Active Surveillance –
Current Trends, Genetic Testing and Patient Selection

Dr. Ilan Gielchinsky

Urologic Oncologic Surgeon

Robotic Surgery | Minimally Invasive Surgery | Focal Therapy

Precision management. Not passive observation.

SELECT • MONITOR • INTERVENE

The question is no longer whether we can safely observe.
It is how **precisely** we can **select**, **monitor** and intervene.

BIOLOGY

MRI

HISTOLOGY

PATIENT

Why Active Surveillance Matters

Excellent long-term outcomes — when surveillance is structured

98–100%

10-y cancer-specific survival

1.4%

10-y metastasis • PASS

0.1%

10-y PCa mortality • PASS

ProtecT: essential context, but not modern AS

- 15-year mortality low and similar among monitoring, surgery and radiotherapy.
- Metastases and clinical progression were more frequent with active monitoring.
- The monitoring arm was largely PSA-driven and lacked today's MRI + targeted biopsy pathway.

Reclassification is not failure — it is the surveillance system working.

EAU 2026 • Hamdy 2023 • Newcomb 2024

Guidelines 2026 — Key Messages

Same philosophy; meaningful differences in follow-up detail

EAU 2026

- AS standard: suitable low-risk
- Selected low-volume ISUP2
- PSA ≥ q6 months
- Biopsy ~q2–3 years
- **PSA-DT <3 y → MRI + biopsy**
- MRI progression → biopsy
- **Cribriform / IDC exclude**

AUA / ASTRO

- AS preferred low-risk
- Discuss favorable intermediate-risk
- Serial PSA + repeat biopsy
- **mpMRI augments risk - PIRADS4-5 immediately re-biopsy.**
- **MRI ≠ biopsy replacement**
- Biopsy ~1–4 y individualized
- **Repeat isolated PSA rise**

NICE / UK *

- **Year 1 PSA q3–4 months**
- DRE at 12 months
- mpMRI ~12–18 months
- **Year 2+ PSA q6 months**
- DRE yearly
- **MRI / biopsy by concern**
- Re-biopsy if discordant

NCCN / ASCO

- Confirm eligibility
- **MRI + biopsy + selected molecular tools**
- More caution in favorable intermediate-risk
- Focal evidence less mature
- **Biomarkers selectively**
- **Only if decision may change**
- **Not routine genomics for all**

Who Is a Candidate for Active Surveillance?

Selection is biology + burden + patient context

FAVOURABLE

- ISUP1: core AS population
- Selected ISUP2: small pattern 4 + low volume
- Usually cT1c–cT2a
- PSAD ~0.15: continuous risk variable
- Reassuring MRI phenotype
- Life expectancy ~10 years or more
- Comorbidity, frailty, preference

CAUTION / EXCLUSION

- Invasive cribriform architecture
- Intraductal carcinoma
- More extensive pattern 4
- Adverse MRI / clinical features
- Generally ISUP3 or higher
- BRCA2: not automatic exclusion; closer confirmation and surveillance

The Modern Active Surveillance Toolbox

Integrated, multiparametric risk assessment

Clinical

PSA • kinetics • PSAD • DRE

Imaging

mpMRI • PI-RADS • PRECISE

Histology

targeted • perilesional • systematic • transperineal

Blood / urine

PHI • 4K • IsoPSA • Stockholm3 • ExoDx • SelectMDx • MPS2

Tissue

Decipher • Prolaris • ProMark • ArteraAI

Emerging

BRCA2 • micro-US • PSMA PET • AI

The goal: reduce uncertainty — not create false precision.

PSA, Kinetics and PSA Density

A trigger to investigate — not a treatment trigger

PSA DENSITY

PSA ÷ PROSTATE VOLUME

≈ 0.15

- PSA at least every 6 months (EAU)
- Repeat a sudden rise after excluding transient causes
- PSA-DT <3 years → MRI + repeat biopsy
- Negative MRI + **low PSAD** is more reassuring than negative MRI + **high PSAD**
- **Treatment change should be driven by confirmed histological progression**

PSA tells you when to look harder.

Multiparametric MRI and PRECISE

Serial MRI asks: has the disease changed?

