The Future of Radiotherapy

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Financial Disclosure

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

Assembly Floor

www.tomotherapy.com

TomoTherapy's 58,000 sqft. Madison WI Facility

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

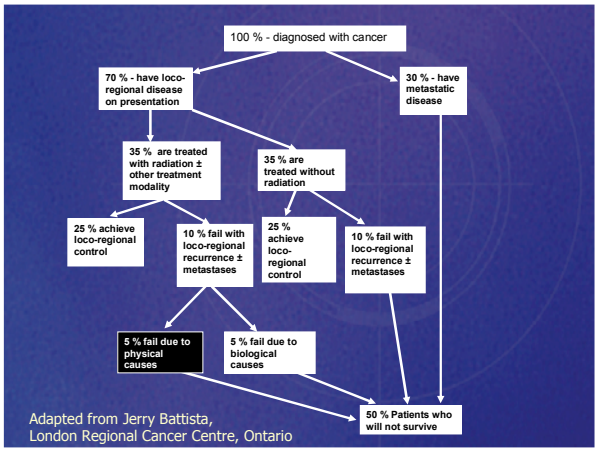
Telegraph from E.A McCulloch to H. Johns 1962

"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 in the U.S., it would surely be considered our most important drug.



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	500 to 3,000

ASCO 1992
*Ontario Ministry of Health, Canada
**Perez IMRT, assuming 10 years gained

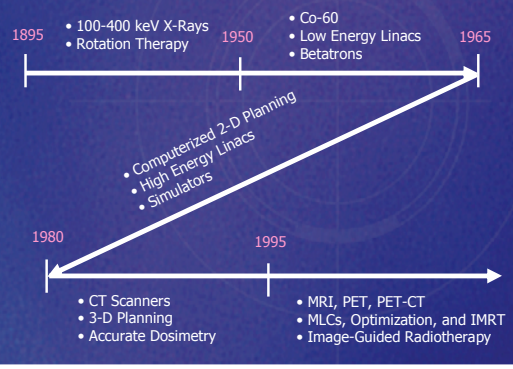
Adapted from Jerry Battista, London Regional Cancer Centre, Ontario

More Costs in Perspective

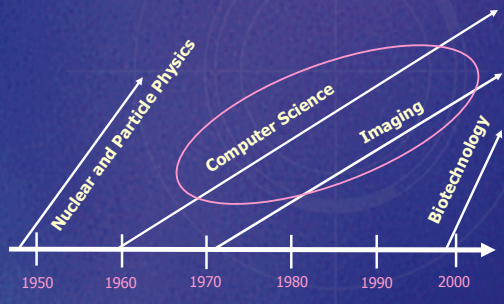
PROCEDURE	COST ($/yr of life saved)
Mine Safety	1,000,000
Radiation Protection	16,000
Auto Safety (Air Bags)	8,000
Traffic Barrier (Median)	5,700
Radiation Therapy	350 to 1,800
Feeding the Poor	125

Adapted from Jerry Battista, London Regional Cancer Centre, Ontario

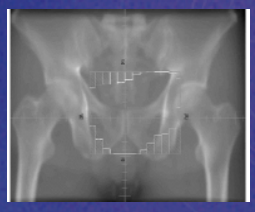
Radiotherapy Timeline



Scientific Forces Behind Our Field

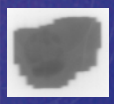


2D Treatment Planning



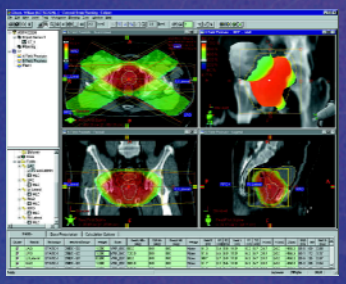
2D **simulation films** or computer-generated **"DRRs"**

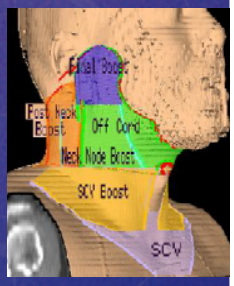
Tumors are hard to see in 2D images, especially port films, and you must rely on "landmarks."



Treatment machine **port films**

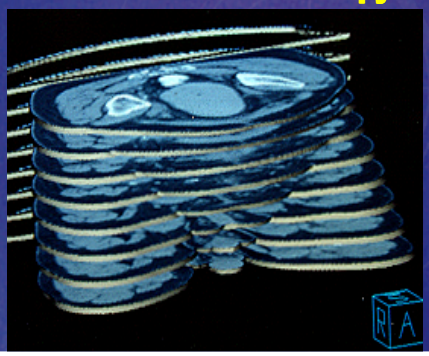
3-D Treatment Planning



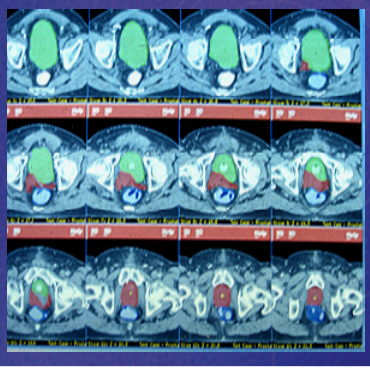


Planning workstations use 3D imaging and accurate dose calculations to allow highly "conformal" treatment planning.

