HEALTHY ARIZONA WORKSITES PROGRAM (HAWP) PRESENTS:

RADIATION THERAPY: WHAT IS IT AND HOW IS COVID-19 IMPACTING CANCER CARE?

Presented by:

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RADIATION THERAPY: WHAT IS IT AND HOW IS COVID-19 IS IMPACTING CANCER CARE?

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Phoenix
12/15/2020

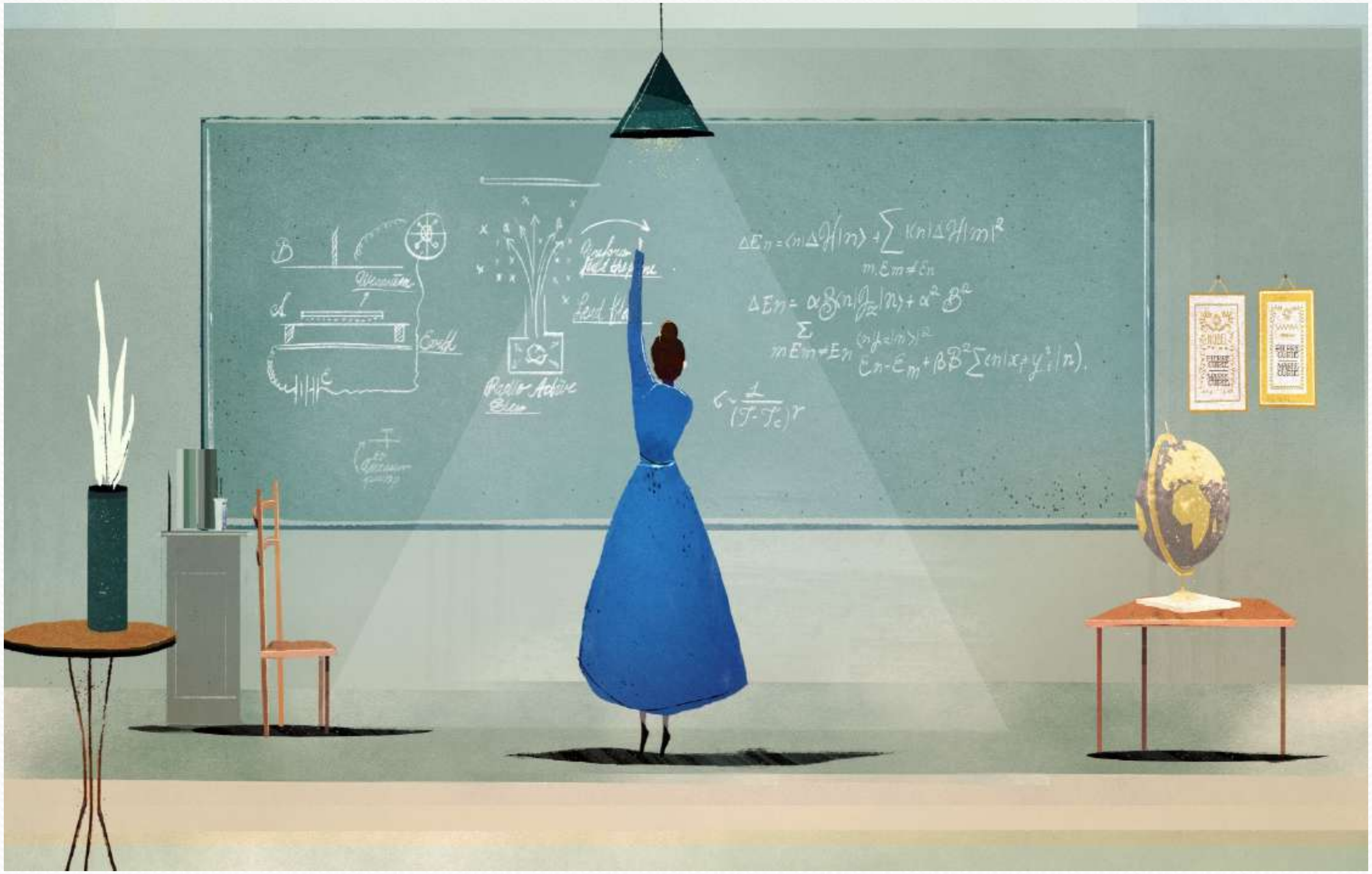
Overview

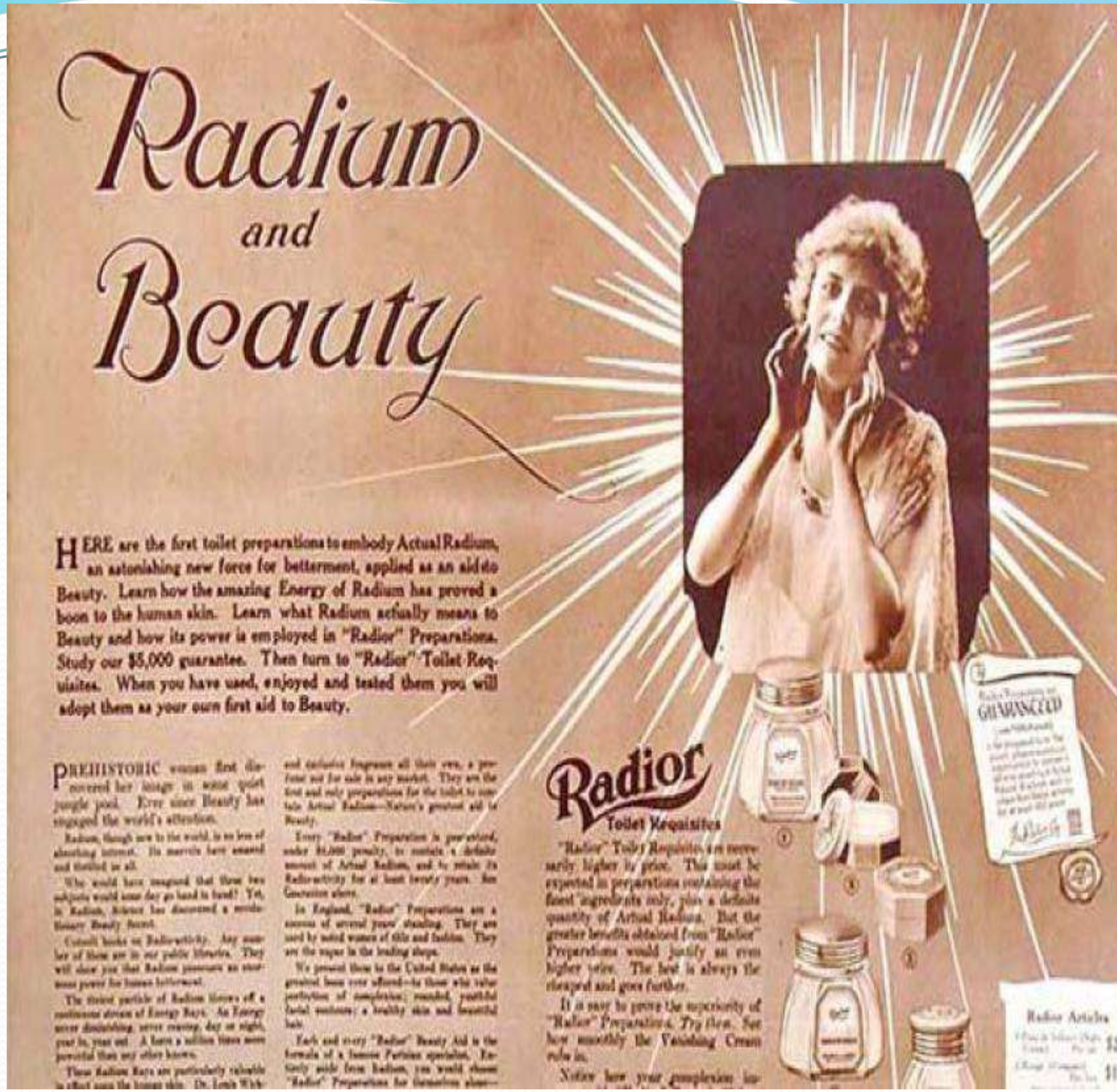
- Role of radiation in Cancer therapy
- Forms and frequency of radiation therapy
- Cancer types that benefit from radiation
- Radiation therapy and the typical 8-5 work schedule
- Covid-19 hit - what does that mean for radiation therapy treatment
- How employers can support employees undergoing radiation therapy treatment

History

History

- 1895- Roentgen Discovers Xrays
- 1896- Becquerel discovers natural radioactive decay.
- 1896-Marie and Pierre Curie further characterize radioactive compounds
- 1896- First patient with Cancer treated by Grubbe
- 1952- First Linear accelerator used for treatment
- 1968- Leksell invents the first Radiosurgery device
- 1980- Proton therapy
- 1988- IMRT
- 2000s- IGRT





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HERE are the first toilet preparations to embody Actual Radium, an astonishing new force for betterment, applied as an aid to Beauty. Learn how the amazing Energy of Radium has proved a boon to the human skin. Learn what Radium actually means to Beauty and how its power is employed in "Radior" Preparations. Study our $5,000 guarantee. Then turn to "Radior" Toilet Requisites. When you have used, enjoyed and tested them you will adopt them as your own first aid to Beauty.
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Notice how your complexion im-
Radior Articles

Radiation in the early 20th Century

Vita Radium Suppositories (ca.1930)

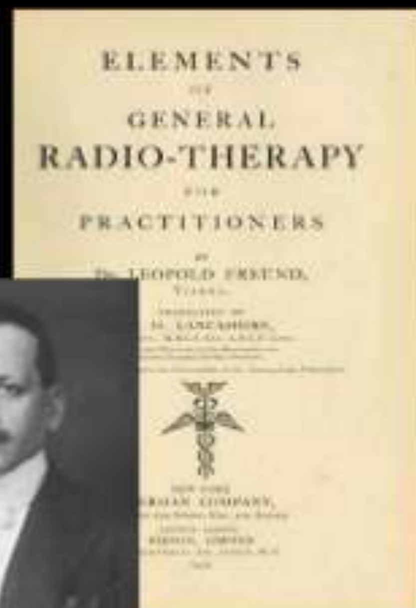
"Weak Discouraged Men!

Now Bubble Over with Joyous Vitality

Through the Use of

Glands and Radium"

1896 : Therapeutic use of X-rays
1903 : Authored first textbook of radiotherapy


ELEMENTS
GENERAL
RADIO-THERAPY
PRACTITIONERS
LEOPOLD FREUND

Leopold Freund

A five yr old girl with pigmented hairy naevus all over her back treated and cured , then lived upto 75 yrs.

In 1903 Gynecological Brachytherapy was first introduced by…….

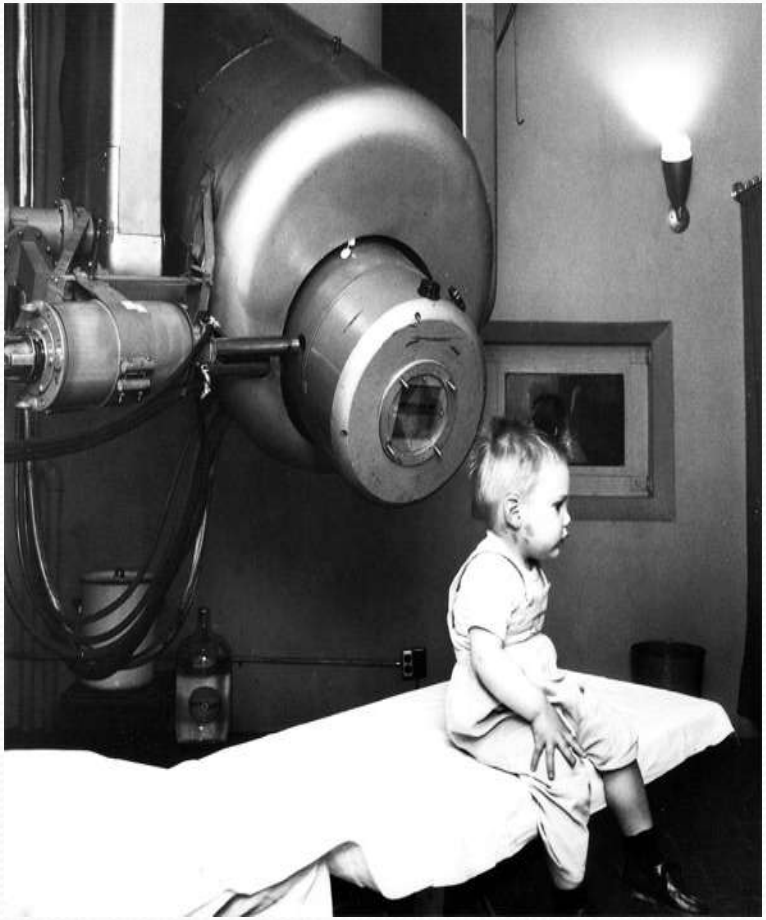
Margaret Abigail Cleaves

On 15 September 1903 she treated an inoperable cancer of the cervix uteri with 700 milligrams of radium bromide sealed in a glass tube.

Two applications of 10 minutes each were made with an interval of 3 days between.

O'Brien, F. w. (1947): Amer. J. Roentgenol., 57, 281.

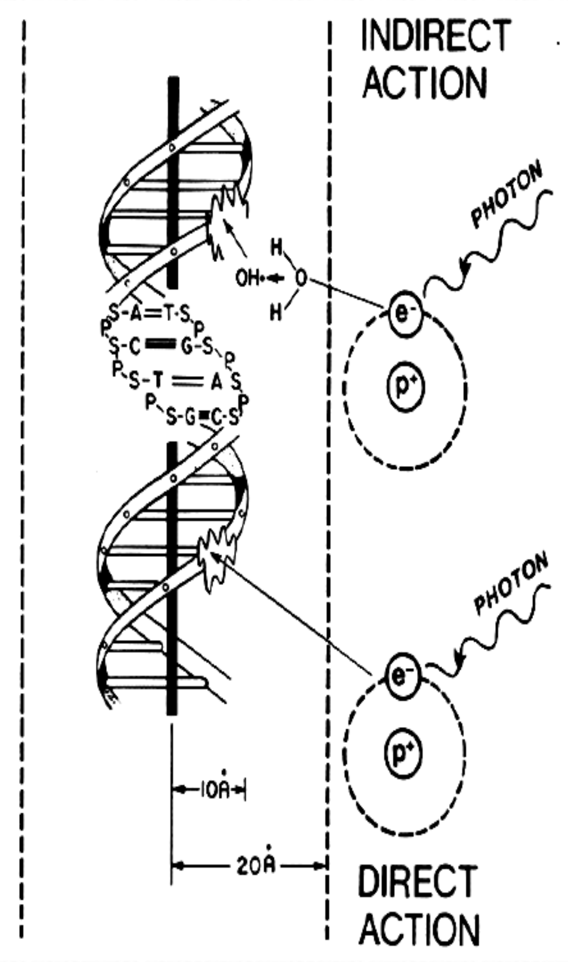
First patient to be treated on a Linear accelerator



Dose

Radiation Biology: How does it work?

- DNA damage is the result of direct and indirect effects of radiation
- Damage / Gy of X-rays:
  - 40 DSBs
  - 150 DNA crosslinks
  - 1,000 SSB
  - 2,500 base damages
  - SSB correlates poorly with lethality
  - DSB most important lesion



From: Hall, "Radiobiology for the Radiologist"

Effects of radiations on the irradiated tissues

EFFECT	RESULTS
Physics	issue, transfer and absorption of energy
Biophysics	ionisation and excitation phenomenon
Physical-chemical	direct alterations of atoms and molecules or indirect damage through the productions of free radical
Chemical	the breaking of bonds, polymerization or depolymerization phenomenon
Biochemical	molecular alterations
Biochemical-biological	damage to DNA, RNA, cytoplasm, enzymes
Biological	aberrations of various cellular components, morpho-functional and metabolic lesions, damage to the genetic material

Evolution of understanding of Dose

- Complications and negative side effects were discovered quick
- Stenbeck- Smaller doses of radiation over longer period of time was effective for skin cancer
- Bergonie and Tribondeau, 1906- Experiments with Rays and Rat testicles. Xrays are most effective on cells having-

a. A high proliferative rate

b. a long-life span with many divisions

c. Unspecialized

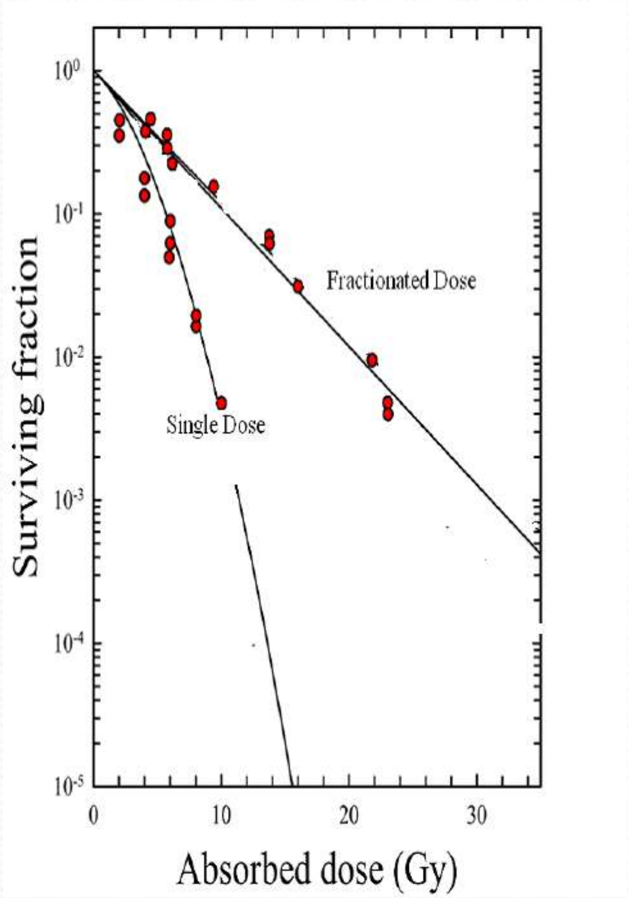
- 1920s animal sterilization experiments in Rams- splitting radiation in smaller fractions allows sterilization with minimal necrosis to the scrotum