PRECISE 1–2

Regression

PRECISE 3

Stability

PRECISE 4–5

Progression

- **If diagnosis was made without MRI, obtain MRI before confirmatory reassessment.**
- **MRI progression → biopsy confirmation before treatment change.**
- mpMRI augments risk stratification but does not replace periodic biopsy.
- **MRI-only surveillance can miss histological upgrading.**
- Stable PRECISE 3 + stable PSAD <0.15 may support biopsy de-intensification in selected low-risk men — weak EAU recommendation.

PI-RADS = suspicion now • PRECISE = change over time

Biopsy Strategy in Modern Surveillance

Each sampling strategy answers a different question

TARGETED

- MRI-visible lesion
- Direct assessment of the radiological target

PERILESIONAL

- Around the target
- Defines boundaries; may detect csPCa just outside target

SYSTEMATIC

- Rest of gland
- Detects MRI-occult disease; maps multifocal burden

TRANSPERINEAL

- Route
- Lower infectious risk; excellent anterior / apical access

Target the lesion. Sample the gland. Prefer the safer route.

Blood and Urine Biomarkers

Probability refinement — mainly around biopsy decisions

PHI

Blood

tPSA + fPSA + p2PSA
PSA-family refinement; improves specificity for csPCa.

4Kscore

Blood

4 kallikreins + clinical variables
Outputs probability of GG2+ on biopsy.

IsoPSA

Blood

PSA structural / isoform signal
Looks at PSA structure—not just concentration.

Stockholm3

Blood

proteins + genetics + clinical data
Integrated proteins + genetics + clinical risk model.

62-year-old man on Active Surveillance
GG1 (3+3), low-volume disease
PSA 6.2 ng/mL → stable
PSA density 0.11
MRI: PI-RADS 3, unchanged
PHI: 58 Management:
→ Earlier repeat MRI / targeted + systematic biopsy
→ **PHI changes surveillance intensity — not treatment itself**

exosomal ERG / PCA3 / SPDEF
No DRE required; exosomal RNA signal for GG2+ risk.

SelectMDx

Urine

HOXC6 + DLX1 after DRE
Post-DRE mRNA; HOXC6/DLX1 linked to aggressive biology.

MPS2

Urine

18-gene assay aimed at GG2+ risk
18-gene urine panel designed for GG2+ detection.

PCA3

Urine

legacy prostate-cancer RNA marker
Legacy post-DRE RNA marker; largely superseded.

68-year-old on AS
GG1, low-volume disease
PSA 7.1 ng/mL
PSA density 0.13
MRI: PI-RADS 3, stable
MPS2: very low predicted risk of GG2+ → Continue surveillance
→ Consider avoiding an immediate repeat biopsy
Take-home:
A reassuring biomarker may help avoid unnecessary biopsy.

Useful when PSA, MRI and pathology are borderline or discordant — not a replacement for imaging or histology.

DO I NEED TO LOOK HARDER?

Tissue Molecular Classifiers — What Is Unique About Each?

DECIPHER

22-gene RNA transcriptomic classifier.

- Continuous genomic-risk score (0–1)
- Reflects tumour aggressiveness / metastatic biology
- **Helpful when conventional features and apparent biology do not align**

MEMORY HOOK

“How aggressive is this tumour biologically?”

PROLARIS

Cell-cycle progression (CCP) RNA signature.

- Measures genes involved in mitosis / proliferation
- Asks how actively the tumour is cycling
- Useful in high-volume ISUP1 / selected ISUP2 when AS vs treatment is uncertain

MEMORY HOOK

“How fast is the biological engine running?”

PROMARK

Proteomic rather than RNA-based.

- Eight proteins measured in biopsy tissue
- Reflects downstream functional cellular behaviour
- Estimates favourable vs unfavourable pathology

MEMORY HOOK

“**Proteins, not genes — what is the cell expressing**?”

DO I TRUST THIS TUMOUR ENOUGH TO SURVEIL IT?

ArteraAI & When Do These Tests Actually Help?

Artera is digital pathology AI — not an RNA-expression genomic assay.

ARTERAAI

INPUT
Digitised routine H&E biopsy slide + clinical variables

- Multimodal AI integrates histological image features + **clinical context**
- No RNA extraction
- No additional staining
- Does not consume tissue
- Prognostic risk stratification
- **Predictive information in radiotherapy — e.g. ADT benefit**

MEMORY HOOK
“The computer reads the H&E slide — NOT a genomic-expression assay.”

WHEN ARE CLASSIFIERS MOST USEFUL?