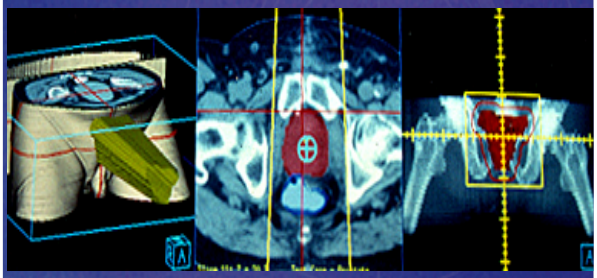
CT Slices Forming a Patient Representation is the Modern Basis for Radiotherapy



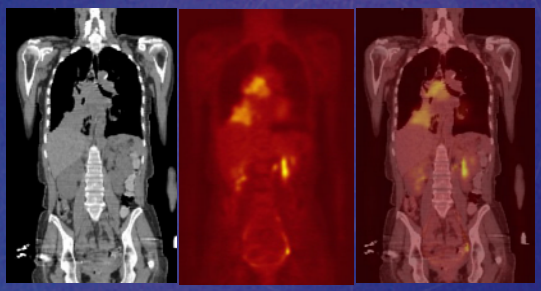
The Tumor and Sensitive Structures are Outlined



The Beam Directions are Chosen



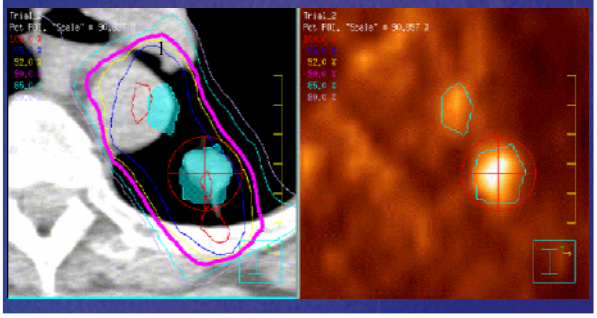
PET/CT will Become the Main Instrument for Radiotherapy Planning



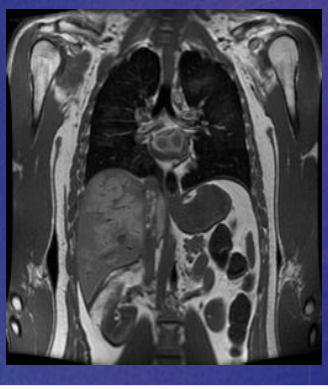
CT PET CT+PET

Sometimes CT Cannot Provide The Target Location

CT: No Target Seen PET Image

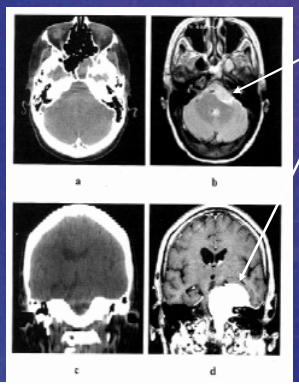


Use of MRI with Grow



Abdominal MRI

Comparison Between CT and MRI

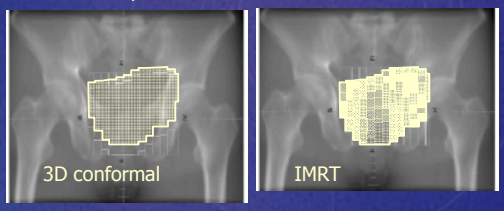


Tumor seen only on MRI.

a) Axial CT
b) Axial MRI
c) Coronal CT
d) Coronal MRI

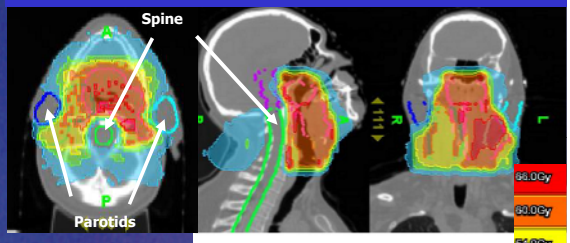
Optimization and Intensity-Modulated Radiotherapy (IMRT)

