

Stakeholder engagement plan for development of personalized decision aid program for prostate cancer treatment decisions after radical prostatectomy



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What is the goal of this prostate cancer research program?

- Personalized “decision aid” for patients faced with treatment choices
- Clinical perspective for genomic testing that predicts risk of cancer spread

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What is a stakeholder engagement?

- “Meaningful involvement of patients, caregivers, clinicians, and other healthcare stakeholders throughout the research process...”
- “...such engagement can **influence research to be more patient centered**, useful, and trustworthy and ultimately lead to **greater use and uptake** of research results by the patient and broader healthcare community.”

- Patient Centered Outcomes Research Institute

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What is the purpose of this meeting today?

- You have been identified as a stakeholder for this topic
- We value your input on the project
- Your input will be recorded in notes
- *Informed consent must be documented*

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The Clinical Decision: Immediate vs Delayed Radiation Therapy after Prostatectomy

Post-Operative Radiation Therapy (RT)

- Adjuvant radiation therapy (ART):
 - Negative PSA + concerning pathology findings after surgery
 - ART is directed to the prostate bed to prevent recurrence
- Observation with PSA testing, use delayed salvage RT (SRT) only if/when PSA rises
 - SRT targets the prostate bed to treat PSA-detected microscopic recurrence
 - RT is more effective when PSA is low

Adjuvant Radiation Therapy

PROS (+)	CONS (-)
High level of evidence (randomized, controlled trials)	Overtreatment. Many men (~40%) would never recur anyways.
Earlier RT may be more effective for some med with highest-risk tumors	Risks of complications applies to all men treated.
Curative. Cure prevents need for hormone therapy and other treatments.	Costs and time. RT is expensive. 7 weeks of daily treatments.

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Salvage Radiation Therapy

PROS (+)	CONS (-)
Multiple sources of evidence (not randomized, controlled trials)	Delayed RT may worsen outcomes for men with aggressive tumors.
Fewer patients treated overall.	Risks of complications.
Curative. Cure = no need for hormone therapy and other treatments.	Costs and time. RT is expensive. 7 weeks of daily treatments.

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Adjuvant and Salvage Radiotherapy After Prostatectomy: AUA/ASTRO Guideline

Ian M. Thompson,* Richard K. Valicenti,* Peter Albertsen, Brian J. Davis,
S. Larry Goldenberg, Carol Hahn, Eric Klein, Jeff Michalski, Mack Roach,
Oliver Sartor, J. Stuart Wolf, Jr. and Martha M. Faraday

From the American Urological Association Education and Research, Inc., Linthicum, Maryland, and the American Society for Radiation Oncology, Fairfax, Virginia

“...the patient, his family and the multi-disciplinary treatment team should engage in a shared decision-making process in which the patient is advised to consider the possibility of additional treatment (i.e. radiotherapy). Whether ART should be administered is a decision best made by the multidisciplinary treatment team and the patient with consideration of the patient’s history, functional status, values, preferences and tolerance for the potential toxicities and QoL effects of radiotherapy”

