Radiation Oncology 101:

A Whole Field, 120 Years, and 100's of Diseases in Under 30 min

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Palo Verde Cancer Specialists &
Phoenix Cyberknife

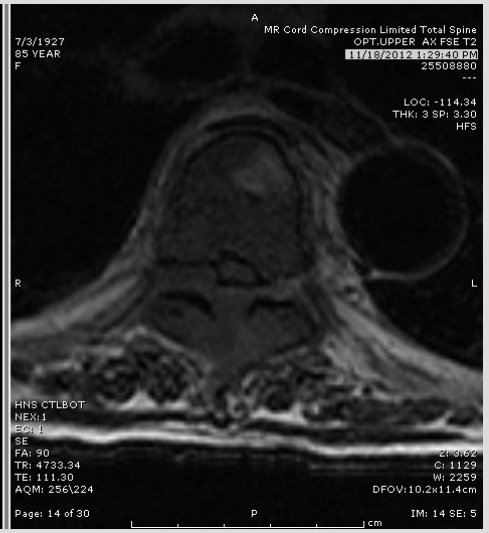
Agenda

- Rad Onc as a Career: Advertisement for the Specialty.
- Uses of Radiotherapy in Clinical Medicine.
- Radiobiology 101.
- Radiation Physics 001.
- Radiation Treatment Modalities including Radiosurgery and Proton Therapy
- Patient Experiences through Treatment / Case Vignettes

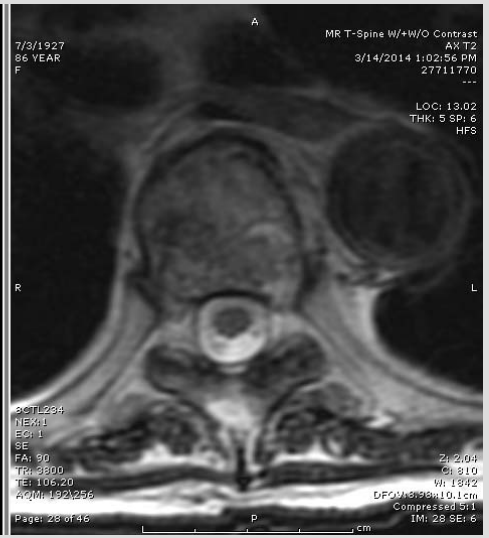
Why am I a Rad Onc?

- 85 yo woman admitted with 1 week of inability to walk, bowel and bladder incontinence after three months of increasing back pain.
  - IDC, 1.5 years prior: pT3 pN3a (ER/PR 25%, Her2-)
  - Anastrozole / Femara / Tamoxifen intolerant due to "joint aches, back and shoulder pain"

Pre XRT
Paralyzed / Incontinent



3.5 years Post XRT
Ambulatory / Continent
Living Independently



PHOENIX CYBERKNIFE

Why am I a Rad Onc?

- I can cure many patients on my own.
- I relieve symptoms for many of those I cannot cure.
- Cancer care requires teamwork.
- I have the time to get to know my patients well, and form close relationships with them during critical and emotional milestones in their lives.
- I treat children and adults.
- I don't just write prescriptions, I do procedures.
- I see fascinating biology and pathology each day.
- Our field strives for evidence-based care.
- It mixes art and science with rapidly advancing technology.

Use of Radiation Therapy

- First effective non-surgical anti-cancer treatment.
- Still the single most potent anti-cancer "drug".
- 60-70% of all cancer patients will receive RT at some point in the course of their disease.
- Utilization is estimated to increase by 20% between 2010 and 2020.

The Future of Radiation Oncology in the United States From 2010 to 2020: Will Supply Keep Pace With Demand?

Benjamin D. Smith, Bruce G. Haffty, Lynn D. Wilson, Grace L. Smith, Akshar N. Patel, and Thomas A. Buchholz

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Table 1. Projected Estimates of Patients Receiving Radiation Therapy in 2010 and 2020

Tumor Site	No. of Patients Receiving Radiation Therapy 2010	No. of Patients Receiving Radiation Therapy 2020	% Increase in Demand for Radiation Therapy From 2010 to 2020
Total	470,000	575,000	22
Breast (invasive)	103,000	119,000	15
Prostate	91,000	123,000	35
Lung	77,000	96,000	25
Oral cavity and pharynx	21,000	25,000	18
Breast (in situ)	20,000	23,000	15
Colorectum	19,000	23,000	22
Esophagus	19,000	23,000	22
Thyroid	15,000	16,000	10
CNS	12,000	14,000	16
Non-Hodgkin's lymphoma	11,000	13,000	18
Uterus	11,000	13,000	22
Larynx	9,300	12,000	24
Cervix	7,000	8,100	16
Pancreas	6,000	7,500	25
Stomach	5,300	6,800	27
Myeloma	4,700	5,800	25
Bladder	3,200	3,900	24
Hodgkin's lymphoma	3,200	3,300	6
Testis	3,000	3,000	2
Kidney	2,500	3,100	21
Melanoma	1,500	1,800	17
Leukemia	1,400	1,600	11
Liver	920	1,200	26
Ovary	380	440	16
All other sites	24,000	29,000	19

NOTE. Cells have been rounded to two significant digits. Percent increase was calculated with unrounded estimates. The total No. includes all invasive sites (excluding nonmelanoma skin cancers) and in situ breast cancers.

