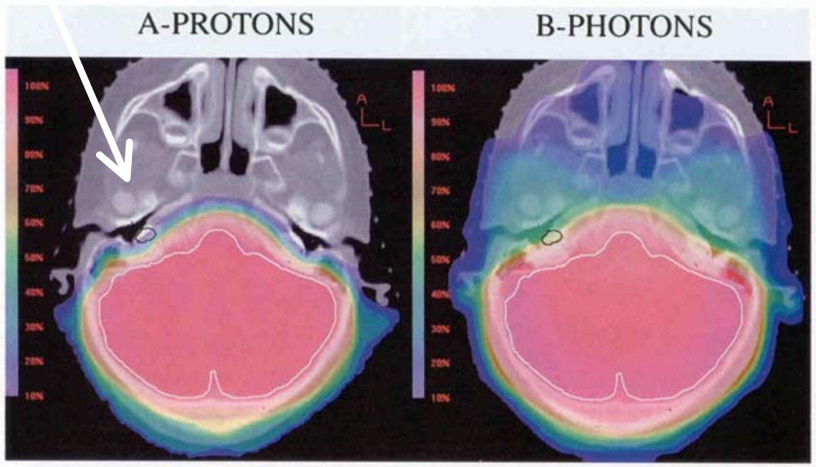
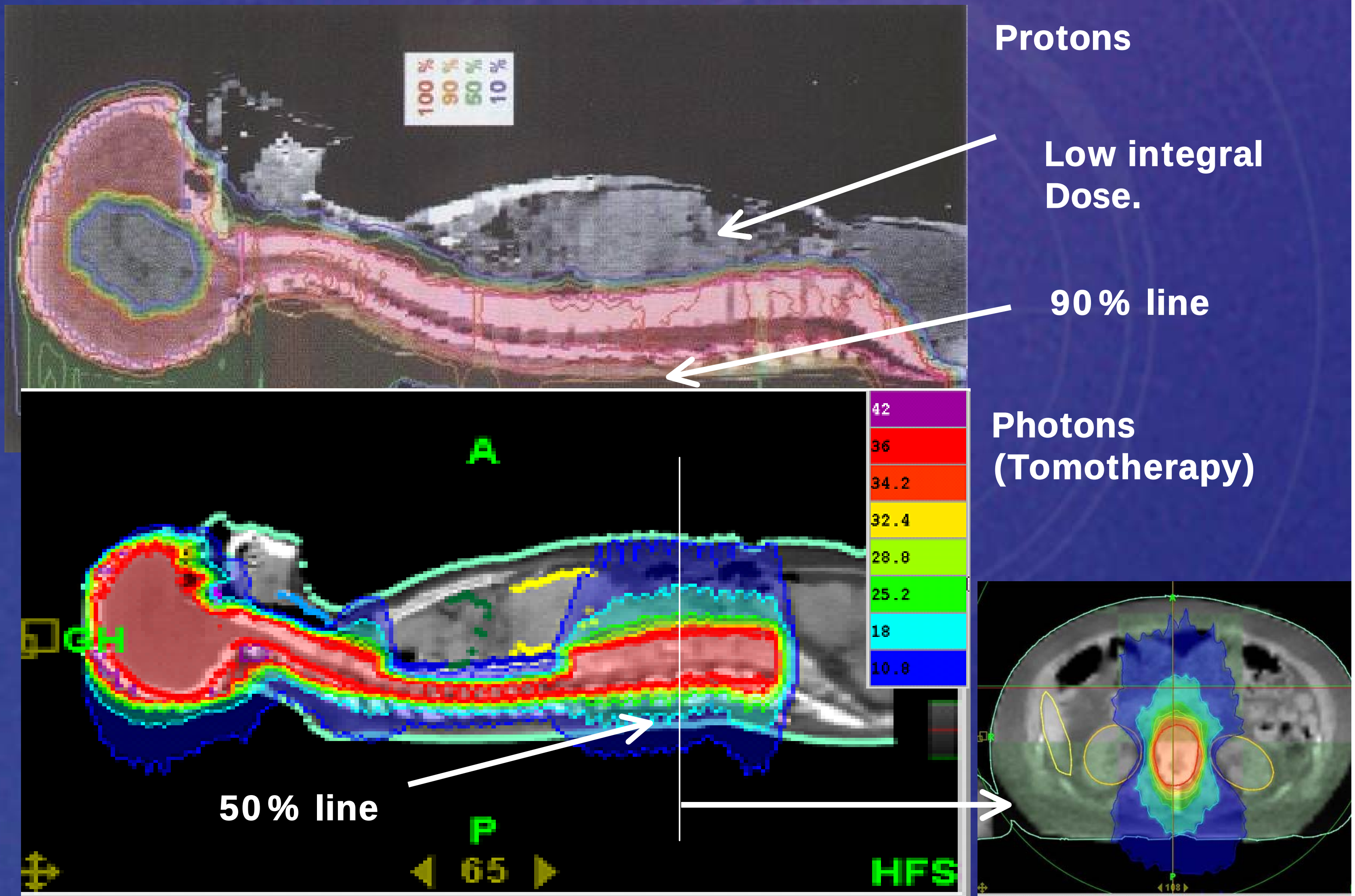


Fig. 3. Radiation treatment of the posterior fossa: color wash dose-distributions ranging from 10% to 100% isodose levels. Comparison of (A) proton with (B) three-dimensional photon plans. (The cochlea is outlined in black).

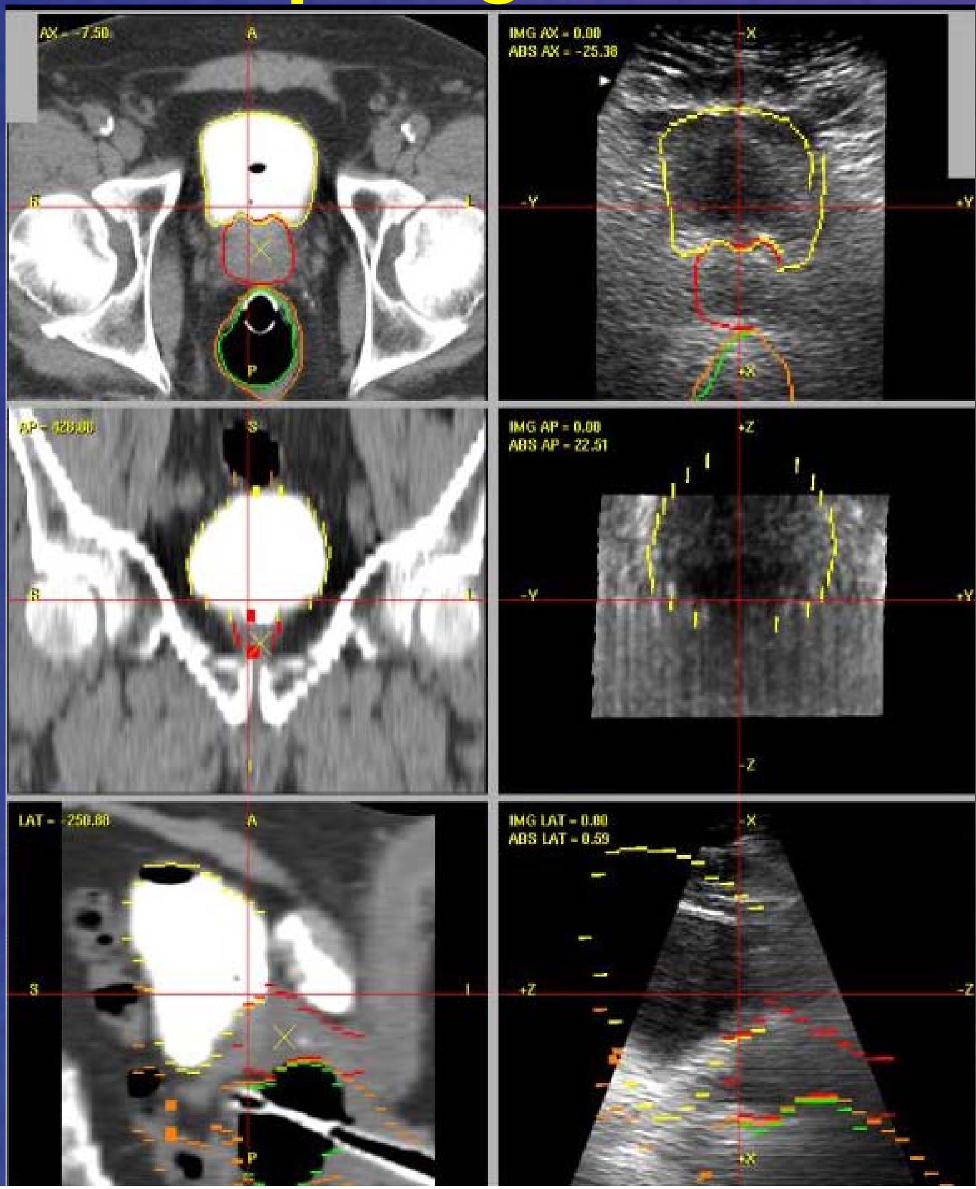
Dose Distribution Comparison



Why 3D Image-Guided Radiotherapy (IGRT)?

- Eventually most radiotherapy will be IMRT, even many palliative treatments, e.g., re-treatments.
- All IMRT should be image-guided:
  - IMRT is justified by sparing critical tissues (conformal avoidance) which produces higher dose gradients.
  - IGRT enables higher gradients to be delivered safely and effectively.
  - IGRT enables a smaller setup margins to be defined.
- In some radiotherapy sites, e.g., prostate, IGRT may be more important than IMRT.
- 2D imaging is inadequate to obtain volume information.

Setup Alignment with Ultrasound

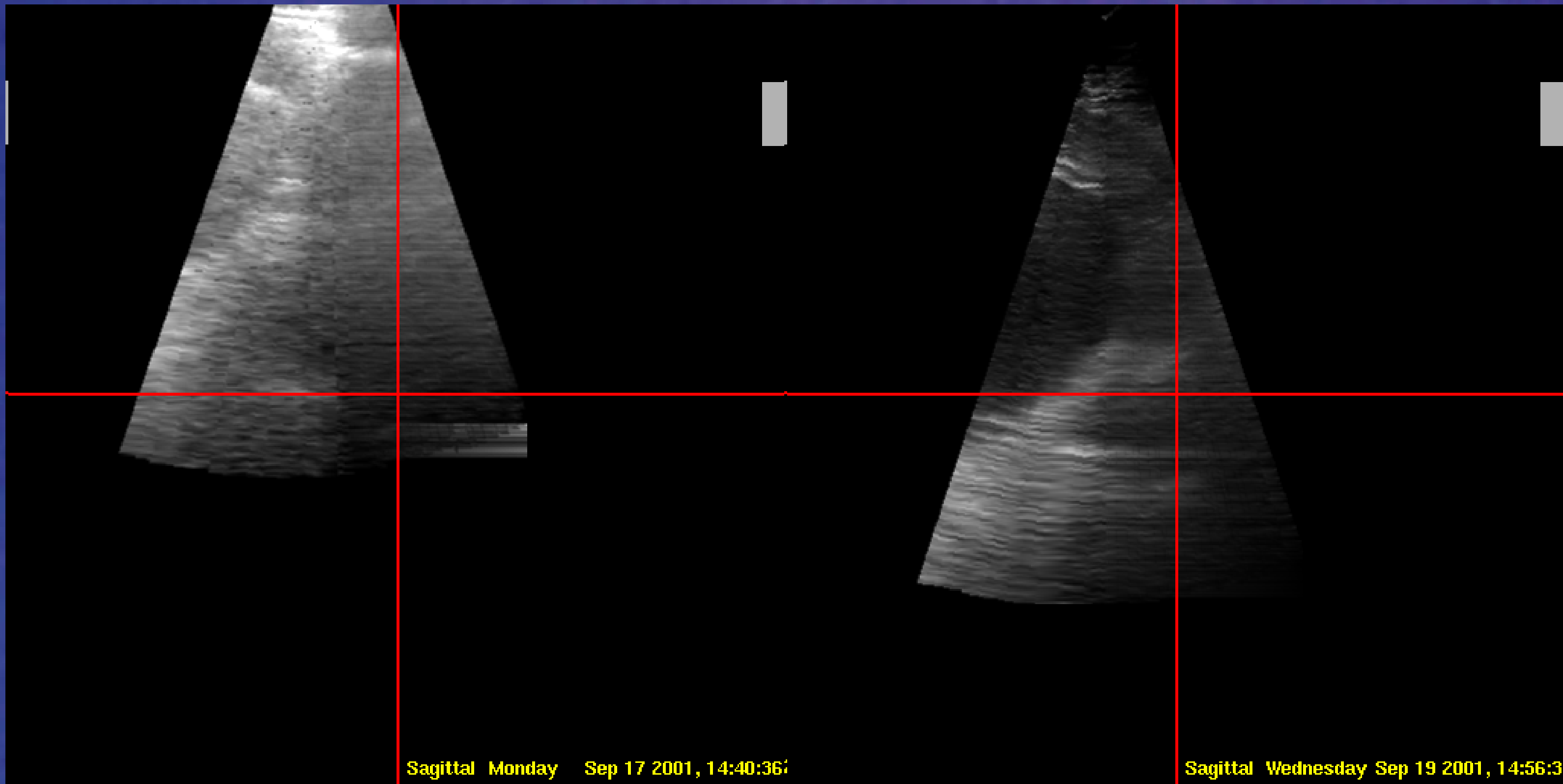


When contour alignment to ultrasound is satisfactory, shift the patient to the new position.