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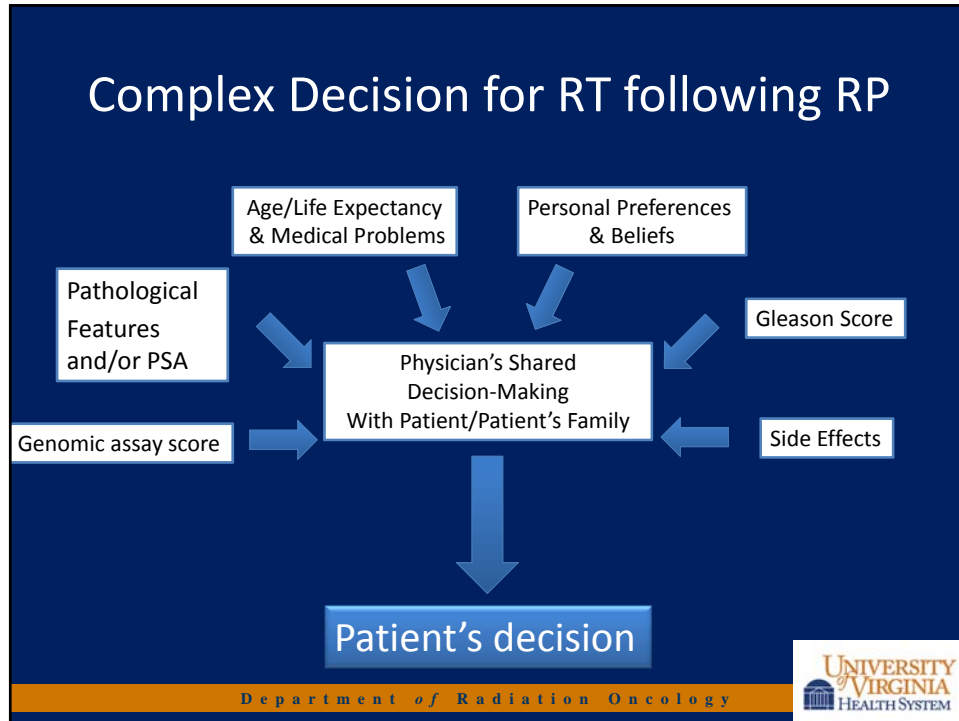


Personal Factors to Consider

- Priorities: aggressive treatment vs. quality of life
- Level of concern for side effects
- Opinions of family and friends
- Physician recommendations (and bias)
- Life expectancy and other medical problems
- Genomic tests: new way to estimate individual risk of cancer spread

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What are the potential opportunities to improve decision making?

- *Our Current Strategy:* Research from grant from American Society for Radiation Oncology (ASTRO)
- Aim 1) Perform decision analysis modeling to evaluate the comparative effectiveness of adjuvant and salvage therapeutic strategies after prostatectomy for locally advanced prostate cancer. Model simulates effects of individual patient's age, preferences, and genomic test results.
- Aim 2) Create a decision support tool to guide personalized, shared decision making regarding adjuvant and salvage therapies after prostatectomy for patients with locally advanced prostate cancer.

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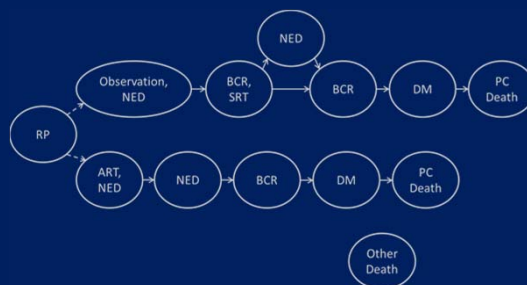
Decision Analysis Modeling (Aim 1)

- Markov model of Adjuvant RT vs. Observation/Salvage RT
 - 10-year time horizon.
- Clinical health states, possible complications, and “utilities” in model.
- Utility is a value that represents an individual patient’s preference for a particular health state, with potential values ranging from 0 (death) to 1 (perfect health).
- Model results: quality adjusted life-years (QALYs)

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Transition State Diagram



This figure shows the overall structure of the Markov model. After prostatectomy (RP), half of the simulated patients are assigned to Observation and half to adjuvant radiation therapy (ART). In monthly cycles over a 10-year time horizon, transitions occur from left to right at a specified probability based on risk of prostate cancer recurrence. In the model, each transition has associated impact on treatments received, side effects of treatment, and changes in utility values. The model also includes a continuous age-based risk of death from other causes (Other Death).