Uses of Radiation Therapy

Use	Definition	% Practice
Definitive	Alone or in combination with sensitizers (cisplatin, 5FU, taxanes, Erbitux, androgen deprivation, etc.) to cure a cancer	33%
Adjuvant	Before or after surgery (or less often chemotherapy) to kill regional microscopic disease for cure	33%
Palliative	Non-curative therapy to reduce or prevent symptoms from incurable cancer	33%
Benign Disease	Non-cancerous conditions	1%

Uses of RT – (NEO)ADJUVANT

ADJUVANT radiation is generally only given when risk of local/regional relapse after surgery or chemotherapy is:

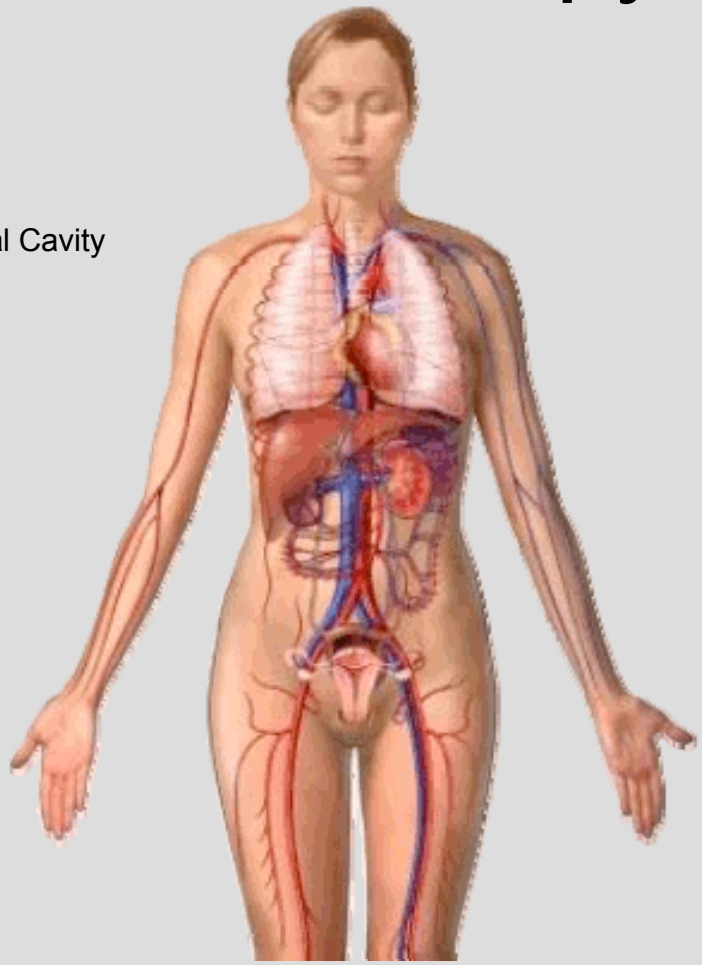
1. ≥ 15% or would be very morbid
2. difficult or morbid to salvage
3. associated with cancer-specific mortality
4. supported by results of Phase 3 RCTs
5. "sanctuary" sites where chemotherapy cannot penetrate (brain / testes)
6. bulky disease

Generally, RCTs of adjuvant radiotherapy show:

- **> 50% RELATIVE REDUCTION** of risk of locoregional relapse
- **5-15% ABSOLUTE IMPROVEMENT** in overall survival

Uses of RT: Definitive Radiotherapy

- Brain Tumors:
  - Meningiomas, Schwannomas, Germinomas
- Head and Neck Cancers:
  - **Oropharynx**, Larynx, Oral, Nasopharynx→Hypopharynx, Nasal Cavity
- Chest:
  - **Lung**, Esophagus
- GI:
  - Pancreas, Gallbladder, Bile Ducts, Anal
- GU:
  - **Prostate**, Penis, Urethra, Bladder
- GYN Cancer:
  - Cervix, Vagina, Vulvar, Uterine
- **Non-melanoma Skin Cancer**
  - Particularly on the face
- Lymphoma (alone or with chemotherapy)
- Pediatrics (usually with chemotherapy):
  - Rhabdomyosarcoma, Ewing's, Lymphomas, …



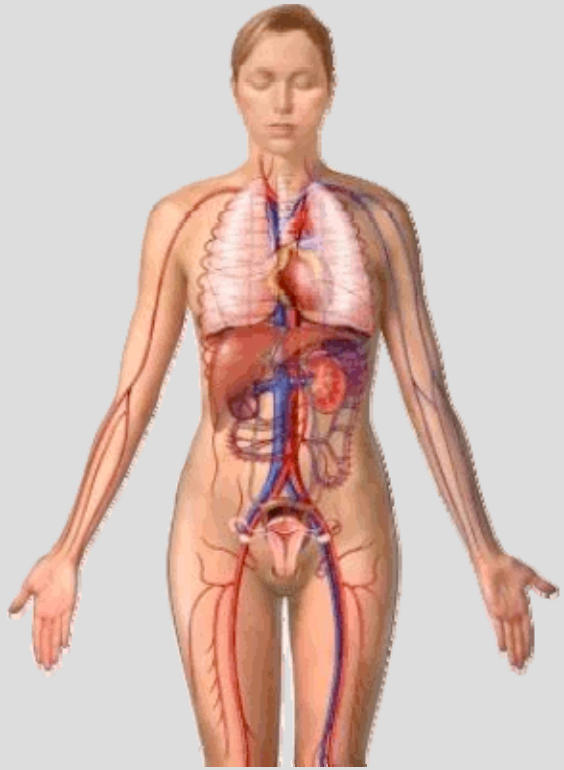
Uses of RT - NEOADJUVANT

- NEOADJUVANT - BEFORE surgery to:
  - **Downstage** tumor to:
    - facilitate resection.
    - allow **function-sparing** surgery.
  - Minimize risk of positive margins and intraoperative tumor spread.
  - Minimize overall side effects of treatment as compared to radiation after surgery.
  - Maximize effectiveness of radiation by treating tumor before it is disrupted.