Using Varian's Ultrasound Localization System

From Dr. Wolfgang Tomé

Pitfall: Pubic Arch Interference

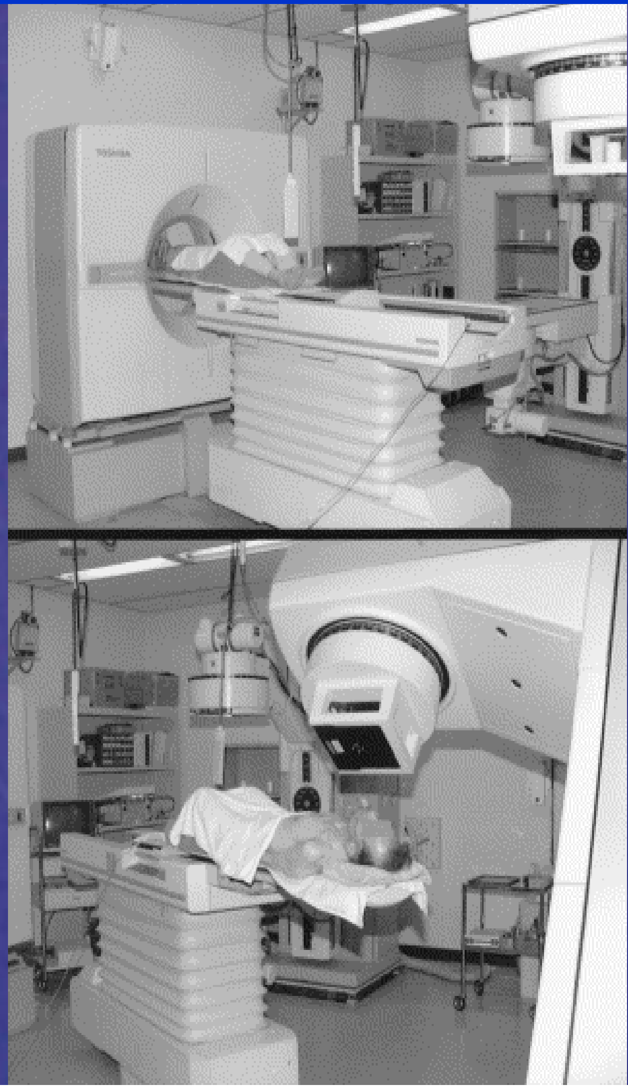


Probe placed over treatment isocenter.

Probe displaced by 1cm superiorly from treatment isocenter.

From Dr. Wolfgang Tomé, UW-Madison

CT in the Treatment Room



First CT

Then Treat

From Minoru Uematsu et al.
IJROBP 48, 432 (2000)

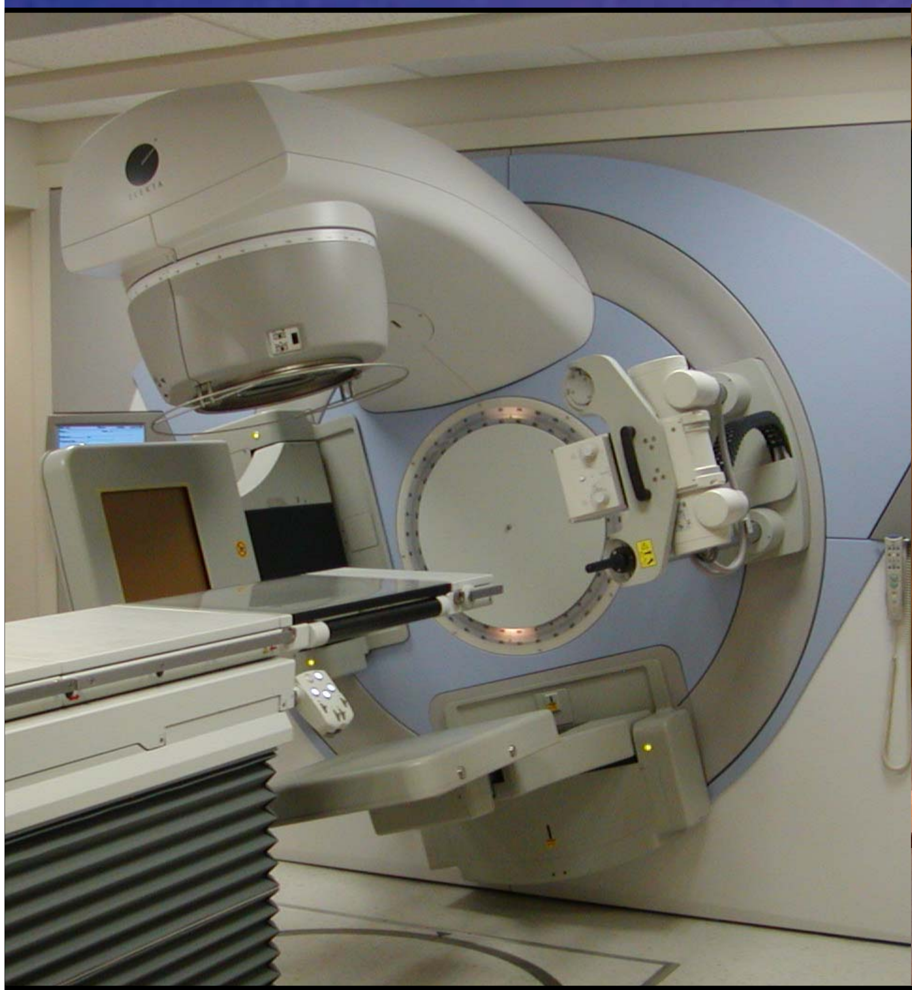
CT in Treatment Room

Siemens Primatom
"CT on Rails"