Evolution of understanding of Dose

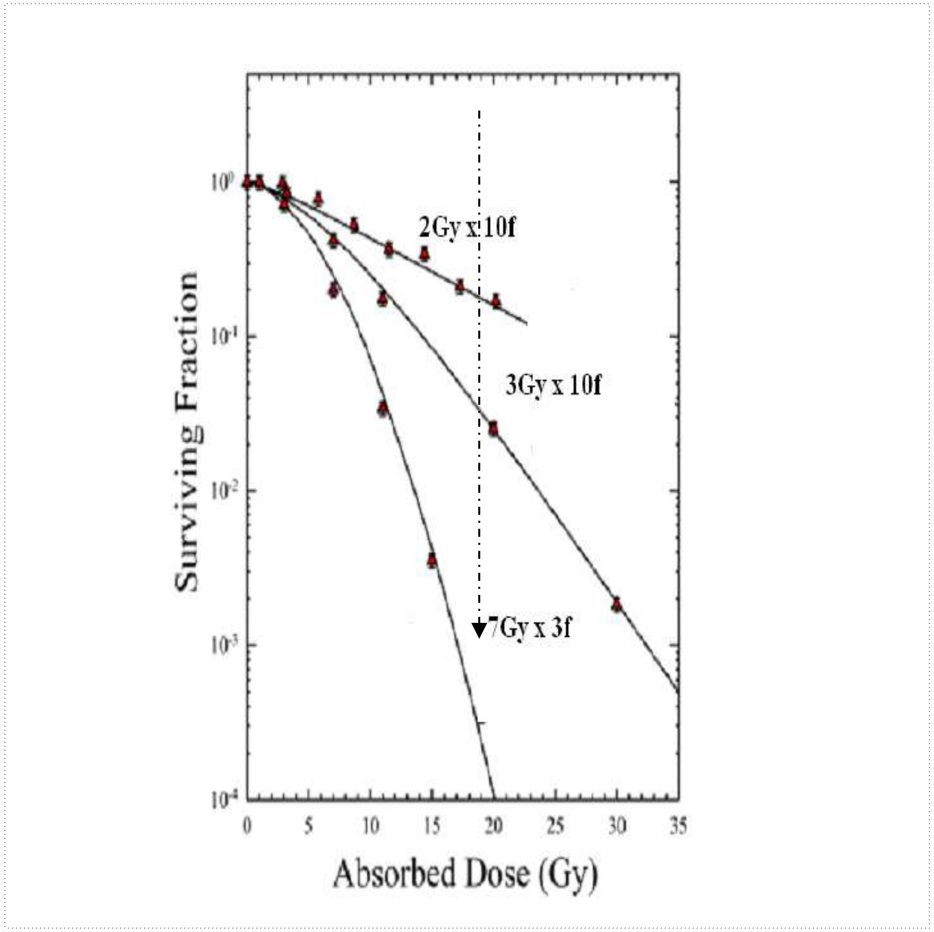
- Conventional fractionation- 1.8-2.0 Gy/d 5 times a week over 3-7 weeks
- Hyperfractionated radiation- conventional doses into smaller doses without change in overall treatment time. 0.5-2.0 Gy/fr with two fractions/day 2-5 times a week over 2-4 weeks
- Accelerated Hyperfractionation- 1.0-1.6 Gy/fr in 5 or more fr/wk
- Hypofractionation- Higher dose in fewer fractions. 8-30 Gy in 1-5 fr

Tumor Control Probability

- Clonogenic tumor cell survival decreases with increasing radiation dosages in most tumor systems
- As clonogenic tumor cell survival decreases, the probability of tumor control increases



Comparison of Hypo Fractionation and Standard Fractionated RT



Radiobiological Effective Dose (BED)

$$BED_{Gy} = TD\ (1 + \underline{\text{dose fraction}})$$

- 2Gy x 10f = 20Gy total dose = 24Gy

  3Gy x 10f = 30Gy total dose = 39Gy

- 7Gy x 3f = 21Gy total dose = 36Gy
  (50% "more effective dose" which can translate into approx. 3 logs of additional cell killing)

  15Gy x 2f = 30Gy total dose = 75Gy
  (92% "more effective dose" which can translate into approx. 5 logs of additional cell killing)

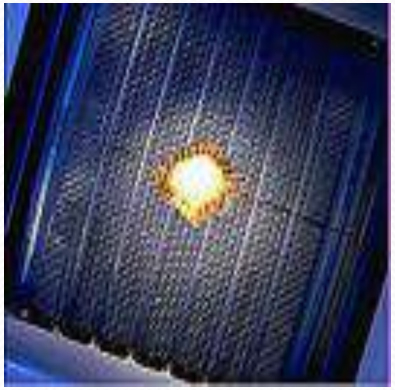
Dose delivery Techniques

And some benign tumors….

Why is it difficult?

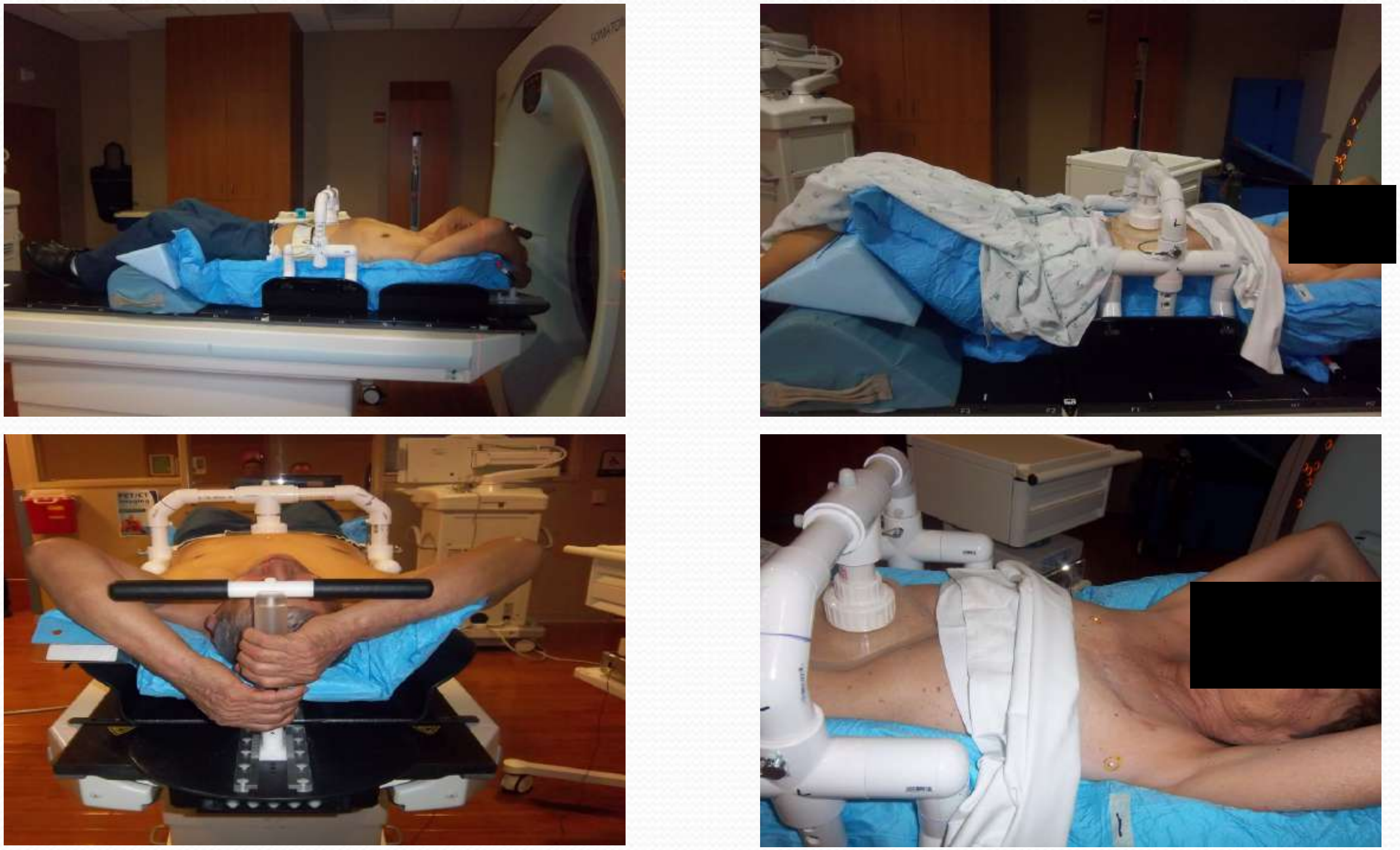
- Organs at risk in the field with tolerance below prescription dose

Linac Based Systems



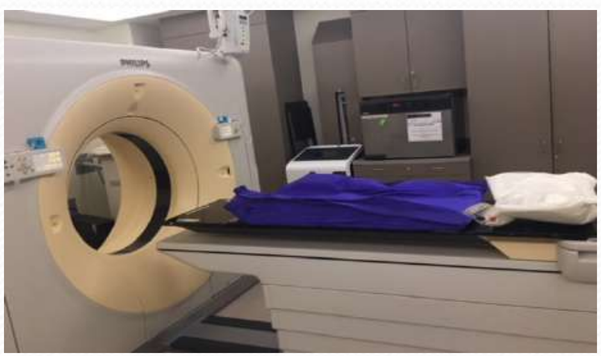
- Use of Linacs with the conventional beam and addition of a Micromini leaf MLC to conform the shape of the target
- Additional devices for immobilization(with or without frame), imaging, target localization and accurate treatment delivery

SBRT patient set-up



Motion Management

- Real time Fluoroscopy (Simulator, OBI, C-arm)
- Acquire 4D CT scan (CT Sin[redacted]
- Assess the tumor motion
- Motion control
- Abdominal compression, gating, breath hold, tr

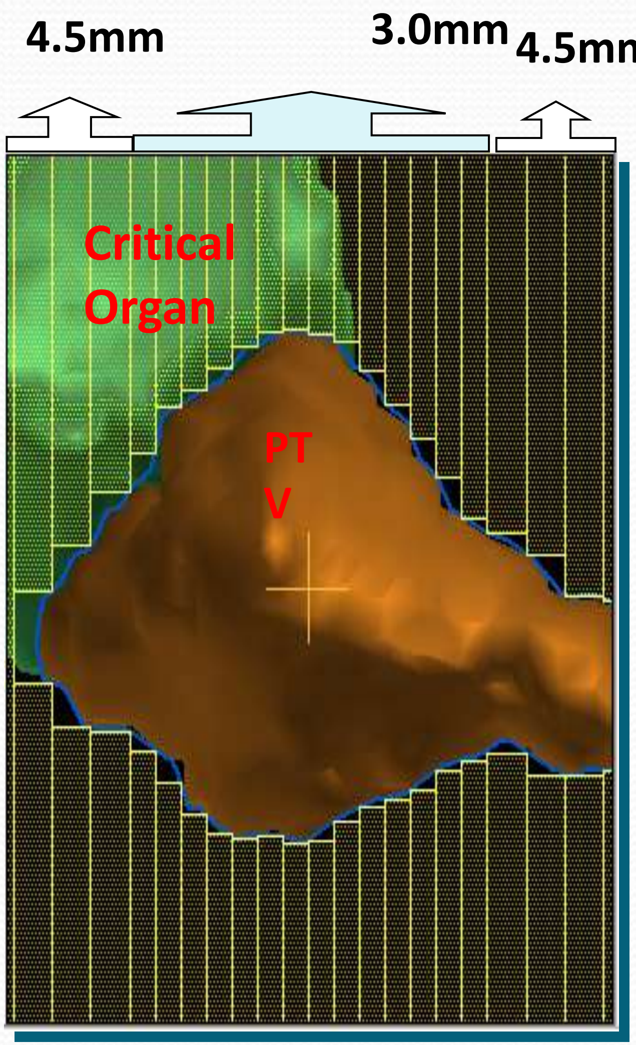


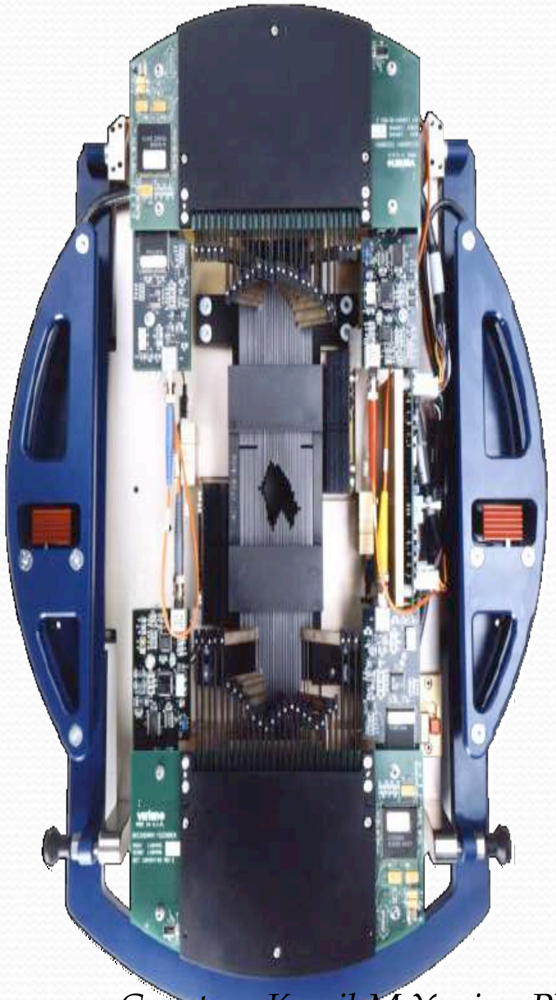
Dignity Health.

Standard Beam Shaping
Circular Cones

- Small fields shaped by precisely machined circular cone inserts (diverging)
- Linear accelerator circles around target while radiation is being delivered
- Multiple non-coplanar arcs

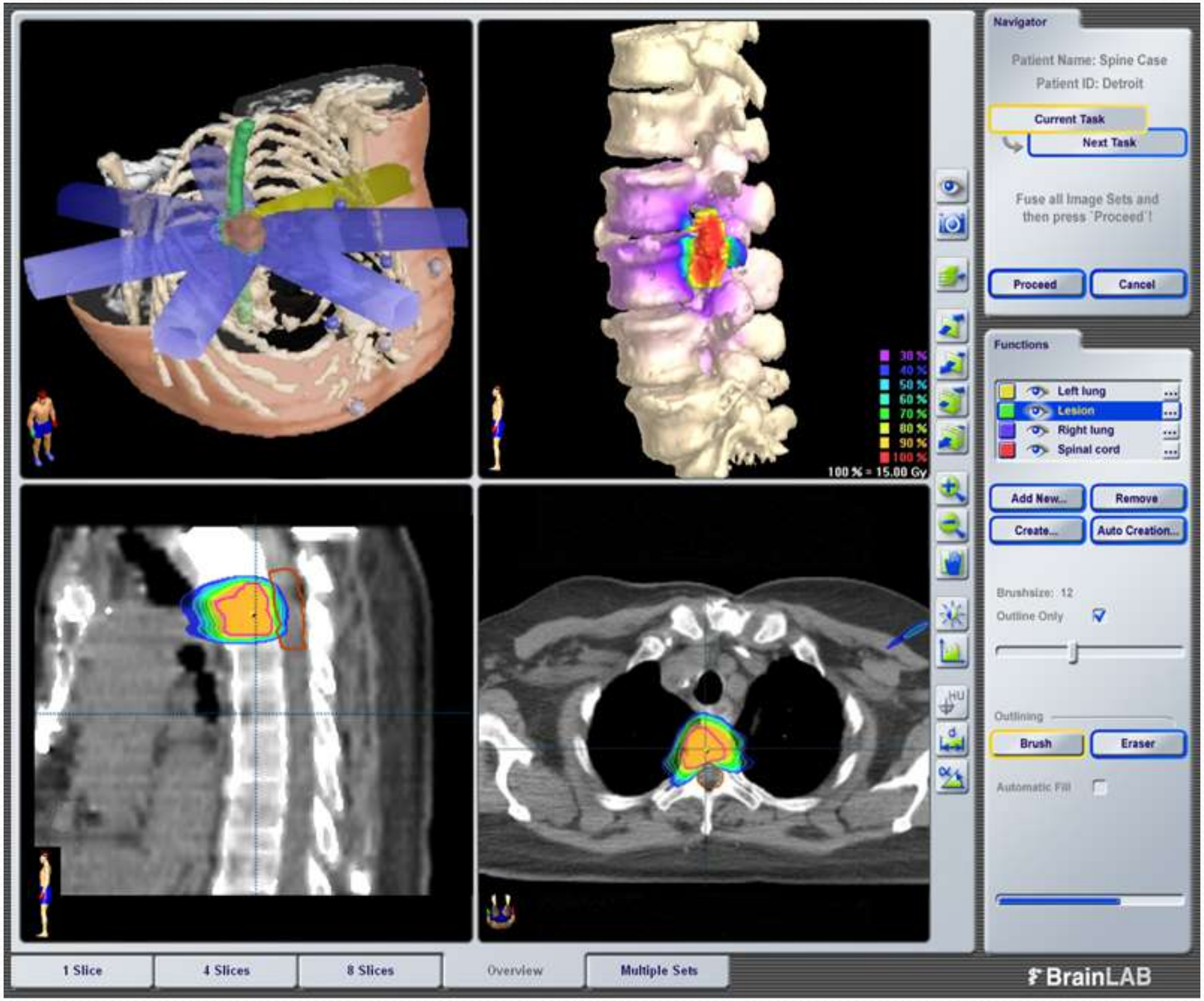
Intensity Modulated Radiosurgery
Micro Multileaf Collimator