  - **DISADVANTAGES**:
    - **Pathological information** from surgical specimen is **not available.**
    - May result in **over-treatment of some patients** whose disease is less extensive than preoperative imaging evaluation suggests.

Uses of RT: Neoadjuvant Treatment

- Lung Cancer:
  - NSCLC (especially Pancoast Tumor)
- GI Cancers:
  - Rectal
  - Esophageal
  - Pancreatic
  - Gastric
- Soft Tissue Sarcoma



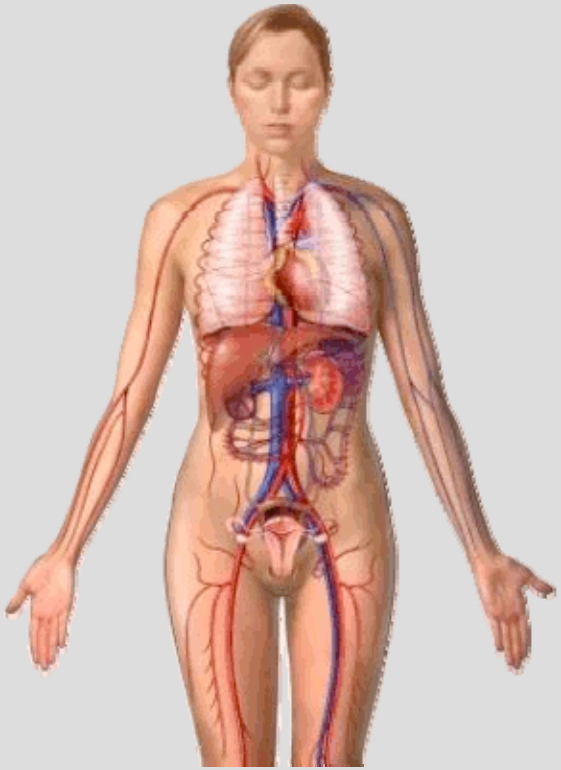
Uses of RT - ADJUVANT

ADJUVANT - AFTER definitive surgery to:

- Minimize risk of **loco-regional recurrence** by sterilizing disease in:
  - unresected draining lymph nodes.
  - the margins of a resection, especially positive margins.
- Contribute to **overall survival**.

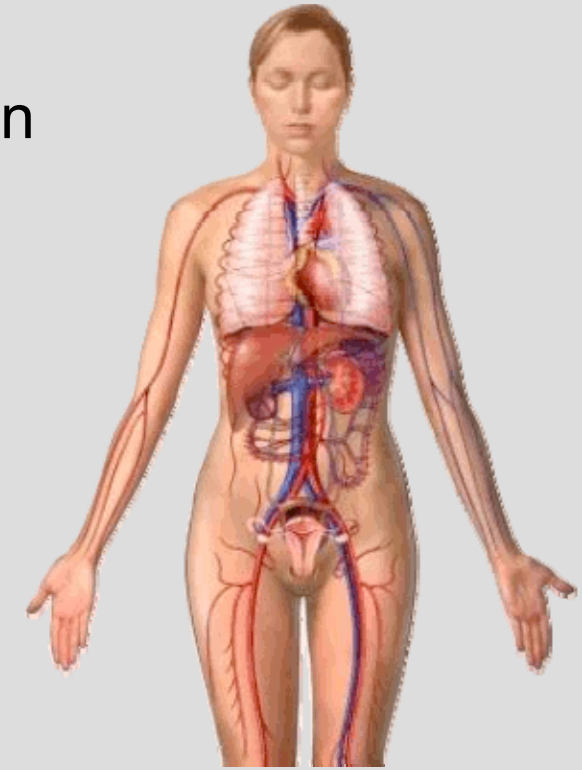
Uses of RT: Adjuvant Treatment

- Brain
- Head and Neck
- Lung
- Breast
- GI Cancers: Gastric, Rectal
- GU: Prostate
- Soft Tissue Sarcoma
- Skin
- Pediatrics:
  - Brain, Rhabdomyosarcoma, Wilm's, Neuroblastoma, …



Uses of RT: Consolidative/Prophylactic RT

- Lymphoma
- Prophylactic Cranial or Craniospinal Irradiation
  - “Sanctuary” due to blood-brain barrier
  - Small Cell Lung Cancer
  - Leukemia / Lymphoma
  - Medulloblastoma and other Pediatric CNS Tumors



Uses of RT - PALLIATIVE

- PALLIATIVE – Relieve symptoms in incurable disease.
  - Pain:
    - Bone mets, uncontrolled head & neck, skin, chest wall, or extremity disease.
  - Neurological Impairment:
    - Brain metastases. spinal cord compression.
  - Obstructions:
    - Airway, bowel, vessels (eg SVC syndrome, extremity edema), dysphagia
  - Hemostasis:
    - Hemoptysis, vaginal bleeding, hematochezia
  - **Success Rate: ≥ 80% for bone pain relief, ≥ 70% for other indications**
  - **Onset: within days to weeks**
  - **Duration of response: Weeks to Years (usually months)**

