

A New Paradigm for Cancer Treatment: Stereotactic Radiation (SBRT/SAbR)

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■ Did You Know...

- There is no such thing as a tumor that cannot be eradicated by irradiation?
- With high enough tumor dose, all essential cellular processes are disrupted.



...so why
don't we kill
every cancer?

Collateral Damage



- Plagued radiotherapy from its start over 100 years ago
 - Normal tissues suffer a fate similar to the tumor.
 - The dose of radiation that kills the tumor cannot be tolerated by surrounding normal organs.
 - Long, protracted treatment courses aim to reduce collateral damage.

But, How Do We Focus Radiation...



**Any sufficiently advanced
technology is
indistinguishable from magic.**

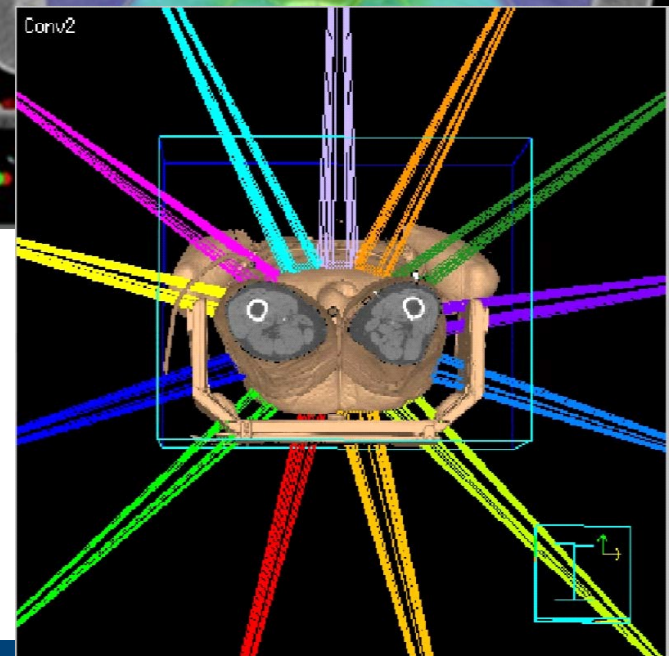
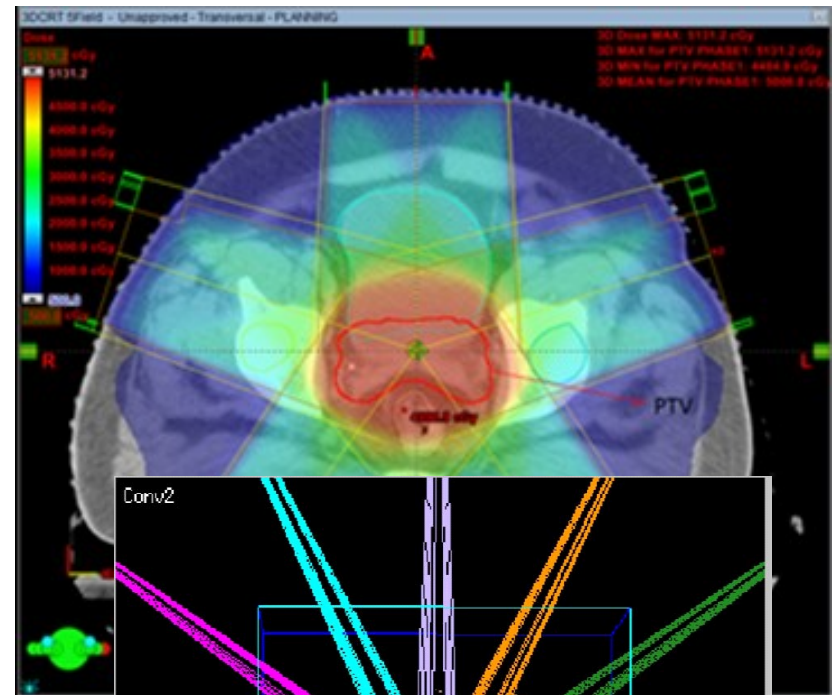
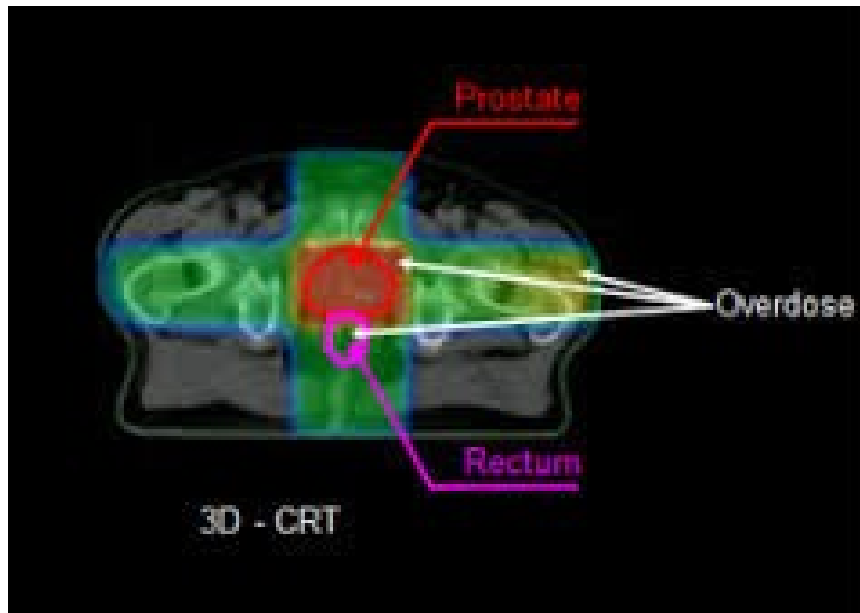
Arthur C. Clarke