Courtesy Kamil M Yenice, Ph.D

Micro MLC SRS



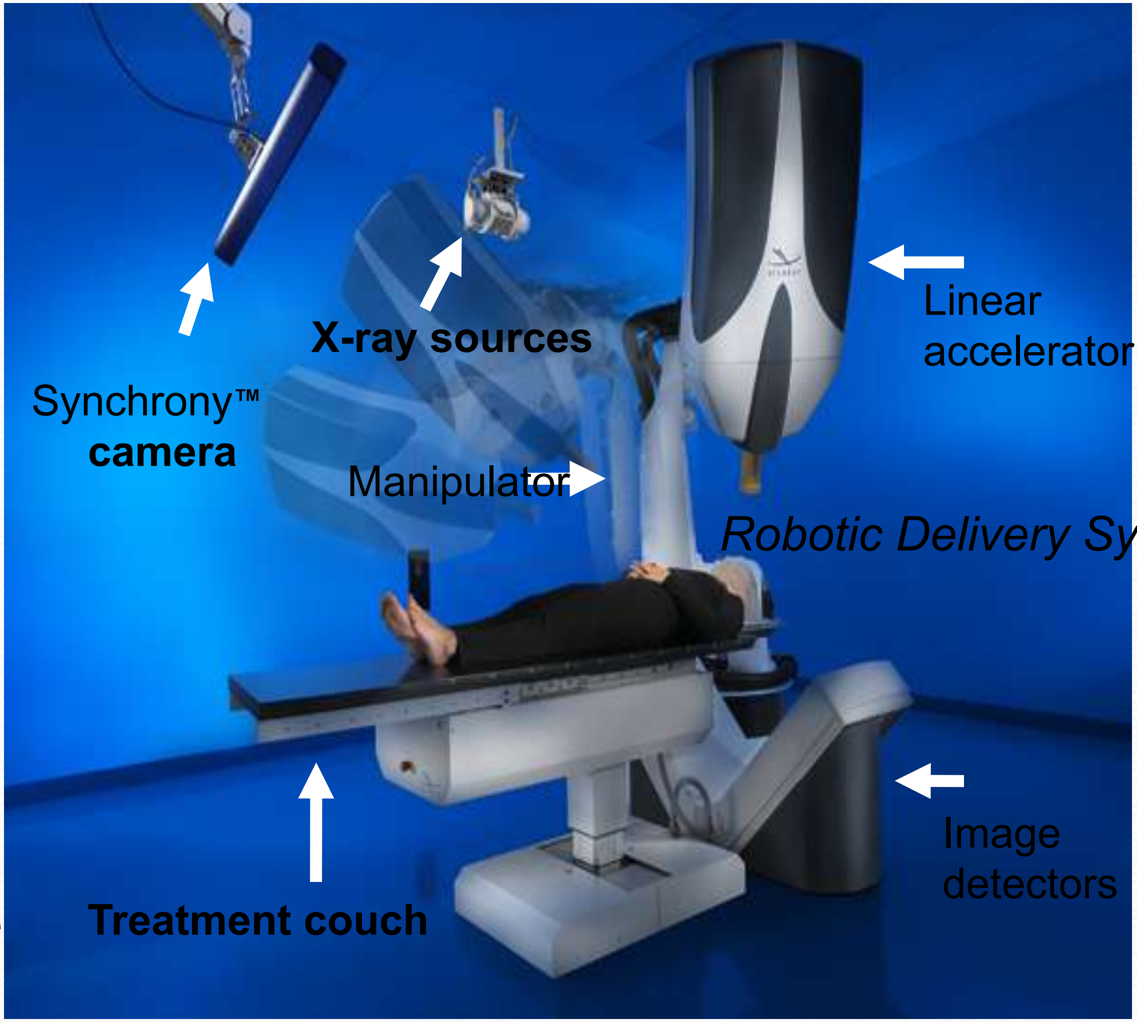
Helical SRS
TomoTherapy HiArt System

- IMRT delivered through continuous 360º rotations
  - Uses binary multileaf collimator

- Patient couch moves continuously during treatment session

- Megavol

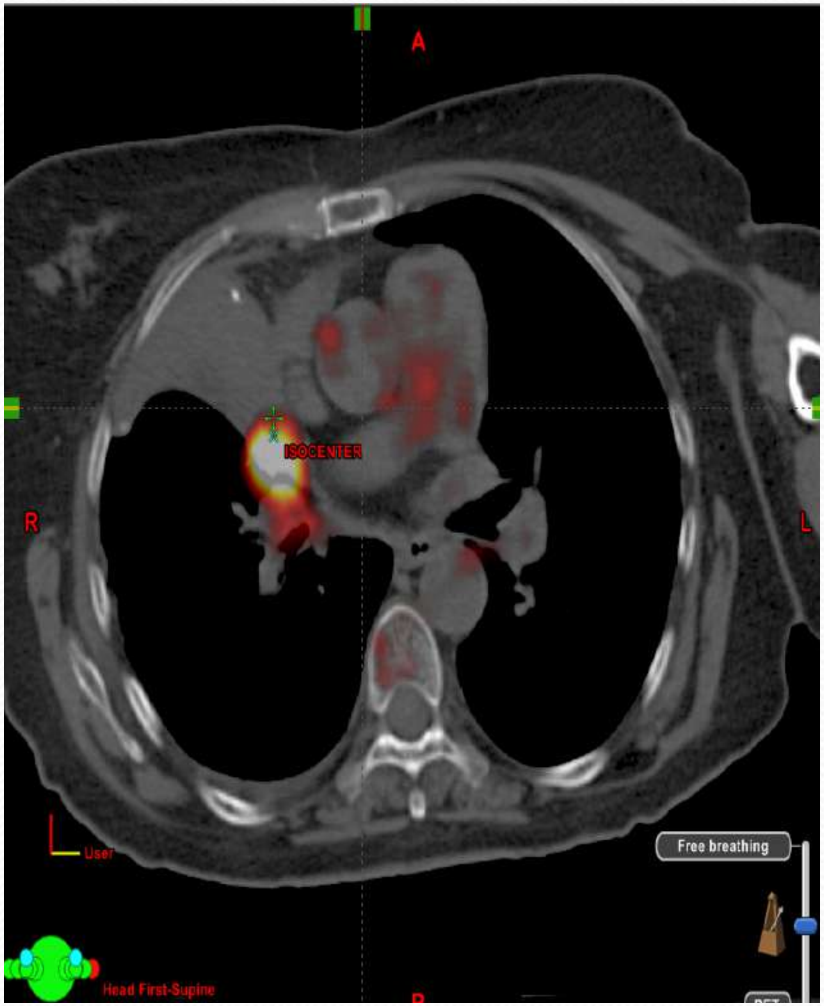
CyberKnife
Robotic Arm Mounted Accelerator



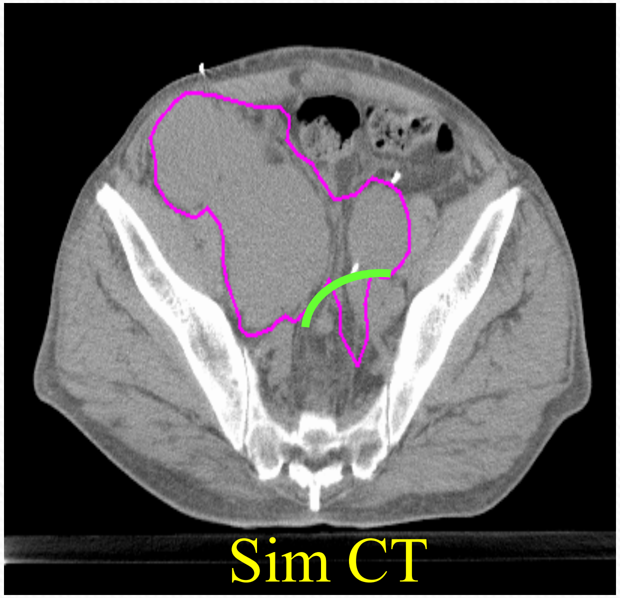
Tre

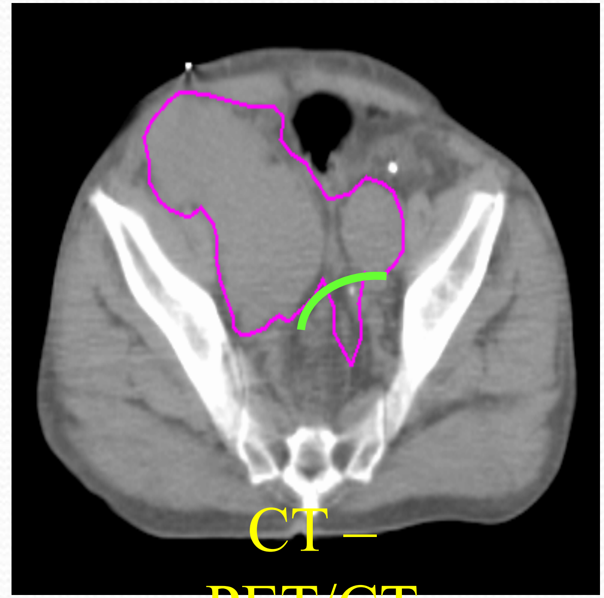
Fiducial placement

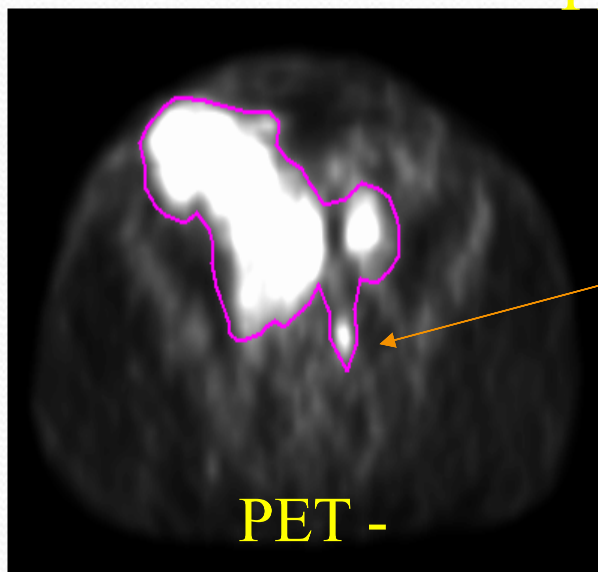
Target Delineation



PET fusion

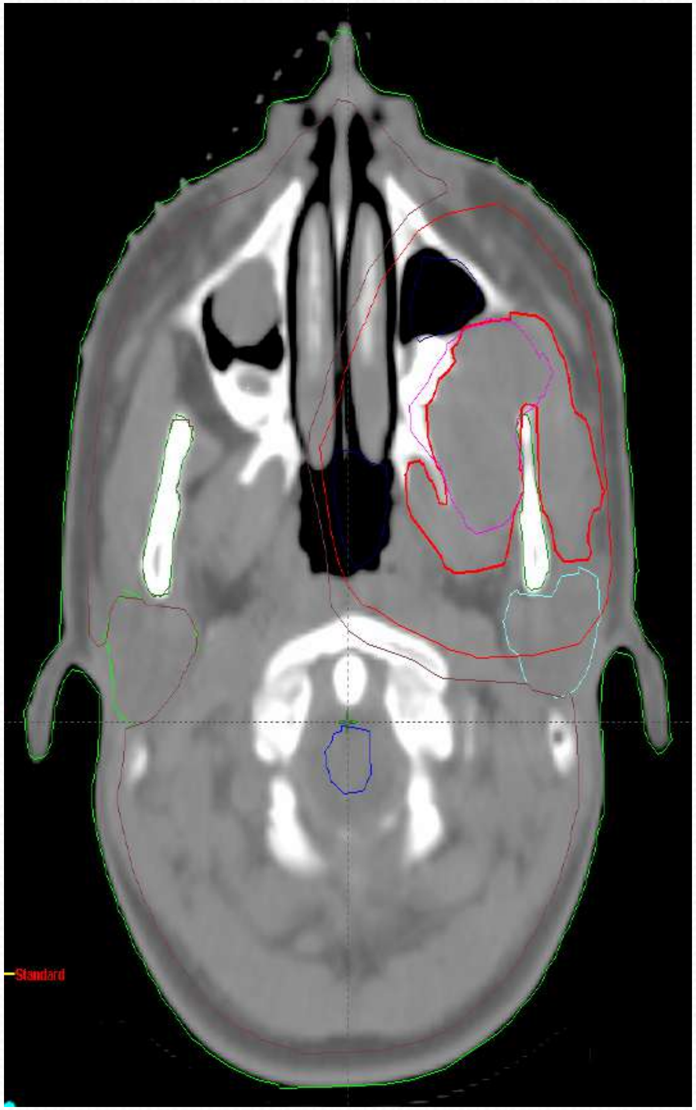


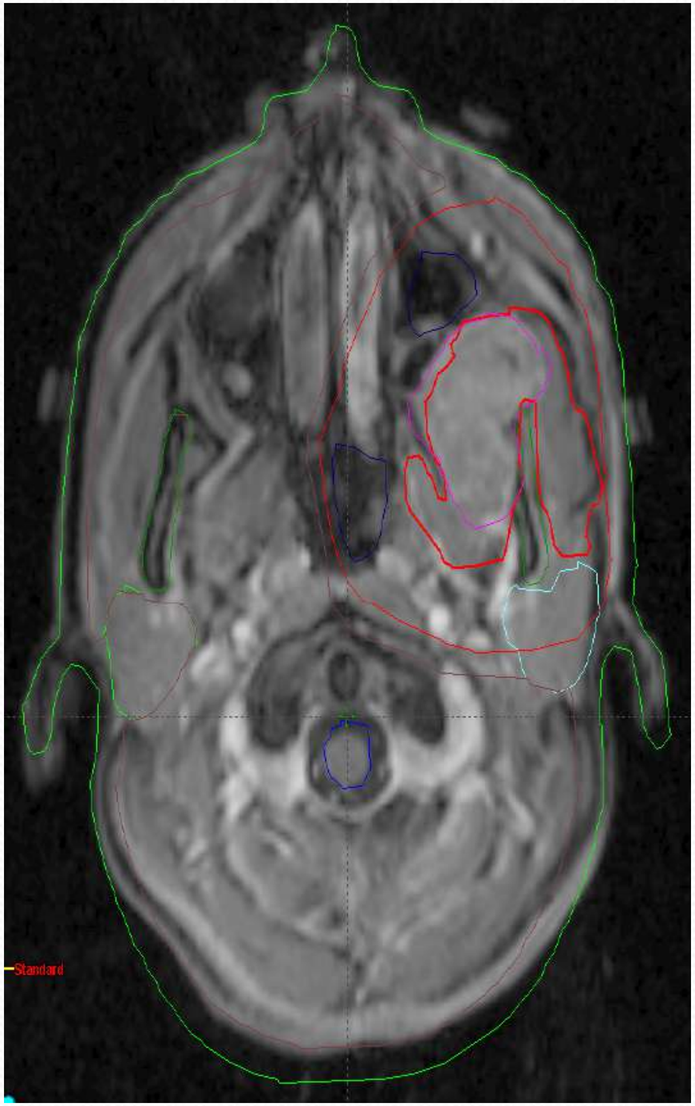




iliac
lymph
node

MRI fusion





Respiratory Gating

- Infrared illuminator / CCD camera
- Reflective external marker placed on abdomen or chest
- Workstation to process signals & generate trigger (CT) or gate beam

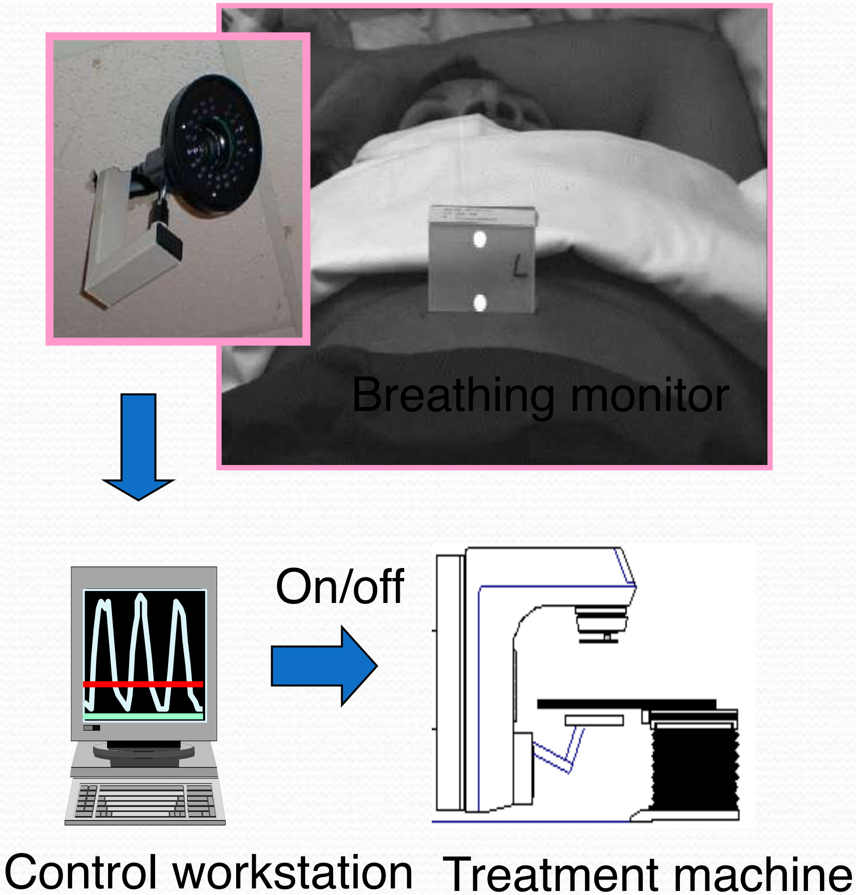
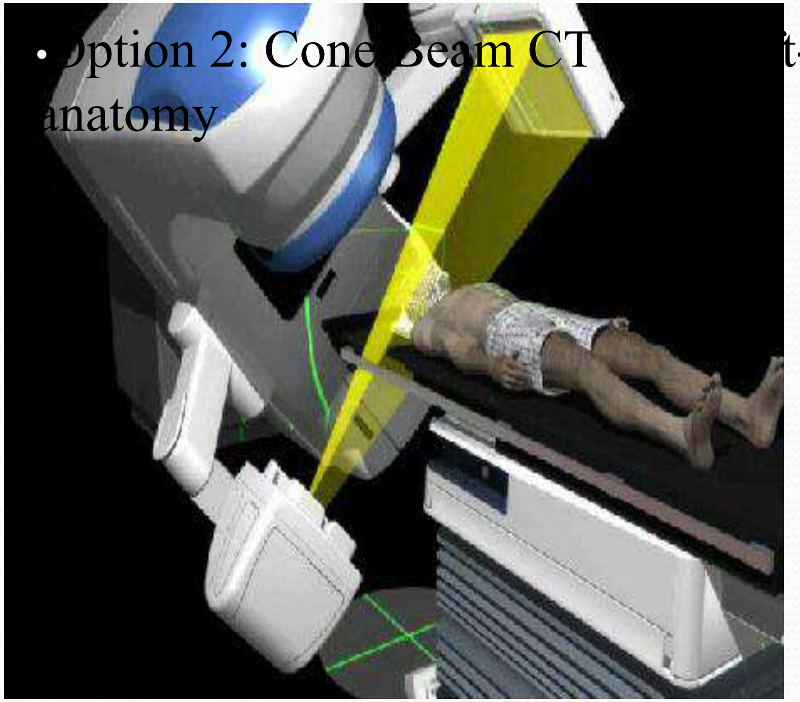


