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

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https://www.utsouthwestern.edu/labs/hannan/
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?
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 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)

Hannan et. al. 2016, EJC 59 (142-151)
### GU Toxicity 45 Gy

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<tr>
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### GI Toxicity 50 Gy

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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

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- 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

POTEN-C Group
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

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
Dose 40 – 45 Gy / 5 fractions

Standard SAbR

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

* 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
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
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