

# Active Surveillance for Low and Intermediate Risk Prostate Cancer: Opinions of North American Genitourinary Oncology Expert Radiation Oncologists

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## Abstract

**The ProtecT trial provides Level 1 evidence supporting active surveillance for low-risk and intermediate-risk prostate cancer. The impact of these findings on the opinions of North American genitourinary oncology expert radiation oncologists regarding the role of active surveillance was investigated; active surveillance is well-regarded for low-risk but not intermediate-risk prostate cancer. These preferences may affect the design of future clinical studies, influencing the adoption of active surveillance in North American clinical practice.**

**Introduction:** The ProtecT trial has provided level 1 evidence supporting active surveillance for prostate cancer patients with low-risk and intermediate-risk disease. The effect of these findings on the opinions of North American genitourinary (GU) experts regarding the role of active surveillance for these patients has not been previously examined. **Materials and Methods:** A survey was distributed to 88 practicing North American GU physicians serving on decision-making committees of cooperative group research organizations. Questions pertained to appropriateness of active surveillance in patients with low-risk and intermediate-risk (Gleason 3+4) disease. Opinions regarding active surveillance were correlated with practice patterns using Fisher exact test. **Results:** Forty-two radiation oncologists completed the survey. Forty percent had been in practice for more than 20 years; 90% practice at an academic center. Forty-five percent see  $\geq 20$  patients per month in consultation. More than 95% (40 of 42) recommended active surveillance for Gleason 6 disease, whereas only 17% recommended active surveillance for Gleason 3+4 disease. There were no demographic differences between supporters or opponents regarding active surveillance with regard to monthly patient volume, practice type, likelihood of self-identifying as an expert brachytherapist, belief in advanced imaging techniques, or preferred default external beam radiation therapy dose/fractionation for either low-risk or intermediate-risk disease. However, there was a trend toward greater support of active surveillance for Gleason 3+4 disease among experts having practiced  $< 10$  years versus  $\geq 10$  years ( $P = .085$ ). **Conclusion:** Active surveillance is almost universally supported by North American GU expert radiation oncologists for low-risk prostate cancer. However, there is very weak support for this strategy in Gleason 3+4 disease despite the ProtecT trial providing level 1 evidentiary support in both risk groups. There were no significant differences between experts supporting versus opposing active surveillance for either low-risk or intermediate-risk disease. These preferences might affect the design of future clinical studies, influencing the adoption of active surveillance in North American clinical practice.

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## Active Surveillance for Non–High-Risk Prostate Cancer

### Introduction

The ProtecT trial randomized 1643 men ages 50 to 69 years in the United Kingdom with clinically localized prostate cancer to active surveillance ( $n = 545$ ), radical prostatectomy ( $n = 553$ ), or radiotherapy ( $n = 545$ ) and reported that at a median of 10 years, there was no difference in prostate cancer-specific mortality regardless of treatment chosen.<sup>1</sup> The results of this trial have provided level 1 evidence supporting active surveillance for prostate cancer patients, particularly low-risk (Gleason 6) patients, which comprised 77% of the study population.<sup>2</sup> Intriguingly, the results also provided evidence supporting active surveillance for intermediate-risk (Gleason 7) disease, which comprised 21% of participants.<sup>2</sup> The effect of these findings on the opinions of North American genitourinary (GU) experts regarding the role of active surveillance for low- and intermediate-risk prostate cancer patients has not been previously examined.

### Materials and Methods

#### Survey Design and Deployment

The survey was designed to identify characteristics of each respondent's typical practice patterns, as well as to assess their personal opinions on the role active surveillance in low-risk and intermediate-risk prostate cancer patients. Survey questions specified Gleason 3+4 when defining intermediate-risk disease. Eighty-eight currently practicing North American GU oncology physicians, who serve on cooperative group research organizations such as NRG Oncology, were contacted via e-mail and invited to complete the survey; their position in cooperative group research organizations served to define them as "experts" for the purposes of this study. The survey was designed and hosted by Research Electronic Data Capture (REDCap), and contained screening questions to ensure respondents were currently practicing, not in training, and specializing in GU oncology.<sup>3</sup>

#### Statistical Analysis

On the basis of responses, participants were categorized as "supporters" or "opponents" of active surveillance for low-risk and intermediate-risk patients. Opinions were correlated with practice patterns using Fisher exact test.

### Results

Analysis was conducted on 42 radiation oncologist respondents. Seventeen participants (40%) had been in practice for  $> 20$  years and 38 (90%) practice at an academic center. Nineteen participants (45%) see  $> 20$  patients per month in consultation. Ninety-five percent (40 of 42) recommended active surveillance for Gleason 6 disease, whereas only 17% (7 of 42) recommended active surveillance for Gleason 3+4 disease (Figure 1). There was no significant difference between supporters and opponents of active surveillance for low-risk or Gleason 3+4 disease with regard to years in practice ( $> 10$  years,  $> 20$  years), monthly patient volume, practice type, belief in advanced imaging techniques, likelihood of self-identifying as an expert brachytherapist, or treatment preferences for external beam radiation therapy dose/fractionation for Gleason 3+4 disease. However, there was a trend toward greater support of active surveillance for Gleason 3+4 disease among experts who practiced fewer than 10 years since residency program completion, compared with experts with  $> 10$  years of professional experience ( $P = .085$ ).