Uses of RT – BENIGN DISEASE

BENIGN DISEASE –

- Inflammatory or Other Etiologies:
  - Heterotopic ossification prophylaxis after hip arthroplasty.
  - Keloids
  - Trigeminal neuralgia
  - AVMs
  - Grave's Ophthalmopathy
  - Pyronie's Disease
  - Hypersalivation
- Benign Tumors
  - Acoustic neuromas, Schwannomas, Meningiomas
  - Desmoid tumors

Radiation Toxicities

DETERMINISTIC:

- Will occur when a given tissue is exposed to given amount of radiation.
- Different tissues have differing susceptibilities.
- Result from cell death, scarring/fibrosis, or physiologic changes.
- May be influenced by medical comorbidities
  - DM, IBD, genetic radiation sensitivities (ataxia telangiectasia, xeroderma pigmentosa, …)
- Depend on functional organization of an organ.

Radiation Toxicities

STOCHASTIC:

- No absolute dose-response relationship.
- May be caused by even very-low dose exposures, e.g.

- **Radiation-induced second primary malignancies**

  Risk increases with:

  - Younger age at treatment.
  - Large volume of body treated.
  - Higher dose delivered.
  - Latency of > 7 years

Radiation Side-Effects

- Limited to the area treated, except:
  - Fatigue
  - Nausea (usually only with abdominal treatments)
- ACUTE:
  - Normal and expected.
  - Build up slowly over course of radiation.
  - Peak 7-10 days after completion of therapy.
  - >90% resolved 3-4 weeks after treatment.