Image Guided Radiation Therapy

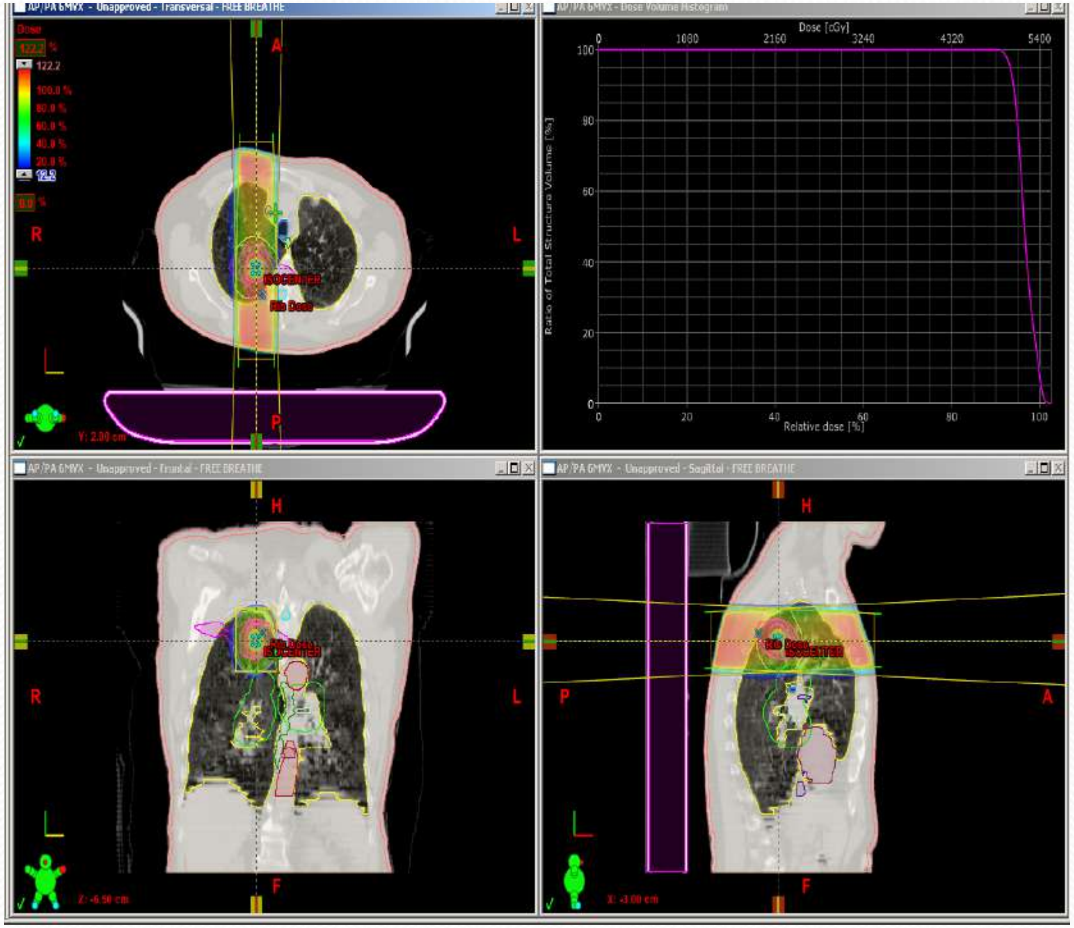
The patient is positioned on the table and image-guidance is used to fine-tune the setup, online, before treatment begins.

Option 1: Radiographs with radiopaque markers

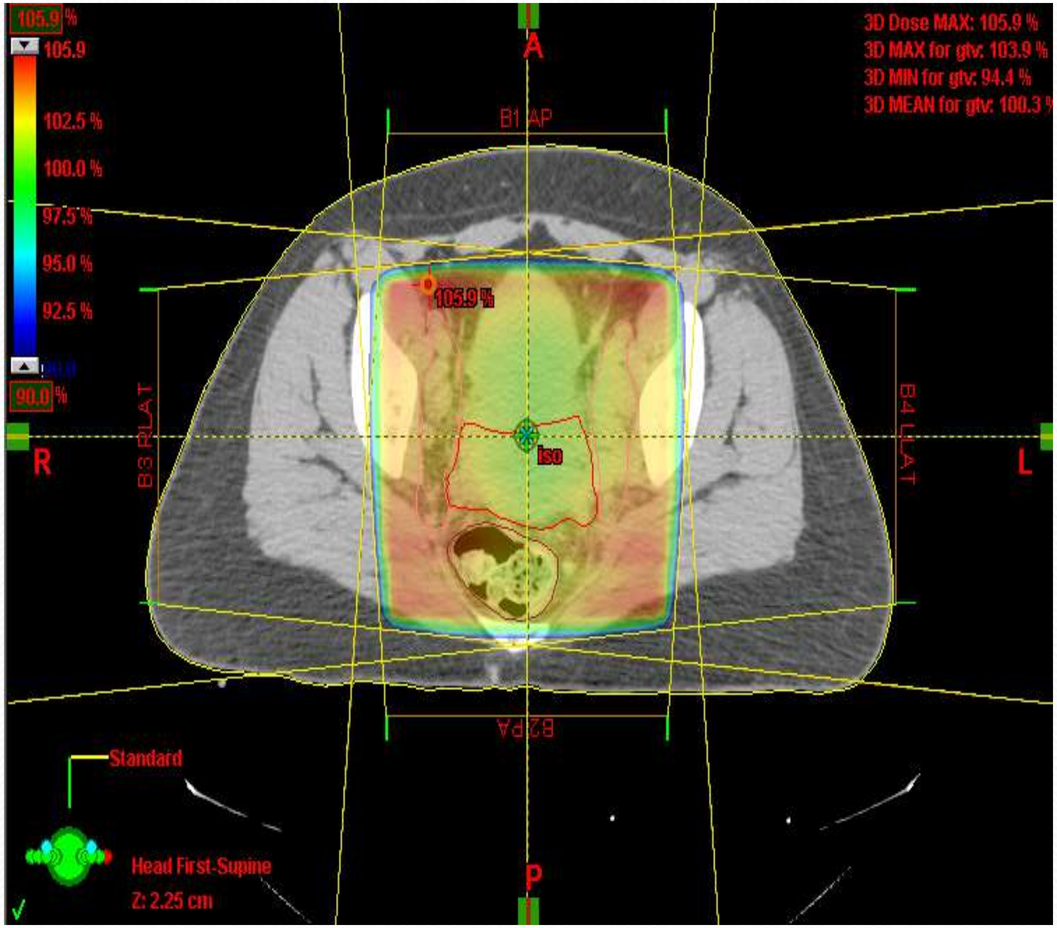
- Option 2: Cone Beam CT [illegible]t-tissue anatomy



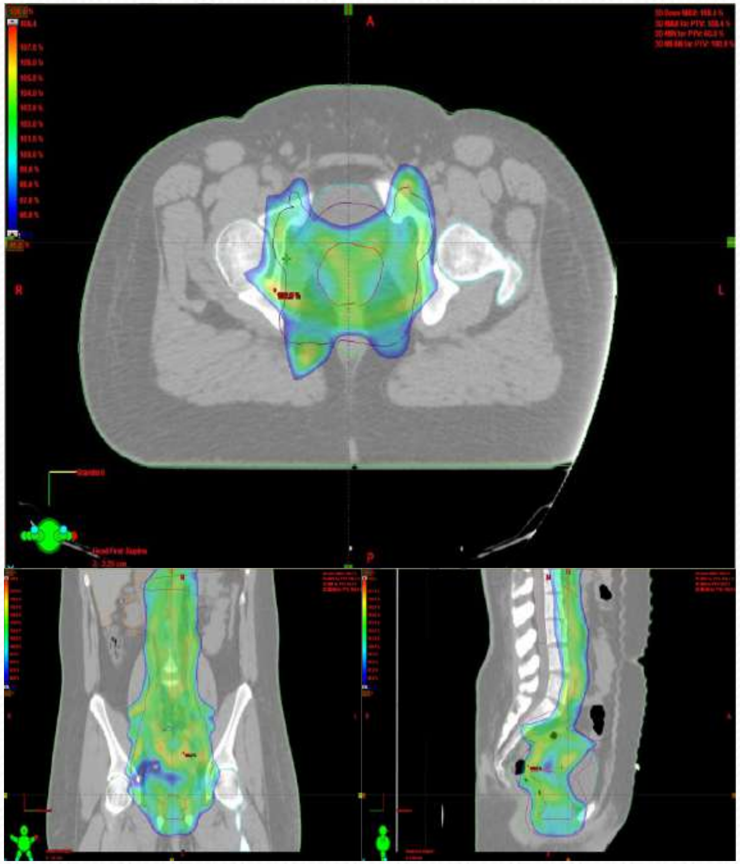
Techniques of radiation therapy-2D



Techniques of radiation therapy-3D

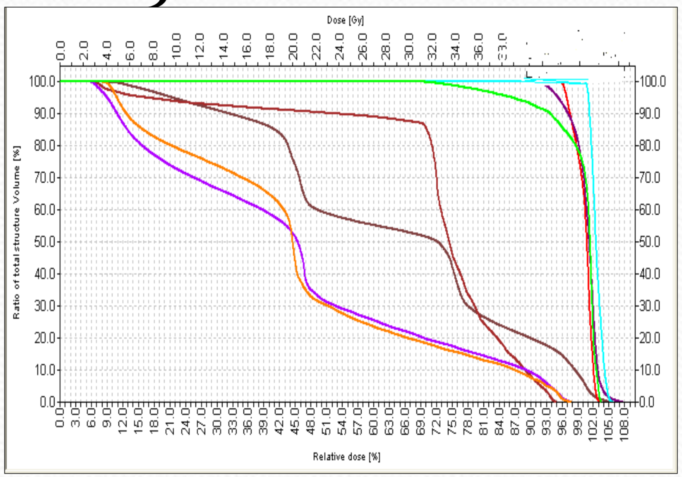


Intensity Modulated radiation therapy(IMRT)



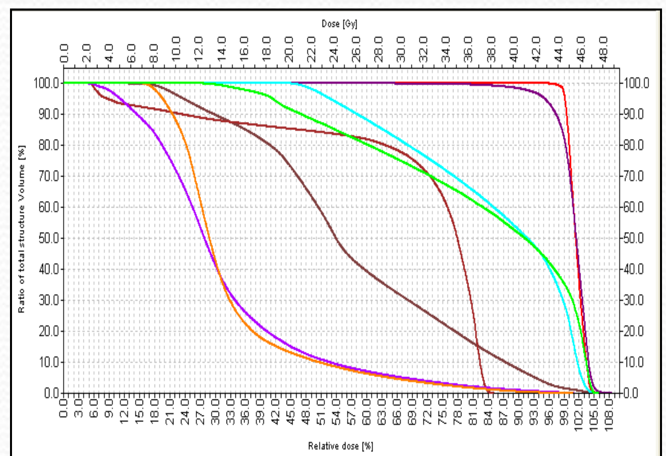
Comparison of Dose Volume Histograms

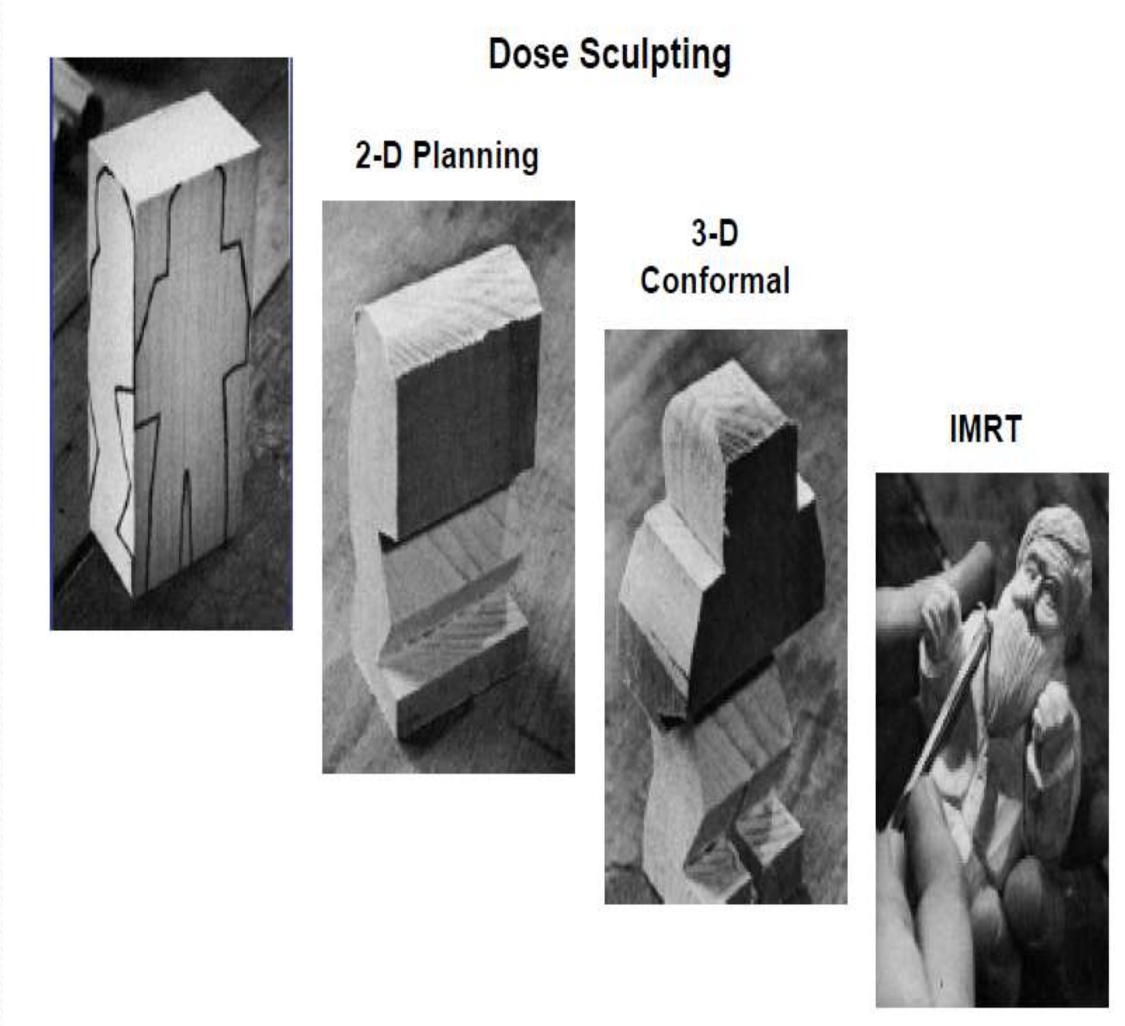
3D Conformal



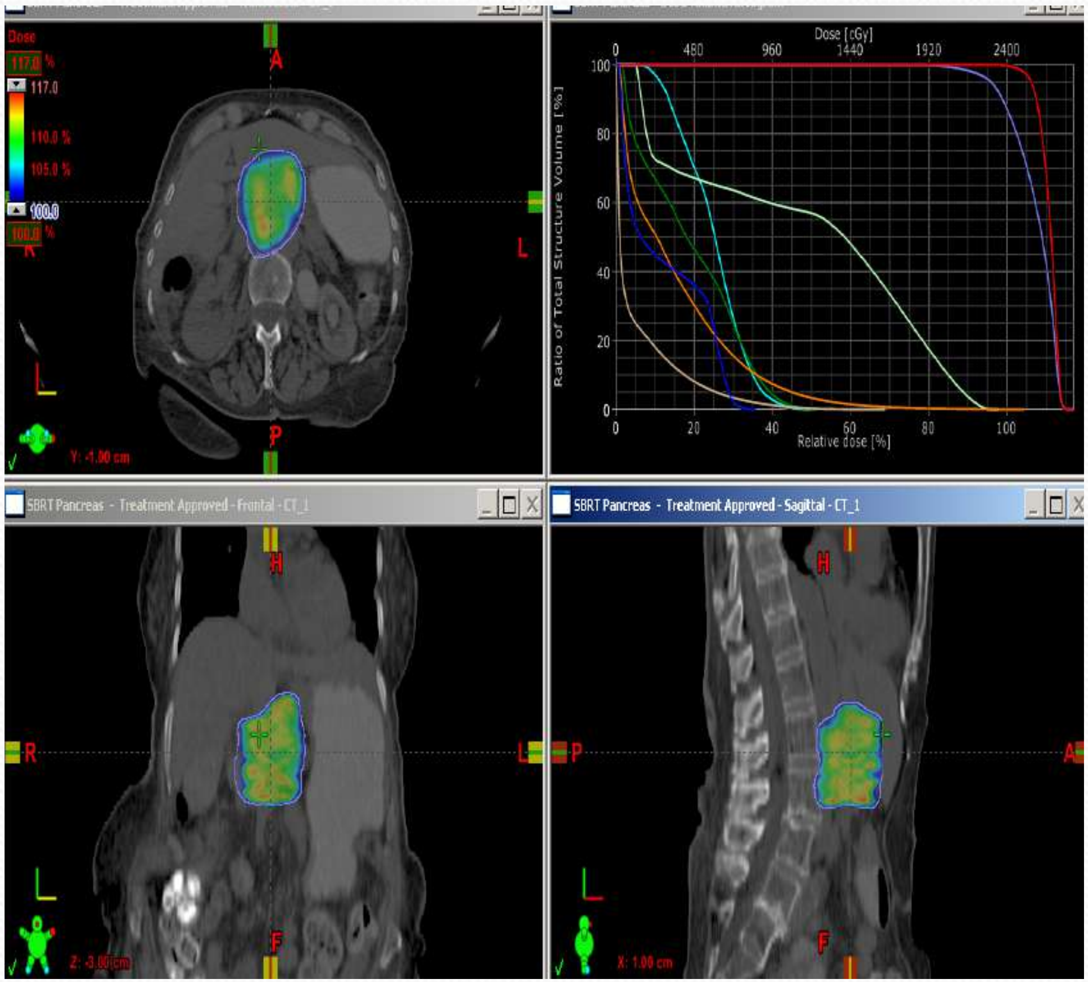
- Bladder
- Rectum
- Gross tumor volume
- Planning tumor volume
- Small bowel
- Spinal cord
- Left Kidney
- Right Kidney

