



Radiation Treatment for Breast and Prostate Cancer

Chris Premo, MD
Radiation Oncology
Madigan Army Medical Center

Disclosures

- ▶ Employed by the US Army. The slides and discussion are my own views/opinion and do not represent the opinion/views of the government, DoD, US Army, or Madigan Army Medical Center.

Outline

- ▶ History of radiation
- ▶ Brief physics and biology review
- ▶ Conditions treated with radiation therapy
- ▶ Logistics of radiation therapy – typical course of therapy
- ▶ Radiation planning –various techniques and considerations
- ▶ Short term side effects
- ▶ Long term side effects
- ▶ Follow up/surveillance

History of Radiation

- Xrays discovered in 1895 by Wilhelm Roentgen
- One of the first pictures of an xray was of his wife's hand.
- Within 3 years radiation was used to treat cancers




History of Radiation

- ▶ Early uses of radiation:
 - ▶ Skin conditions such as acne
 - ▶ Removal of unwanted hair
 - ▶ Treatment of tonsils and adenoids
 - ▶ Scalp treatment for ringworm
 - ▶ Treatment of enlarged thymus

RADIUM THERAPY

The only scientific apparatus for the preparation of radio-active water in the hospital or in the patient's own home.

This apparatus gives a high and measured dosage of radio-active drinking water for the treatment of gout, rheumatism, arthritis, neuralgia, sciatica, tabes dorsalis, catarrh of the antrum and frontal sinus, arterio-sclerosis, diabetes and glycosuria, and nephritis, as described in Dr. Saubermann's lecture before the Roentgen Society, printed in this number of the "Archives."



DESCRIPTION.

The perforated earthenware "activator" in the glass jar contains an insoluble preparation impregnated with radium. It continuously emits radium emanation at a fixed rate, and keeps the water in the jar always charged to a fixed and measurable strength, from 5,000 to 10,000 Maché units per litre per diem.

SUPPLIED BY
RADIUM LIMITED,
93, MORTIMER STREET, LONDON, W.
Telephone: 6N 8477A.



order that his cooperation may be secured more relatively still.

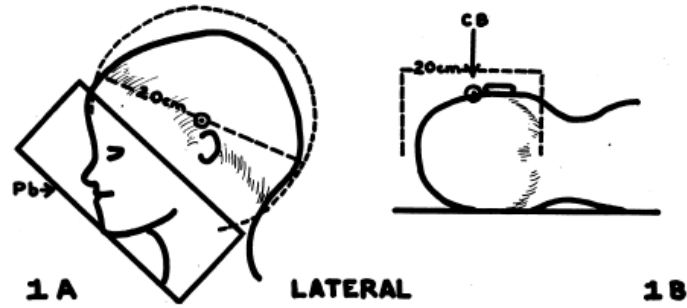


Diagram 1, A and B.—Lateral: Position of the head and direction of the central beam for irradiation of the lateral field(a).

March, 1949

RADIATION THERAPY OF RINGWORM OF SCALP

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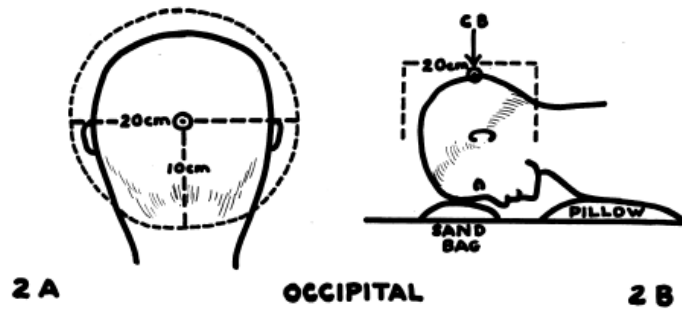


Diagram 2, A and B.—Occipital: Position of the head and direction of the central beam for irradiation of the occipital field.

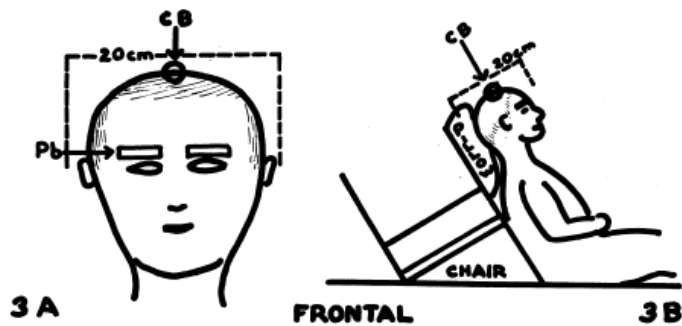
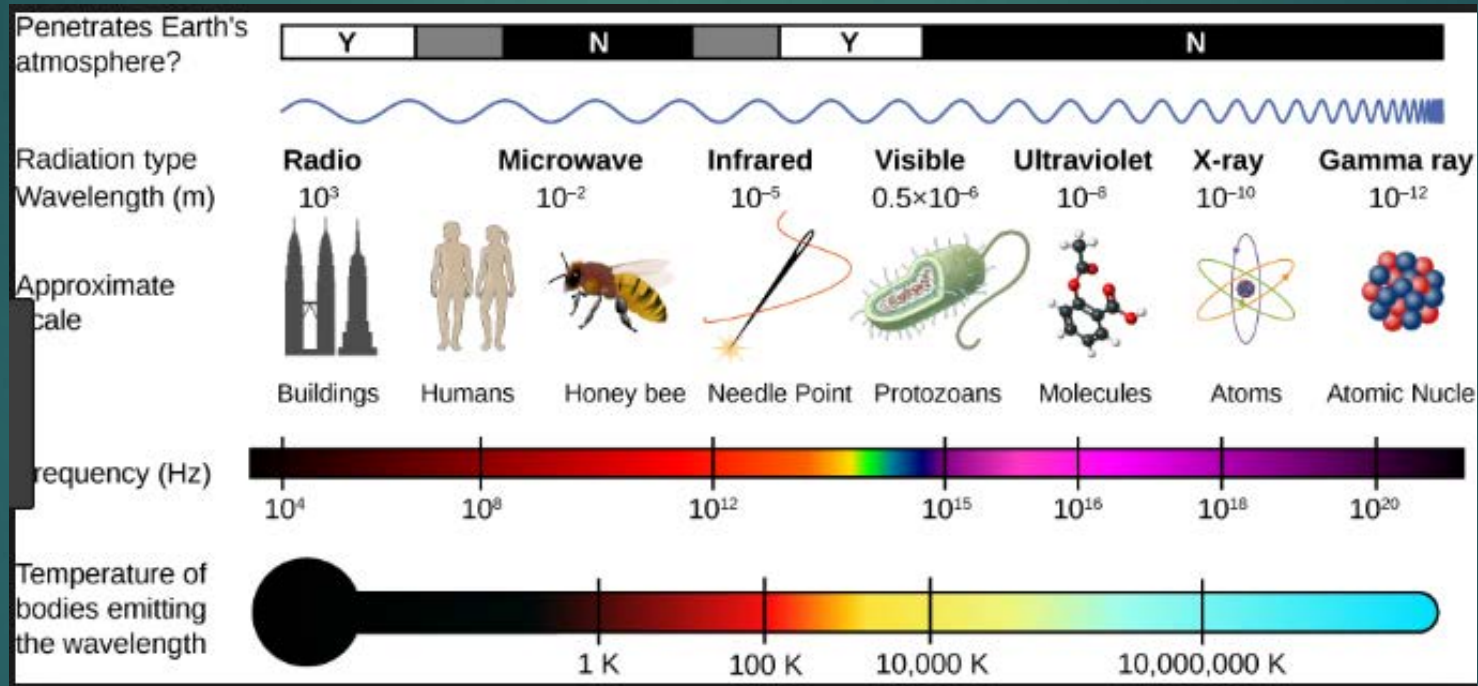


Diagram 3, A and B.—Frontal: Position of the head and direction of the central beam for irradiation of the frontal field.