The Magic of Delivering Focused Radiation

Stereotactic Ablative Radiation Therapy (SBRT/SAbR)

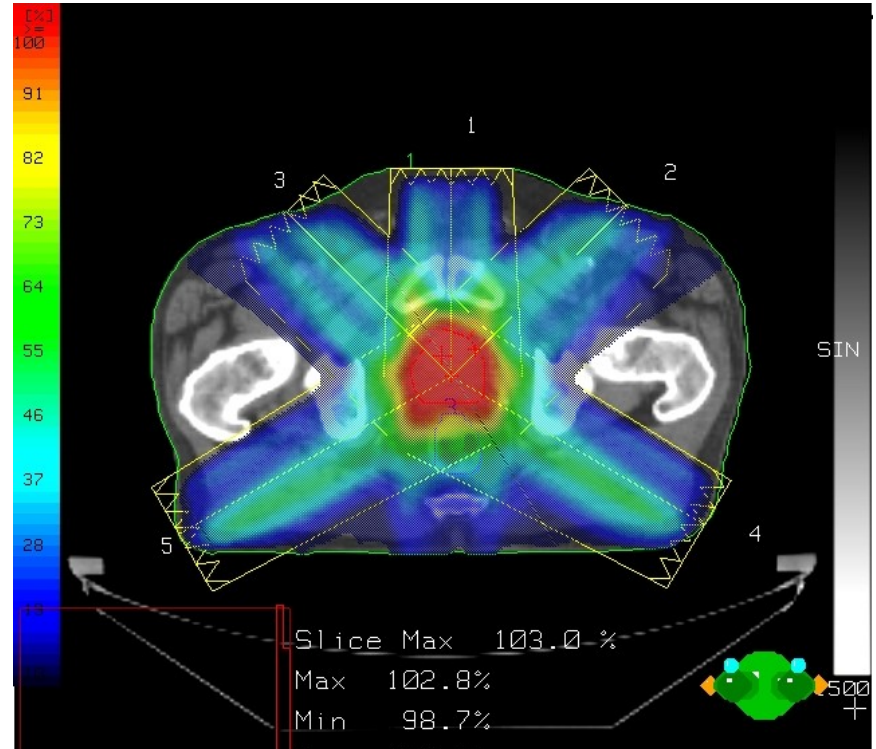
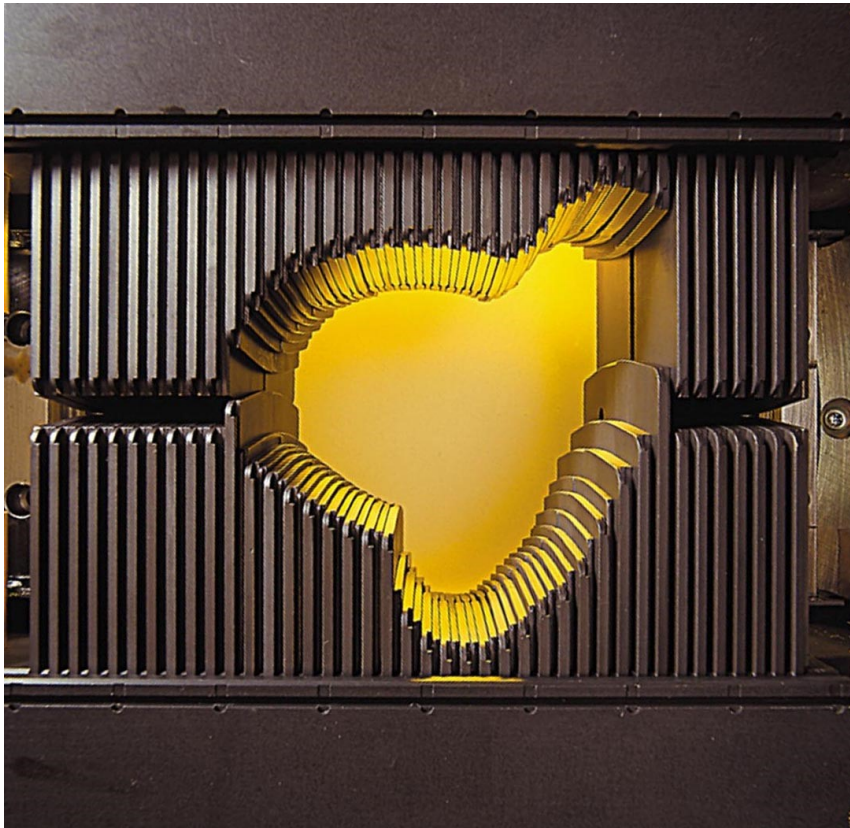
- Goes by many names:
 - SAbR, SBRT, CyberKnife, Gamma Knife
- Builds upon previous technological advances
 - 3D Conformal Radiation Therapy (3D-CRT),
 - Intensity Modulated Radiation Therapy (IMRT),
 - ARC Radiation Therapy (ARC-IMRT),
 - Image-Guided Radiation Therapy (IGRT),
 - Tumor motion management (4D CT and tracking)