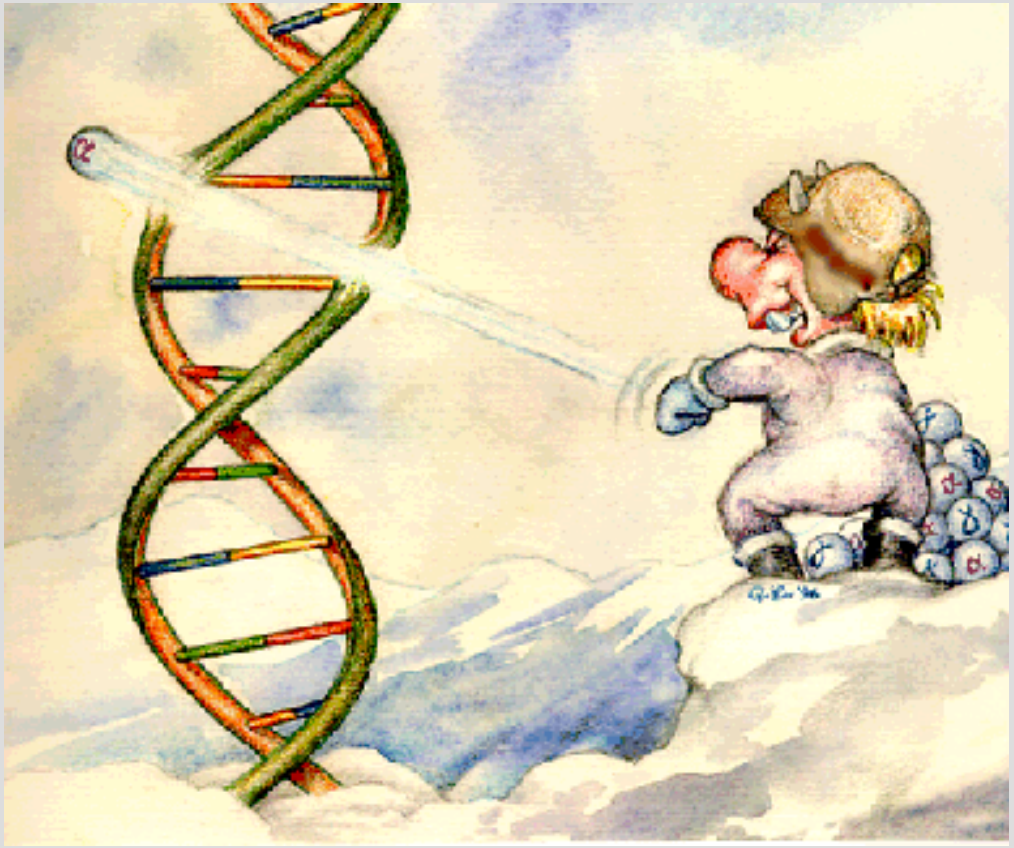
Radiation Side-Effects

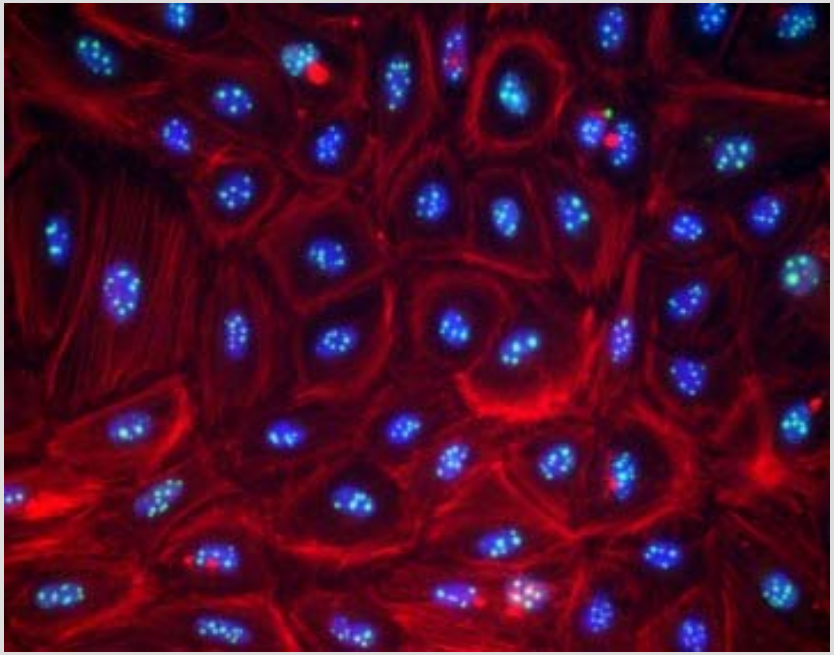
- Common Chronic :
  - Slowly manifest over 1-2 years after treatment.
  - Usually of mild intensity, such as:
    - Brain: Short-term memory loss
    - Prostate: Obstructive urinary symptoms (eg slow stream, nocturia, frequency, ...), erectile dysfunction
    - Head & Neck: Dry mouth, fibrosis
    - Abdomen: Frequency, intermittent diarrhea, intolerance of fatty foods
    - Breast: Tissue fibrosis.

Radiation Side-Effects

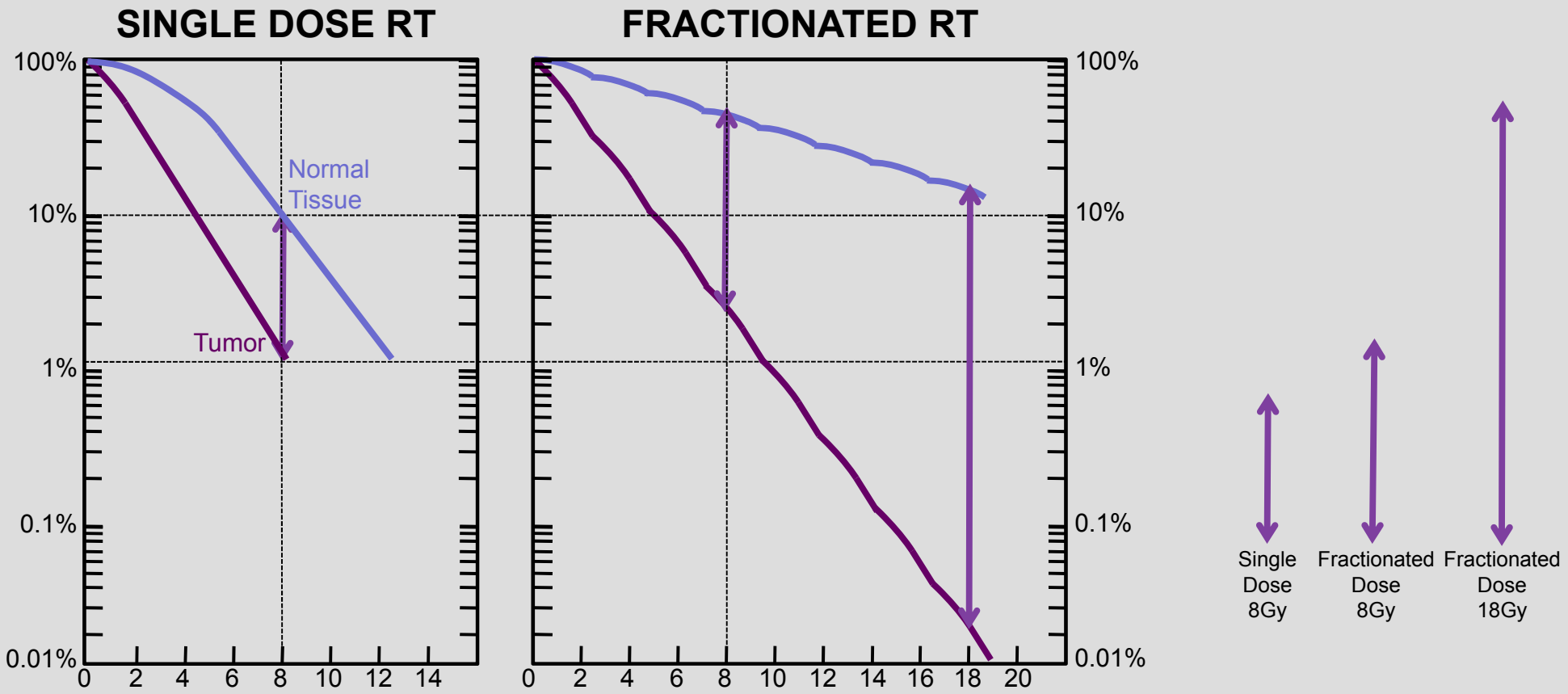
- CHRONIC:
  - SEVERE complications such as bowel obstruction, fistulae, radionecrosis, strictures, etc. are RARE (<5%)
  - Risk increases with higher-dose, larger fields
  - Retreatment (Reirradiation)
  - Concurrent chemotherapy
  - Diabetes, Smoking, Procedures in Treated Areas
  - Genetic Predispositions (ATM, XP, etc.)