GE CT + Varian Linac

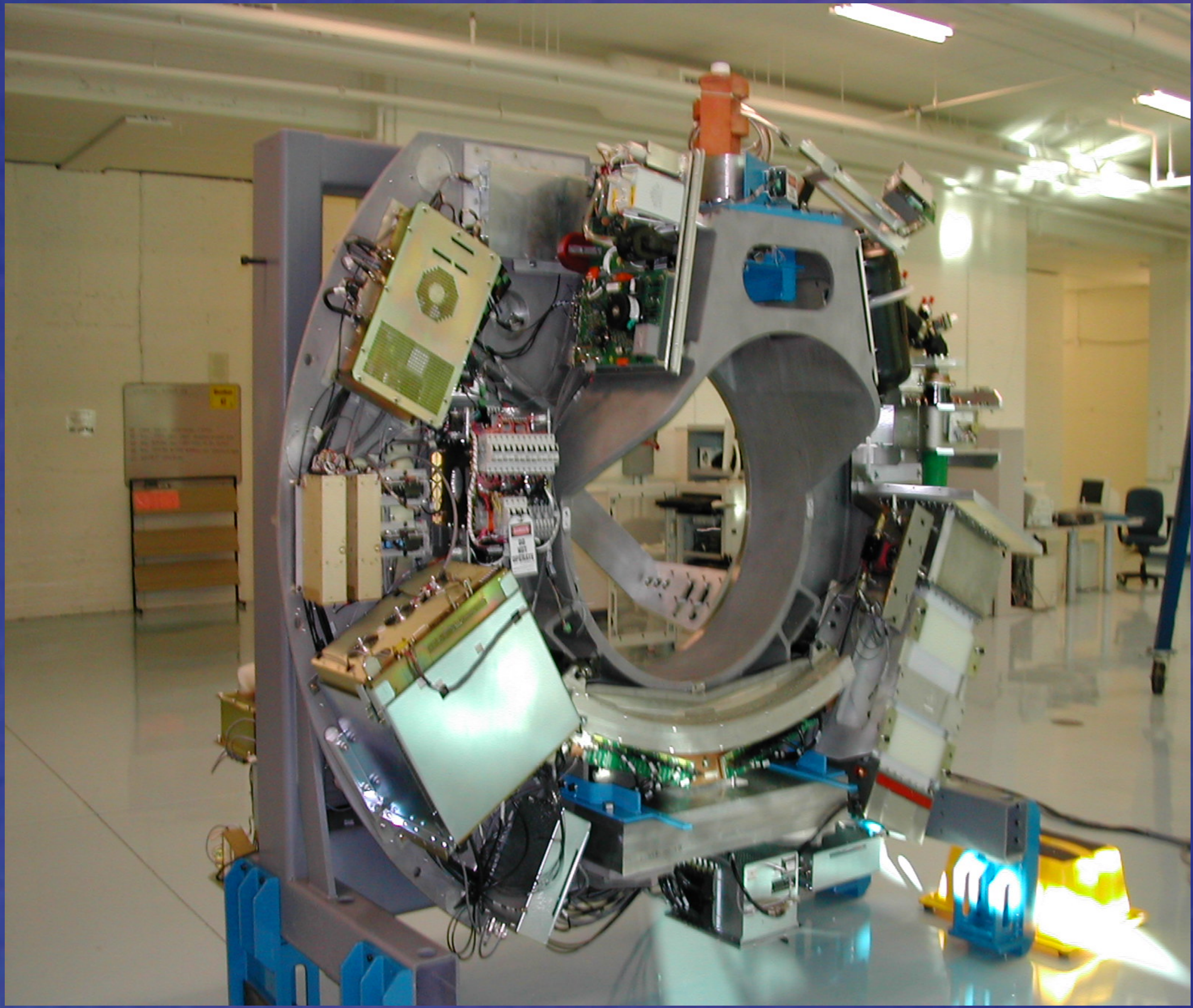
From Tim Holmes, St. Agnes Hospital

Cone Beam Imaging

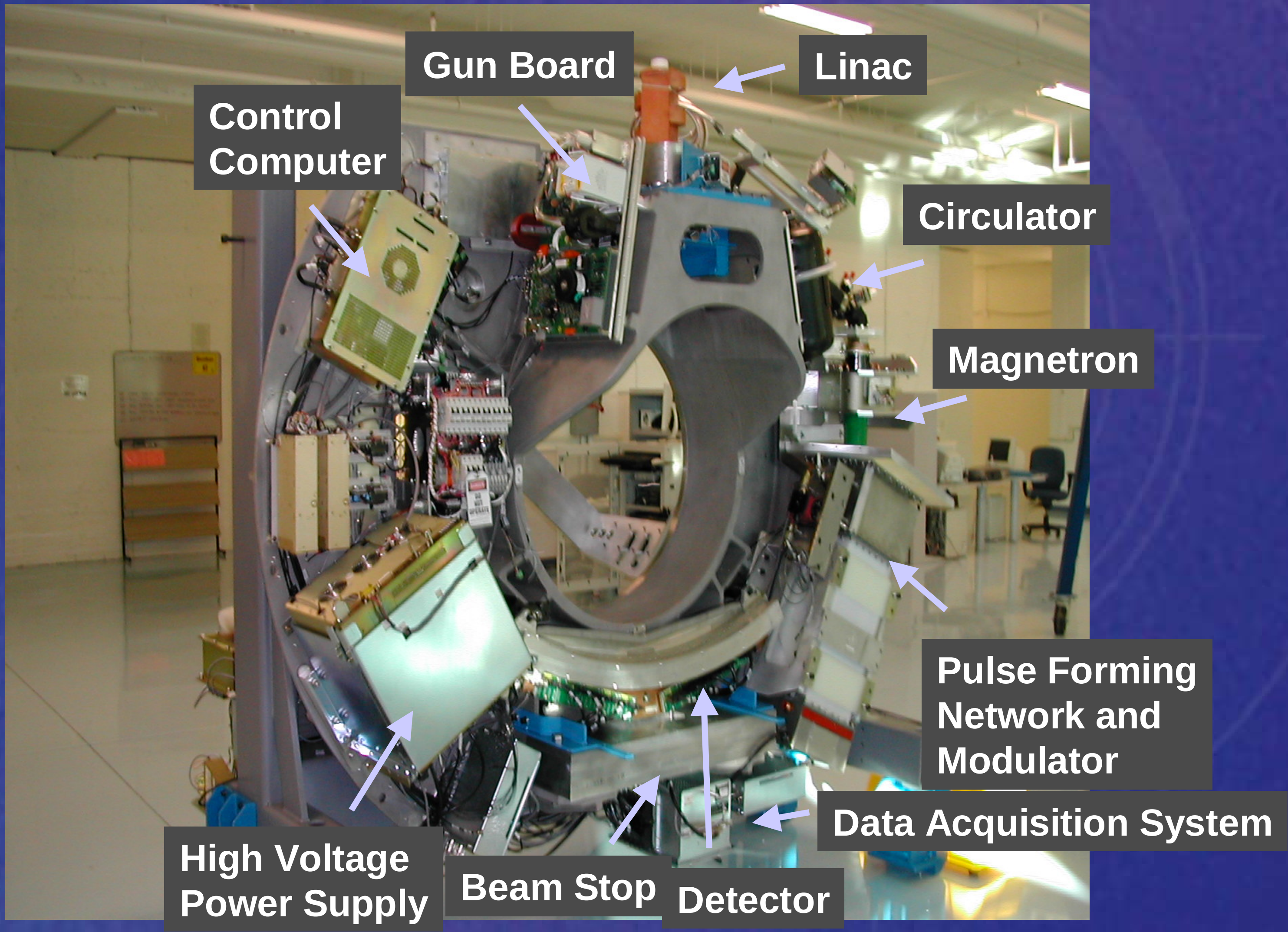


Elekta Synergy **Varian Trilogy**

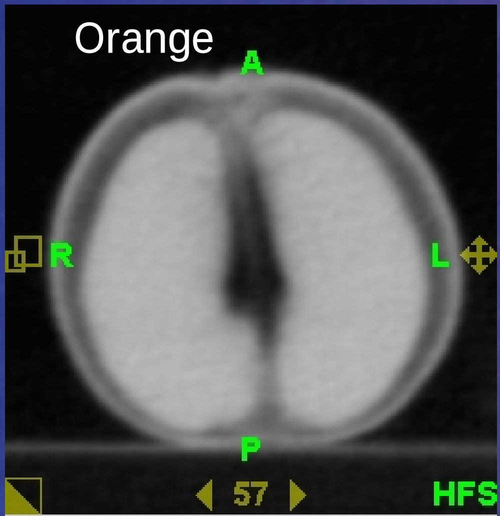
Helical Tomotherapy Unit

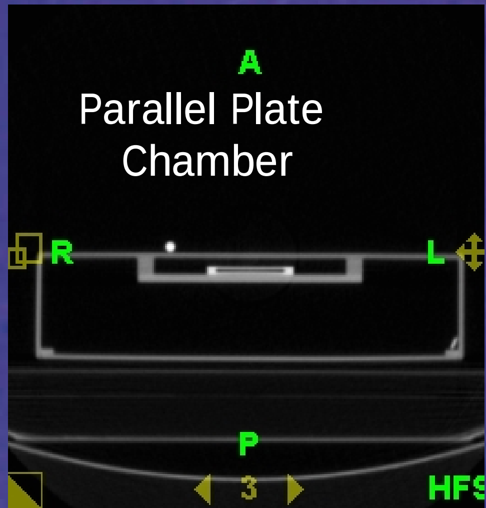


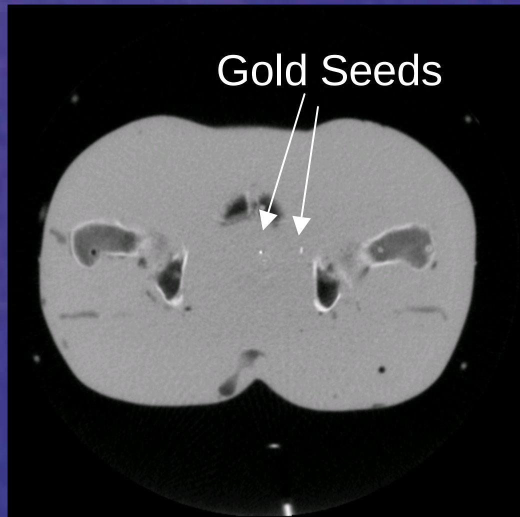
Helical Tomotherapy Unit

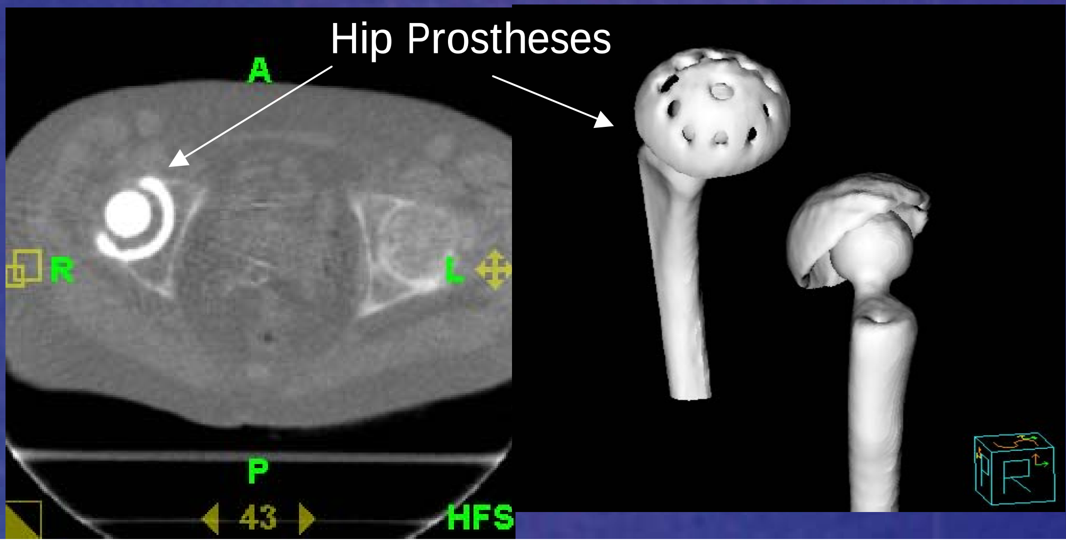


Tomotherapy Verification Scanning With the Treatment Beam

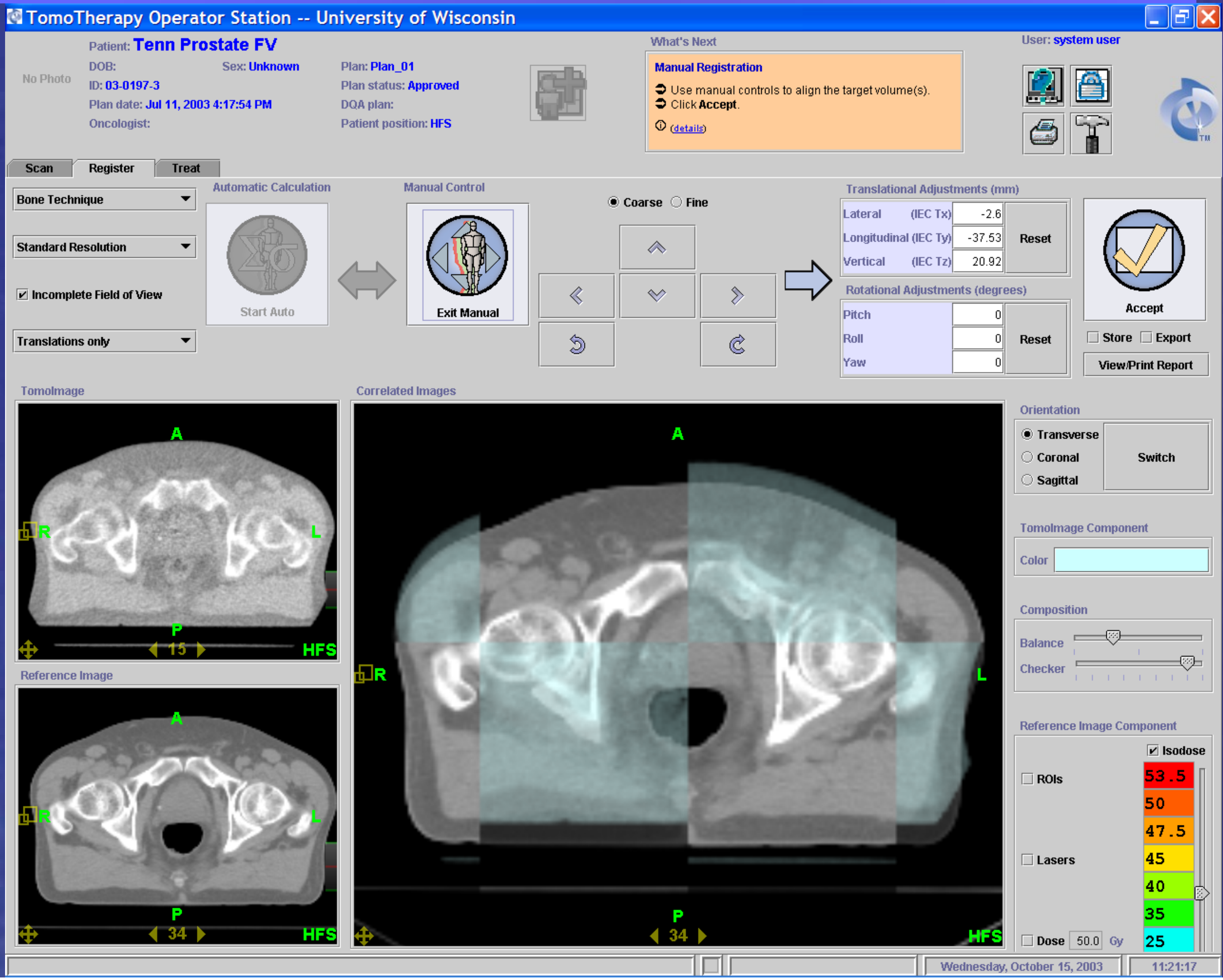




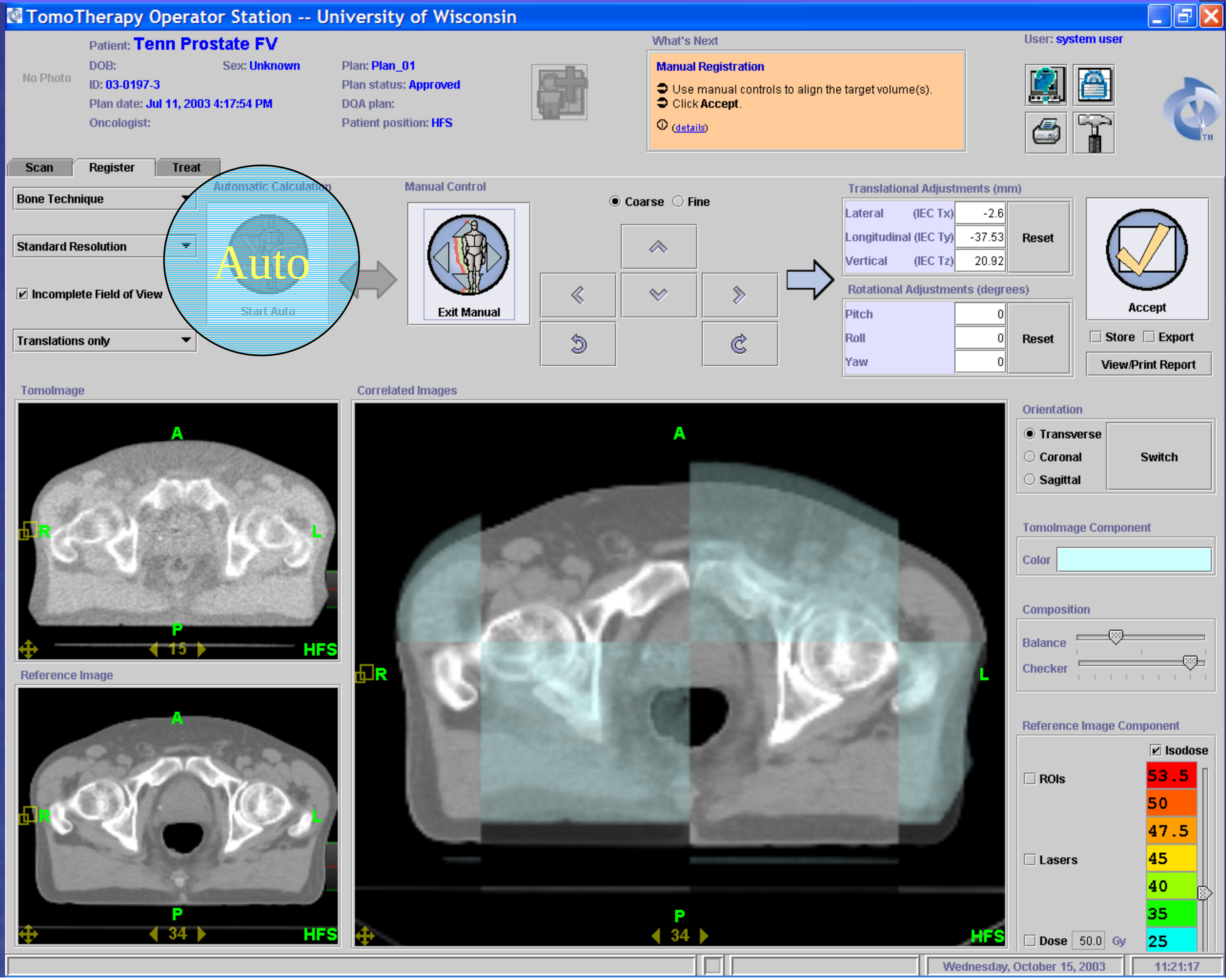