- *Let the computer do the work…*



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

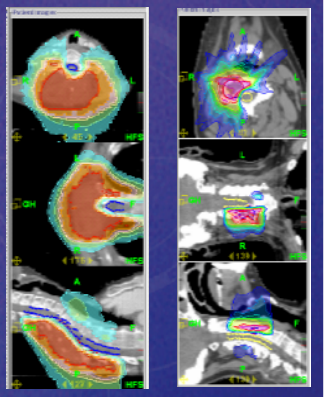
Tomotherapy IMRT Plan



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

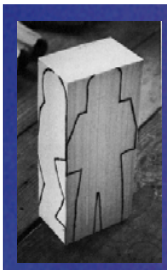
Re-Treatments

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



Patients courtesy of UAB

Dose Sculpting



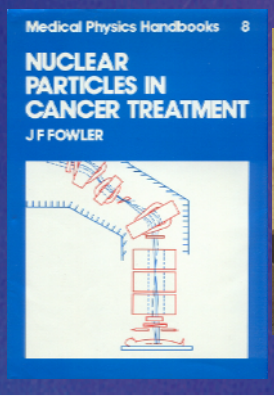
2-D Planning

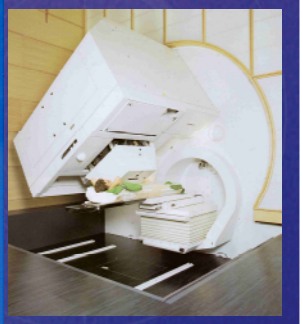
3-D Conformal

IMRT

Courtesy of J. Schreiner Kingston Regional Cancer Centre, Ontario

Protons and Heavy ("Light") Ions

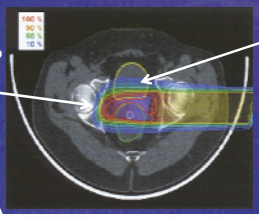




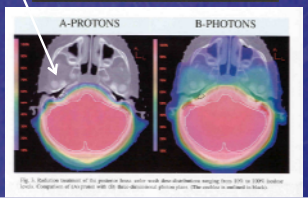
PSI Switzerland

Will the Long Term Future Be Protons?

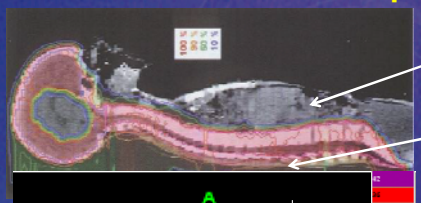
Protons stop so integral dose is less.



Not so great lateral penumbra.



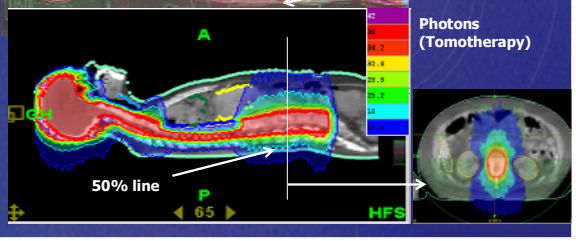
Dose Distribution Comparison



Protons

Low integral Dose.

90% line



Photons (Tomotherapy)

50% line

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.

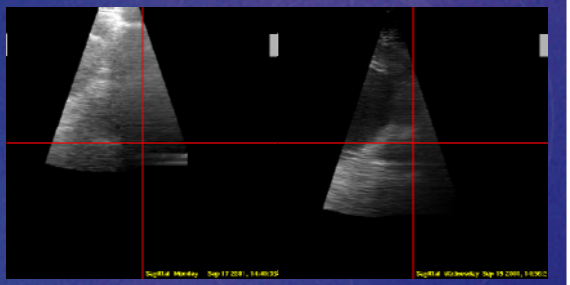
Setup Alignment with Ultrasound

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

Using Z-Med'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

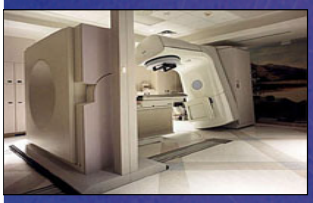
CT in the Treatment Room

First CT

Then Treat

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

CT in Treatment Room

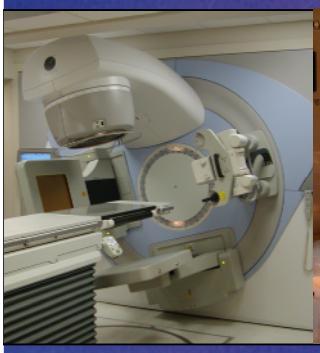


Siemens Primatom "CT on Rails"