Radiation Physics

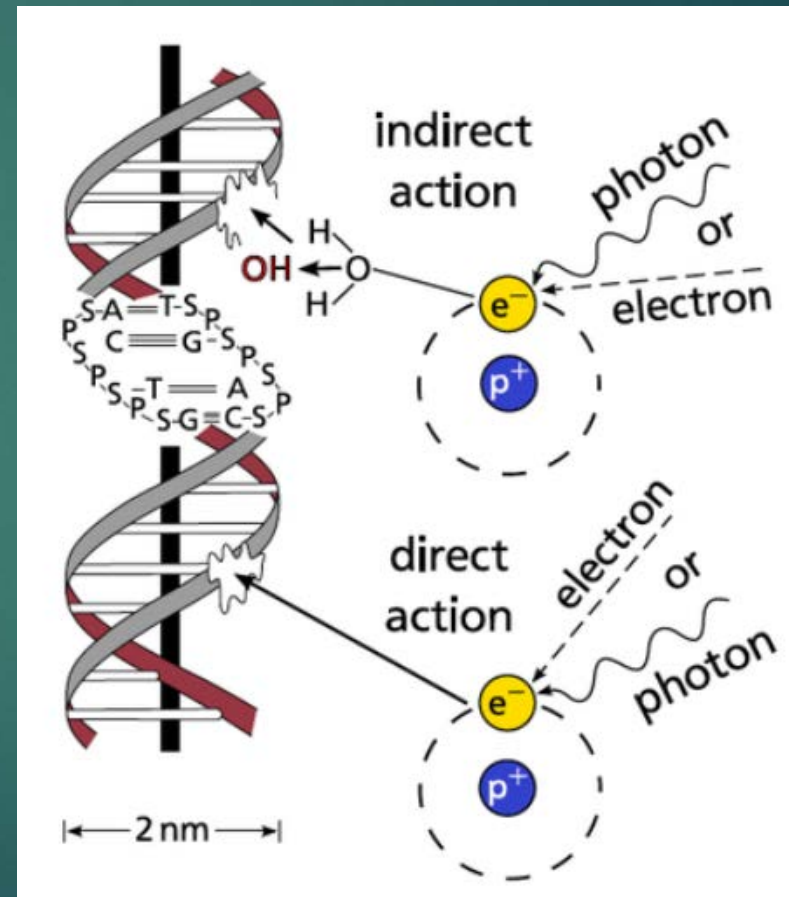


Radiation Physics



- ▶ Common types of radiation used for therapy:
 - ▶ Photon
 - ▶ Electron
 - ▶ Proton
 - ▶ Neutron
 - ▶ Carbon ion
 - ▶ Radioisotopes

Radiobiology



- ▶ Radiation causes cell damage by 2 main mechanisms which ultimately lead to cell death via apoptosis or, more commonly, during mitosis
 - ▶ Directly causes double stranded DNA breaks – 1/3
 - ▶ Generates free radicals in cells which then cause DNA damage – 2/3
- ▶ Normal cells can repair radiation damage within 6 hours



Estimated New Cases

			Males	Females			
Prostate	174,650	20%			Breast	268,600	30%
Lung & bronchus	116,440	13%			Lung & bronchus	111,710	13%
Colon & rectum	78,500	9%			Colon & rectum	67,100	8%
Urinary bladder	61,700	7%			Uterine corpus	61,880	7%
Melanoma of the skin	57,220	7%			Melanoma of the skin	39,260	4%
Kidney & renal pelvis	44,120	5%			Thyroid	37,810	4%
Non-Hodgkin lymphoma	41,090	5%			Non-Hodgkin lymphoma	33,110	4%
Oral cavity & pharynx	38,140	4%			Kidney & renal pelvis	29,700	3%
Leukemia	35,920	4%			Pancreas	26,830	3%
Pancreas	29,940	3%			Leukemia	25,860	3%
All Sites	870,970	100%			All Sites	891,480	100%

Estimated Deaths

			Males	Females			
Lung & bronchus	76,650	24%			Lung & bronchus	66,020	23%
Prostate	31,620	10%			Breast	41,760	15%
Colon & rectum	27,640	9%			Colon & rectum	23,380	8%
Pancreas	23,800	7%			Pancreas	21,950	8%
Liver & intrahepatic bile duct	21,600	7%			Ovary	13,980	5%
Leukemia	13,150	4%			Uterine corpus	12,160	4%
Esophagus	13,020	4%			Liver & intrahepatic bile duct	10,180	4%
Urinary bladder	12,870	4%			Leukemia	9,690	3%
Non-Hodgkin lymphoma	11,510	4%			Non-Hodgkin lymphoma	8,460	3%
Brain & other nervous system	9,910	3%			Brain & other nervous system	7,850	3%
All Sites	321,670	100%			All Sites	285,210	100%

Conditions Treated With Radiation

- ▶ Cancerous:
 - ▶ Brain tumors
 - ▶ Head/Neck cancers
 - ▶ Breast cancer – typically used after surgery to reduce the risk of recurrence
 - ▶ Lung cancer
 - ▶ Gastrointestinal – esophagus, stomach, pancreas, rectum, anus
 - ▶ GU – bladder, prostate – used as definitive treatment or after surgery to reduce the chance of recurrence.
 - ▶ Gyn – endometrial, cervical, vulvar
 - ▶ Soft tissue tumors – sarcomas
 - ▶ Skin cancer

Conditions Treated With Radiation

- ▶ Benign conditions
 - ▶ Heterotopic ossification prevention
 - ▶ Dupuytren's/Ledderhose disease
 - ▶ Plantar Fasciitis
 - ▶ Keloids
 - ▶ Pigmented villonodular synovitis (PVNS)
 - ▶ Pterygium
 - ▶ Benign tumors
 - ▶ Graves' ophthalmopathy
 - ▶ Peyronie's disease
 - ▶ Trigeminal neuralgia