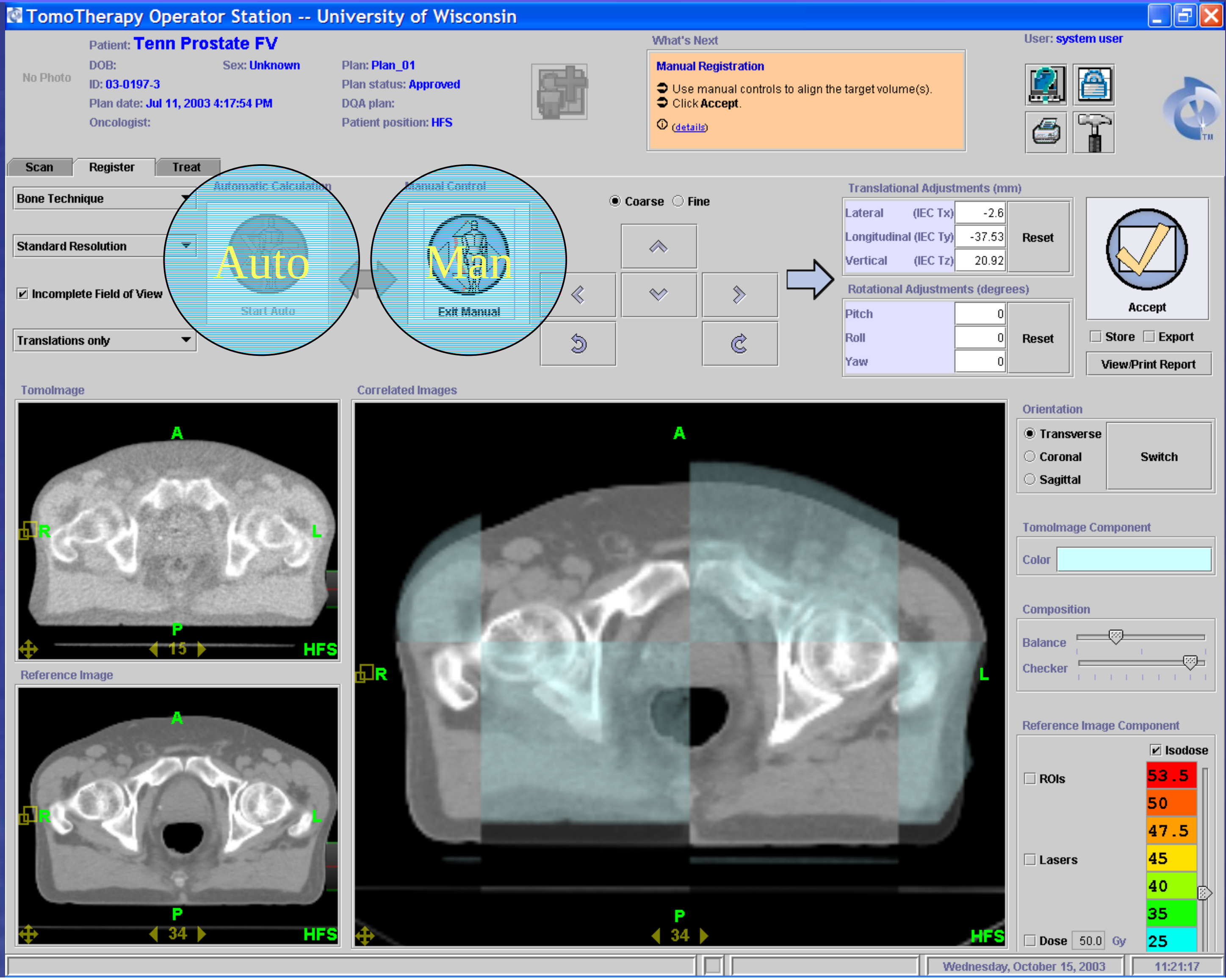
Register Verification CT to Planning CT



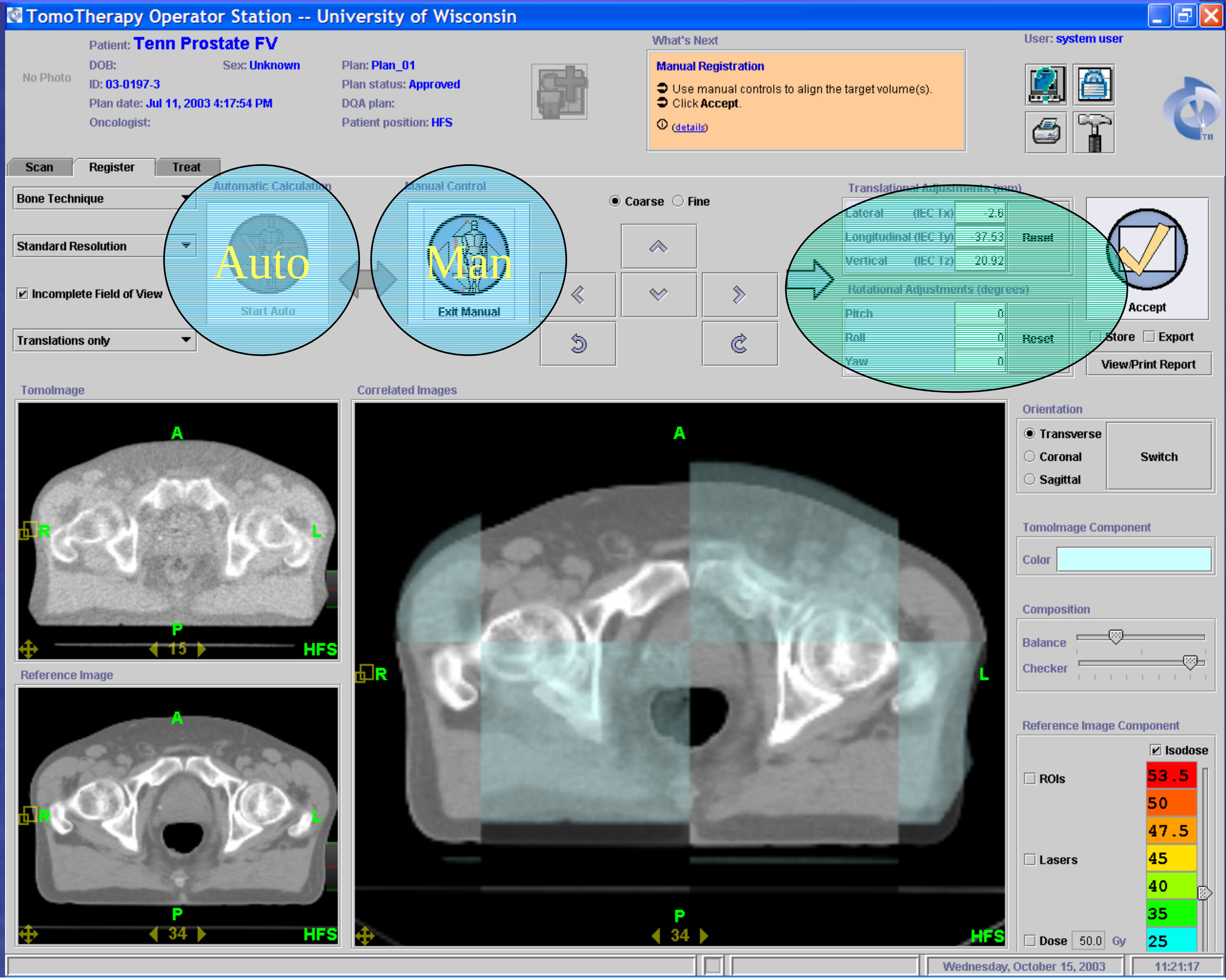
Register Verification CT to Planning CT



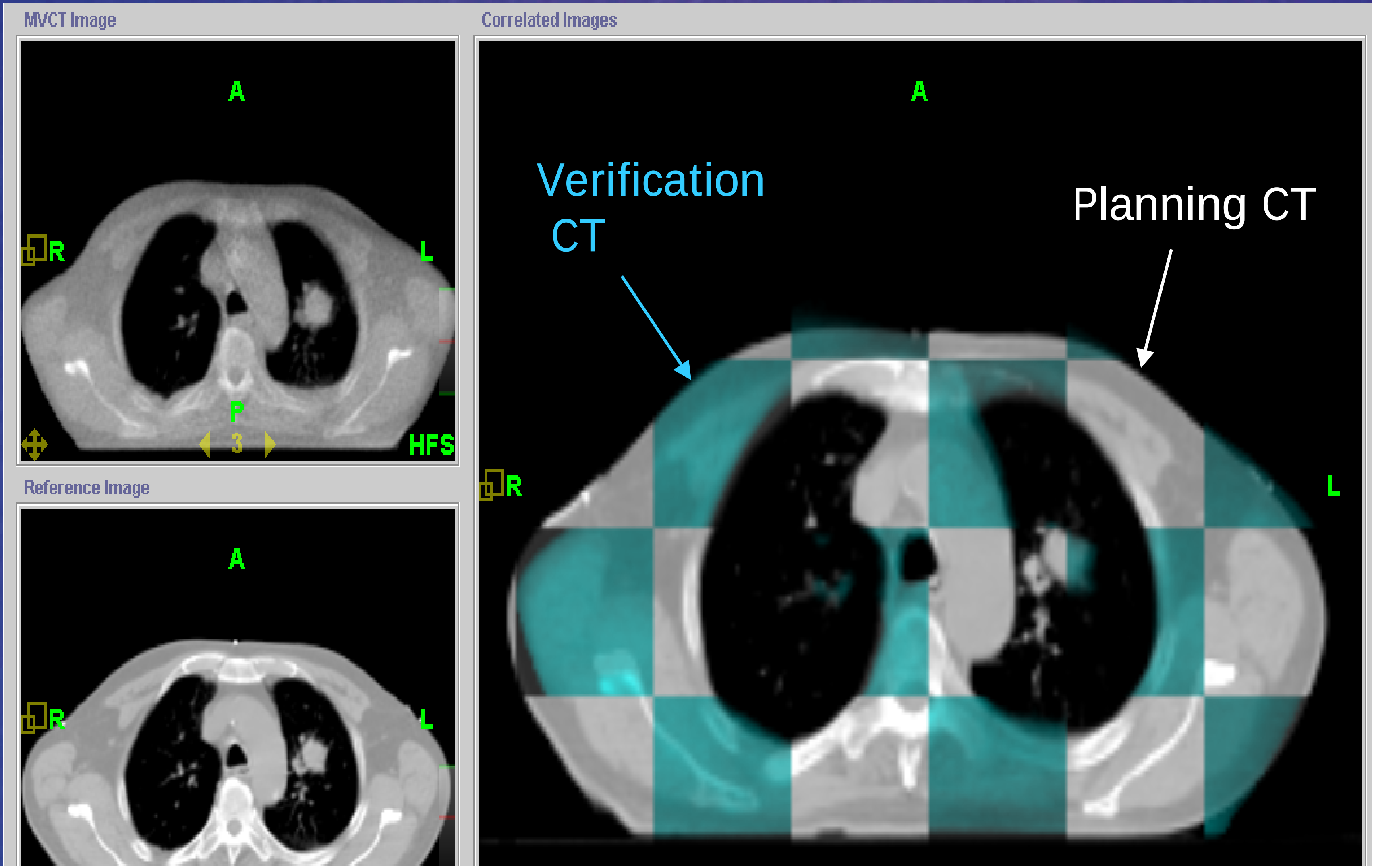
Register Verification CT to Planning CT



Register Verification CT to Planning CT



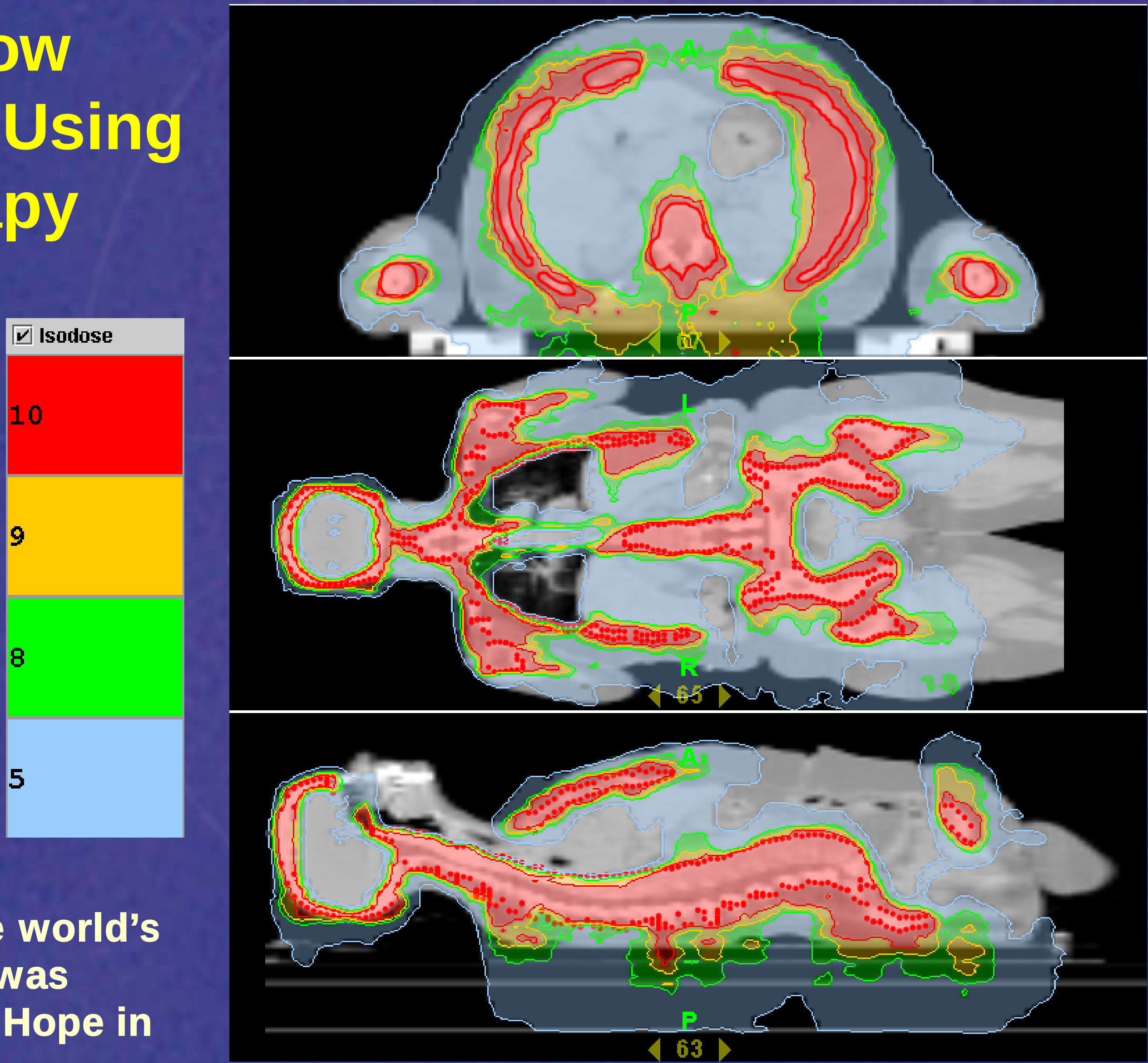
Tomotherapy Registration of Lung Case



Strategy for Conformal Avoidance Radiotherapy

- Use generous treatment volumes.
- Outline normal sensitive tissues and concentrate on avoiding them.