GE CT + Varian Linac

From Tim Holmes, St. Agnes Hospital

Cone Beam Imaging

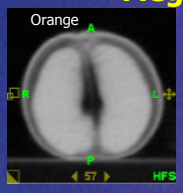


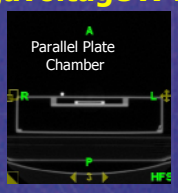
Elekta Synergy

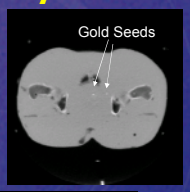
Varian Trilogy

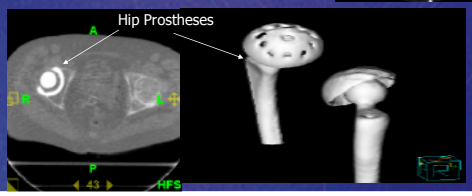
Helical Tomotherapy

Tomotherapy Scanning With Megavoltage X-Rays

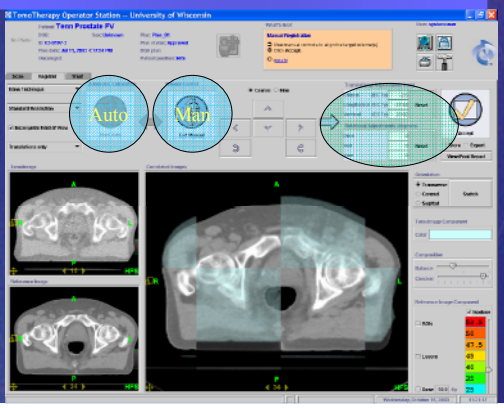




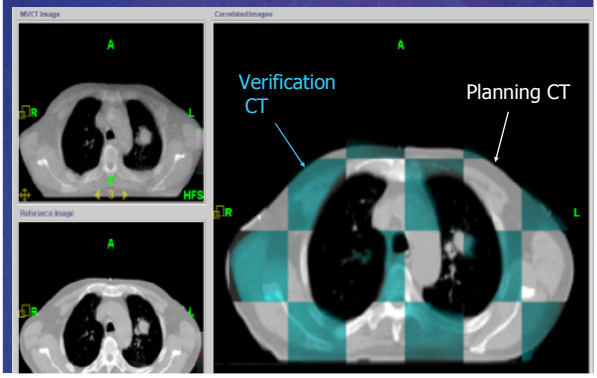




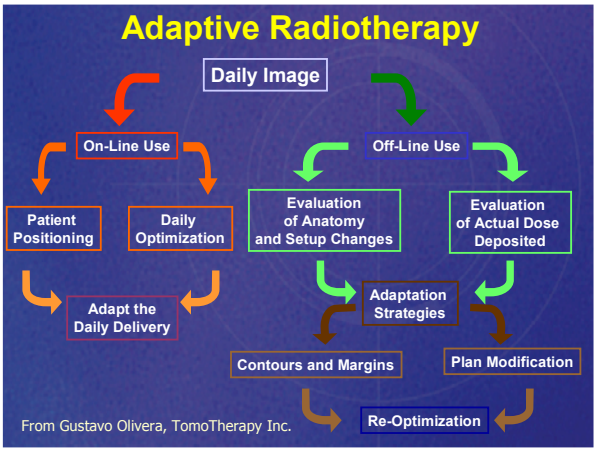
Register Verification CT to Planning CT



Tomotherapy Registration of Lung Case



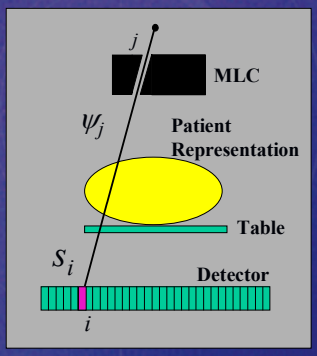
Adaptive Radiotherapy



From Gustavo Olivera, TomoTherapy Inc.

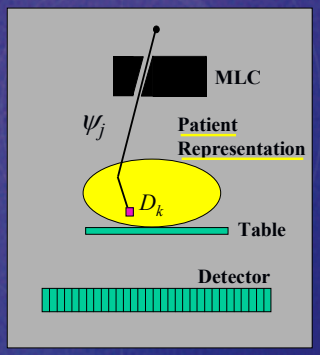
Theory of Dose Reconstruction

The leaf *j* produces a beam intensity ψ_j which is detected after the patient in detector element S_i .

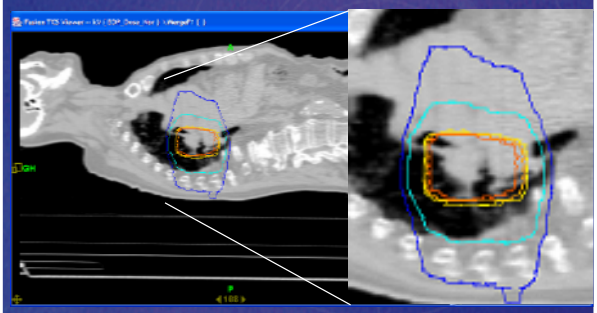


Theory of Dose Reconstruction

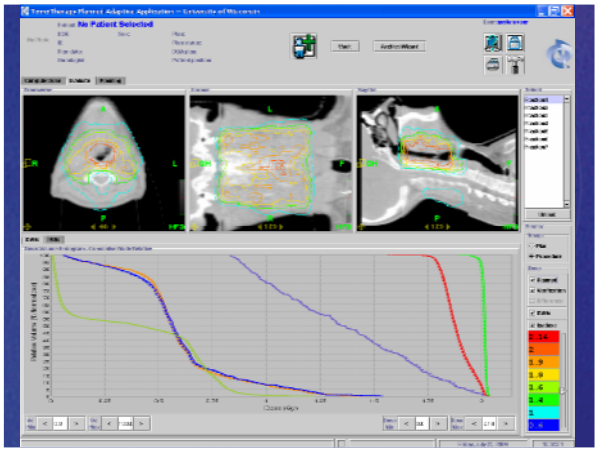
Using the same dose calculation algorithm used for planning, the beam intensity ψ_j is used to compute the dose in volume element D_k .