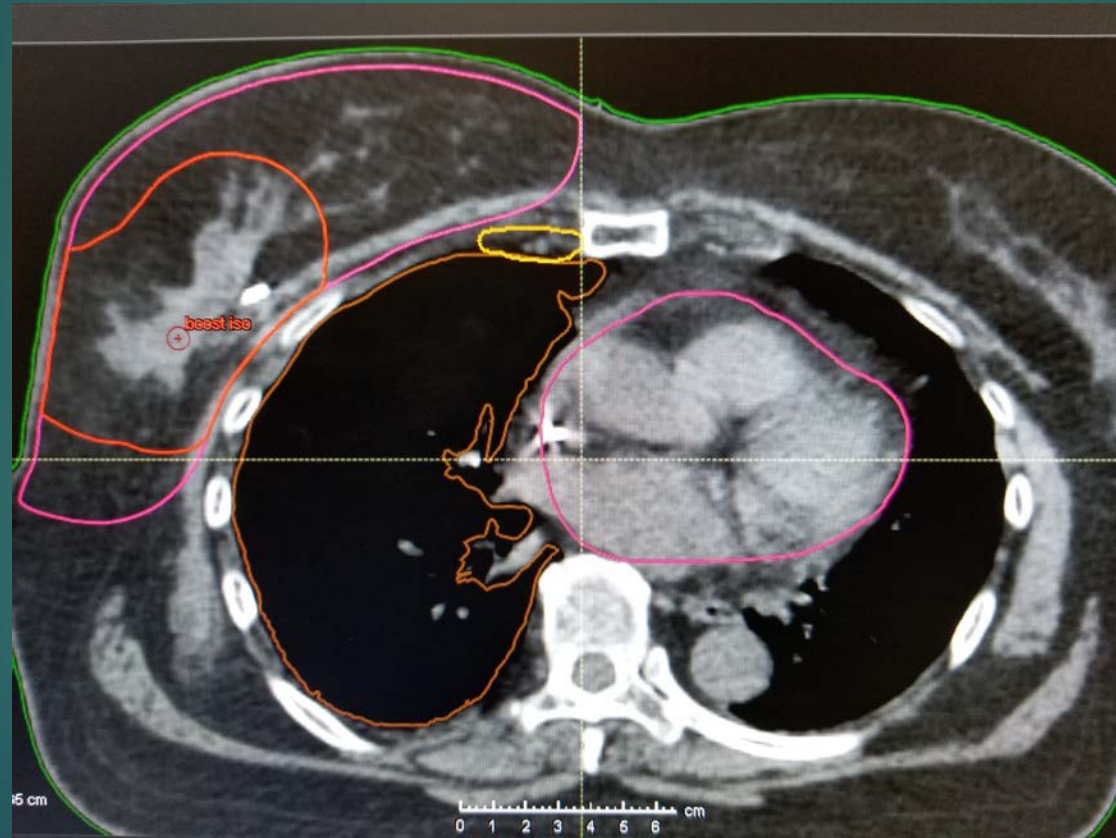
Logistics of Radiation Therapy

- ▶ CT simulation – “dry run” or planning scan
- ▶ Radiation planning – 1-2 weeks
- ▶ Treatment - typically daily treatments, M-F, for several weeks
 - ▶ Breast cancer: 1-6 weeks
 - ▶ Prostate cancer: 1-8 weeks
- ▶ Treatment generally takes 10-15 minutes a day
- ▶ In general, radiation therapy is very safe and well tolerated with low risk of severe complications
- ▶ Many patients can work full time and exercise during radiation therapy – i.e. minimal disruption to their daily activities