- Use image-guidance to assure that the normal tissues are being avoided.
- Conformal avoidance radiotherapy is the complement of conformal radiotherapy.

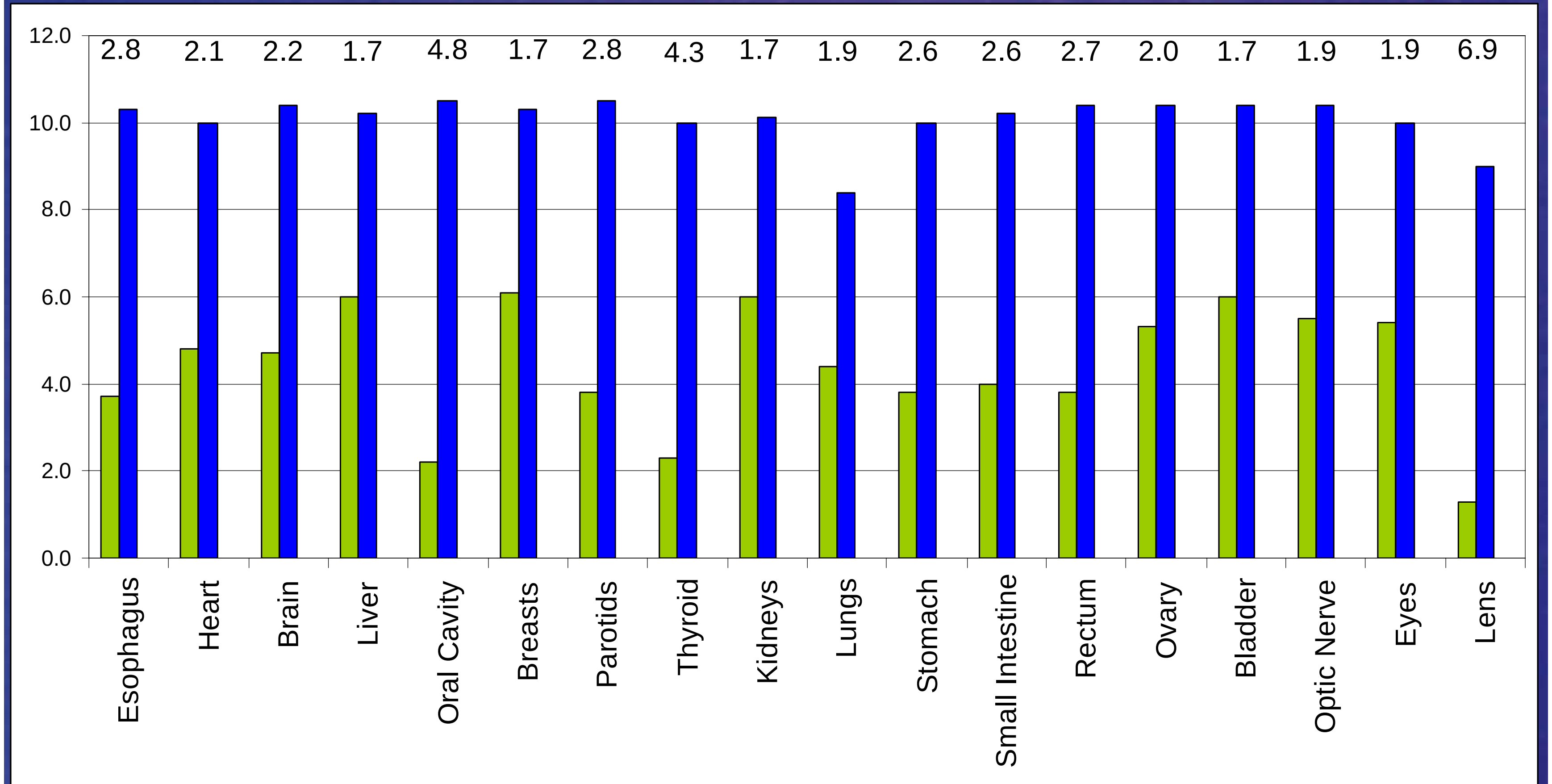
Total Marrow Irradiation Using Tomotherapy



In June 2005, the world's first TMI patient was treated at City of Hope in Los Angeles.

From Dr. An Liu

Total Marrow Irradiation (TMI) vs. Total Body Irradiation (TBI)



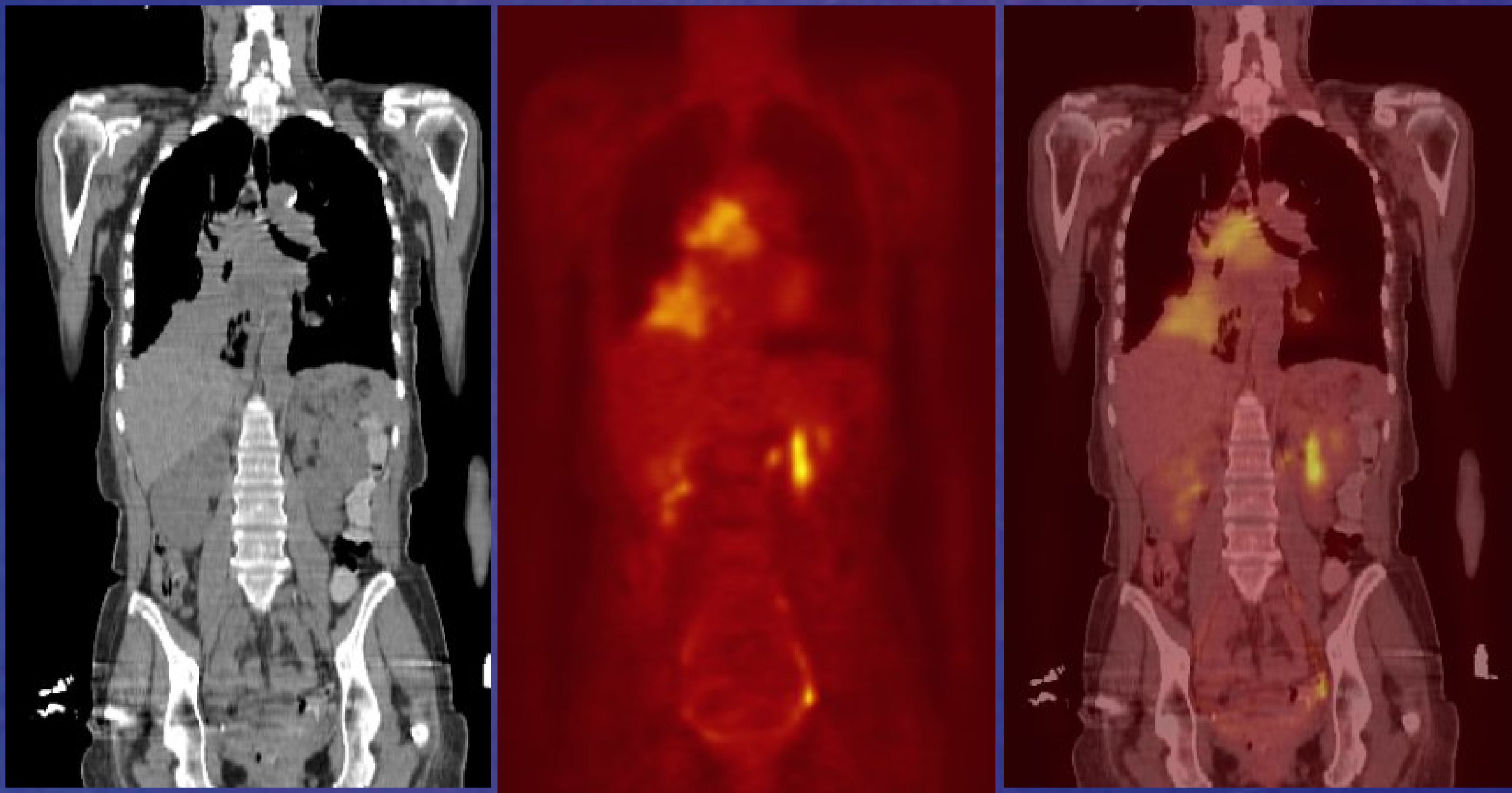
• TMI • TBI

From Dr. An Liu

With Better Avoidance of Normal Tissue Can We Shorten Courses of Therapy?

