Radiologic Progression of Disease in a patient on Active Surveillance of Prostate Adenocarcinoma

VALERIE SANDS, MD
STEVEN EBERHARDT, MD
UNIVERSITY OF NEW MEXICO HOSPITAL
Goal of Active Surveillance of Prostate Adenocarcinoma

- Delay the initiation of curative treatment and avoid possible side effects of treatment of early state prostate adenocarcinoma
  - Following radical therapy, 60% of patients experience erectile dysfunction (Hugosson, 2011)
  - Up to 30% experience some urinary incontinence (Unlisted author, 2013)
Typical Enrollment Criteria (Barrett & Haider, 2017)

- Gleason score $\leq 3+3$
- PSA $\leq 10$ ng/ml
- Stage $\leq T2$ (tumor confined to prostate)
- Biopsy $\leq$ two positive cores and/or $\leq 50\%$ of core
  - Thought to underestimate disease and possibly miss 30-40% of clinically significant tumors (Hu, et al, 2012)

*MRI not typically included*
Typical Active Surveillance Monitoring Methods

- PSA every 3 – 6 months
- Digital rectal examination every 3-6 months
- Biopsy as frequently as every 12 months and as infrequently as every 3-4 years or as indicated by PSA doubling time or digital rectal examination findings
  - Transrectal ultrasound guided biopsy is associated with a complication rate of 10% (Nam, 2010)

*MRI not typically included*
More than half of patients eligible for surveillance choose initial radical treatment (Miller et al, 2006)
Role of multiparametric MRI in Active Surveillance (Barrett & Haider, 2017)

- Not currently included in enrollment criteria or active surveillance protocols but often used for both and can be beneficial

- Goal:
  - Prior to enrollment, detect significant cancer not identified by biopsy
  - During active surveillance,
    - Prompt repeat biopsy and/or change from active surveillance to active treatment
    - Identify biopsy target
    - Possibly supplement or replace biopsy, minimizing the invasive nature of follow up and improving quality of life

- May increase clinician faith and patient tolerance of active surveillance, increasing the number of patients who choose it
Reclassification of Disease (Barrett & Haider, 2017)

- Little consensus on what constitutes progression of disease
- Typically includes:
  - No longer meeting conditions of enrollment
  - Detection of higher volume or higher grade cancer on follow up biopsy
  - PSA doubling time of less than 3 years
  - Unequivocal clinical progression
Progression of Disease by mpMRI
(Barrett & Haider, 2017)

- Change in size or stage
- Upgrade in PIRADS score
- Appearance of new lesions
- Functional characteristics such as DWI and dynamic contrast enhancement parameters (not widely used)
Our Patient:

- Highly educated man initially diagnosed in his late 60s, approximately 10 years ago, who reads extensively on prostate cancer and prefers to delay treatment as long as possible.
2010-2014: Patient placed on Active Surveillance. Within this time period, patient had two Gleason 3+3 biopsies of the right prostate and one benign biopsy, all in line with continued surveillance, though with gradual rise in PSA, such that by...

Mid 2016 - PSA is 6.3 ng/ml (increased from 3.0 in 2010), such that in...

Late 2016 - First MRI is performed which demonstrated...
PIRADS 3 Lesion in the left apical anterolateral peripheral zone: Focal moderate hypointense on ADC, isointense on DWI and DCE negative.
Early 2017 – New biopsy Gleason 3+4, left prostate

Mid 2017 – Based on rising PSA, new Gleason sum 7 disease by biopsy and intermediate suspicion lesion on MRI, clinician recommends external beam radiotherapy with neoadjuvant androgen deprivation therapy. Patient elects continued surveillance and one year later another biopsy is performed...

Early 2018 – Gleason 3+4, left and right prostate

Late 2018 – Continued sinusoidal rise in PSA, now 10.4 ng/mL

Early 2019 – Follow up MRI demonstrates...
PIRADS 5 lesion in the left apical anterolateral gland:
Focal markedly hypointense on ADC and markedly hyperintense on DWI, measuring ≥ 1.5 cm.
No gross extracapsular extension.

Incidental note of enhancement along the posterior lateral gland on the left and mid gland bilaterally, thought to reflect inflammation/prostatitis.
Patient Timeline Continued

- Early 2019 - Clinician again recommends localized treatment with radiation therapy. Patient requests additional biopsy and states he would be amenable to treatment if Gleason 8 or above. PSA 13.7 ng/ml.
- Early 2019 – Repeat biopsy Gleason 3+4, left lateral apex, left medial apex, middle and base, and right lateral base.
- Early 2019 – Patient elects not to proceed with treatment but requests to start Finasteride.
- Late 2019 – PSA 9.96 ng/ml, which is higher than the expected 50% decrease six months after commencement of Finasteride and is concerning for disease progression.
- Late 2019 – Patient discontinued Finasteride secondary to side effects.
- Early 2020 – PSA 19.3 ng/ml, again concerning, though an increase would be expected following discontinuation of Finasteride.
- Mid 2020 – Additional MRI performed by patient request and his own initiative to obtain insurance approval, demonstrating...
Increased size of dominant PIRADS 5 lesion in the left apical anterolateral peripheral zone, suggestive of disease progression. No gross extraglandulararular extension.
New PIRADS 4 lesion in the left apical posteromedial peripheral zone

Several new small PIRADS 4 lesions in the left mid gland PZ and a new small PIRADS 3 lesion in the right mid gland posteromedial PZ
Slight increase in size of an oval left external iliac node, now measuring 1.2 x 0.8 cm, previously 1.0 x 0.5 cm; non-enlarged by size criteria and unchanged in morphology. Attention to be given on follow up MRI, if treatment is not pursued.
Patient Timeline Continues...

- Scheduled for follow up appointment.
- Repeat targeted biopsy anticipated given disease progression by imaging and patient preference to withhold treatment until Gleason 4+4 disease identified, though perhaps patient will consider treatment given imaging findings.
Role of mpMRI in Active Surveillance for the Patient’s Prostate Cancer

- Initial MRI helped to clarify clinical picture in the setting of gradually rising PSA with relatively nonsuspicious biopsy results and may have helped to identify target for biopsy.

- Second MRI demonstrates disease progression but allowed for treatment adverse patient to continue on surveillance (though against clinician recommendations) with some peace of mind. Again identification of biopsy target.

- Third MRI demonstrates further progression of disease. Provides the patient and clinician with additional information so that they can continue making an informed decision based on patient preference. Also clarifies the clinical picture, given PSA was slightly confounded by interim Finasteride therapy.
Teaching Points

- Active Surveillance delays radical treatment in early prostate adenocarcinoma, reducing associated side effects

- Role of mpMRI in active surveillance
  - Ensure enrollment of appropriate patients only
  - Identify sites for biopsy to obtain adequate pathology
  - Document disease progression and assist the clinician and patient with making an informed decision, especially for the treatment adverse patient
  - Eventually could reduce the frequency of biopsies during surveillance, making surveillance a more appealing choice for some men
The hope is that prostate mpMRI will continue to increase clinician confidence and patient tolerance of active surveillance and thereby reduce the morbidity associated with early treatment of prostate adenocarcinoma.