3D Conformal RT (3D-CRT)



Red = high dose ("Hot")
Orange-Green=Intermediate dose
Blue = low dose ("Cold")

Intensity-Modulated Radiation Therapy (IMRT)



ARC Radiation Therapy/ ARC-IMRT

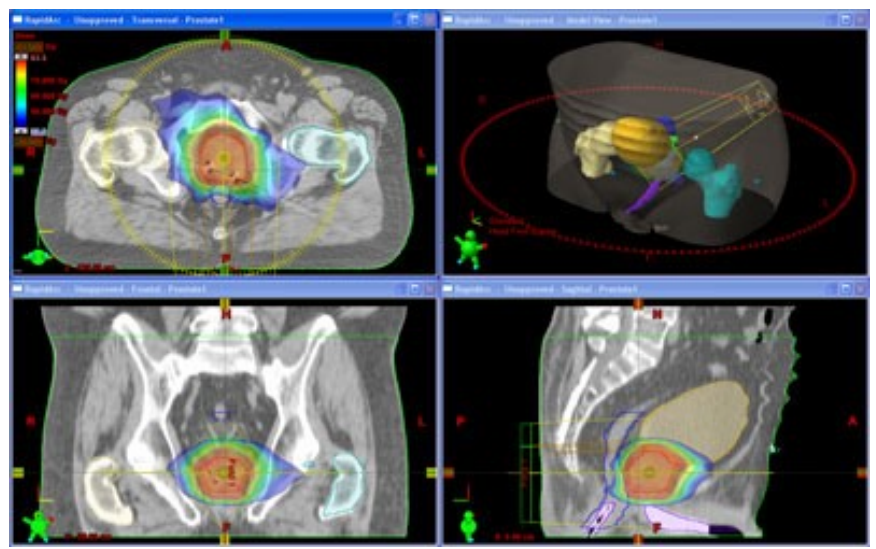
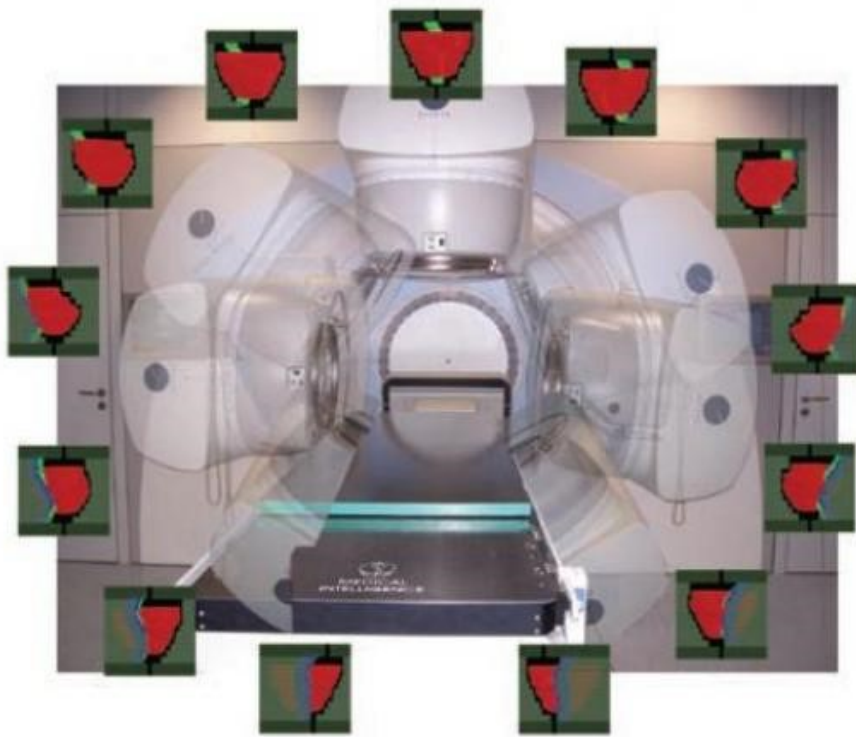