- In prostate CA, the tumor may repair even better than the normal tissues.
- In lung CA, rapid proliferation reduces the treatment control probability as the treatment is extended in duration.
- Provided better avoidance of sensitive tissues is maintained, fewer fractions of higher dose/fraction will provide both better tumor control <u>and</u> be less expense to deliver.
- Carefulness can be cost effective.

PET/CT will Become the Main Instrument for Radiotherapy Planning



CT PET CT+PET

Image-Guided Radiotherapy of the Future

- Image-based staging of the primary and regional field.
  - Determine hypoxic and highly proliferative regions using bioimaging and paint in higher dose.
  - Conformally avoid sensitive structures in the regional field.
- IMRT with 3-D image verification.
  - Less fraction quantity – greater fraction quality.
  - Adaptive radiotherapy to provide patient-specific QA of the whole course of therapy.

Image-Guided Radiotherapy of the Future (Cont.)

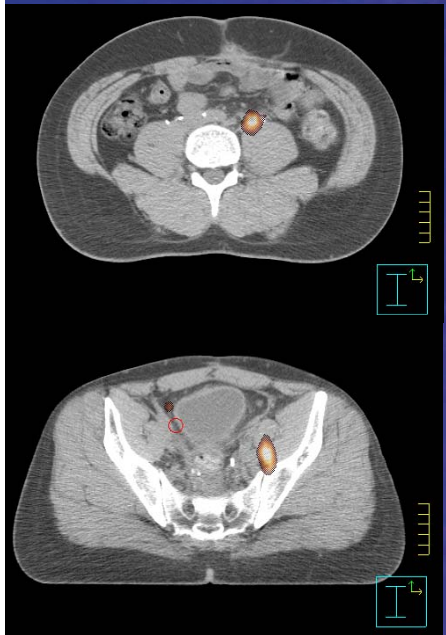
- Image-based monitoring of outcome.
  - e.g., PET scans for regional or metastatic development using a priori information.
- Aggressive treatment of recurrences or distant metastases using conformal avoidance to spare critical structures.
  - Better QA of first treatment will allow safer retreatments.
  - “Weeding the garden” with image-guided radiotherapy and prevent spread with chemotherapy and immunotherapy.

Oligometastases or “Weeding the Garden”

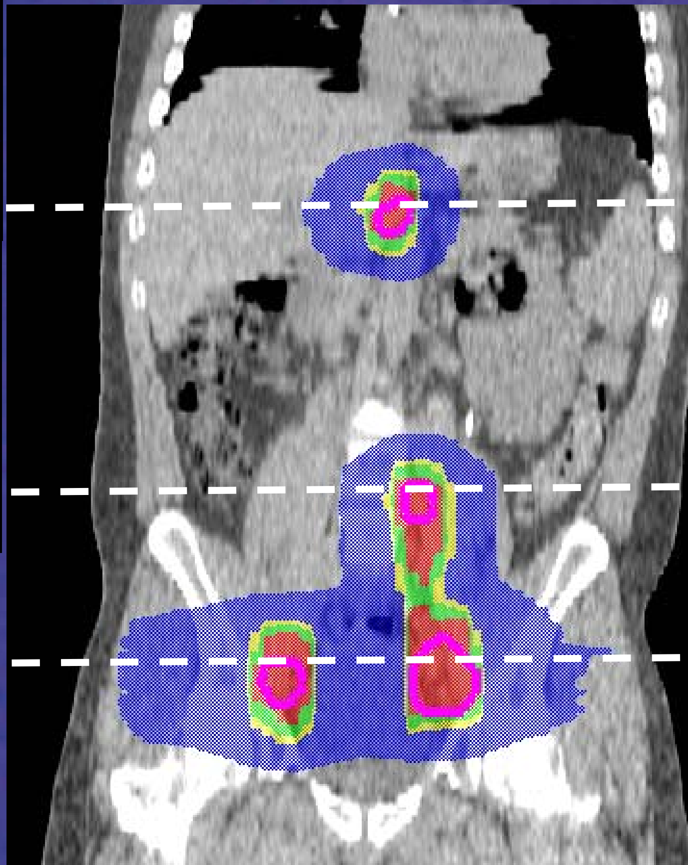
- Following definitive radiotherapy with local control we often have metastatic progression.
- Chemotherapy (analogous to pre-emergent herbicides) may be effective against 100 to 1000 cell tumorlets.
- With PET it is possible to infer the presence of tumorlets with 100,000 to 1,000,000 labeled cells.
- Perform PET scan followups to catch the emergent tumorlets.
- Weed with conformal avoidance hypofractionated radiotherapy before they can seed more metastases.
- Keep careful track of the cumulative dose delivered so the process can be repeated several times if necessary.

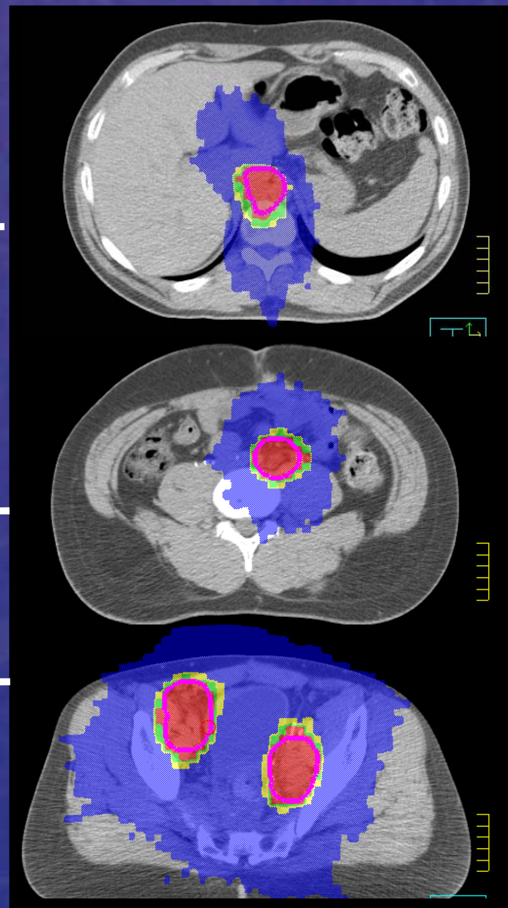
Treating Multiple Metastases Determined From PET Scans