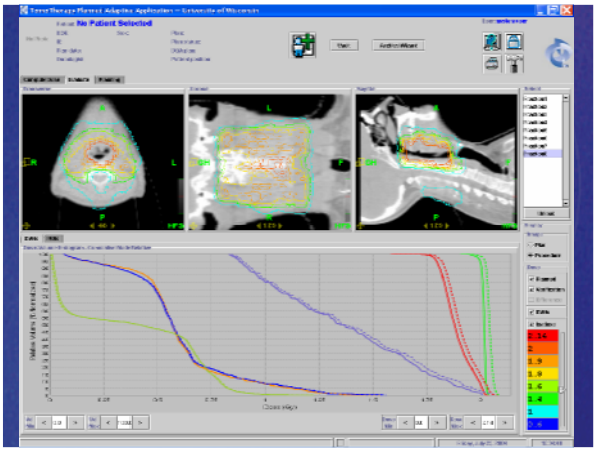


Verifying the Dose Delivered



Planned ———
Actual - - - -



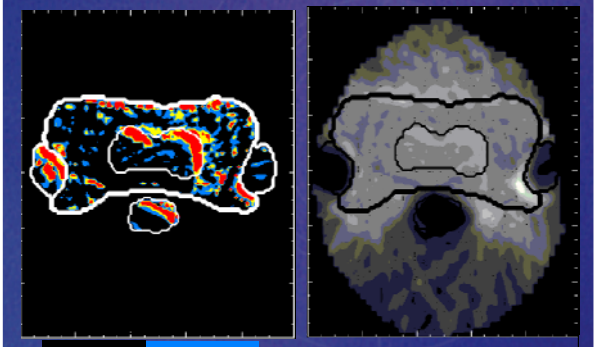


PET-CT for In-Vivo Dosimetry

Brahme et al 2003

Image of Regret

Adapted Dose Distribution

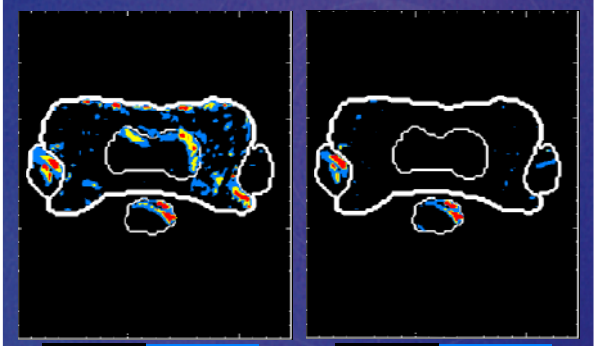


0 to 3 mm(%) | 3 to 6 mm(%)
6 to 9 mm(%) | 9 to 12 mm(%)

Dose to deliver to correct regret.

Incorrect +Perfect

Incorrect +Corrected



0 to 3 mm(%) | 3 to 6 mm(%)
6 to 9 mm(%) | 9 to 12 mm(%)

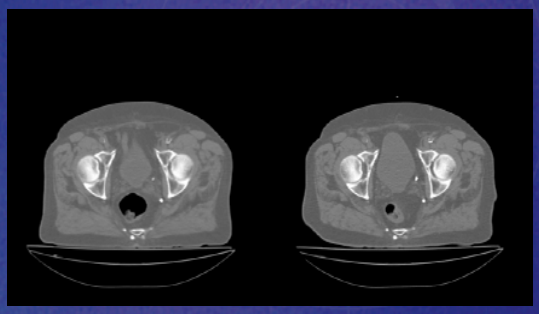
0 to 3 mm(%) | 3 to 6 mm(%)
6 to 9 mm(%) | 9 to 12 mm(%)

Deformable Registration Will Be a Foundation Technology for Radiotherapy and Radiology

- Deformable registration maps one 3-D distribution to another.
- Enabling technology for use of 4-D imaging.
- Allows anatomy and/or dose to be combined onto one time point to account for motion.
- Makes atlas-based auto-contouring possible.
- Enables longitudinal comparison of anatomy for diagnosis, treatment progress and outcome studies.