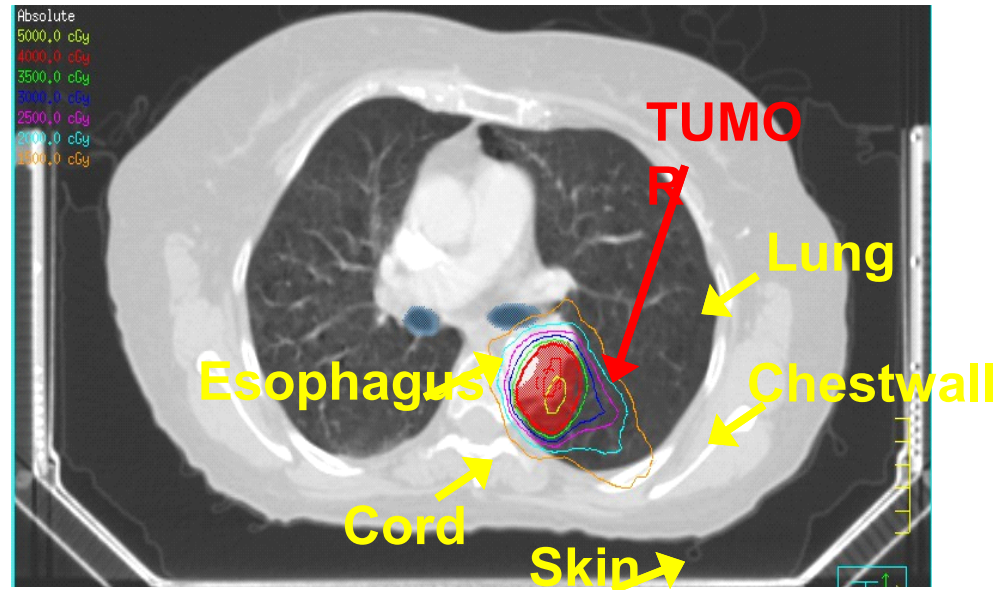
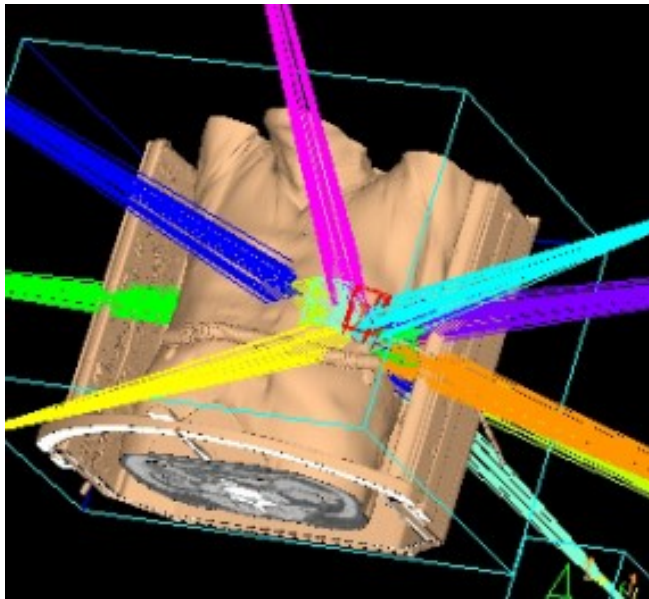
Image-Guided Radiation Therapy (IGRT)



Tumor Motion



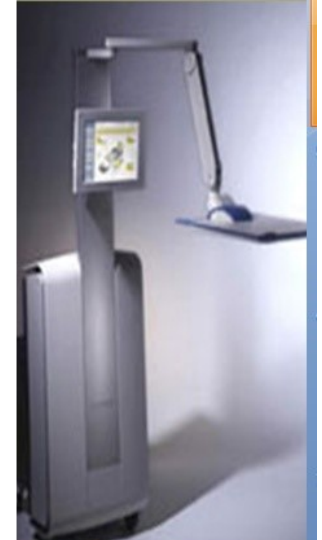
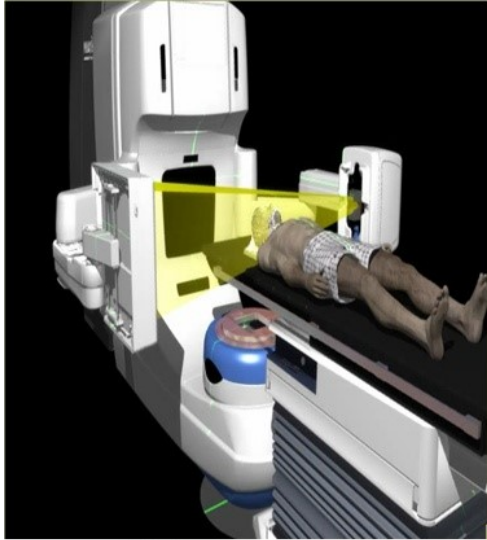
Stereotactic Radiation Therapy (SBRT/SAbR)