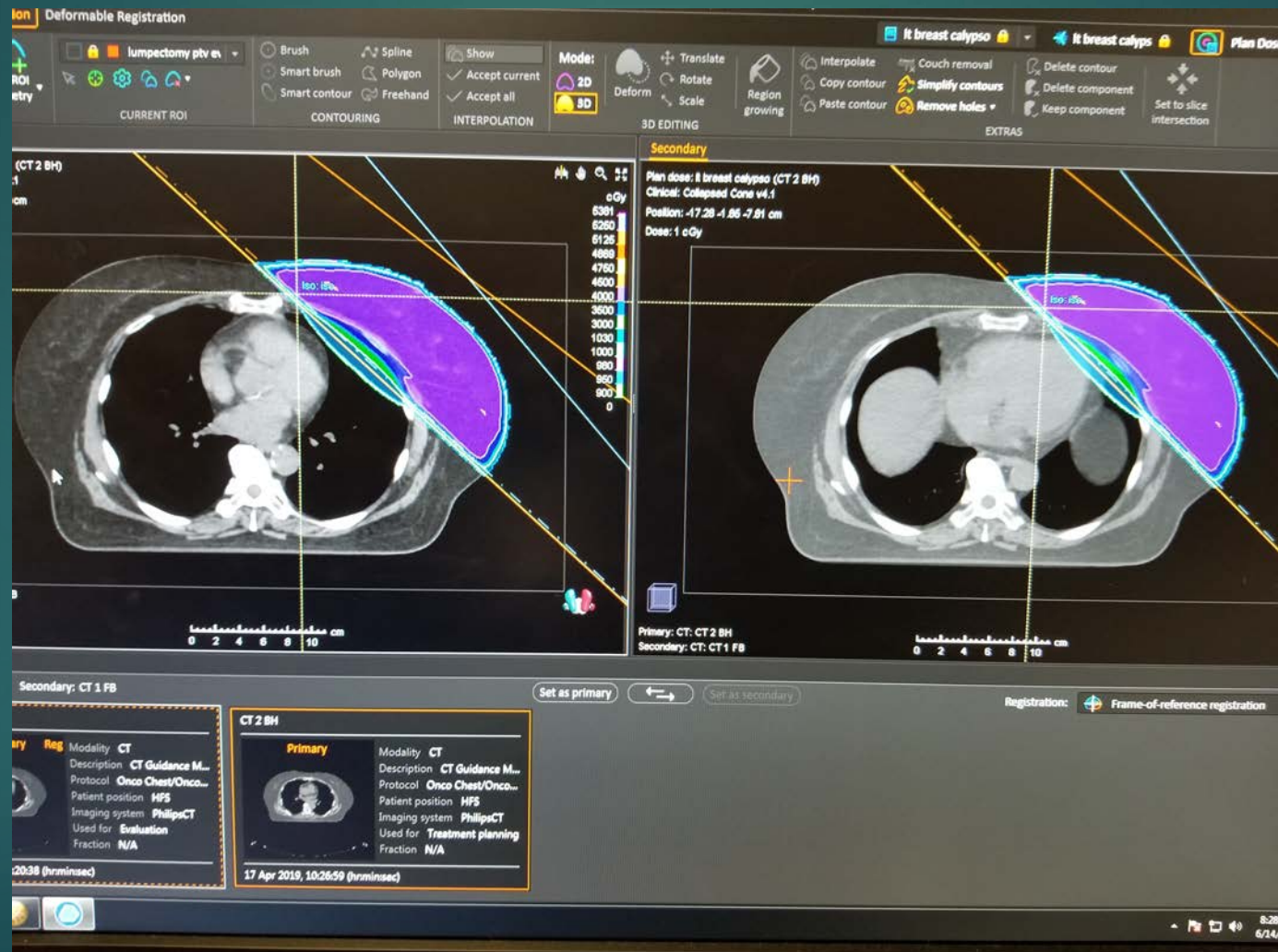
CT Simulation/Radiation Planning Scan



Radiation Planning



Radiation Planning

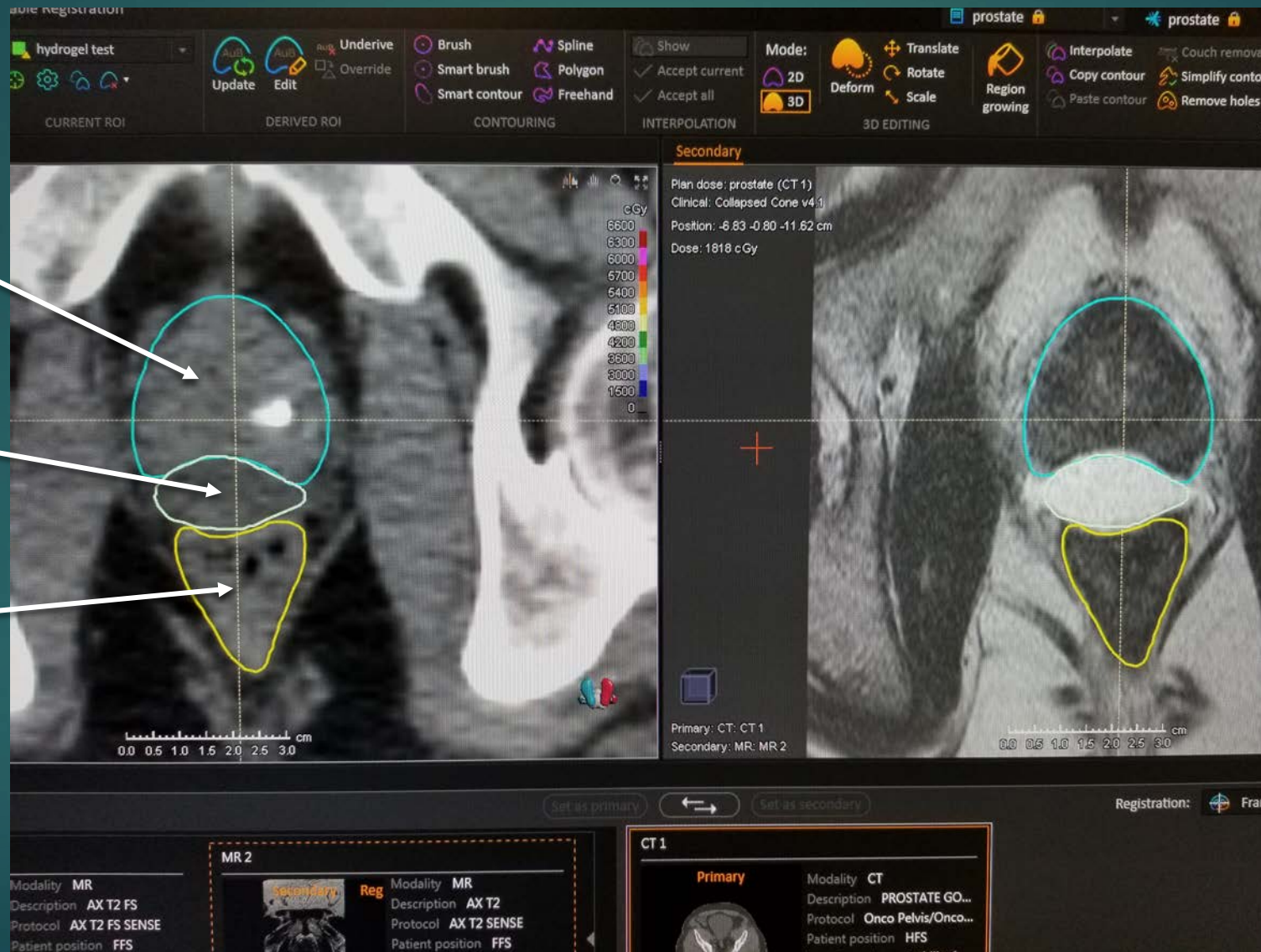


Radiation Planning

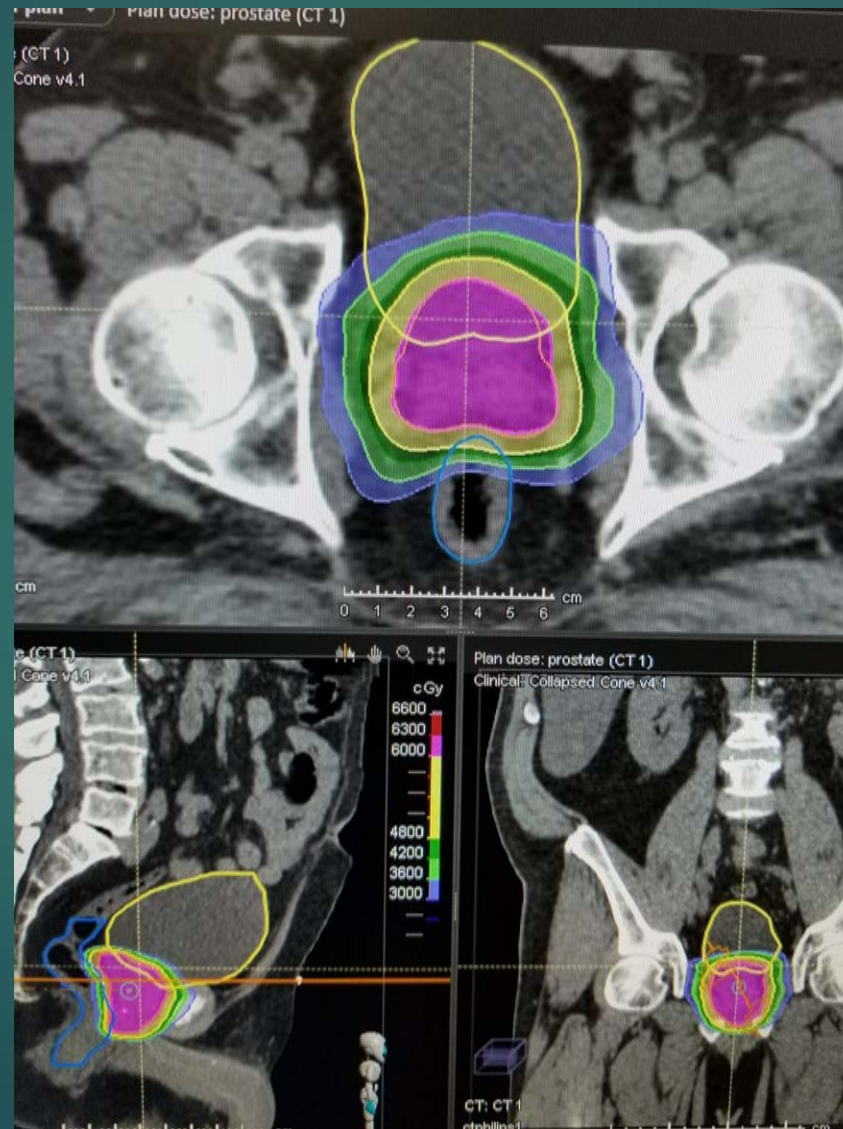
prostate

Hydrogel spacer

rectum



Radiation Planning



Treatment Techniques for Breast Cancer

- ▶ Whole breast radiation is standard for most patients
- ▶ Partial breast radiation for select women