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Model Inputs

- Published literature for average values
- Individualized-range inputs designed to simulate wide differences among patients:
 - Age-adjusted mortality risk: based on life tables maintained by US governmental agency
 - Genomic classifier score
 - Utilities: full reported range
 - Complication risks over wide range

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Overall Findings

- On average, Observation/SRT (8.1 QALYs) preferred over ART (6.73 QALYs).
- Observation/SRT favored even when model inputs varied dramatically (including utilities).
- However, genomic-based risk changes results:

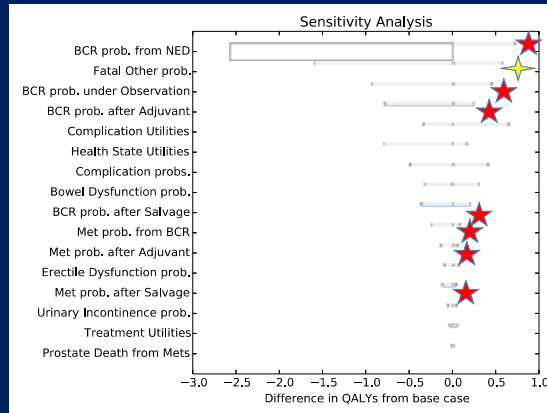
HIGH RISK Genomic Score

- ART strongly preferred (~80% of paired sample runs).

LOW RISK Genomic Score

- Observation/SRT strongly preferred (98% of paired sample runs).

Factors that Alter Optimal Treatment



- ★ = from genomic test score
- ★ = based on patient age

*All other factors were based upon the best average estimates published in literature, with sensitivity analyses based on broadest range:

- Utilities were lowest and higher reported values
- Complication probabilities from ½ to 2x average

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Our Modeling Conclusions

- Genomic test results most influential in model
- Age-based risk of death is also important
 - Opportunity to refine/adjust methods
- Across broad range of values, utility inputs (patient preferences for outcomes) had relatively small effect on outcomes
- Genomics-based recurrence inputs creates new opportunity for this approach to be used to provide personalized reports

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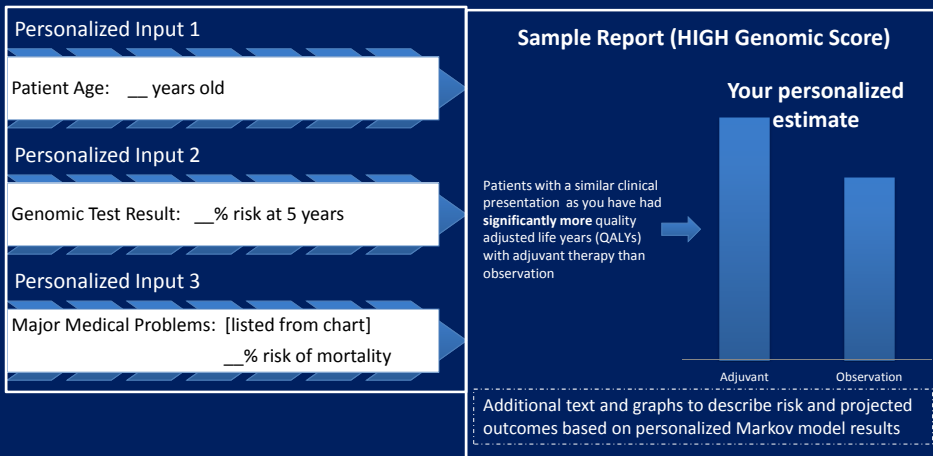
Leveraging Model Results for Personalized Decision Aid

- We plan to develop a decision aid program that uses Markov modeling to provide personalized guidance for adjuvant vs observation decisions based on individualized data for:
 - genomic test result
 - Patient age +/- additional comorbidities
- A simplified pictorial approach will be used for reporting

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Hypothetical Decision Aid Format



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Feedback

- Is this a useful addition to genomics info?
- How should information be presented?
 - Numbers vs. general themes
 - Graphs/pictures vs. numerical format
- Where should this be available?
 - Only in MD office?
 - Direct to patient beforehand?

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What are potential barriers?

- Who would patients want to discuss this with (MD or nurse)?
- How can we make this be understandable?
- Would web-based portal be accessible?
- Is more information needed to provide a helpful guide?

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