The result is:

- Tumor-killing dose → Maximized tumor control (>90%)
- Minimized toxicity (collateral damage) (<5%)
- Performed in 1-5 fractions/settings
- Completely non-invasive, convenient and cost effective

UTSW – We Have the Technology....



UTSW Success with SAbR

- Multiple clinical trials
 - NIH funded phase I/II trials
 - DOD funded phase II trials
 - NIH and Industry sponsored phase III trials
- CPRIT funded biological research
- NIH funded physics research
- >100 UTSW publications and textbooks

SBRT for Prostate Cancer

- In a DOD-funded Phase II clinical trial
 - 91 Prostate cancer patients were enrolled
 - Patients were treated with SAbR of only 5 treatments
 - 5-year cure rate was 98.6% (90/91)

UTSW SBRT Prostate Experience. Hannan et. al. EJC 59 (2016)

GU Toxicity 45 Gy				
Grade	Acute		Late	
	No.	%	No.	%
0	8	53.3%	8	53.3%
1	2	13.3%	4	26.7%
2	5	33.3%	3	20.0%
3	0	0.0%	0	0.0%
4	0	0.0%	0	0.0%
5	0	0.0%	0	0.0%

GI Toxicity 45 Gy				
Grade	Acute		Late	
	No.	%	No.	%
0	8	53.3%	14	93.3%
1	6	40.0%	1	6.7%
2	1	6.7%	0	0.0%
3	0	0.0%	0	0.0%
4	0	0.0%	0	0.0%
5	0	0.0%	0	0.0%

GU Toxicity 47.5 Gy				
Grade	Acute		Late	
	No.	%	No.	%
0	6	40.0%	9	60.0%
1	8	53.3%	1	6.7%
2	1	6.7%	4	26.7%
3	0	0.0%	1	6.7%
4	0	0.0%	0	0.0%
5	0	0.0%	0	0.0%

GI Toxicity 47.5 Gy				
Grade	Acute		Late	
	No.	%	No.	%
0	7	46.7%	9	60.0%
1	4	26.7%	5	33.3%
2	4	26.7%	1	6.7%
3	0	0.0%	0	0.0%
4	0	0.0%	0	0.0%
5	0	0.0%	0	0.0%

GU Toxicity 50 Gy				
Grade	Acute		Late	
	No.	%	No.	%
0	13	21.3%	28	45.9%
1	34	55.7%	17	27.9%
2	14	23.0%	12	19.7%
3	0	0.0%	3	4.9%
4	0	0.0%	1	1.6%
5	0	0.0%	0	0.0%

GI Toxicity 50 Gy				
Grade	Acute		Late	
	No.	%	No.	%
0	21	34.4%	39	63.9%
1	24	39.3%	5	8.2%
2	14	23.0%	11	18.0%
3	1	1.6%	4	6.6%
4	1	1.6%	2	3.3%
5	0	0.0%	0	0.0%