Deformable Registration

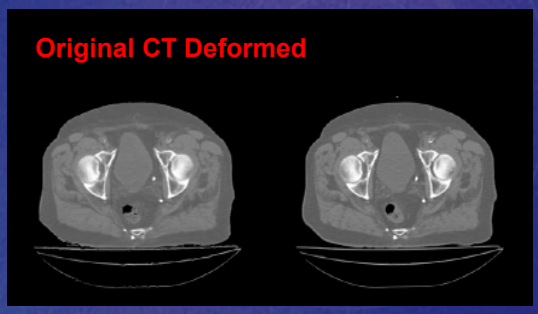
CT Fraction 1 CT Fraction 9



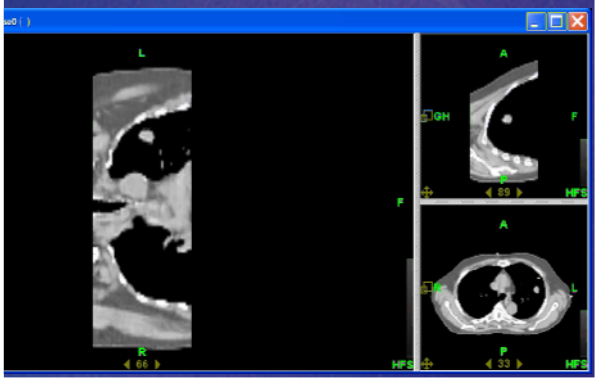
Deformable Registration

CT Fraction 1 CT Fraction 9

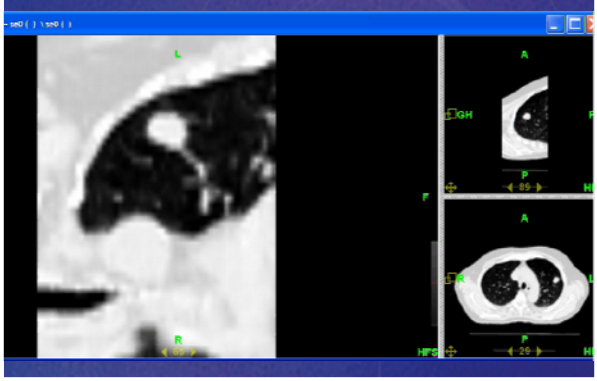
Original CT Deformed

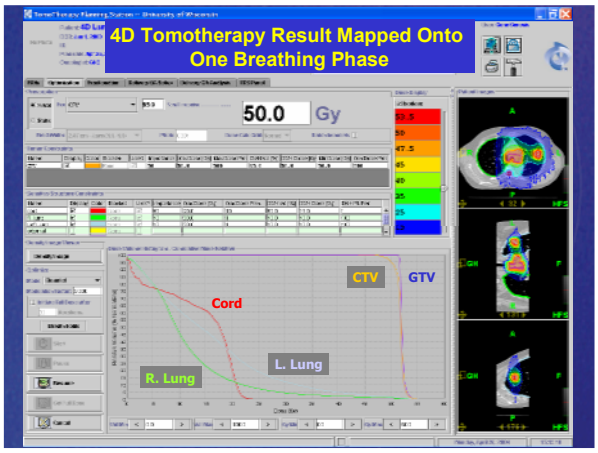


4-D CT Scan



4D CT Scan with Deformation Vectors





Indications for Conformal Avoidance

- The tumor volume may not be visible using 3-D imaging.
- There may be uncertainty in defining the clinical margins.
- There may be suspected regional/nodal involvement.
- The margin to account for setup variation or organ motion may be uncertain.
- The target dose is limited by normal sensitive tissue.

Strategy for Conformal Avoidance Radiotherapy

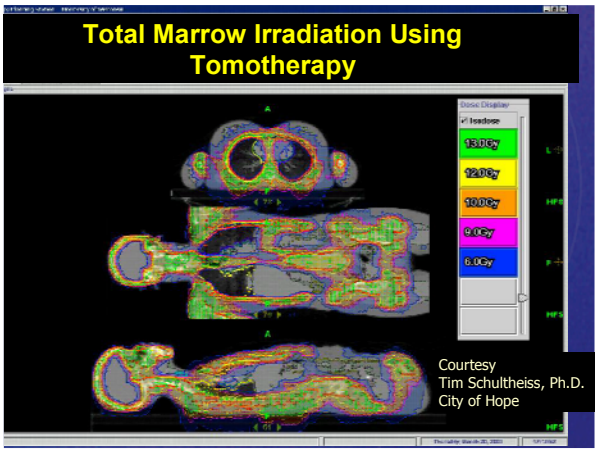
- Use generous treatment volumes.
- Outline normal sensitive tissues and concentrate on avoiding them.
- Use image-guidance to assure that the normal tissues are being avoided.
- Conformal avoidance radiotherapy is the complement of conformal radiotherapy.

Continuum Between Conformal Tx and Conformal Avoidance Tx

Conformal Tx — **Know where tumor is but will not harm sensitive tissue.**

Conformal Avoidance Tx — **Don't really know where tumor is and may harm sensitive tissue.**

Total Marrow Irradiation Using Tomotherapy

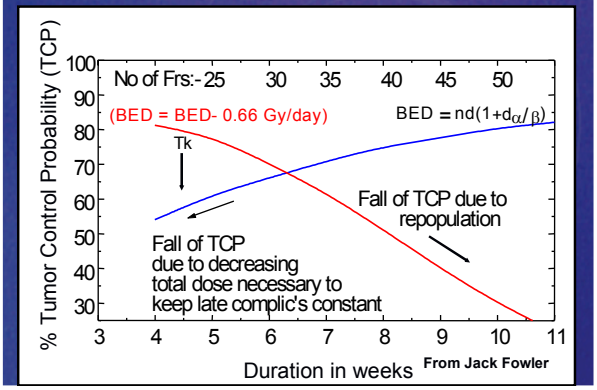


Courtesy
Tim Schultheiss, Ph.D.
City of Hope

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 and be less expense to deliver.
- Carefulness can be cost effective.

Optimizing Tumor Control



Hypofractionation of Lung CA May Yield Much Better Results

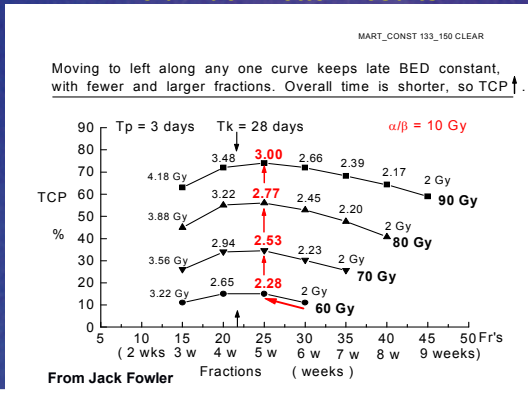


Image-Guided Radiotherapy of the Future

- 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.