- 1. Placement**

The closed applicator is inserted into the lumpectomy cavity through a single incision. Placement of the catheter can be done at the time of the lumpectomy or as a post-operative procedure.
- 2. Expansion**

Once the applicator is placed in the cavity, rotation of the expansion tool deploys the catheters, conforming to the size of the cavity.
- 3. Treatment**

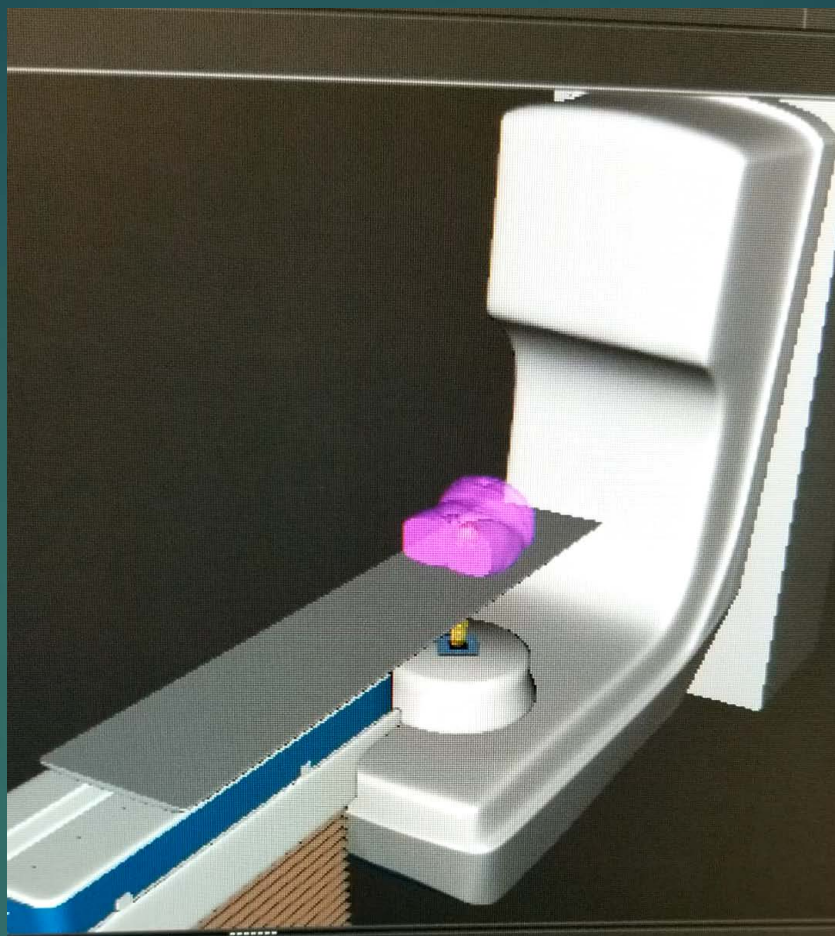
The individual catheters are connected to an HDR afterloader for delivery of the radiation source. With the close proximity of the catheters to the targeted tissue, the radiation dose around each catheter can be modulated to protect the skin, heart, lungs and other healthy tissue.
- 4. Removal**

After the final treatment, the applicator is collapsed and easily removed.

Radiation Techniques for Prostate Cancer

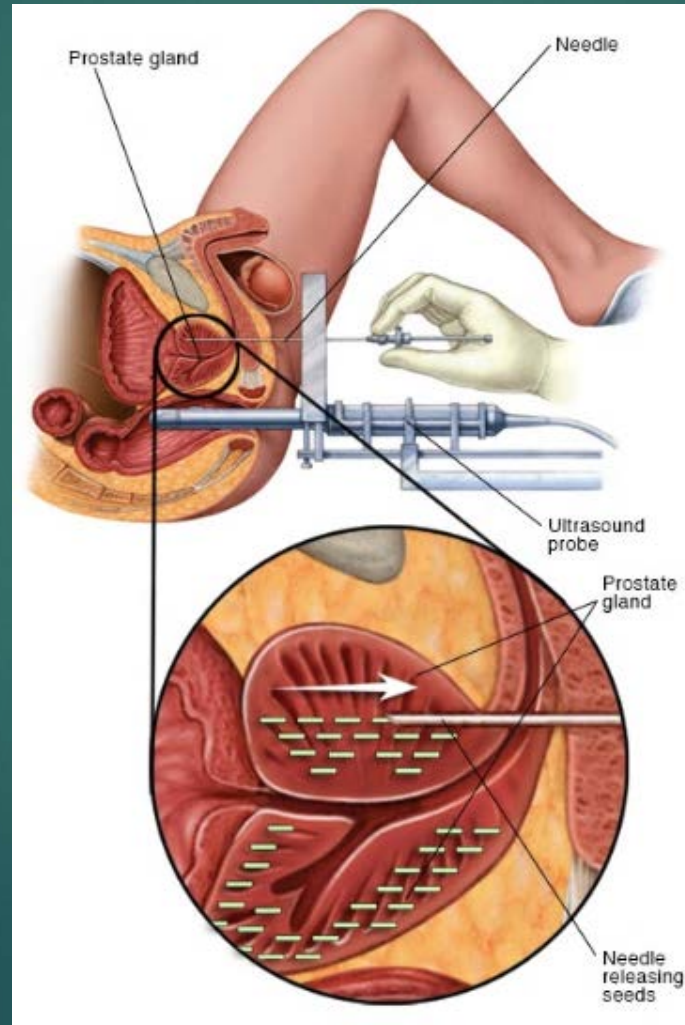
- ▶ External beam radiation therapy for 1-8 weeks





Radiation Techniques for Prostate Cancer

► Brachytherapy



Short-Term Side Effects

Side effects from radiation are limited to the area treated

- ▶ Breast Cancer –
 - ▶ Fatigue/tiredness
 - ▶ Skin redness, darkening, desquamation (peeling), pain/discomfort on the skin
 - ▶ Fullness/tightness in the breast/chest wall
- ▶ Prostate Cancer –
 - ▶ Fatigue/tiredness
 - ▶ Bladder: urinary frequency, urgency, pain with urination
 - ▶ Bowel: soft/loose stools or diarrhea



Mid treatment



Last day



Three weeks post-radiation



Last day

Long Term Side Effects

- ▶ Breast Cancer
 - ▶ Mild-moderate cosmetic changes. Majority of women report good-excellent cosmetic outcome
 - ▶ Residual skin darkening or telangiectasias (visible red blood vessels)
 - ▶ Breast pain, swelling, increase/decrease in breast size
 - ▶ Rib fracture
 - ▶ Lung inflammation (<1%)
 - ▶ Heart disease – rare, dose dependent
 - ▶ Radiation-related cancer (<1%) – develops years later
 - ▶ Lymphedema (lymph node dissection is biggest risk) – dependent on surgery, BMI/weight, whether the lymph nodes were treated with radiation, etc.
 - ▶ Radiation can increase complications of future surgeries on the treated side