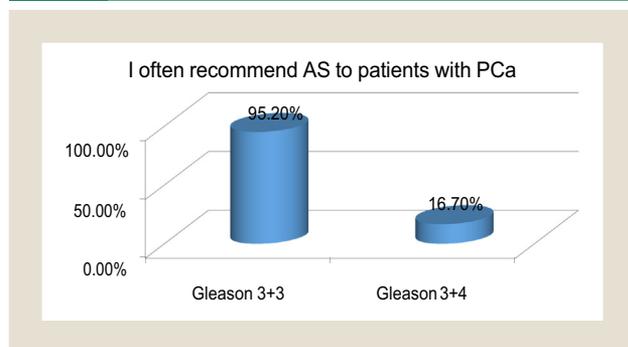
### Discussion

Committees of cooperative group research organizations play an integral role in the design of clinical studies and consequently the degree of acceptance or rejection of treatment modalities.<sup>4</sup> These experts also take part in decision-making committees of organizations that issue national treatment guidelines, often are faculty members teaching the next generation of clinicians, and render expert opinions for patients seeking care at large academic institutions. Their opinions shape the current and future national guidelines and recommendations and the design of clinical trials. The ProtecT trial has had a major effect on the GU oncologic community; for some it has resulted in dramatic changes in the standard of care, whereas others have resisted its implications of active surveillance being comparable with radical prostatectomy or radiotherapy for low-risk and intermediate-risk prostate cancer.<sup>5,6</sup> Because of the effect of cooperative research group organizations on shaping the future direction of care, we sought to determine the acceptance of active surveillance among North American GU experts in light of the ProtecT results.

Our findings indicate that although active surveillance has been widely adopted for low-risk prostate cancer (95%), it has largely failed to achieve adoption for Gleason 3+4 disease, with more than 80% of participants in our study opposed to active surveillance for this group of patients. The findings that there were no significant demographic differences between supporters and opponents of active surveillance recommendation for low-risk and Gleason 3+4 disease serve as a window into the direction of active surveillance in present as well as future North American clinical trials. Although it did not reach statistical significance, it is noteworthy to mention that opposition to active surveillance for Gleason 3+4 disease approached significance for experts having practiced at least 10 years versus less than 10 years; this might indicate that radiation oncologists having finished residency more recently might be more comfortable with advising active surveillance for Gleason 3+4 disease, which is consistent with the more recent evidence supporting active surveillance for low-risk disease.

Limitations of this study include its small sample size, because the target population was GU physicians who served on cooperative

**Figure 1** Depiction of Survey Results From 42 North American Genitourinary Oncology Expert Radiation Oncologists



Abbreviations: AS = active surveillance; PCa = prostate cancer.

group research organizations. Furthermore, because responses were in the format of multiple choice, the full range of opinions might not have been adequately captured. Additionally, survey fatigue can result in responses that are not genuine; we sought to curb this by not offering an incentive (financial or otherwise) to complete the survey that we hope maximized the rate of legitimate responses. Another limitation is that this survey did not assess whether responders saw patients for the first time together with the surgeon (in multidisciplinary clinic), or only after being referred by the urologist; this is important because the multidisciplinary clinic approach is associated with increased selection of active surveillance, adherence to National Comprehensive Cancer Network guidelines, and minimization of overtreatment in low-risk prostate cancer patients.<sup>7</sup> Finally, an important consideration is the underrepresentation of minorities in these patient populations with regard to clinical trials; a recent publication warned that the failure of the ProtecT trial to stratify results according to patient race might put its overall recommendation of active surveillance for low-risk prostate cancer on thinner ice for African-American than for Caucasian men, particularly because < 1% of ProtecT participants were of African descent, a number far smaller than the true proportion of African-Americans in the United States, which was 13% in the most recent US Census.<sup>2,8,9</sup> Support for active surveillance in African-American patients, particularly for intermediate-risk but also for low-risk disease, is on even thinner ice because African-American individuals might harbor more aggressive disease than Caucasian individuals.<sup>10</sup> This study limitation might be because of the lack of granularity in the survey questions regarding the racial demographic characteristics of patients being treated, and is an important area for future studies to address.

## Conclusion

Active surveillance is well supported by North American GU expert radiation oncologists for low-risk but not intermediate-risk prostate cancer, despite the results of the ProtecT trial providing level 1 evidentiary support for active surveillance in both risk groups. There were no significant differences between experts supporting versus opposing active surveillance for either low-risk or intermediate-risk disease. These preferences might affect the design of future clinical studies, and thus influence the adoption of active surveillance in North American clinical practice.

## Clinical Practice Points

- The ProtecT trial has provided Level 1 evidence supporting active surveillance for prostate cancer patients with low-risk and intermediate-risk disease. The impact of these findings on the opinions of North American genitourinary (GU) experts regarding the role of active surveillance for these patients has not been previously examined.
- Active surveillance is almost universally supported by North American GU expert radiation oncologists for low-risk prostate cancer. However, there is very weak support for this strategy in Gleason 3+4 disease despite the ProtecT trial providing Level 1 evidentiary support in both risk groups. There were no significant differences between experts supporting versus opposing active surveillance for either low-risk or intermediate-risk disease.
- These preferences may affect the design of future clinical studies, influencing the adoption of active surveillance in North American clinical practice.

## Disclosure

The authors have stated that they have no conflicts of interest.

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