Mechanism of Action





Maximizing Therapeutic Ratio - Fractionation Radiobiology

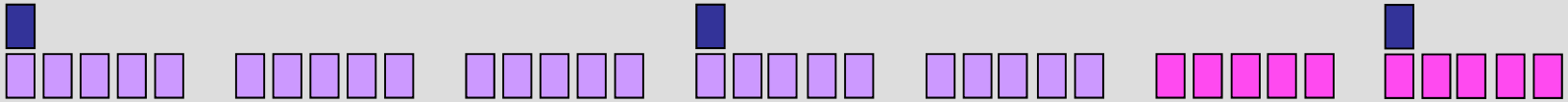


Conventional RT Schedules

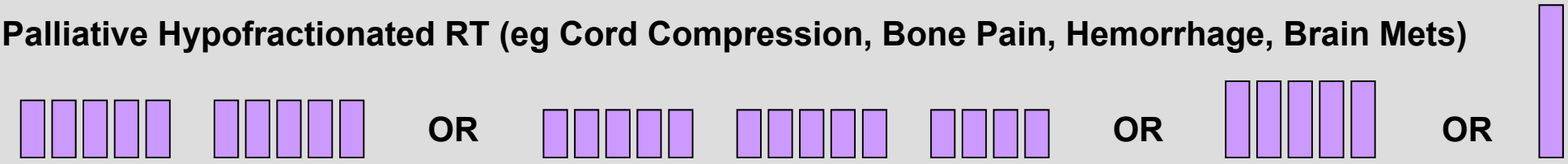
Definitive RT Alone (eg Prostate Cancer, 200 cGy/d, 50 Gy to pelvis boost prostate to 80Gy)

Adjuvant RT (eg Breast Cancer, 200 cGy/, 50 Gy to whole breast boost lumpectomy bed to 60Gy)

Definitive Chemo RT (eg Head & Neck Cancer, 200 cGy/d, 50 Gy to neck, boost gross tumors to 70Gy)



Palliative Hypofractionated RT (eg Cord Compression, Bone Pain, Hemorrhage, Brain Mets)



300 cGy x 10

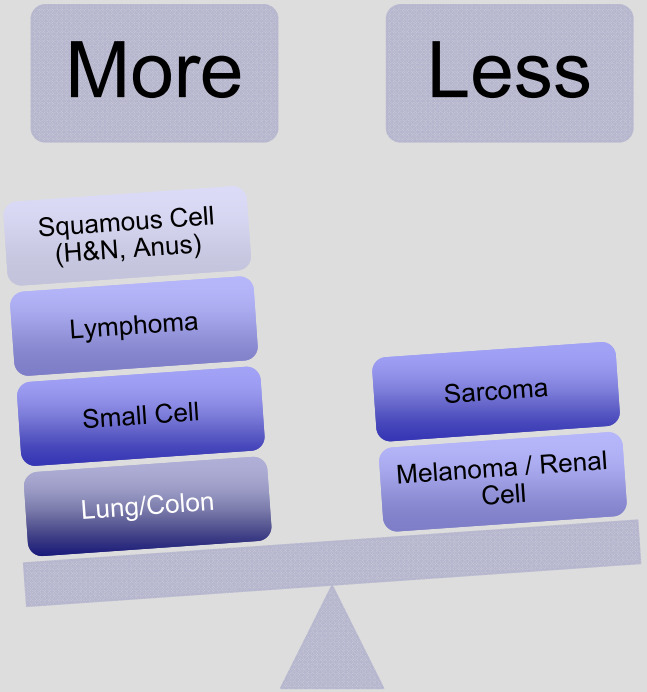
250 cGy x 14

400 cGy x 5

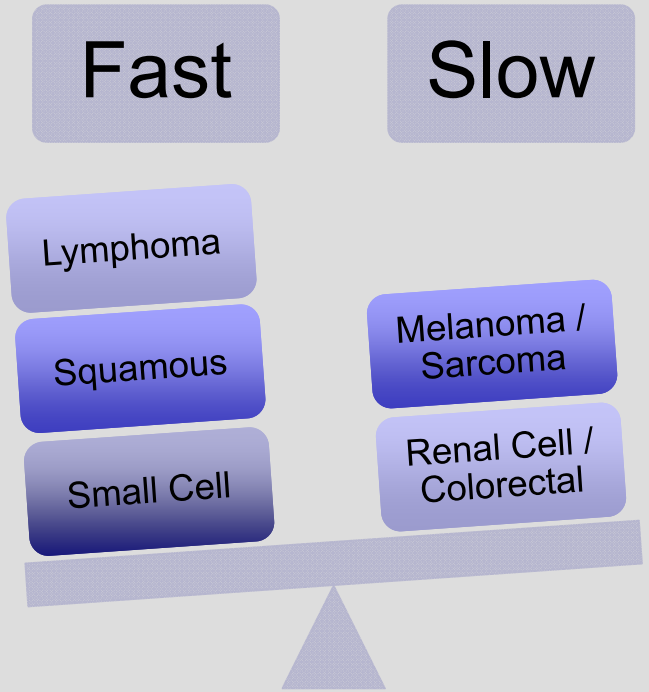
800 cGy x 1

SENSITIVITY and RESPONSIVENESS

How SENSITIVE to Killing



How FAST does tumor Shrink



Radiosurgery

- Focus 1-5 massive doses of radiation on a tumor or organ.
- Non-invasively kill nearly everything in the target volume.
- Forfeit most radiobiological sparing of normal tissues.
- More like surgery, RFA or cryotherapy.

- Rely on physics, imaging, and technology to maximally focus radiation on target and AVOID normal tissues.