IMRT




Dose Sculpting
2-D Planning
3-D
Conformal
IMRT

Radiosurgery/ Stereotactic Body Radiation Therapy (SBRT) / Stereotactic Body Ablative Radiotherapy(SABR)



Conventional radiotherapy Vs. Stereotactic radiation

- Conventional Radiotherapy:
  - Exploits differences in radiation responses of normal tissue and the tumor tissue to effect eradication of tumor without unduly damaging normal tissue
  - Fractionated therapeutic programs over few weeks
- Stereotactic Radiosurgery:
  - Exploits differences in dose distribution to destroy effectively the tumor while sparing normal tissue
  - Single fraction to a maximum of five fractions therapeutic regimens

Stereotactic Radiosurgery Vs. Stereotactic radiotherapy

Radiosurgery

- Single treatment
- Usually used for intracranial / intra-spinal tumors with achievable dose distribution to spare close organs at risk
- Invasive (frame) immobilization

Stereotactic radiation

- Fractionated
- Used for small and well circumscribed tumors where fractionation is preferred and critical structures are close
- Requires target motion management

Stereotactic Radiosurgery Vs. Stereotactic radiotherapy

Radiosurgery

- Single treatment
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Stereotactic radiation

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Brachytherapy

- Low dose Rate brachytherapy

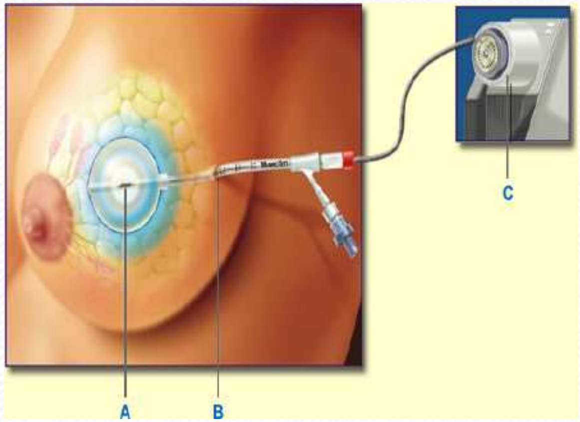
  Radioactive seed implant

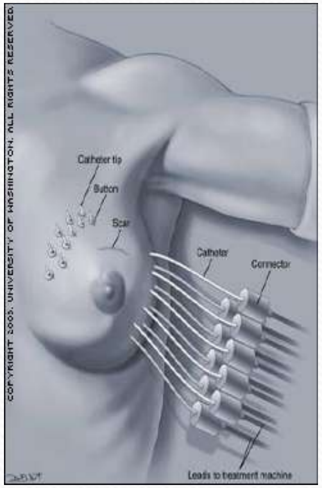
- High dose rate

  After loading catheters with a remote radioactive source Ir-192.

Brachytherapy

Breast Cancer





Indication

- Boost after EBRT, or as monotherapy in early stage breast cancer (NSABP B39)

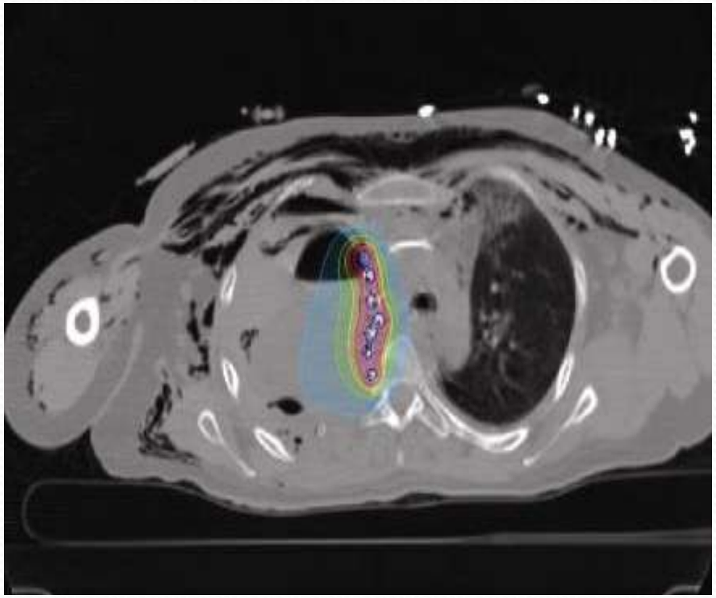
Type of Implant/technique

- Mammosite/ Savi
- Interstitial Implant

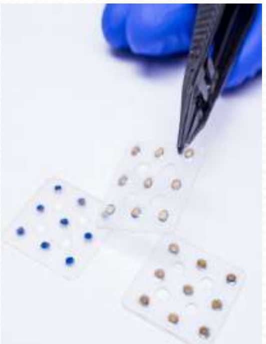
Radioactive source/regimen

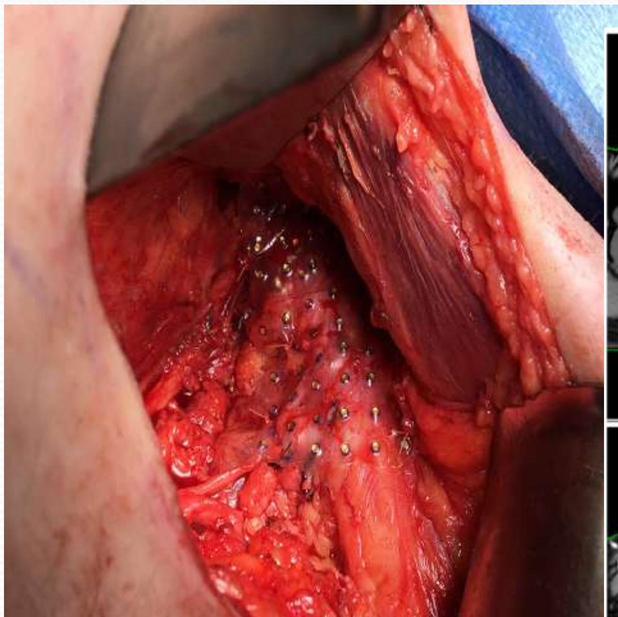
- 34 Gy in 3.4 Gy fractions given twice daily via HDR Brachytherapy