Tomotherapy Treatment Plan



PET-CT Scans

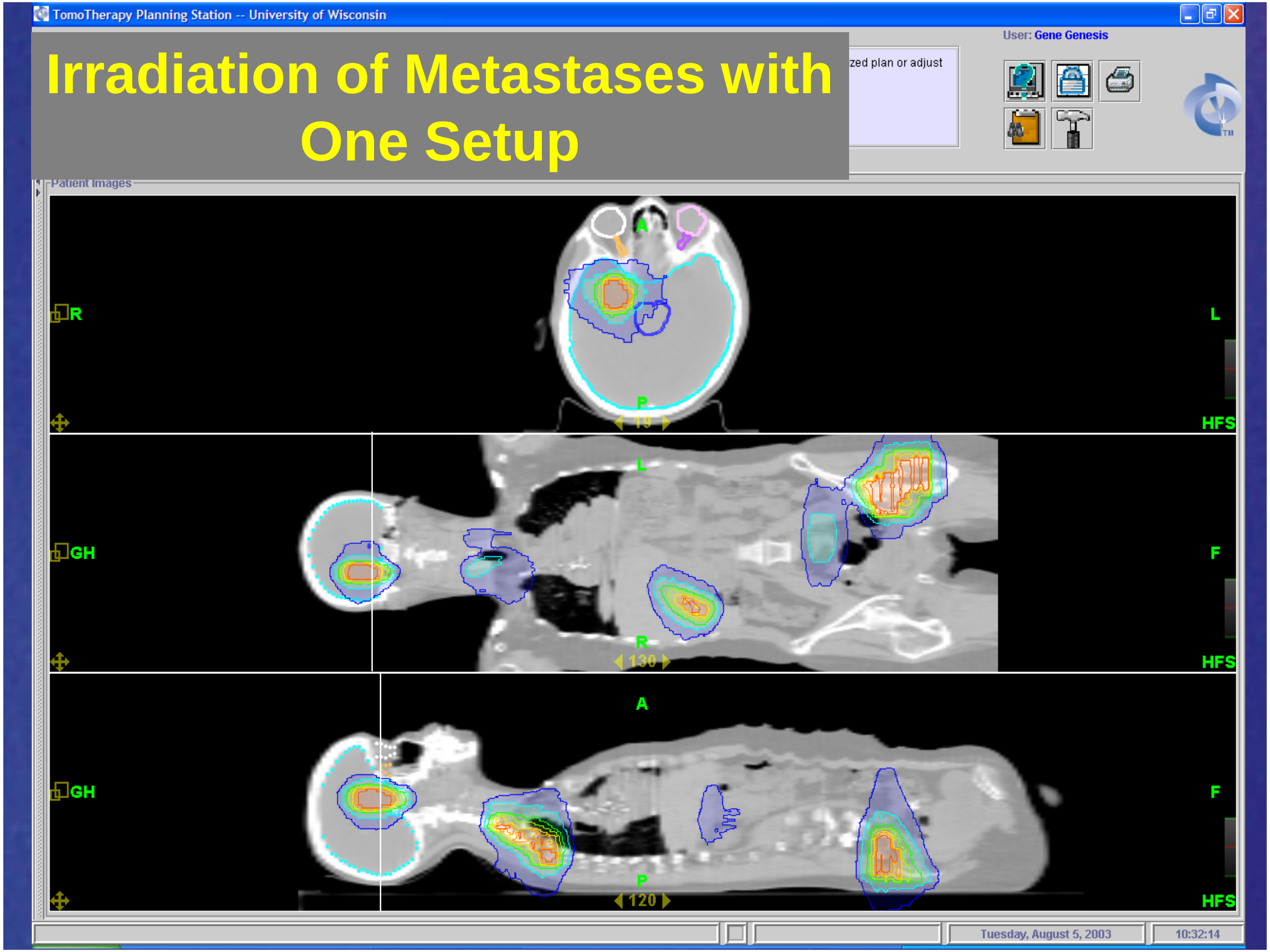


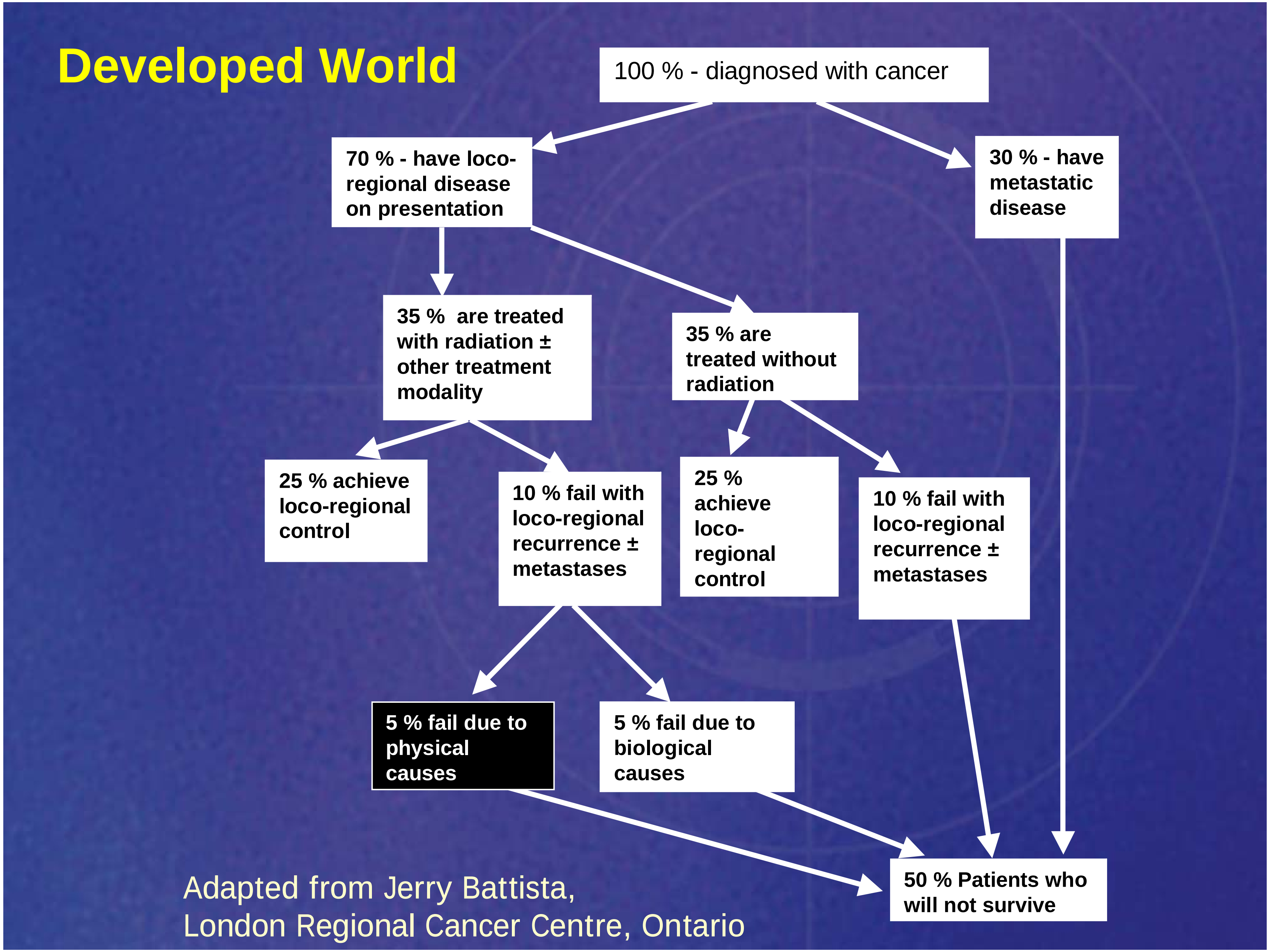


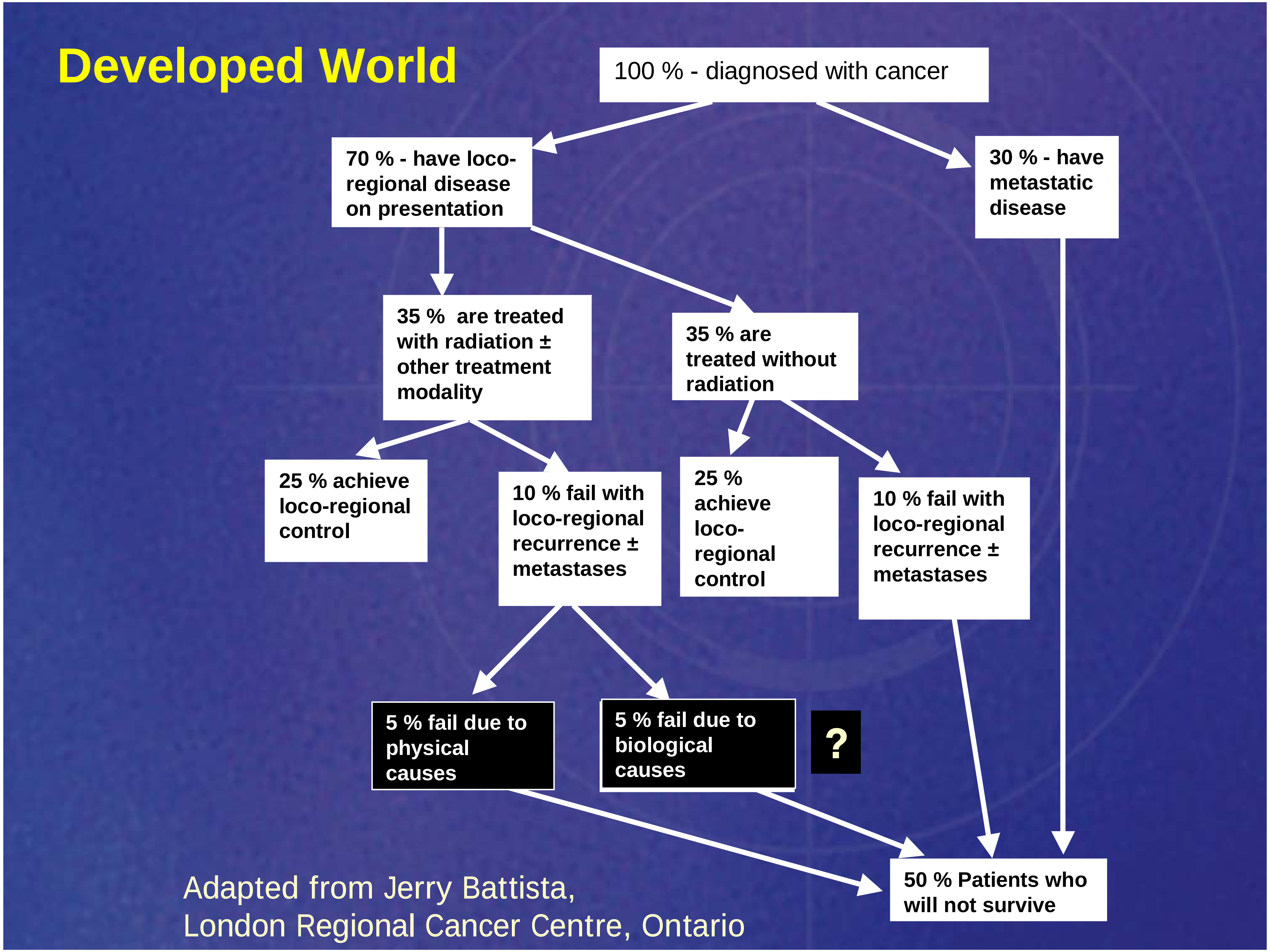
Planned
Using PET-CT

Courtesy of Chet Ramsey, Thompson Cancer Survival Center

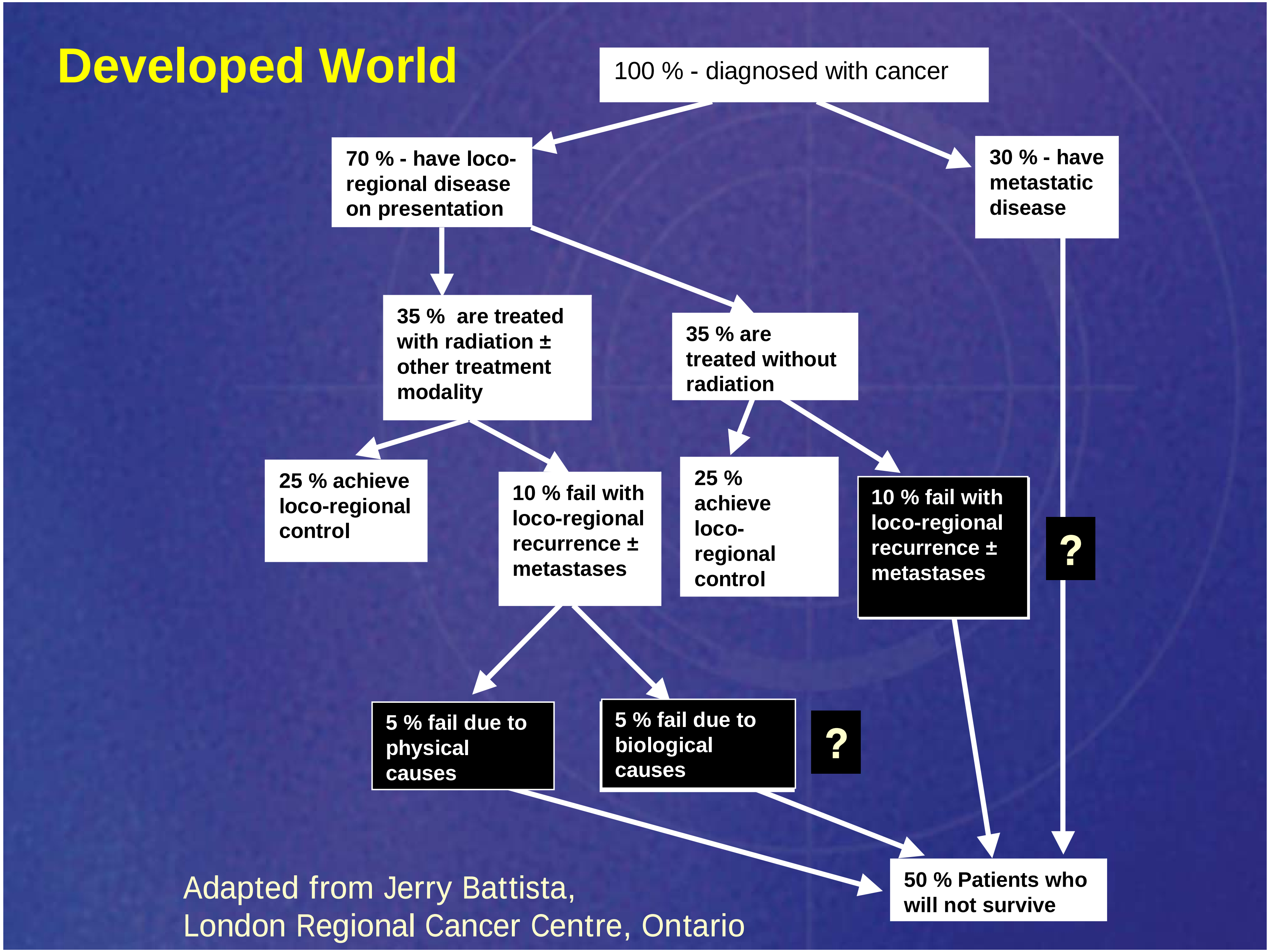
Irradiation of Metastases with One Setup

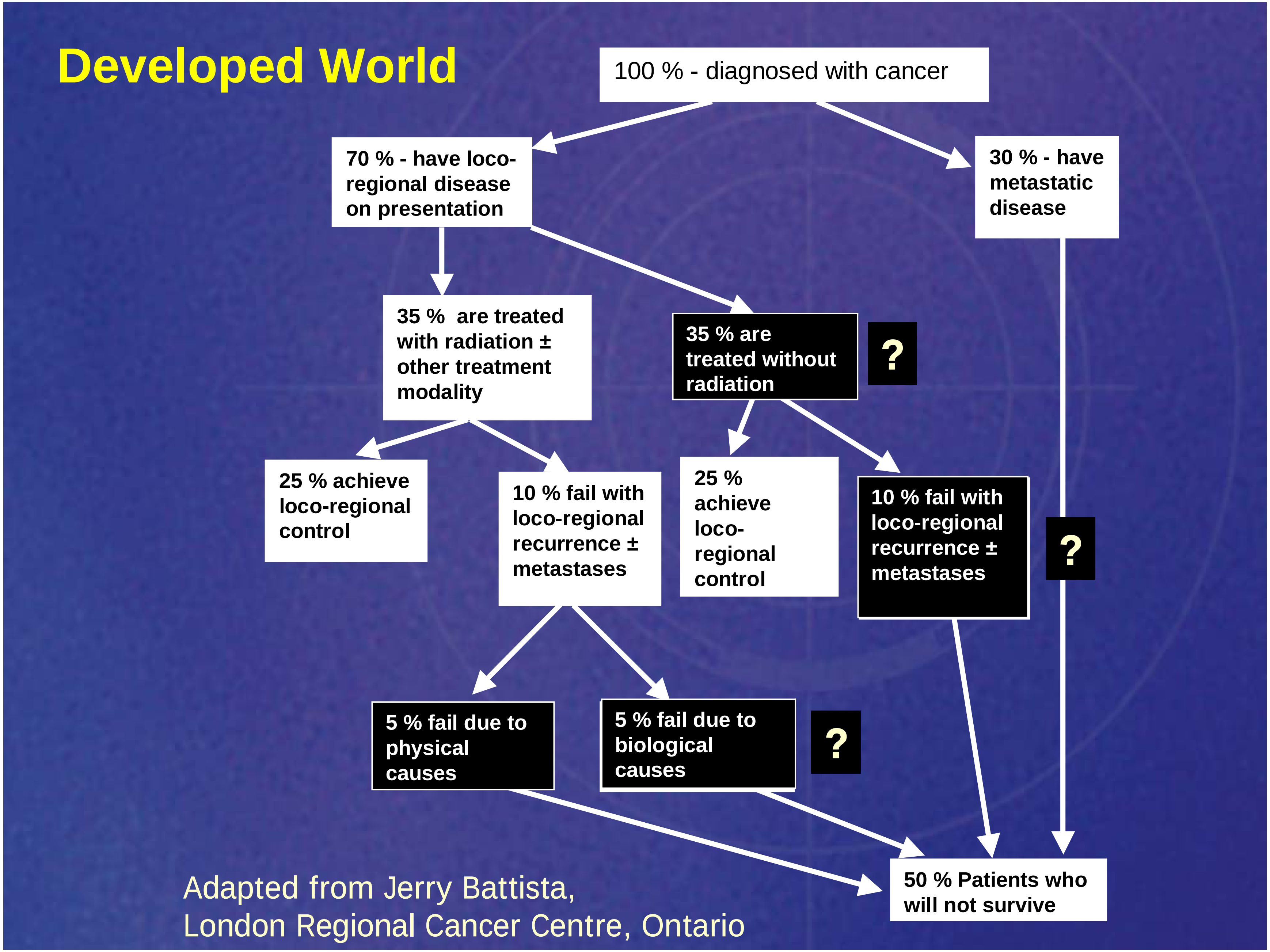



Developed World
100 % - diagnosed with cancer
70 % - have loco-regional disease on presentation
30 % - have metastatic disease
35 % are treated with radiation ± other treatment modality
35 % are treated without radiation
25 % achieve loco-regional control
10 % fail with loco-regional recurrence ± metastases
25 % achieve loco-regional control
10 % fail with loco-regional recurrence ± metastases
5 % fail due to physical causes
5 % fail due to biological causes
50 % Patients who will not survive
Adapted from Jerry Battista,
London Regional Cancer Centre, Ontario