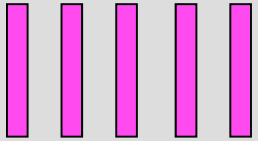
- Radiobiology of large single dose treatment may induced more death of tumor neovasculature to result in better tumor killing.

RADIOSURGERY = RADIATION ABLATION

Definitive RT Alone **(eg 80 Gy to prostate in 40 fx daily)**

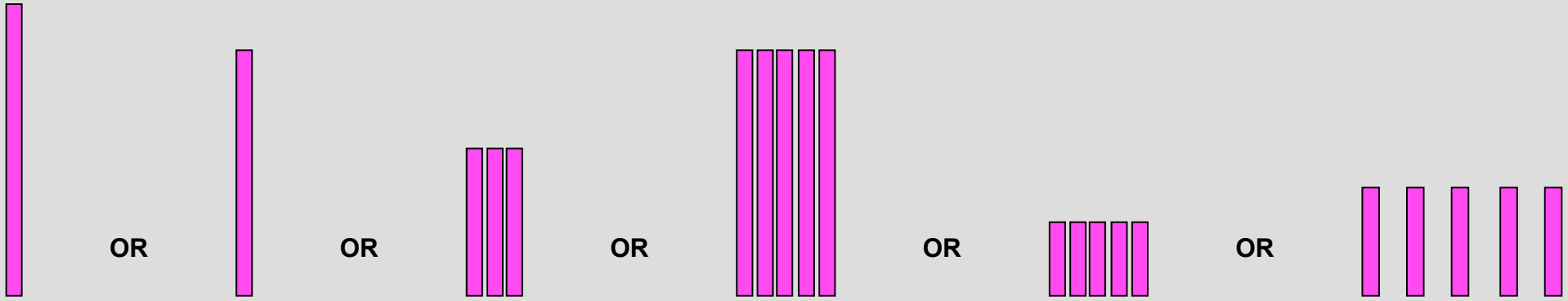
Keep the prostate
Kill the cancer.

Radiosurgery **(eg 38 Gy in 5 fx)**



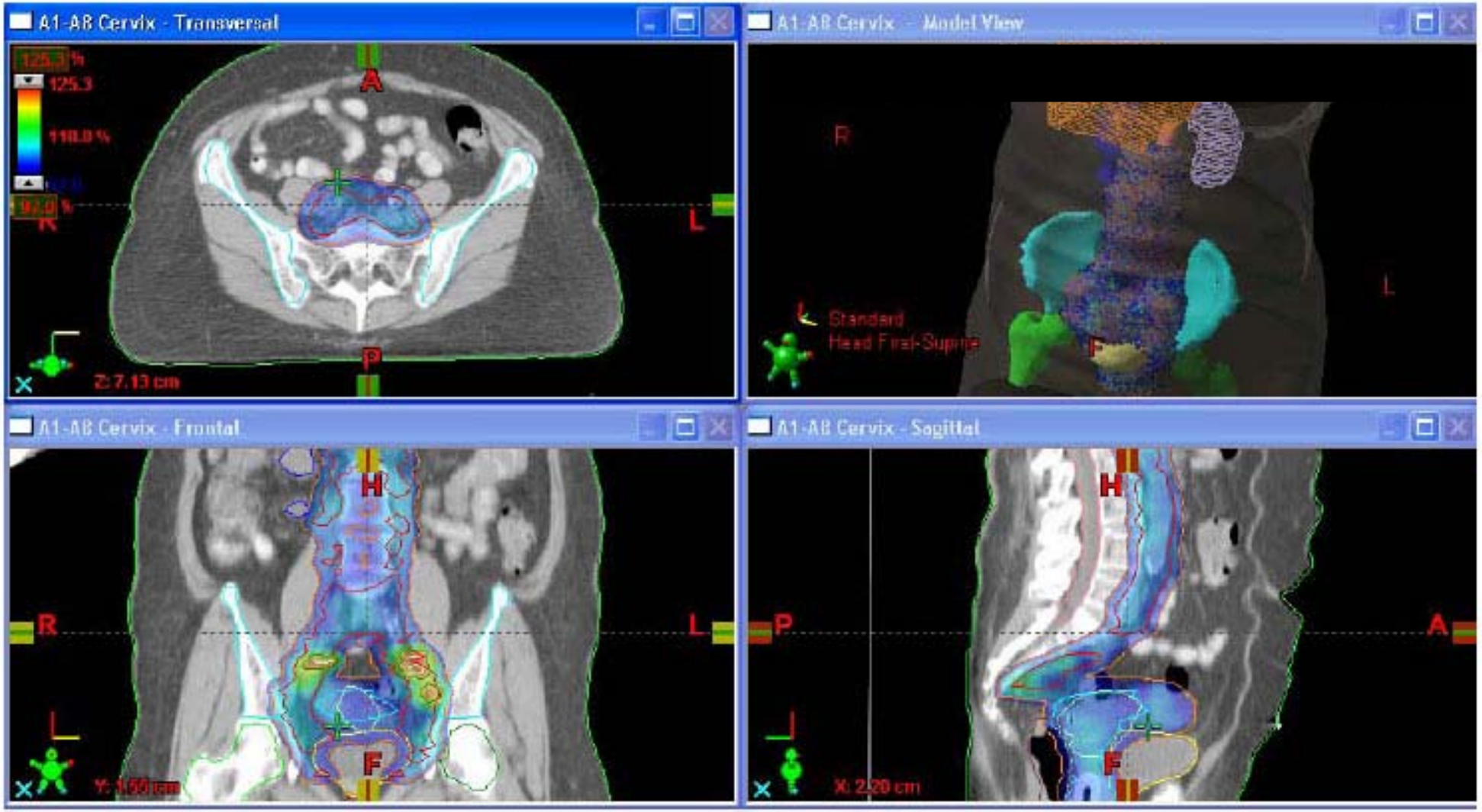
Radiosurgical
Prostatectomy

Radiosurgery Schedules



Maximizing Therapeutic Ratio

- How do I FOCUS it? **PHYSICS**
  - External Beam and/or Brachytherapy
  - Alphabet Soup:
    IGRT, IMRT, Tomotherapy, Protons, HDR, LDR, SBRT, SRS, Cyberknife, TrueBeam, Novalis, Vero, …