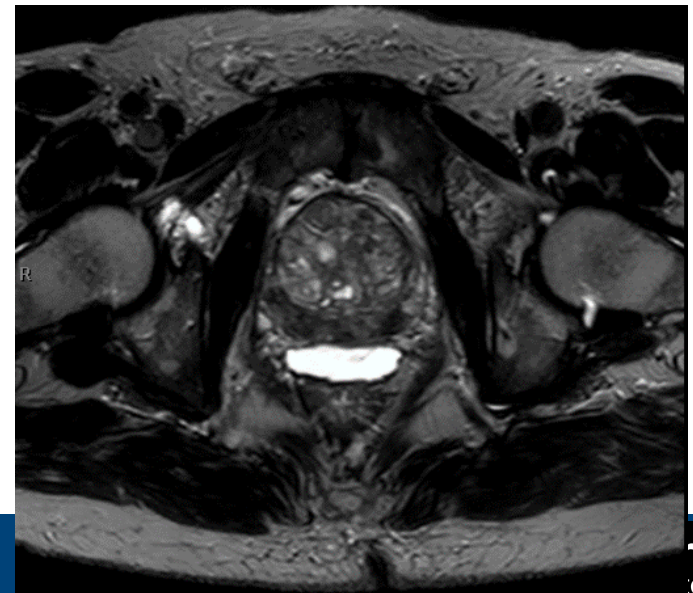
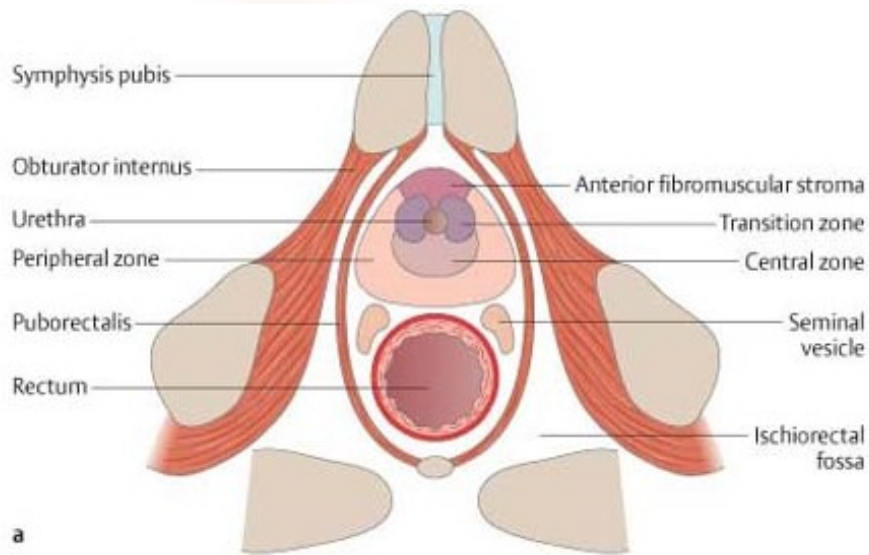
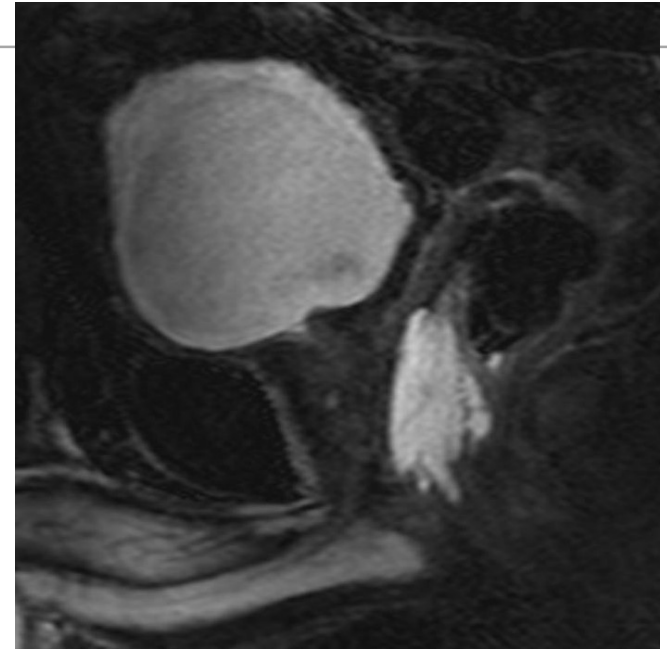
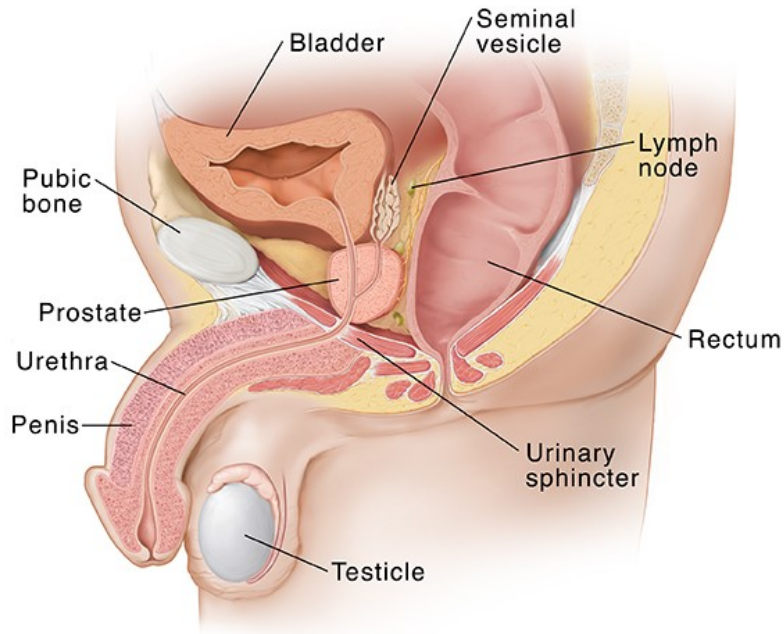
Summary of Phase I/II Trial

- SBRT at 45-47.5 Gy seems safe and effective
 - PSA cure rate at 5 years: 98.6%
 - Late side effect rates 0-6%

- SBRT at more potent dose leads to low rates of rectal injury

- Can we further decrease radiation-induced rectal injury?