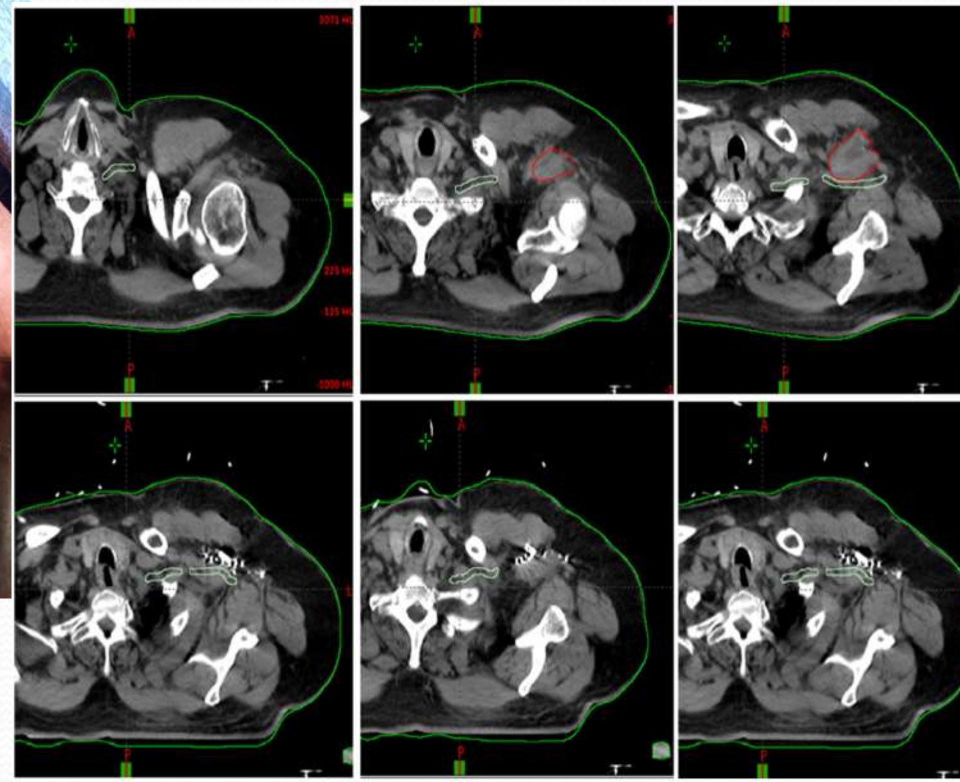
Lung Mesh Implant



Civa Sheet

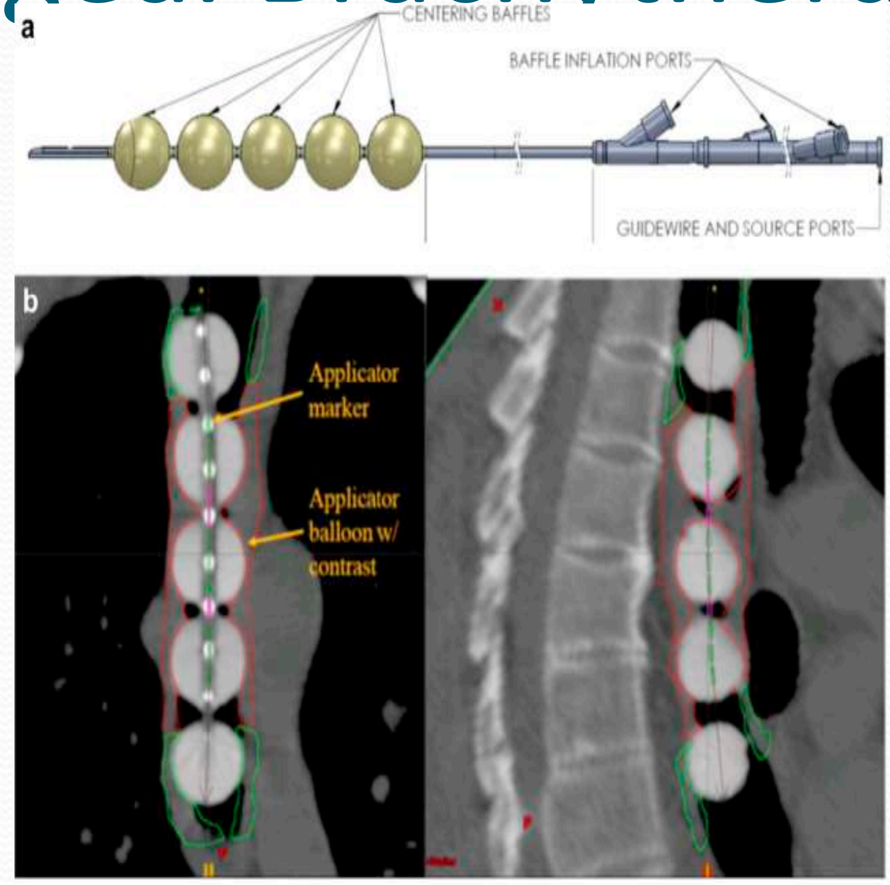




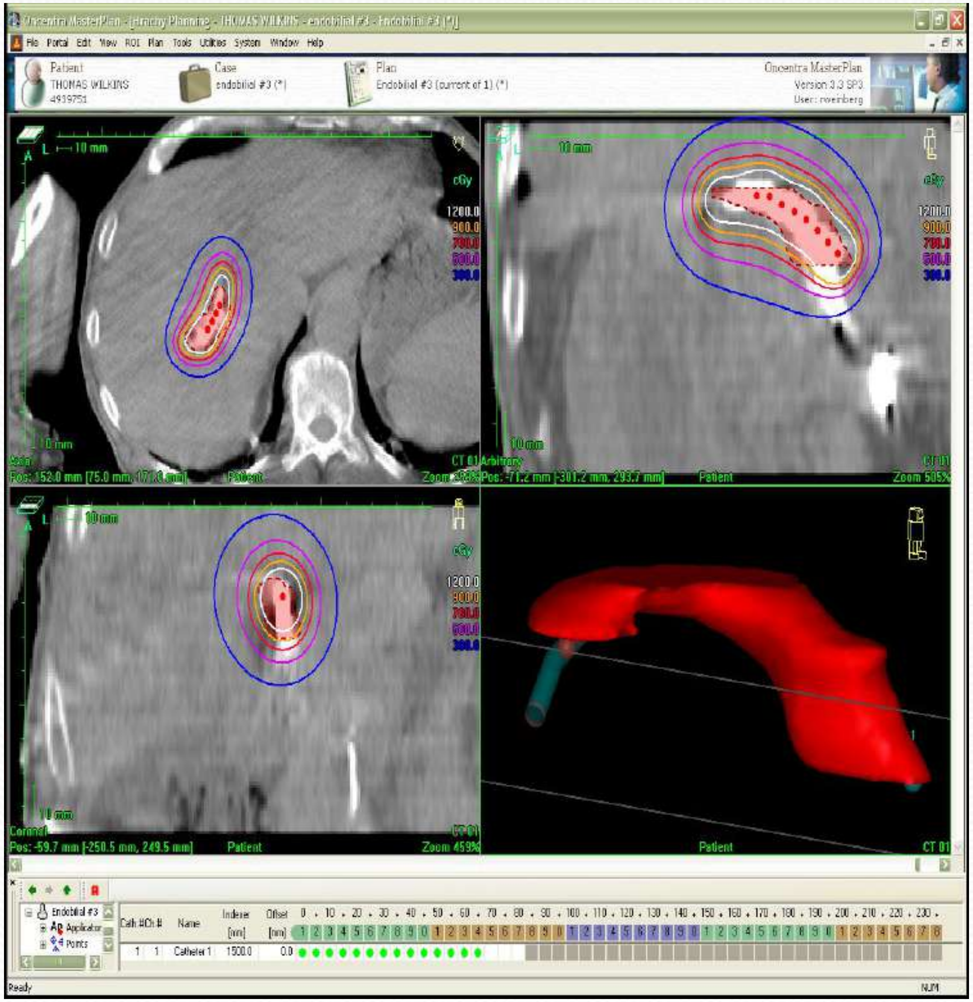


http://www.civatechoncology.com/civasheet.htm

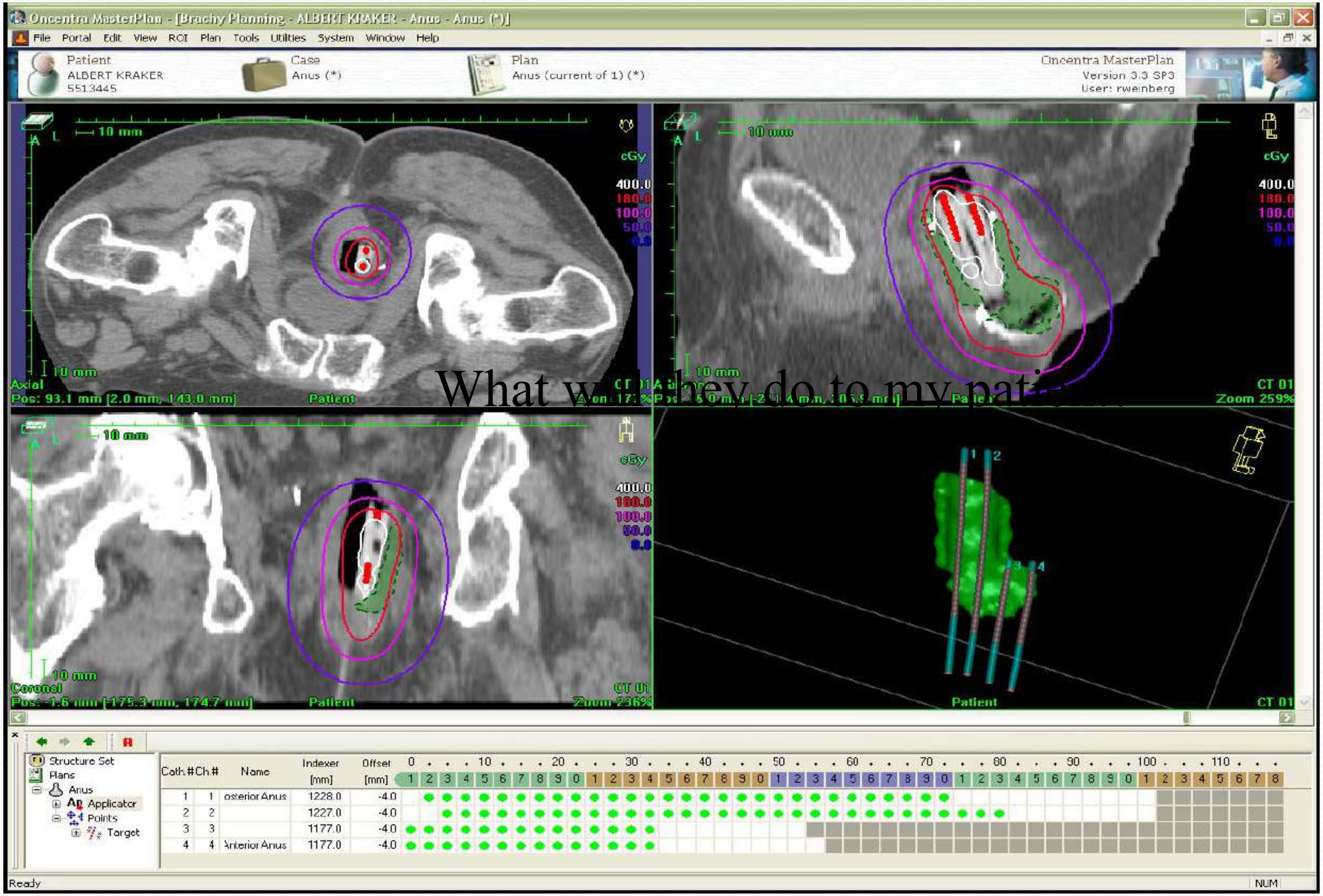
Esophageal Brachytherapy



Endobiliary HDR

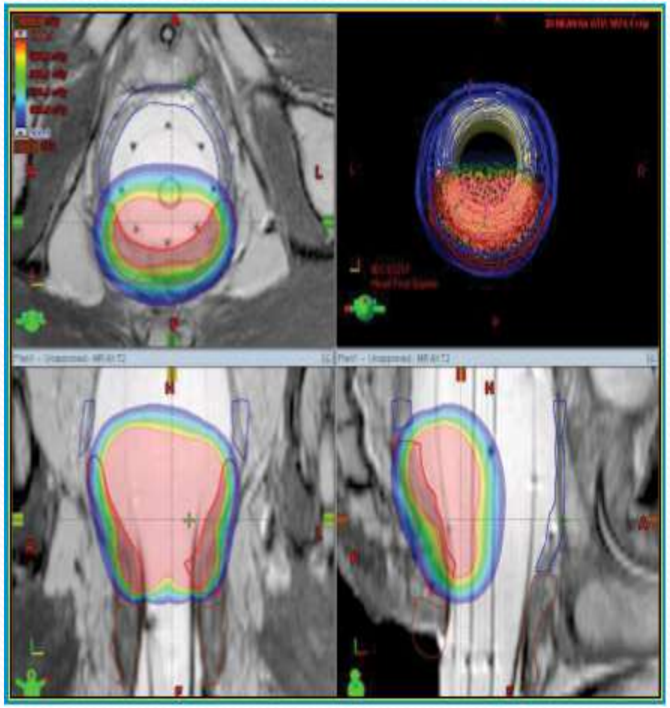


Anal Canal HDR

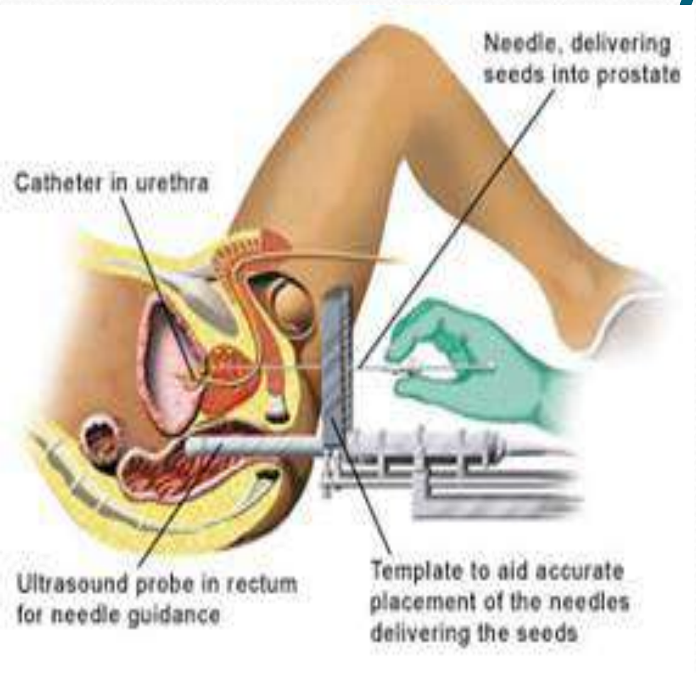


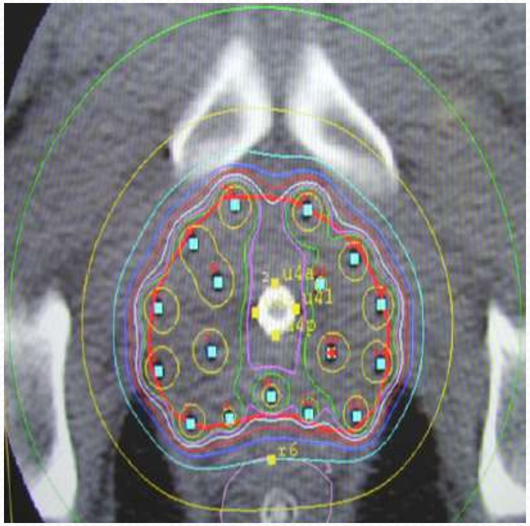
What w... hey do to my pati...