Long Term Side Effects

	Moderate or marked events (n/patients; %)	Estimated proportion of patients with event by 5 years (%; 95% CI)	Estimated proportion of patients with event by 10 years (%; 95% CI)	Crude hazard ratio (95% CI)	p value*
Breast shrinkage†					
50 Gy	256/1003 (25.5%)	15.8% (13.6–18.3)	31.2% (27.9–34.9)	1.00	..
40 Gy	221/1006 (22.0%)	11.4% (9.5–13.6)	26.2% (23.1–29.6)	0.80 (0.67–0.96)	0.015
Breast induration (tumour bed)†					
50 Gy	153/1003 (15.3%)	12.1% (10.2–14.4)	17.4% (14.9–20.3)	1.00	..
40 Gy	129/1006 (12.8%)	9.6% (7.9–11.6)	14.3% (12.1–16.9)	0.81 (0.64–1.03)	0.084
Telangiectasia					
50 Gy	52/1081 (4.8%)	3.8% (2.8–5.2)	5.8% (4.4–7.7)	1.00	..
40 Gy	34/1094 (3.1%)	1.8% (1.1–2.8)	4.2% (2.9–5.9)	0.62 (0.40–0.96)	0.032
Breast oedema†					
50 Gy	86/1003 (8.6%)	8.1% (6.6–10.1)	9.0% (7.3–11.0)	1.00	..
40 Gy	49/1006 (4.9%)	4.7% (3.5–6.2)	5.1% (3.9–6.7)	0.55 (0.39–0.79)	0.001
Shoulder stiffness‡					
50 Gy	4/73 (5.5%)	2.9% (0.7–11.0)	8.2% (2.9–21.8)	1.00	..
40 Gy	3/81 (3.7%)	3.1% (0.8–11.9)	3.1% (0.8–11.9)	0.76 (0.17–3.39)	0.71
Arm oedema‡					
50 Gy	7/73 (9.6%)	6.0% (2.3–15.3)	13.5% (6.4–27.0)	1.00	..
40 Gy	3/81 (3.7%)	2.8% (0.7–10.7)	4.7% (1.5–14.0)	0.42 (0.11–1.63)	0.21
Other					
50 Gy	77/1082 (7.1%)	5.6% (4.3–7.2)	8.1% (6.5–10.2)	1.00	..
40 Gy	53/1095 (4.8%)	3.3% (2.4–4.6)	6.4% (4.8–8.4)	0.65 (0.46–0.93)	0.018

*Assessed by Wald test compared with 50 Gy. †Only assessed in women who had breast-conserving surgery. ‡Restricted to women who received lymphatic radiotherapy (to axilla or supraclavicular fossa).

Table 5: Physician-assessed normal tissue effects by fractionation schedule in START-B

The UK Standardisation of Breast Radiotherapy (START) trials of radiotherapy hypofractionation for treatment of early breast cancer: 10-year follow-up results of two randomised controlled trials

Joanne S Haviland, J Roger Owen, John A Dewar, Rajiv K Agrawal, Jane Barrett, Peter J Barrett-Lee, H Jane Dobbs, Penelope Hopwood, Pat A Lawton, Brian J Magee, Judith Mills, Sandra Simmons, Mark A Sydenham, Karen Venables, Judith M Bliss*, John R Yarnold*, on behalf of the START Trialists' Group†

	START-A			Total (n=2236)	START-B		
	50 Gy (n=749)	41.6 Gy (n=750)	39 Gy (n=737)		50 Gy (n=1105)	40 Gy (n=1110)	Total (n=2215)
Symptomatic rib fracture*							
Reported	5 (0.7%)	8 (1.1%)	9 (1.2%)	22 (1.0%)	17 (1.5%)	24 (2.2%)	41 (1.9%)
Confirmed†	0	0	1 (0.1%)	1 (<0.1%)	3 (0.3%)	3 (0.3%)	6 (0.3%)
Symptomatic lung fibrosis							
Reported	6 (0.8%)	9 (1.2%)	8 (1.1%)	23 (1.0%)	19 (1.7%)	19 (1.7%)	38 (1.7%)
Confirmed†	0	2 (0.3%)	1 (0.1%)	3 (0.1%)	2 (0.2%)	8 (0.7%)	10 (0.5%)
Ischaemic heart disease‡							
Reported	14 (1.9%)	11 (1.5%)	8 (1.1%)	33 (1.5%)	23 (2.1%)	17 (1.5%)	40 (1.8%)
Confirmed†							
Total	7 (0.9%)	5 (0.7%)	6 (0.8%)	18 (0.8%)	16 (1.4%)	8 (0.7%)	24 (1.1%)
Left sided	4 (0.5%)	1 (0.1%)	4 (0.5%)	9 (0.4%)	5 (0.5%)	4 (0.4%)	9 (0.4%)
Brachial plexopathy	0	1 (0.1%)	0	1 (<0.1%)	0	0	0

Data are n (%). *Reported cases include seven after trauma (five in START-A, two in START-B), and ten after metastases (five in START-A and five in START-B). †After imaging and further investigations. ‡26 patients in START-A and 22 in START-B had pre-existing heart disease at enrolment and were excluded.

Table 3: Incidence of other late adverse effects according to fractionation schedule

Long Term Side Effects

- ▶ Prostate Cancer:
 - ▶ Bladder symptoms: ~10-15% risk of mild-moderate persistent urinary bother symptoms such as frequency or urgency. May require medications. Incontinence is unlikely and not an expected complication.
 - ▶ More severe complications like persistent hematuria (blood in the urine) or urinary stricture is ~1-3%
 - ▶ Bowel symptoms: ~ 5% risk of bothersome rectal/bowel issues such as diarrhea, urgency with bowel movements, blood in the stool, etc
 - ▶ More severe complications are rare
 - ▶ Erectile dysfunction/sexual health: worsening erectile function in about 30-50% of patients over a few years.