Spacer Hydrogel for Prostate SBRT



Multi-institutional Phase II Trial of SBRT with Temporary Hydrogel Spacer for Low- and Intermediate-Risk Prostate Cancer

Eligibility:

- Gleason 3+3 or 3+4
- PSA \leq 10

Treatment:

- 45Gy in 5 fractions
- Rectal Hydrogel Spacer

Preliminary results at 1 year:

- PSA cure-rate: 100%; Rectal injury (>Grade 3): 0%!

UTSW Experience with SBRT for Prostate Cancer

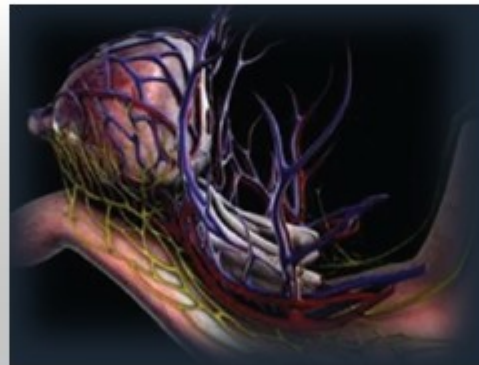
- 250 patients treated in the past 5 years
- Low (9.2%), intermediate (85.2%), high-risk (5.6%)
- PSA cure (bRFS) was 96.33% at 3 years

	Genitourinary				Gastrointestinal			
	Acute		Late		Acute		Late	
Grade	No.	%	No.	%	No.	%	No.	%
0	32	12.8	73	29.2	172	68.8	198	79.2
1	180	72	114	45.6	60	24	41	16.4
2	37	14.8	60	24	18	7.2	10	4
3	1	0.4	3	1.2	0	0	1	0.4
4	0	0	0	0	0	0	0	0

- 17.3% decline in the rate of erectile dysfunction (ED)

Prostate Oncologic Therapy While Ensuring Neurovascular Conservation

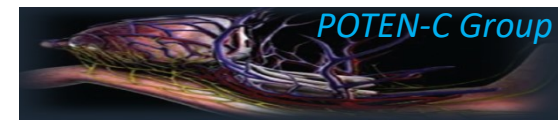
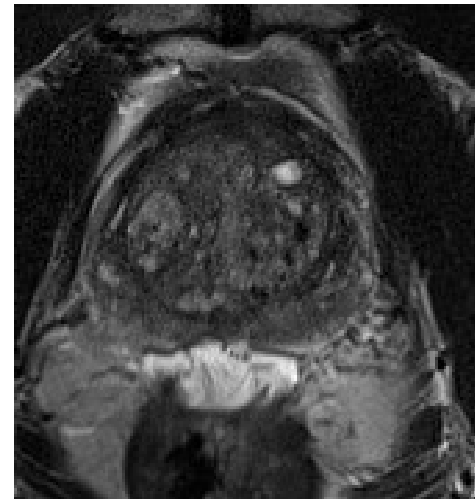
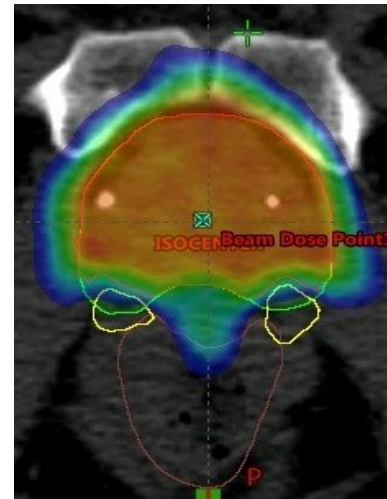
(SAbR POTEN-C)



***A Phase II Randomized Trial of Stereotactic Ablative Body
Radiotherapy (SAbR) with or without Neurovascular Sparing for
Erectile Function Preservation***

Taking the next step

- MR/CT planning with precise contouring tight tolerances on planning/delivery
- SAbR
 - Rectal spacer gel to displace prostate from key structures
 - Randomization to demonstrate meaning



SAbR POTEN-C Trial Schema

Phase II randomized controlled trial of stereotactic ablative body radiotherapy (SAbR) with or without neurovascular sparing for erectile function preservation in localized prostate cancer

Eligibility:

- Low/Intermediate risk PCa (exclude if all intermediate risk factors present*)
- No androgen deprivation therapy
- Baseline erectile potency by EPIC sexual domain 60-100
- No lesion within 5mm of one neurovascular bundle by MRI

* cT2b-cT2c, Gleason 7, >50% cores involved, PSA >10
 ** internal pudendal artery, neurovascular bundle, penile bulb
 *** Recommend CT w/ IV contrast push to simulate arteriogram