Anorectal Brachytherapy

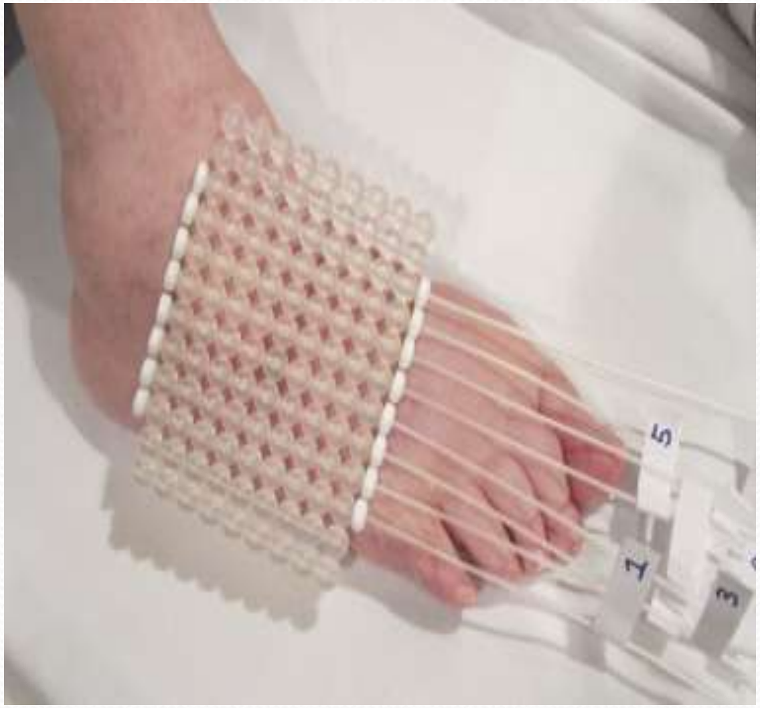


Prostate brachythe

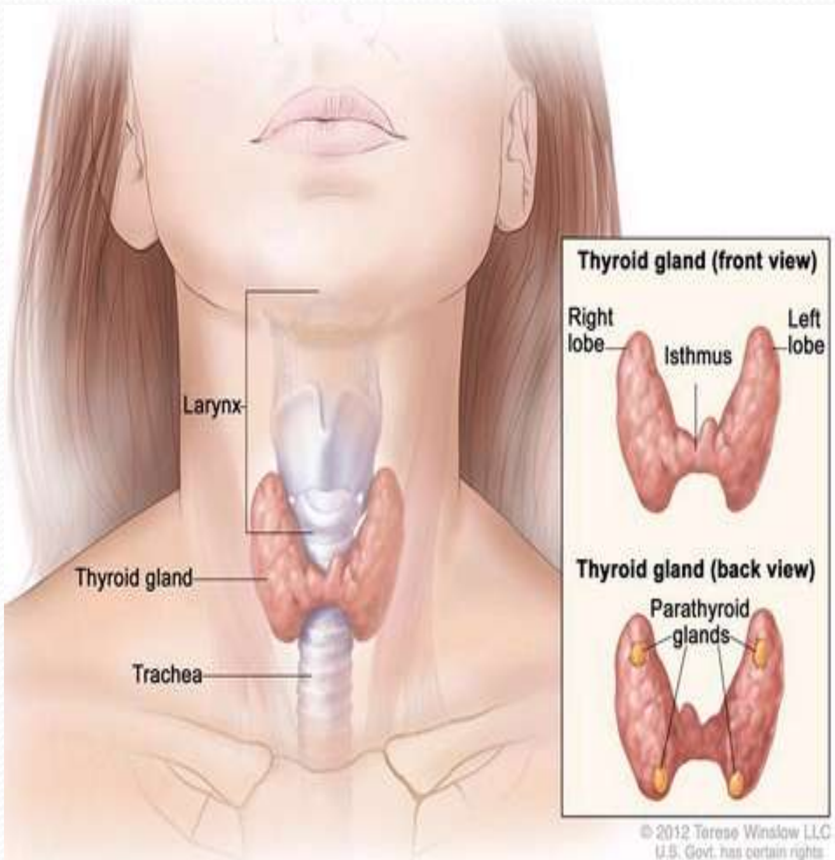




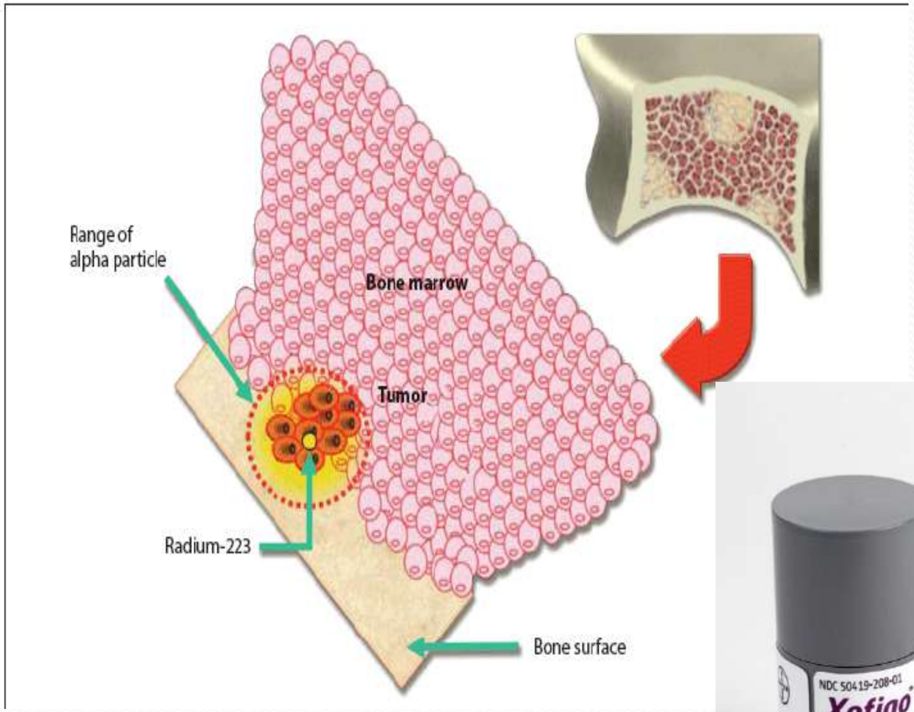
Skin Cancer



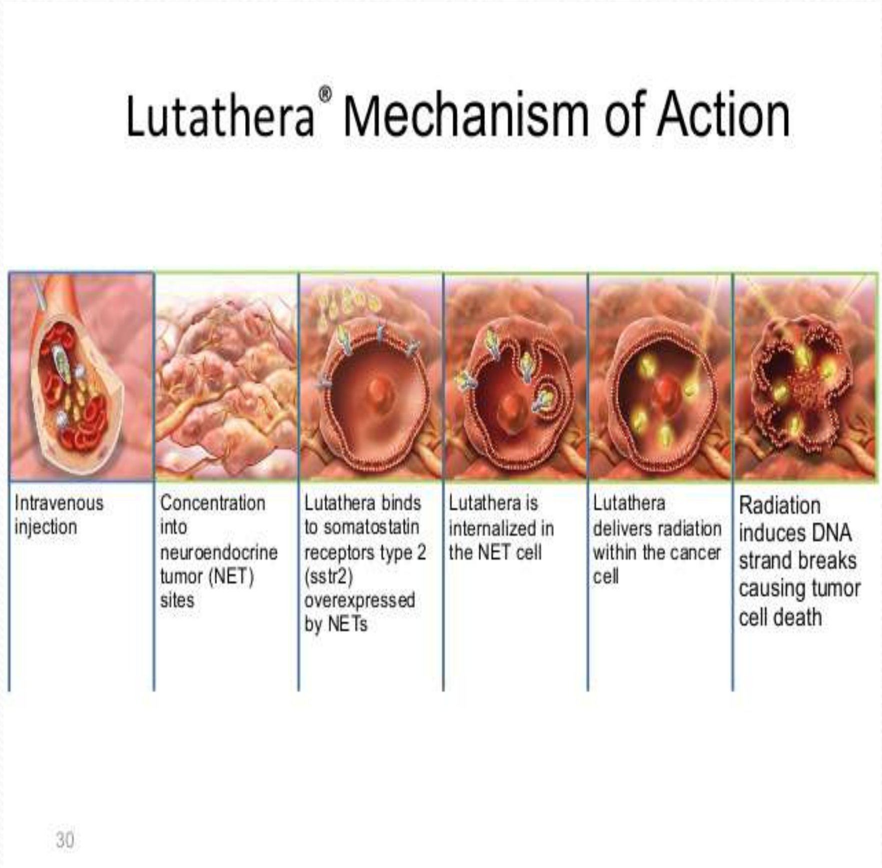
Unsealed Sources- radioactive Iodine



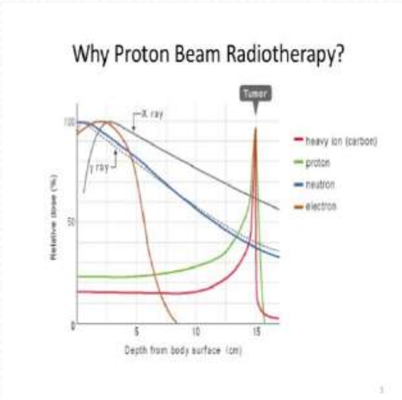
Xofigo-Rn223



Peptide Receptor Radionuclide Therapy



Proton beam Therapy



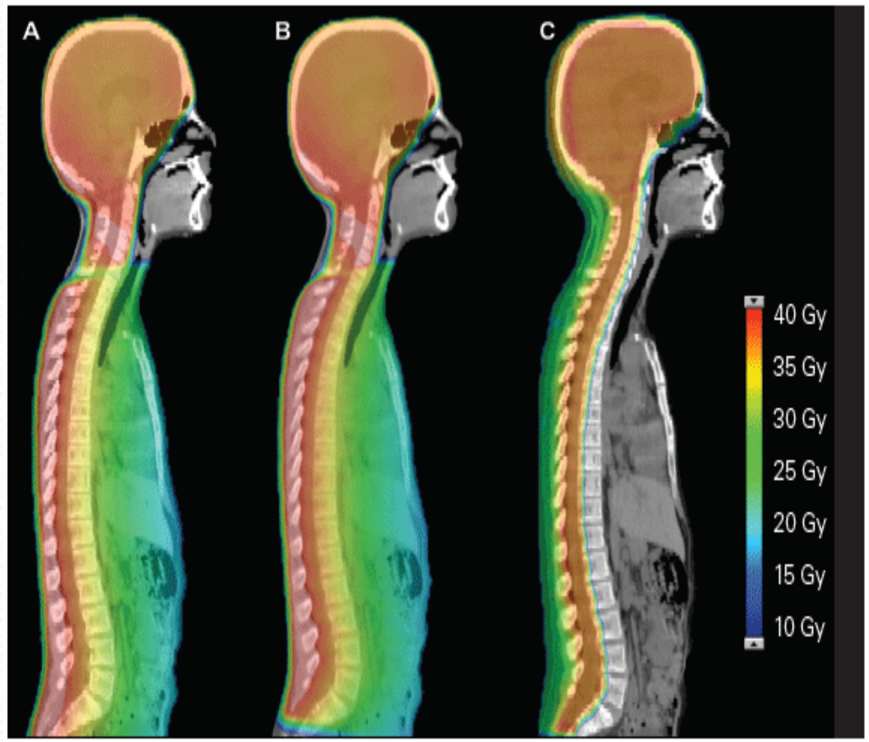
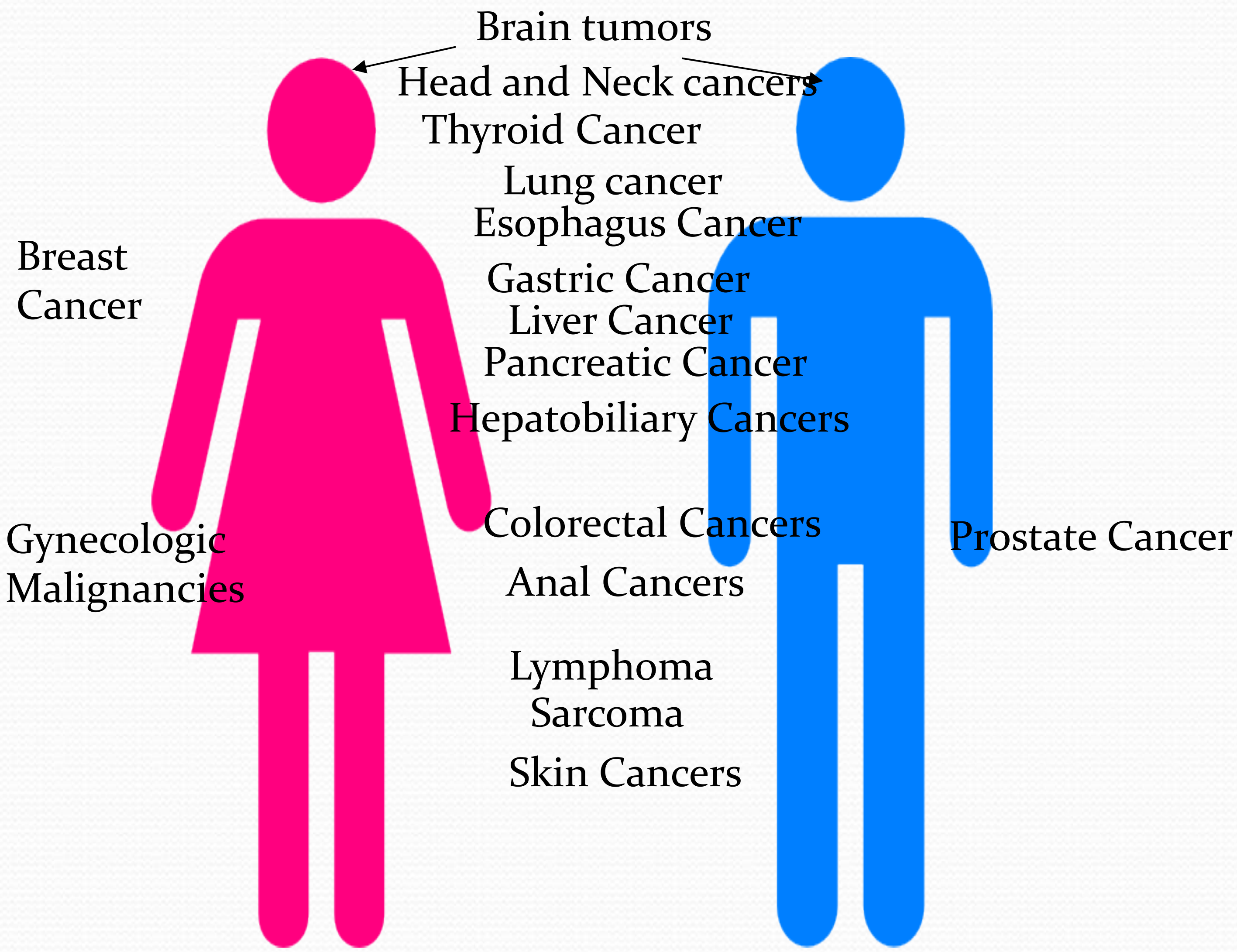


Figure 2. Dosimetric Comparison of Photon and Proton Treatment Plans for a Child Treated With Craniospinal Radiation—(A) Photon 3D-CRT plan with a single posterior spinal field and lateral opposed cranial fields; **(B)** photon IMRT plan; **(C)** intensity-modulated proton therapy plan.

3D-CRT = three-dimensional conformal radiation therapy; IMRT = intensity-modulated radiation therapy.

Clinical Perspective

Indications for Radiation therapy



JAMA. 2010 March 17; 303(11): 1070–1076. doi:10.1001/jama.2010.261.

Stereotactic Body Radiation Therapy for Inoperable Early Stage Lung Cancer

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Abstract

Context—Patients with early stage but medically inoperable lung cancer patients have a poor rate of primary tumor control (30-40%) and a high rate of mortality (3-year survival 20-35%) with current management.

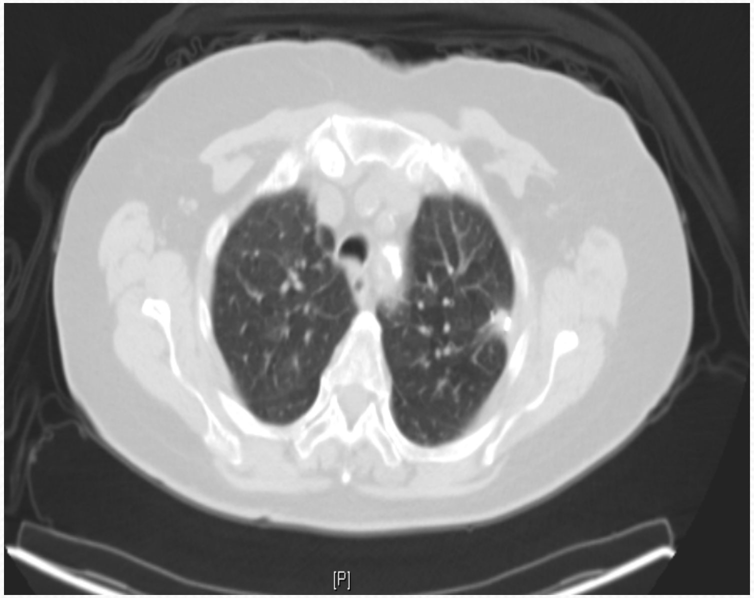
Objective—To evaluate the toxicity and efficacy of stereotactic body radiation therapy in a high risk population of patients with early stage but medically inoperable lung cancer.

Design, Setting, and Patients—Phase 2 North American multicenter study of patients with biopsy-proven peripheral T1-T2, N0, M0 non-small cell tumors less than 5 cm in diameter and medical conditions precluding surgical treatment. The prescription dose was 18 Gy per fraction times 3 fractions (54 Gy total) delivered in 1½-2 weeks. The study opened May 26, 2004, and closed October 13, 2006; data were analyzed through August 31, 2009.

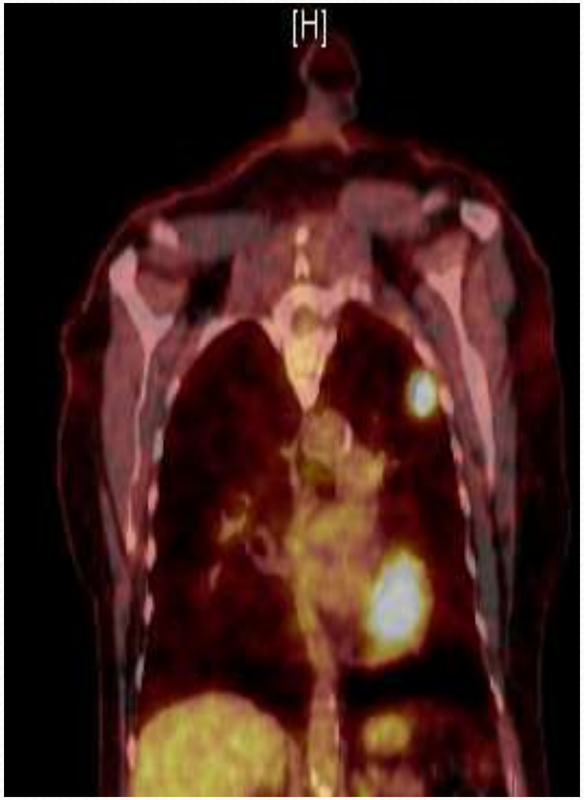
Local control at 3 years 98.6%
3 yr OS 55%
Median OS 48.1 months

Pre Treatment Fiducial markers on CT

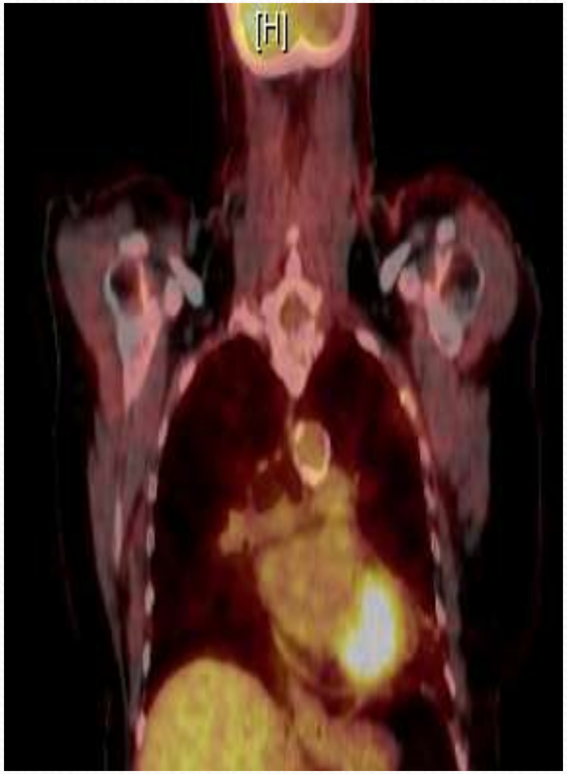
Post Treatment CT Scan



Pre treatment



Post treatment PET

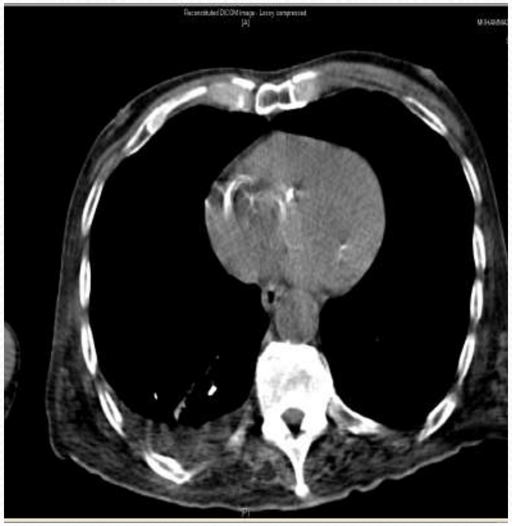


Eaton Lambert Syndrome

Dosimetry


PTV RA2 - Treatment Approved - Transversal - FREE BREATHE
Dose
140.8
130.0 %
120.0 %
110.0 %
A
R
L
P
Isocenter
Y: 0.00 cm
PTV RA2 - Dose Volume Histogram
Dose [cGy]
0
1080
2160
3240
4320
5400
6480
7560
Ratio of Total Structure Volume [%]
100
80
60
40
20
0
20
40
60
80
100
120
140
Relative dose [%]
PTV RA2 - Treatment Approved - Frontal - FREE BREATHE
H
R
L
F
Isocenter
PTV RA2 - Treatment Approved - Sagittal - FREE BREATHE
H
P
A
F
Isocenter

Post treatment imaging



Clinically, Able to walk 2 months after radiation.

Genitourinary malignancies

Indications

- Prostate cancer- LDR,HDR,SBRT,EBRT

  Low risk Prostate Cancer

  Intermediate risk prostate cancer- with hormone therapy

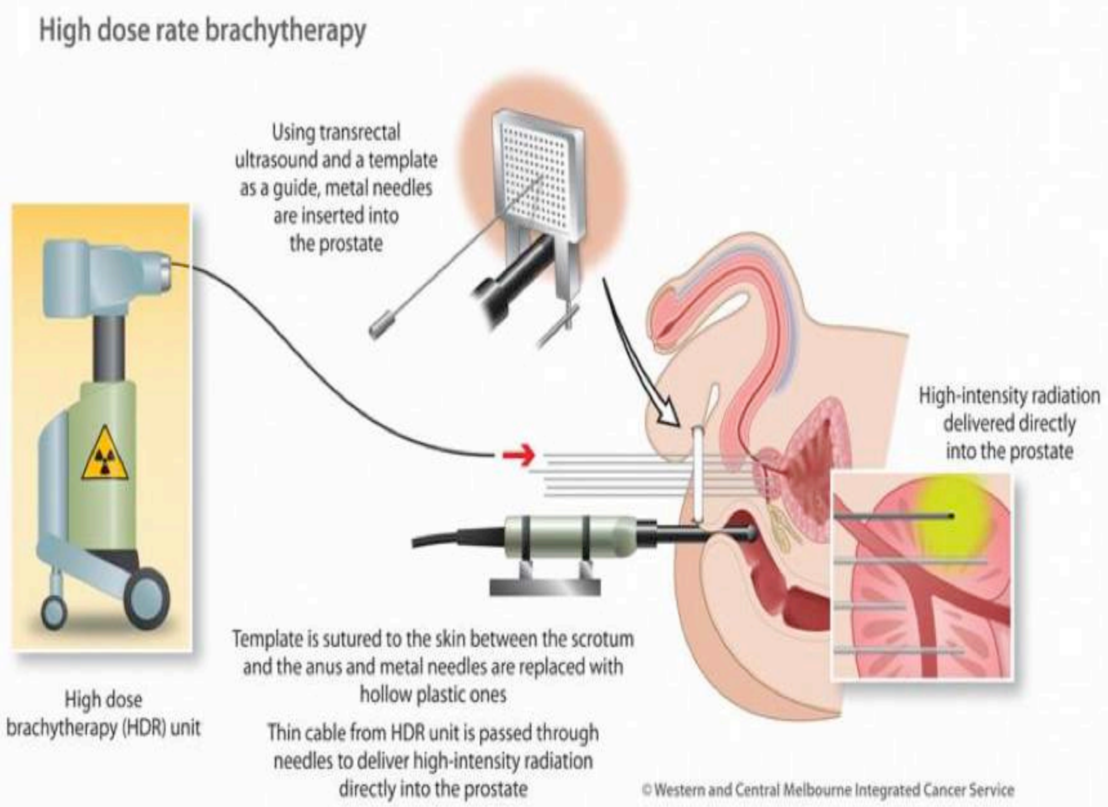
  High Risk Prostate cancer

- Renal cell carcinoma

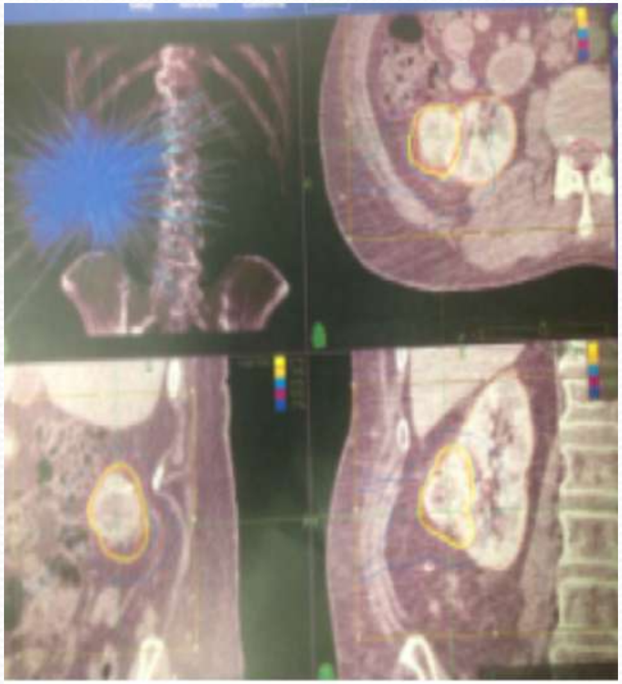
  Post op

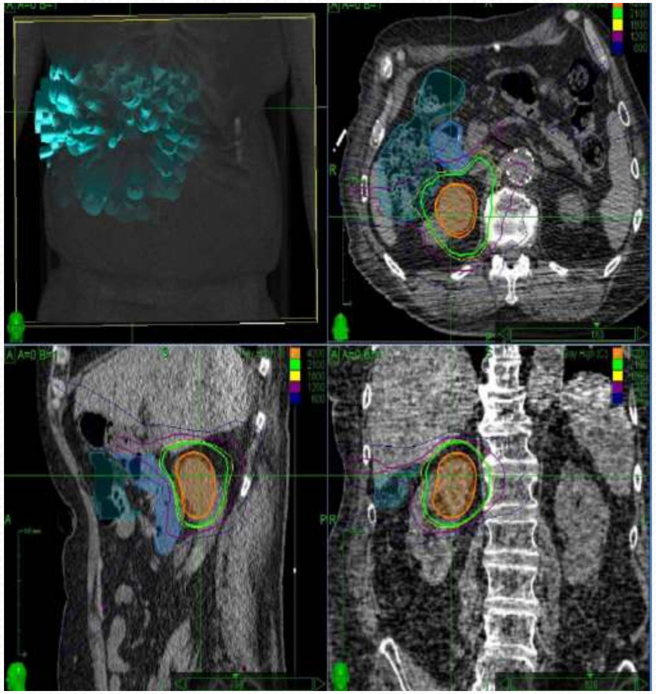
  Medically Inoperable

Prostate HDR



84 year old with RCC





Lymphoma

- TLI
- Consolidative radiation
- Low grade lymphoma
- MALT- gastric

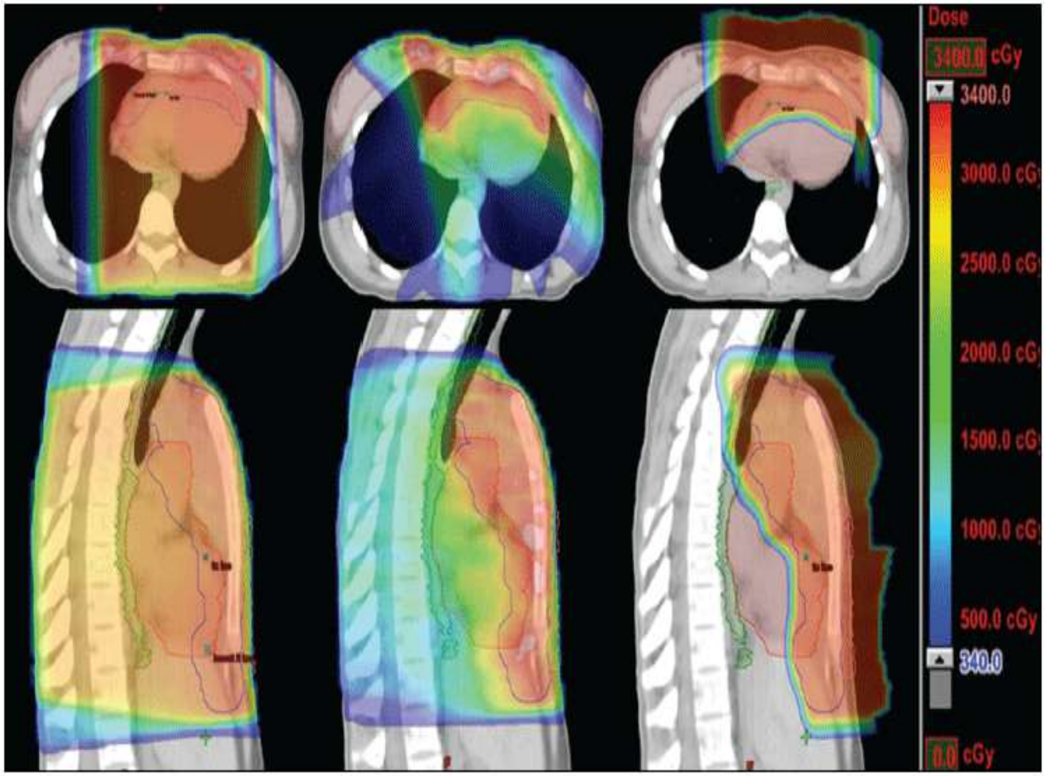


Figure: Color-Wash Dose Distribution for Three Plans for a Representative Patient With Mediastinal Involvement of Hodgkin Lymphoma—3-Dimensional conformal radiotherapy using an anterior-posterior (AP)/posterior-anterior (PA) field arrangement (left); intensity-modulated radiotherapy (middle); and proton therapy using a single AP field arrangement (right). The planned target volume (PTV) is outlined in purple, the heart is outlined in red, and the esophagus is outlined in green.