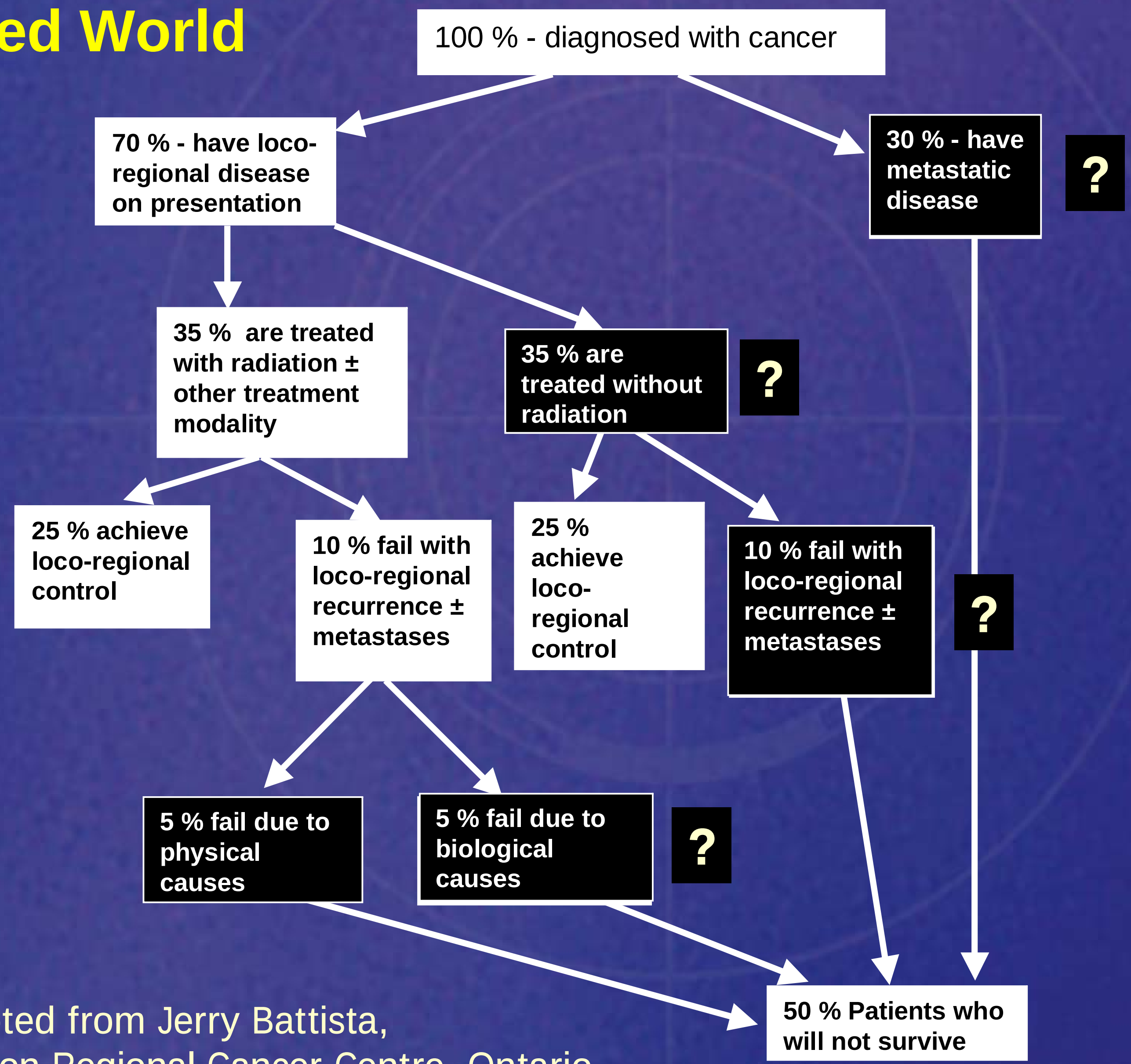


Developed World
100 % - diagnosed with cancer
70 % - have loco-regional disease on presentation
30 % - have metastatic disease
35 % are treated with radiation ± other treatment modality
35 % are treated without radiation
25 % achieve loco-regional control
10 % fail with loco-regional recurrence ± metastases
25 % achieve loco-regional control
10 % fail with loco-regional recurrence ± metastases
5 % fail due to physical causes
5 % fail due to biological causes
?
50 % Patients who will not survive
Adapted from Jerry Battista,
London Regional Cancer Centre, Ontario

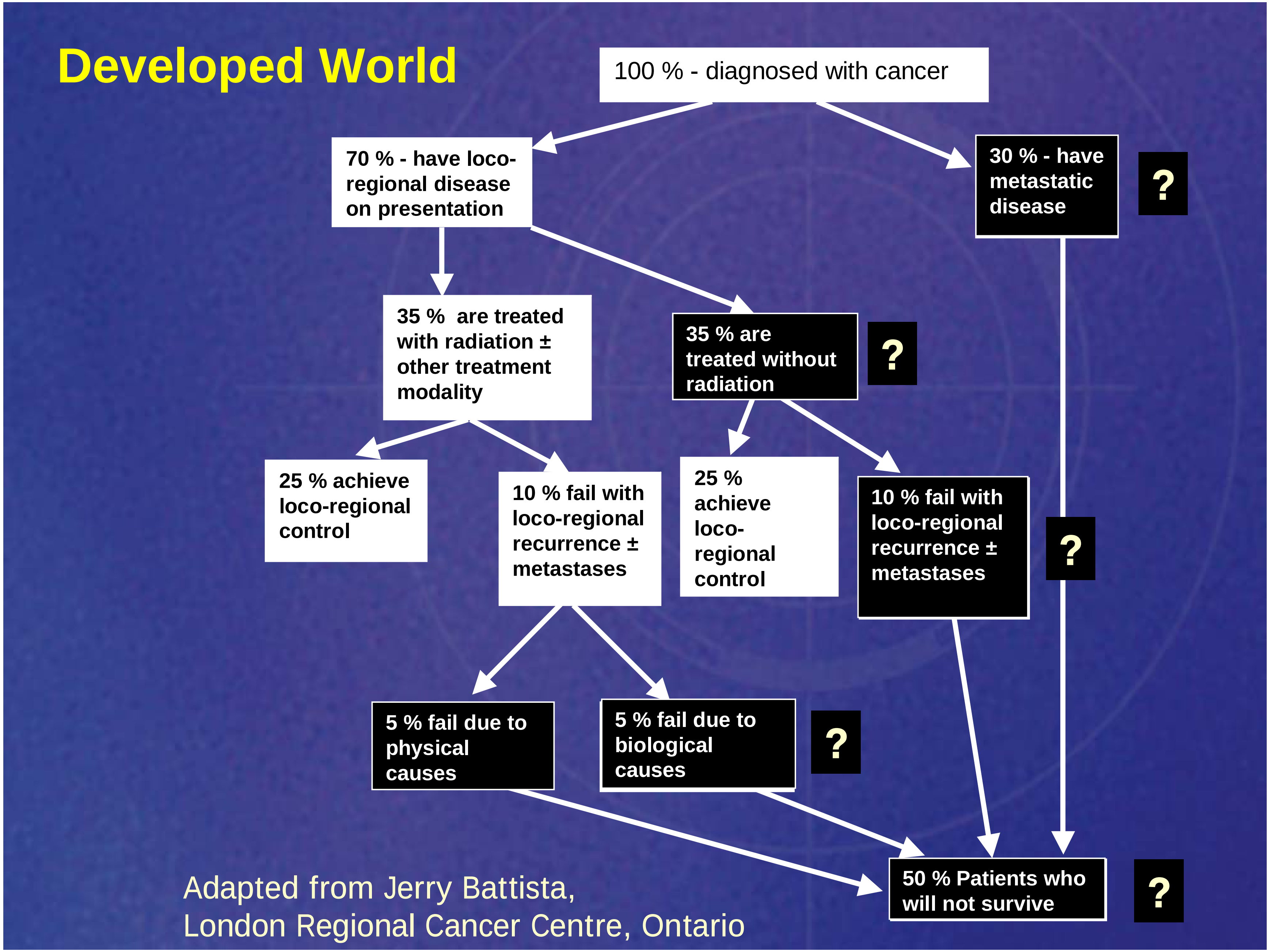

Developed World
100 % - diagnosed with cancer
70 % - have loco-regional disease on presentation
30 % - have metastatic disease
35 % are treated with radiation ± other treatment modality
35 % are treated without radiation
25 % achieve loco-regional control
10 % fail with loco-regional recurrence ± metastases
25 % achieve loco-regional control
10 % fail with loco-regional recurrence ± metastases
?
5 % fail due to physical causes
5 % fail due to biological causes
?
50 % Patients who will not survive
Adapted from Jerry Battista,
London Regional Cancer Centre, Ontario


Developed World
100 % - diagnosed with cancer
70 % - have loco-regional disease on presentation
30 % - have metastatic disease
35 % are treated with radiation ± other treatment modality
35 % are treated without radiation
?
25 % achieve loco-regional control
10 % fail with loco-regional recurrence ± metastases
25 % achieve loco-regional control
10 % fail with loco-regional recurrence ± metastases
?
5 % fail due to physical causes
5 % fail due to biological causes
?
50 % Patients who will not survive
Adapted from Jerry Battista,
London Regional Cancer Centre, Ontario

Developed World



Adapted from Jerry Battista,
London Regional Cancer Centre, Ontario


Developed World
100 % - diagnosed with cancer
70 % - have loco-regional disease on presentation
30 % - have metastatic disease
?
35 % are treated with radiation ± other treatment modality
35 % are treated without radiation
?
25 % achieve loco-regional control
10 % fail with loco-regional recurrence ± metastases
25 % achieve loco-regional control
10 % fail with loco-regional recurrence ± metastases
?
5 % fail due to physical causes
5 % fail due to biological causes
?
50 % Patients who will not survive
?
Adapted from Jerry Battista,
London Regional Cancer Centre, Ontario

Physics is Key to Radiation Therapy

Economic Forces Driving Our Field

- Cost containment.
- Demand for higher quality done more easily.
- In the developed world, radiotherapy is about 40 times more medical physics intensive than radiology.
- Expect that radiotherapy will be economically driven to be more like radiology where medical physicists are mainly quality assurance experts and radiation oncologists ultra-specialized.
- Much of that QA will be imaging related.
- Like medicine as a whole, radiotherapy will specialize around disease sites.

Change from Individual QA to QA of Automated Processes

- Machine QA processes will be built in to the machines.
- QA processes for individual patients will be generated automatically.
- Physicists will be responsible for checking that the automated processes are performing correctly.
- Role will become more like that of a physicist working in radiology.

Future of Radiotherapy Physics

- For the next 20 years, in the developed world, there will be a steady increase in therapy medical physicists employed.
- The end of the baby boom and increased automation will end the rapid growth in the developed world.
- Radiotherapy physicists will require more training in imaging.
- Like radiology physicists, radiotherapy physicists will become QA experts.

Conclusions

- Imaging and computer science is increasing the capability but also the complexity of radiotherapy.
- Radiotherapy is achieving better sparing of normal tissues.
- Radiotherapy will be used for more indications.
- More therapy physicists are needed with increased knowledge of imaging and QA.