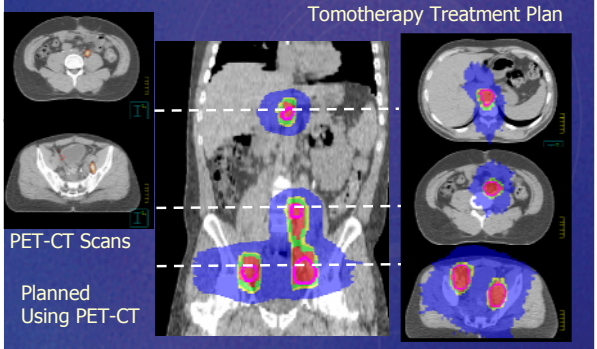
Image-Guided Radiotherapy of the Future (Cont.)

- 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.

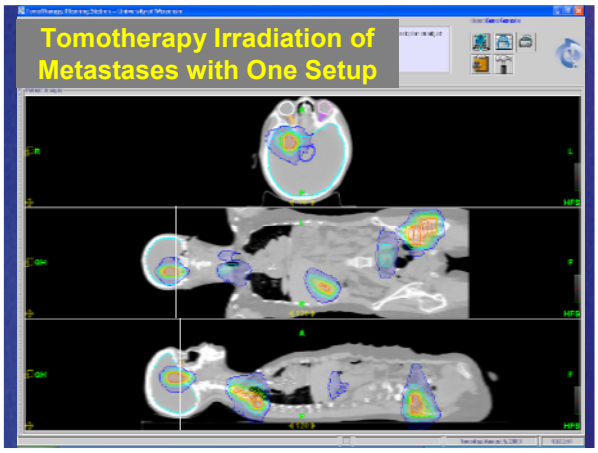
Oligometastases or "Weeding the Garden"

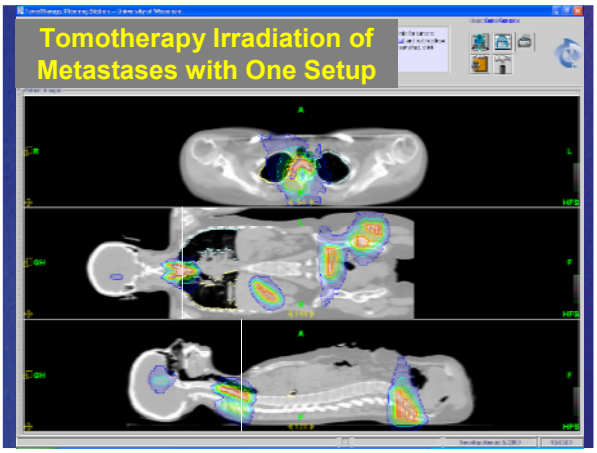
- Following definitive radiotherapy with local control we often have metastatic progression.
- Chemotherapy (analogous to pre-emergent herbicides) may be effective against 100 to 1000 cell tumorlets.
- With PET it is possible to infer the presence of tumorlets with 100,000 to 1,000,000 labeled cells.
- 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



Courtesy of Chet Ramsey, Thompson Cancer Survival Center


Tomotherapy Irradiation of
Metastases with One Setup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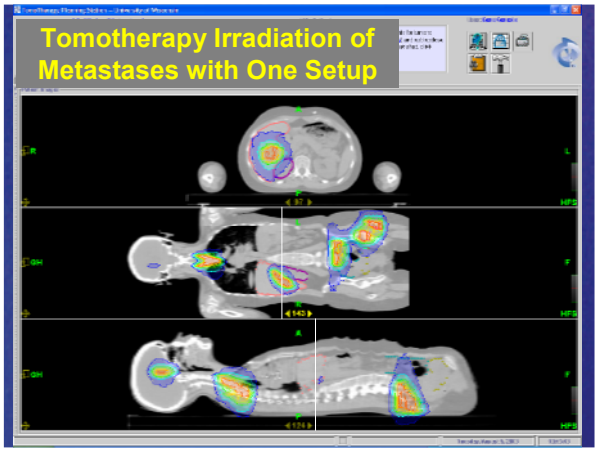
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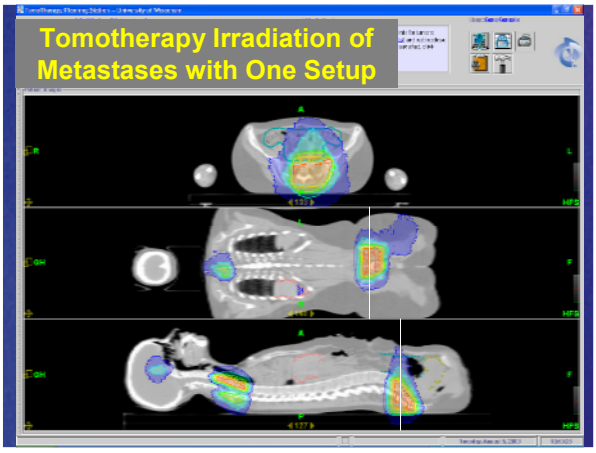
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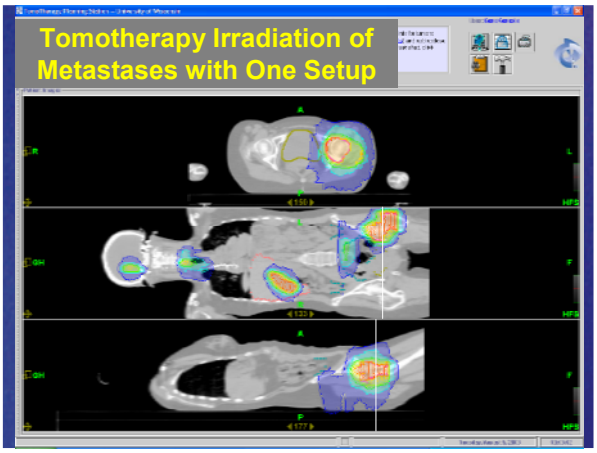