A1-AB Cervix - Transversal
125.3 %
125.3
118.8 %
A
L
P
Z: 7.13 cm
A1-AB Cervix - Model View
R
L
Standard
Head First-Supine
F
A1-AB Cervix - Frontal
H
R
L
F
A1-AB Cervix - Sagittal
H
P
A
F
X: 2.20 cm

Simulation

- Position patient as they will be treated.
- Fabricate immobilization devices (mask, arm-rest, body cradle, leg-rest, abdominal compression belt to minimize respiratory motion).
- Obtain treatment-planning CT scan of the target area.
- Place marks (often tattoos) as reference for repositioning.

Planning

- Rad Onc works with team to define treatment:
  - Fuse different imaging modalities to the planning CT
  - Draw targets and normal structures to avoid
  - Specify Dose-Volume Constraints, for example:
    - Max dose to spinal cord < 50 Gy
    - No more than 27% of lungs to get 20 Gy
    - Lowest dose in PTV should be 95% of the prescription
  - Work with team to optimize treatment
  - Quality assurance

Image-Guided IMRT - Delivery

X-ray Sources

Linear Accelerator

ROBOTIC DELIVERY SYSTEM

IMAGING SYSTEM

Manipulator

TARGETING SOFTWARE

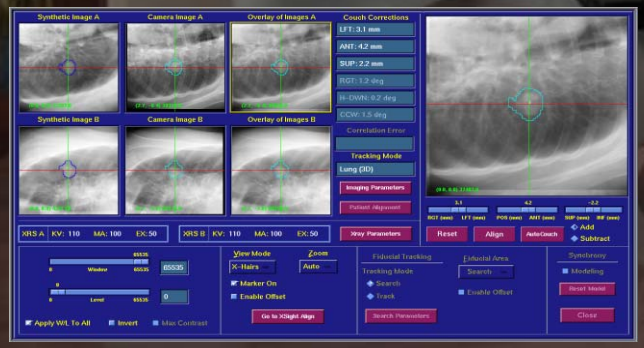
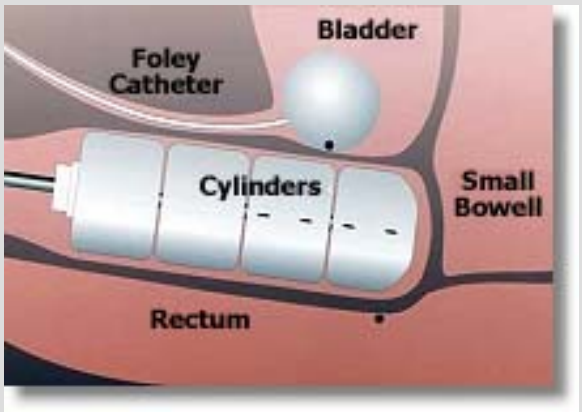


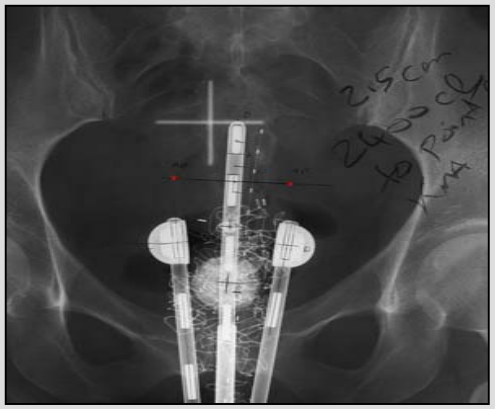
Image Detectors

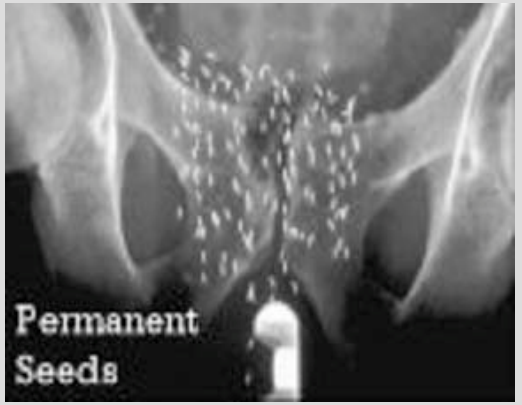
PHOENIX CYBERKNIFE

Brachytherapy – Implant Types

- Temporary
  - "Applicator" = device or catheters placed within tumor-bearing tissue to hold radioactive sources.
  - Applicator removed at end of therapy.
- Permanent
  - Permanent implantation of radioactive seeds into tumor which decay to inert metal







Brachytherapy – Dose Rate

- Low Dose Rate
  - Low activity radioactive seeds slowly deliver radiation over days to months.

- High Dose Rate
  - High activity source pushed in & out of applicator by robot (Afterloader)