Low dose radiation

Format: Abstract ▾ Send to ▾

Lancet Oncol. 2014 Apr;15(4):457-63. doi: 10.1016/S1470-2045(14)70036-1. Epub 2014 Feb 24.

4 Gy versus 24 Gy radiotherapy for patients with indolent lymphoma (FORT): a randomised phase 3 non-inferiority trial.

Hoskin PJ[1], Kirkwood AA[2], Popova B[2], Smith P[2], Robinson M[3], Gallop-Evans E[4], Coltart S[5], Illidge T[6], Madhavan K[7], Brammer C[8], Diez P[9], Jack A[10], Syndikus I[11].

⊕ Author information

Abstract

BACKGROUND: Follicular lymphoma has been shown to be highly radiosensitive with responses to doses as low as 4 Gy in two fractions. This trial was designed to explore the dose response for follicular lymphoma comparing 4 Gy in two fractions with 24 Gy in 12 fractions

METHODS: FORT is a prospective randomised, unblinded, phase 3 non-inferiority study comparing radiotherapy given as 4 Gy in two fractions with a standard dose of 24 Gy in 12 fractions. Entry criteria included all patients aged over 18 years, having local radiotherapy for radical or palliative local control, with follicular lymphoma or marginal zone lymphoma, who had received no previous treatment for at least 1 month before. The primary outcome was time to local progression analysed on an intention-to-treat basis. Randomisation was centralised through the Cancer Research UK and University College London Cancer Trials Centre. Radiotherapy target sites were randomised (1:1) with minimisation stratified by histology (follicular lymphoma vs marginal zone lymphoma), treatment intent (palliative or curative) and centre. This trial is registered with ClinicalTrials.gov number, NCT00310167.

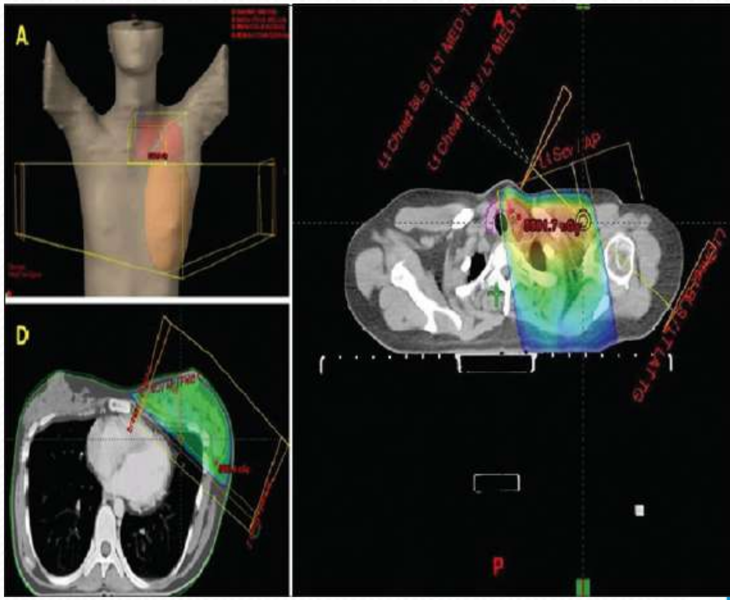
FINDINGS: 299 sites were randomly assigned to 24 Gy and 315 sites to 4 Gy between April 7, 2006, and June 8, 2011, at 43 centres in the UK. After a median follow-up of 26 months (range 0·39-75·4), 91 local progressions had been recorded (21 in the 24 Gy group and 70 in the 4 Gy group). Time to local progression with 4 Gy was not non-inferior to 24 Gy (hazard ratio 3·42, 95% CI 2·09-5·55, p<0·0001). Eight (3%) of 282 patients in the 24 Gy group and four (1%) of 300 in the 4 Gy group had acute grade 3-4 toxic effects. Four (1%) patients in the 24 Gy group and four (1%) patients in the 4 Gy group had late toxic effects. Mucositis was the most common event in the 24 Gy group (two patients with acute mucositis and two with late mucositis; all grade 3) and was not reported in the 4 Gy group. The most common acute effect was pain at the site of irradiation (two patients in the 4 Gy group, one patient in the 24 Gy group; all grade 3), and the most common late effect was fatigue (two patients in the 4 Gy group, one patient in the 24 Gy group; all grade 3).

INTERPRETATION: 24 Gy in 12 fractions is the more effective radiation schedule for indolent lymphoma and should be regarded as the standard of care. However, 4 Gy remains a useful alternative for palliative treatment.

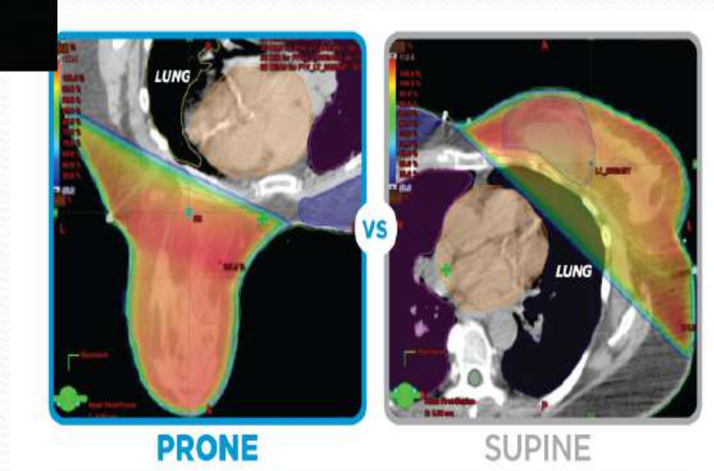
FUNDING: Cancer Research UK.

Sarcoma

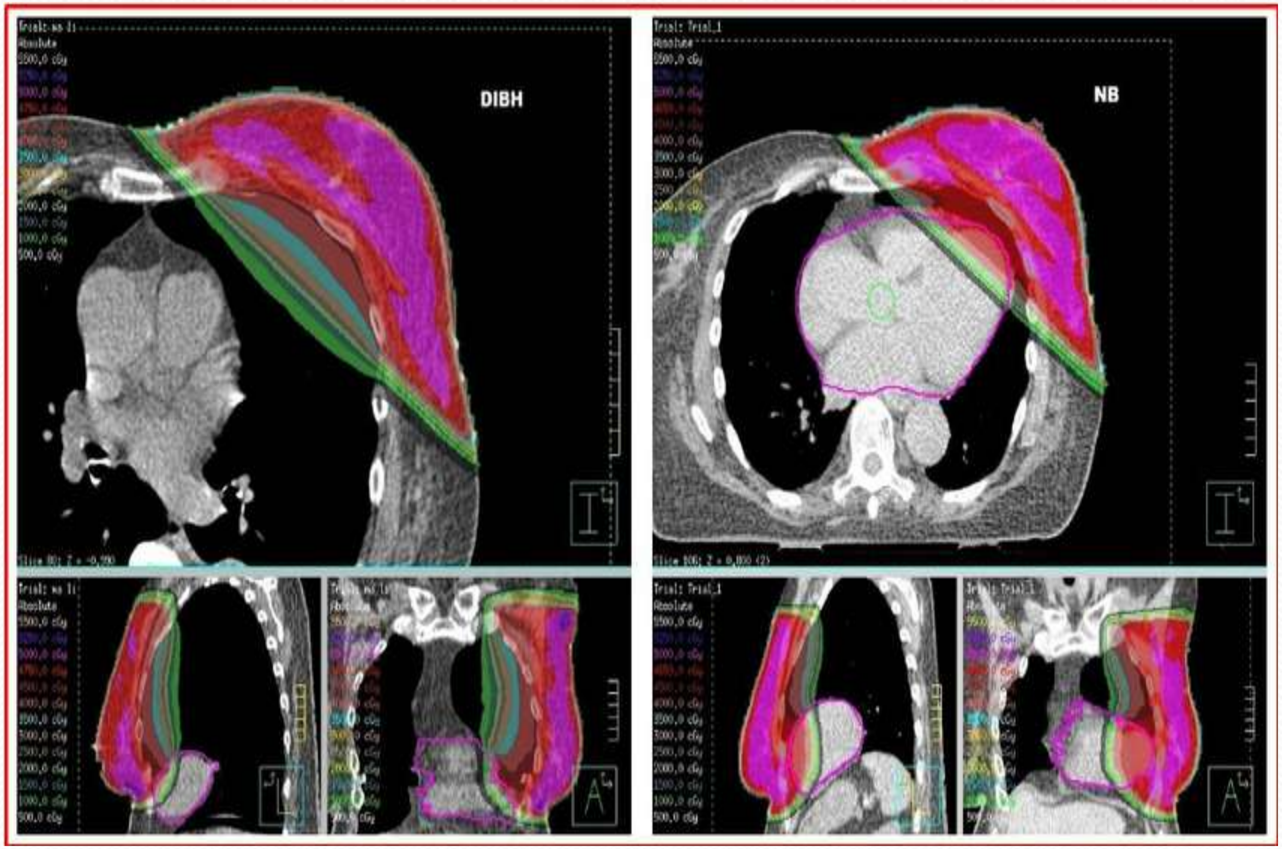
Breast Cancer



Early Stage Breast cancer-
Conventional radiation 5-6 weeks, 5 days/wk
UK FAST trial- 1 day/wk for 5 weeks
Hypofractionated- 3-4 weeks
APBI- brachytherapy- twice daily 5 days
EBRT partial breast- twice daily 5 days



Breast Cancer

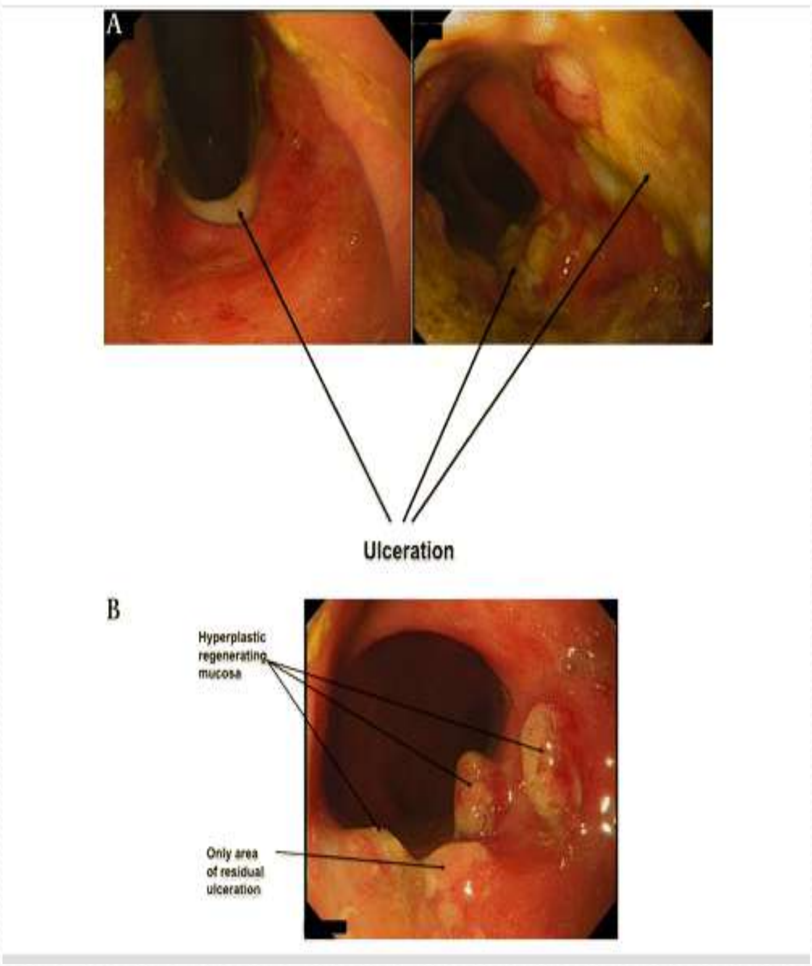


Post radiation changes

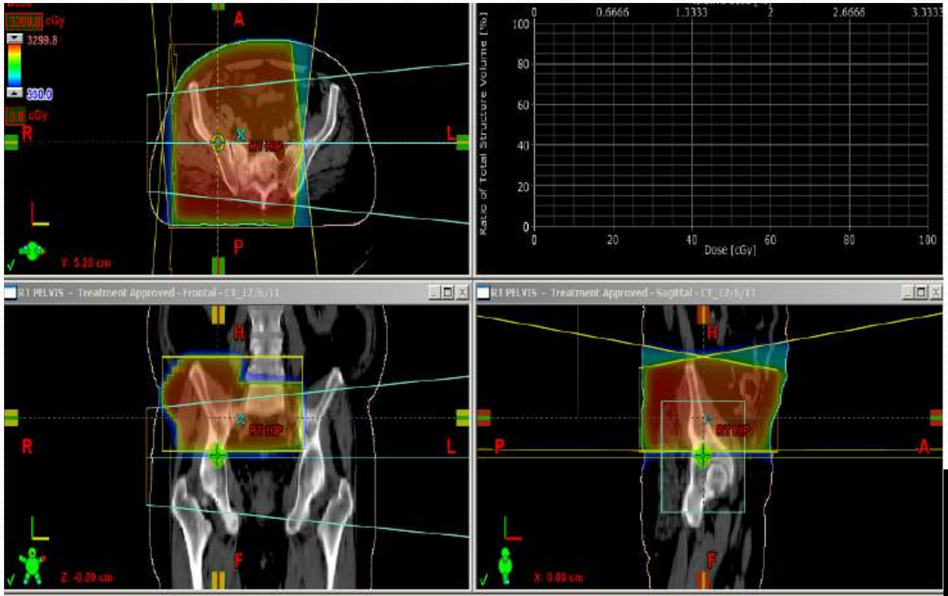
Mid gland

Apex of gland

Endoscopy- bleeding ulcer



Radiation Colitis



Bone metastasis

- 20 Gy in 5 fractions
  - 4 Gy per fraction
- **30 Gy in 10 fractions**
  - **3 Gy per fraction**
- 37.5 Gy in 15 fractions
  - 2.5 Gy per fraction

Bone metastasis

- RTOG 9714
- Randomized Controlled trial compared 8 Gy in 1 fraction vs 30 Gy in 10 fractions
  - 898 patients with breast and prostate cancer metastasis
- Pain relief similar in both arms
- Acute toxicity higher in 10 fraction arm
- Retreatment higher in single fraction arm

- Hartsell WF. J Natl Cancer Inst. 2005 Jun 1;97(11):798-804.

What's new?

Covid-19 Hit -What did it mean for Radiation Oncology

- Oncology care was considered essential during the pandemic
- Social distancing, appropriate protective practices, and prioritization of patient needs
- Oncology care is multidisciplinary- everyone needed to learn Zoom, remote meetings
- Telemedicine- evaluation and consents
- Pretreat testing
- Staff Protection- PPE/ Scrreening

Covid 19 prioritization

- Level 1 (Continue radiation) Patients already on treatment at that onset of the COVID-19 pandemic will continue unless they become COVID-19 positive (COVID+)/person under investigation (PUI). Patients who convert to COVID+/PUI will be placed on a treatment break unless they meet other criteria for urgent treatment. This level allows treatment for emergency and urgent patients where alternative management to radiotherapy is not possible.
- Level 2 (Short delay of radiation acceptable if needed) Routine situations requiring radiotherapy. Within each disease site, specific recommendations have been made. Patients should be contacted at frequent intervals to ensure they have not progressed to Level 1.
- Level 3 (Hold radiation) It may be possible to delay these cases until the pandemic is over or omit radiation all together. These are patients with benign disease or patients amenable to other therapy first (systemic therapy, surgery, etc., when appropriate)

How employers can help employees during radiation treatment?

- Understanding which cancers need treatment
- What are the side effects of the different treatments?
- Help to select sites that are cost effective and outcomes based(not all radiation is equal)
- Understand the limitations during radiation treatment
- Support the work scheduling around radiation treatment
- Cancer as an emotional challenge

Oncology is a team sport!!!

Questions?

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THANK YOU
FOR WATCHING!

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