What About Targeted Therapies?

- Targeted therapies like radioimmunotherapy and BNCT will unlikely be stand-alone therapies.
- Getting an target agent to all of the tumor cells is like committing genocide with letter bombs.
- Before an agent can be a successful therapeutically, it should prove itself a fantastic diagnostic contrast agent.
- NM404 is an example of a "diapeutic" agent.
- Targeted therapies will be useful in conjunction with conventional radiotherapy.

Economic Forces Driving Our Field

- Cost containment.
- Demand for higher quality done more easily.
- 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.
- Much of that QA will be imaging related.
- Like radiology, radiotherapy will specialize around disease sites.

Year 2014 - Merging of Technologies

	Tomotherapy	Conventional
High Quality Fast Scanning	Faster rotation times for scanning.	Faster rotation will demand a ring gantry.
	Multrow detectors using CT electronics.	Limited field cone beam and a translating couch.
High Quality Fast Delivery	Faster delivery times will lead to larger fields and higher outputs.	Faster delivery times will lead to faster leaves and higher linac outputs.
	Non-uniform gantry and couch velocities.	More treatment directions.

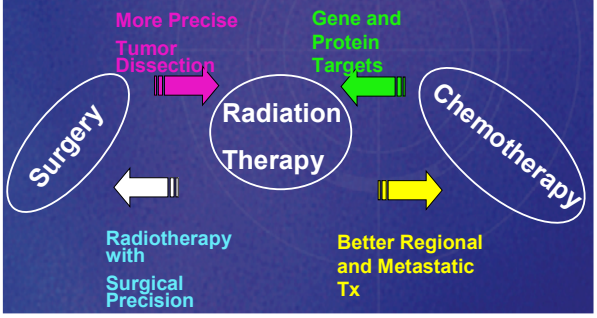
Change from Individual QA to QA of Automated Processes

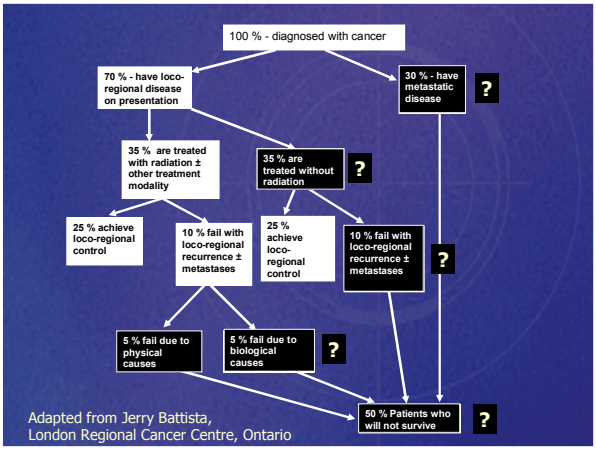
- Machine QA processes will be built in to the machines.
- QA processes for individual patients will be generated automatically.
- Physicists will be responsible for checking that the automated processes are performing correctly.
- Role will become more like that of a physicist working in radiology.

Radiotherapy and Radiology Futures

- Radiotherapy will employ fewer medical physicists in the future.
- Radiology procedures will be done more and more by other disciplines, e.g. cardiologists, neurologists, oncologists.
- Radiotherapy physicists will require more training in imaging.
- Like radiology physicists, radiotherapy physicists will become QA experts.

Shifting Balance Between Rival Treatment Technologies





Be a Booster for Our Field !

- Remind your colleagues that radiotherapy physics is the basic science behind radiotherapy.
- Radiation therapy has far better quality control as compared to surgery or chemotherapy.
- Question why radiotherapy research (including molecular radiation bioeffect) accounts for less than 3% of cancer research.
- Support research and innovation in our field.
- Encourage your colleagues to partake in prospective random clinical trials.
- Educate your community to be well informed about radiation and radiotherapy.
- Don't be second class citizens in the cancer establishment.
- Don't be apologetic about our field, it is currently vital to cancer management and will continue to improve.