Registration:

- Rectal SpaceOar & fiducials
- Labs
- EPIC baseline
- CT/MR*** simulation & delineation of neurovascular structures for sparing in *all* pt

Stratify:

- EPIC sexual domain score ≥ 80 vs. 60-79
- Institution
- Baseline sexual aid or medication use

RANDOMIZE

Neurovascular sparing SAbR with dose-painting approach

Standard SAbR

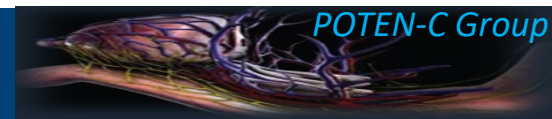
Dose 40 – 45 Gy / 5 fractions

Primary endpoint/stats:

- 2-year decline in EPIC sexual domain
- N=124 pts
- 15% attrition, stdev 20, effect size 0.50, alpha 0.1

Secondary endpoints:

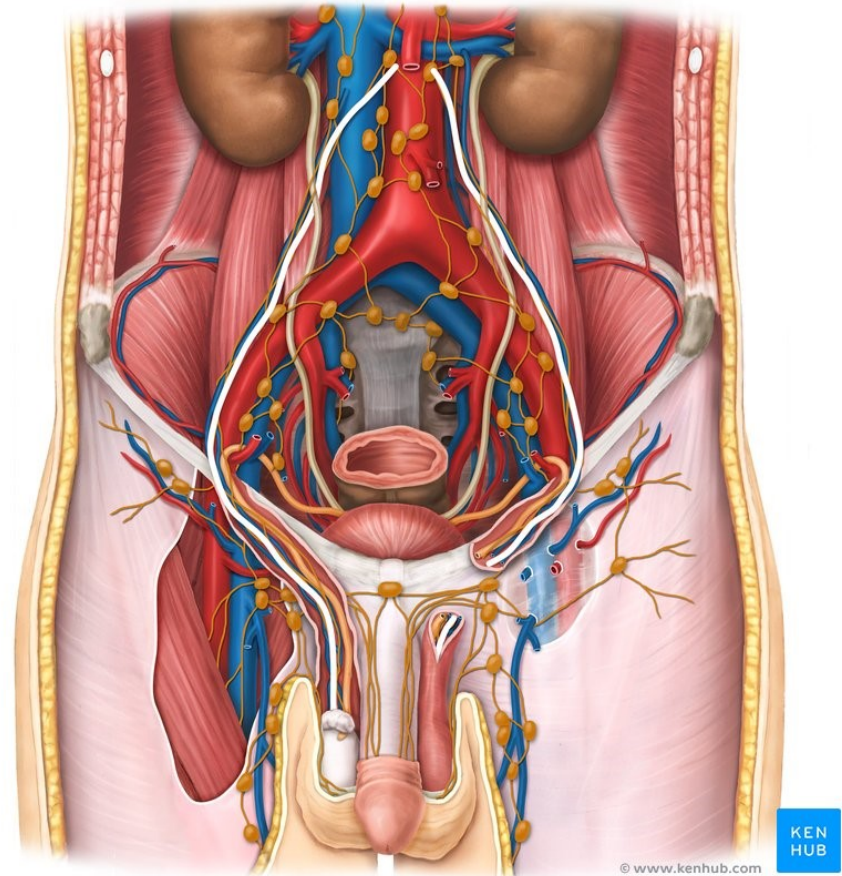
- Biochemical failure, DMFS, CSS
- Other HRQOL EPIC domains
- Comparison of both arms vs historical SBRT prostate control without rectal spacer



Phase I Trial of SBRT for High-Risk Prostate Cancer

Eligibility:

- Gleason ≥ 8 or PSA ≥ 20 or cT3+
- In 5 fractions
 - 47.5Gy to the Prostate and Seminal Vesicles
 - 25.0Gy to pelvic lymph node regions
 - 55Gy to MRI visible prostate tumors
- Rectal Spacer Hydrogel
- Two years of Hormonal therapy



Phase I Trial of SBRT for High-Risk Prostate Cancer

- Completed enrollment of 60 patients

Preliminary Results:

- Evaluation of the first 23 patients
- median of 16.3 month follow up
- No >Gr 3 side effects; 2 patients had grade 3 that resolved
- No one experienced biochemical failure
- All 2-year post-SBRT biopsy returned as **negative** for viable cancer cells
- Based on the preliminary results, we have started offering this treatment outside the trial as standard of care

Take Home Message

- SBRT for prostate cancer is safe and effective
- SBRT for prostate cancer is highly effective for low-intermediate risk patients (98.6% bRFS at 5 years)
- Nerve-sparing SBRT may be the future of prostate cancer treatment for low and intermediate-risk patients
- For high-risk patients it is under investigation
 - Preliminary results appear promising

Thank You