Long Term Side Effects

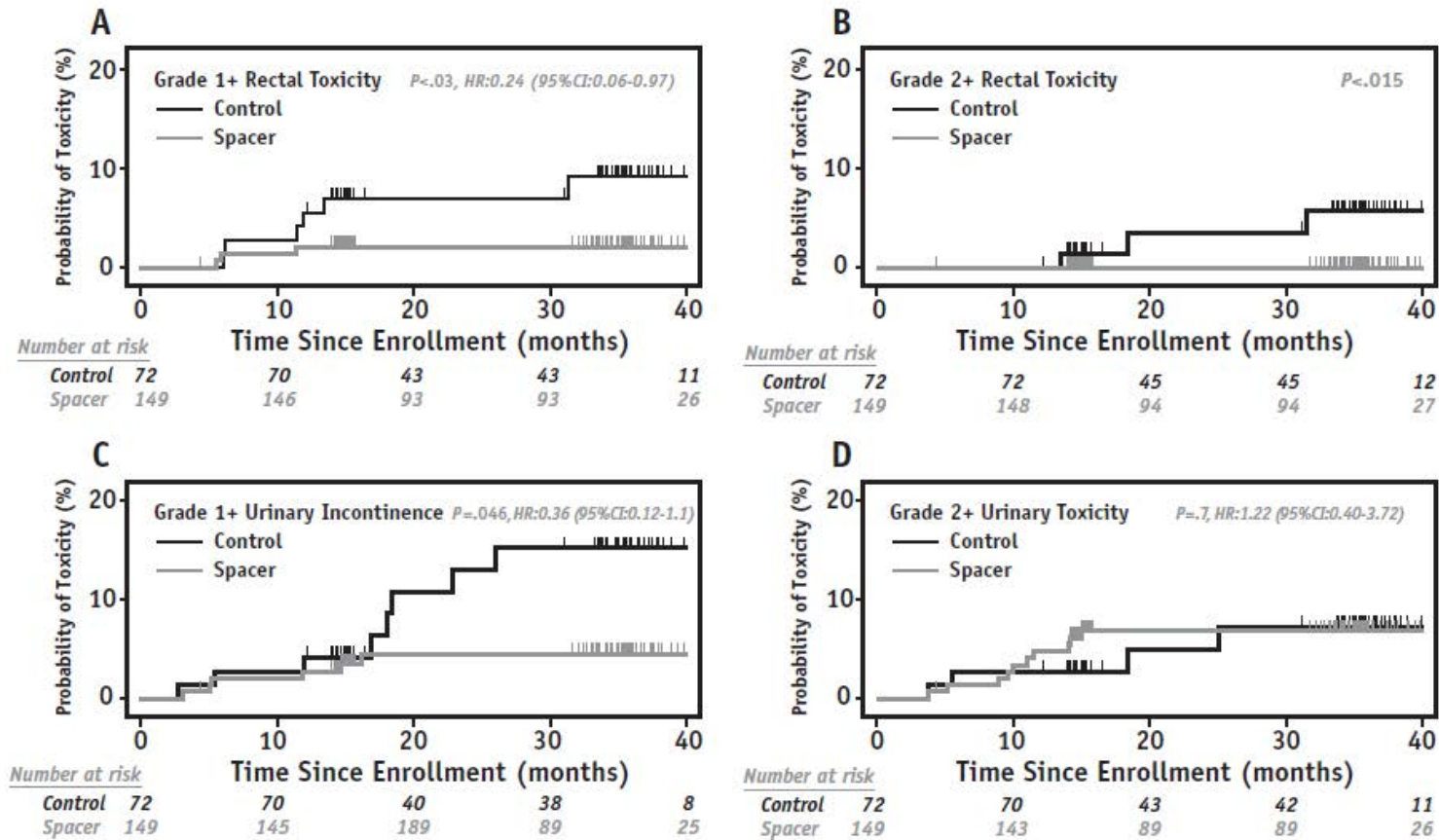
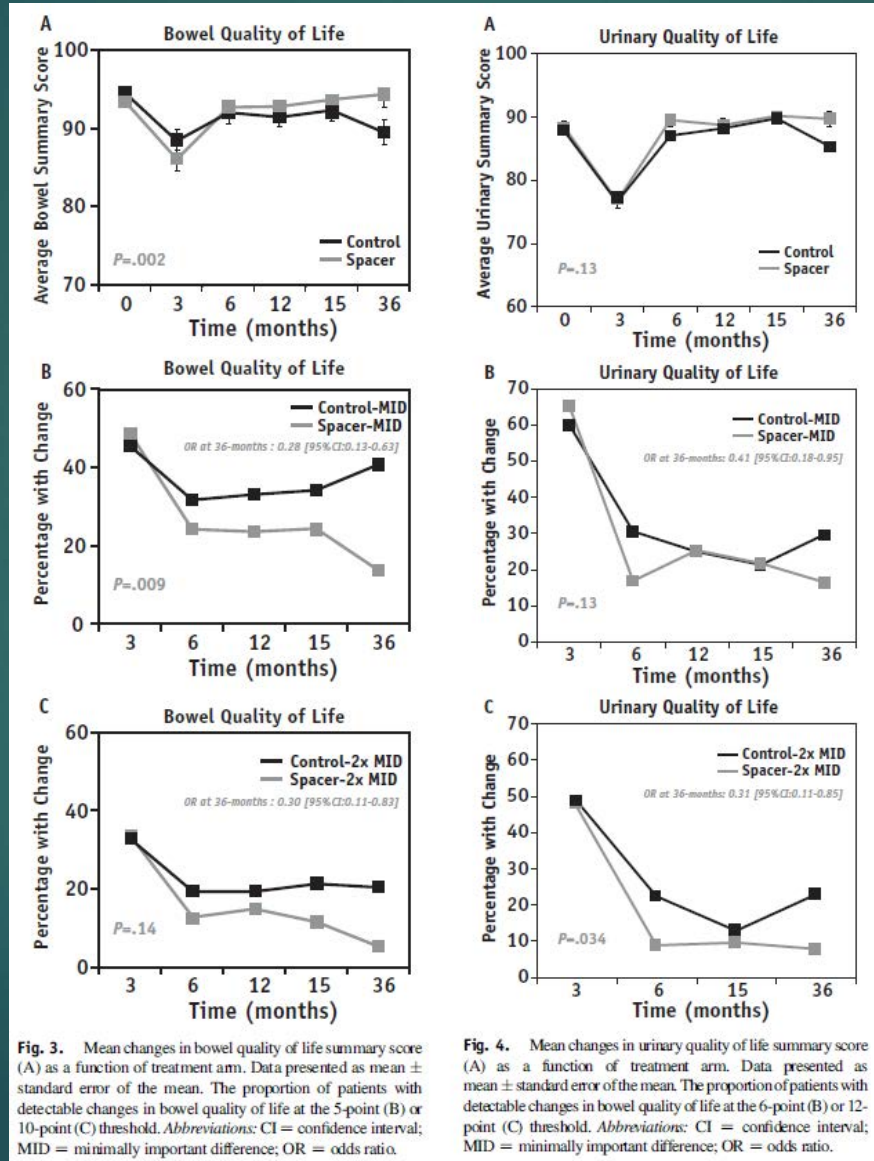


Fig. 2. The cumulative incidence of grade ≥ 1 (A) and ≥ 2 (B) bowel toxicity and grade ≥ 1 urinary incontinence (C) and grade ≥ 2 urinary toxicity (D). *Abbreviations:* CI = confidence interval; HR = hazard ratio.

Long Term Side Effects



Onset of Symptoms

- ▶ Breast Cancer:
 - ▶ At 1 month post treatment - most side effects have resolved.
 - ▶ Skin darkening can linger for months.
 - ▶ Breast edema, telangiectasias, and fibrosis can occur months to several years after treatment.
 - ▶ Lymphedema may occur months to several years later
 - ▶ Radiation pneumonitis/lung inflammation – typically 6 weeks to 6 months after treatment
 - ▶ Heart disease – typically years later
 - ▶ Radiation-related cancer – many years later

Onset of Symptoms

► Prostate Cancer

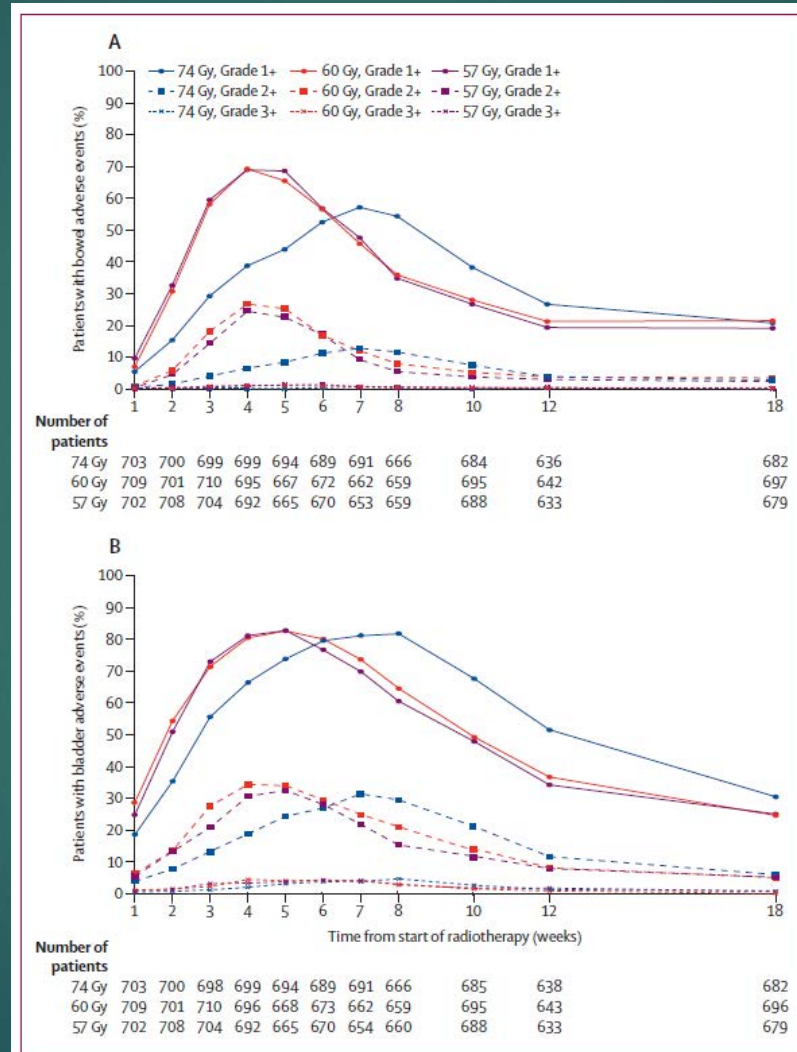


Figure 4: Acute RTOG toxicity by timepoint and randomised treatment group
 (A) Prevalence of bowel toxicity and (B) prevalence of bladder toxicity. RTOG=Radiation Therapy Oncology Group. Grade 1+=grade 1 or worse adverse event. Grade 2+=grade 2 or worse adverse event. Grade 3+=grade 3 or worse adverse event.

Treatment/Management Options

- ▶ Breast Cancer:
 - ▶ Skin Care:
 - ▶ Erythema/redness – moisturizing creams such as A&D creams, eucerin, aquaphor, biafene, radiaguard, hydraguard, aloe, calendula, etc.
 - ▶ Desquamation – A&D, zinc oxide, bacitracin, medihoney, silvadene
 - ▶ Mometasone steroid cream shown to reduce rates of desquamation
 - ▶ Avoid skin friction/irritation
 - ▶ Non-stick dressings
 - ▶ Fibrosis or lymphedema:
 - ▶ Physical therapy
 - ▶ Lymphedema therapy
 - ▶ Massage therapy
 - ▶ Trental/Vit E for 6 months
 - ▶ Chronic pain
 - ▶ OTC pain medications, gabapentin

Treatment/Management Options

- ▶ Prostate Cancer
 - ▶ During treatment:
 - ▶ Medications such as tamsulosin, NSAIDs, tolterodine, or pyridium can be tried for urinary symptoms.
 - ▶ Dietary changes or medications such as Imodium, proctofoam, or Anusol can be tried for bowel symptoms
 - ▶ Long-term complications:
 - ▶ Medications to help relax the bladder or improve urinary flow may be required
 - ▶ Intermittent use of Imodium
 - ▶ Radiation proctitis may require topical treatments from a gastroenterologist for rectal bleeding or may require medications such as sucralfate or steroid enema
 - ▶ Erectile dysfunction: Medications, vacuum devices, rings, injections, surgery, etc

Ways to Minimize Complications

- ▶ Breast Cancer:
 - ▶ Breath hold when treating left side
 - ▶ Hypofractionated treatment
 - ▶ Partial breast radiation?
 - ▶ Minimizing “hot spots” of radiation during planning
 - ▶ Proton therapy?
- ▶ Prostate Cancer:
 - ▶ Use advanced radiation techniques
 - ▶ Daily image-guidance with fiducials, beacons, CT scans, etc
 - ▶ Rectal spacers – decreased rates of rectal irritation and erectile dysfunction.
 - ▶ Maintain full bladder and empty rectum from treatment

Efficacy of Treatment

- ▶ Breast Cancer:
 - ▶ Locoregional recurrence rates are LOW in the modern era. For stage I-III breast cancer treated with lumpectomy/mastectomy, radiation, +/- systemic therapy such as chemo or anti-estrogen therapy the recurrence at 10 years is ~4% (in the breast or lymph nodes)
- ▶ Prostate Cancer treated curatively with radiation: 5-10 year biochemical control (PSA remains low) –
 - ▶ Many variables but risk group most important predictor:
 - ▶ Low risk - >90%
 - ▶ Intermediate - ~80-90%
 - ▶ High risk – 60-80%
 - ▶ Following radiation, it can take several years for the PSA to nadir

Surveillance

- ▶ Breast Cancer
 - ▶ Exam at least every 6 months for 5 years and then annually
 - ▶ Mammogram annually
 - ▶ Breast MRI in select women
 - ▶ CT, bone scan, or PET/CT scan as needed.
- ▶ Prostate Cancer
 - ▶ PSA every 6 months for 5 years and then annually
 - ▶ Imaging studies/scans as clinically indicated

Salvage Treatment

- ▶ What if my cancer comes back? Can I get more radiation?
- ▶ Breast cancer:
 - ▶ If cancer returns after lumpectomy and radiation – generally the recommendation is for a mastectomy
 - ▶ If cancer returns after mastectomy – surgical excision if possible followed by radiation if no prior radiation.
- ▶ Prostate cancer:
 - ▶ PSA rise of > 2 above the nadir is technically considered a cancer recurrence after definitive radiation.
 - ▶ Don't be fooled by a PSA “bounce” – a temporary rise in PSA within a couple years of radiation.
 - ▶ Surgery, cryotherapy, HIFU, brachytherapy, systemic therapy such as androgen-deprivation therapy/anti-testosterone therapy.

Surgery After Radiation

▶ Breast:

- ▶ Radiation can complicate reconstruction surgery or increase the risk of fibrosis/scarring or cause delayed/complicated healing.
 - ▶ Reconstruction is commonly done after radiation – surgeons may wait up to a year after radiation before completing reconstruction surgery.
- ▶ Radiation can be delivered with a tissue expander/implant in place.

▶ Prostate:

- ▶ Surgery can be performed after radiation but it's more complicated and there is a higher risk of post-op complications.
- ▶ Surgery is rarely needed after radiation therapy.

Questions?