Tissue classifiers are best used in a **genuine grey zone**:

- High-volume ISUP1
- Selected low-volume ISUP2
- Discordant MRI / biopsy / clinical features
- Patient genuinely balanced between surveillance and treatment

ASCO PRINCIPLE
Use selectively when the result is likely to change management.

THE LIMITATION: Genomics can only characterize the tumour you actually sampled (Heterogenicity).

Can We Extend the Boundaries of Active Surveillance?

From observation alone to prostate-preserving active management

OBSERVE

Low-risk disease
Structured surveillance

→

SELECTIVELY TREAT

Clinically significant
index lesion

→

CONTINUE TO SURVEIL

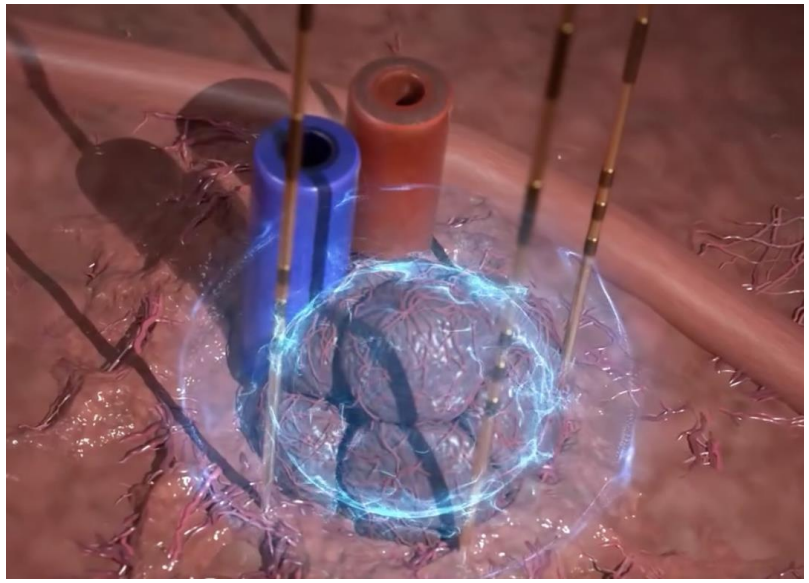
Preserved prostate
Ongoing risk assessment

**Can focal therapy extend the philosophy of Active Surveillance —
without calling focal therapy Active Surveillance?**

Avoid unnecessary radical treatment while maintaining oncological control.

Focal IRE — Irreversible Electroporation

A prostate-preserving focal ablation strategy



HIGH-VOLTAGE ELECTRICAL PULSES

→ irreversible membrane permeabilization

→ targeted cell death

NON-THERMAL FOCAL ABLATION

Preserving the prostate and surrounding structures

2017–18
ST VINCENT'S
SYDNEY

2018–19
HADASSAH
JERUSALEM

2019–PRESENT
MEDICA
TEL AVIV

2025
IMPERIAL COLLEGE
LONDON

Blazevski et al. 2020 • Scheltema et al. 2023

How Do We Surveil the Partially Treated Prostate After IRE?

PSA remains measurable. The **treated field** and **untreated gland** must both be assessed.

PSA

- PSA remains **detectable** after focal IRE
- **Nadir / kinetics may trigger investigation**
- **No validated PSA-only definition of failure**

mpMRI

- **Post-ablation change can mimic recurrence**
- Full mpMRI; **DCE** is particularly important

BIOPSY

- Protocol histology remains important
- **Sample treated field + any suspicious lesion**
- **Sample untreated gland systematically / regionally**

RECURRENCE

- Distinguish i**n-field** persistence / recurrence from **out-of-field** disease
- **Low-grade out-of-field disease may still be surveilled**

Lebastchi 2020 • TARGET 2024 • PI-FAB • contemporary reviews

Post-IRE Surveillance — Three Clinical Pathways

My clinical experience across London, Sydney and Israel

IMPERIAL COLLEGE LONDON

PSA
Every 3 months

MRI
At 12 months

BIOPSY
For cause only

Triggered by PSA rise or abnormal MRI

ST VINCENT'S, SYDNEY

PSA
3 months • 6 months • then q6 months

MRI
At 6 months

BIOPSY
Protocol biopsy at 12 months

Then MRI approximately every 2–3 years

MY PRACTICE — ISRAEL

PSA
Australian schedule

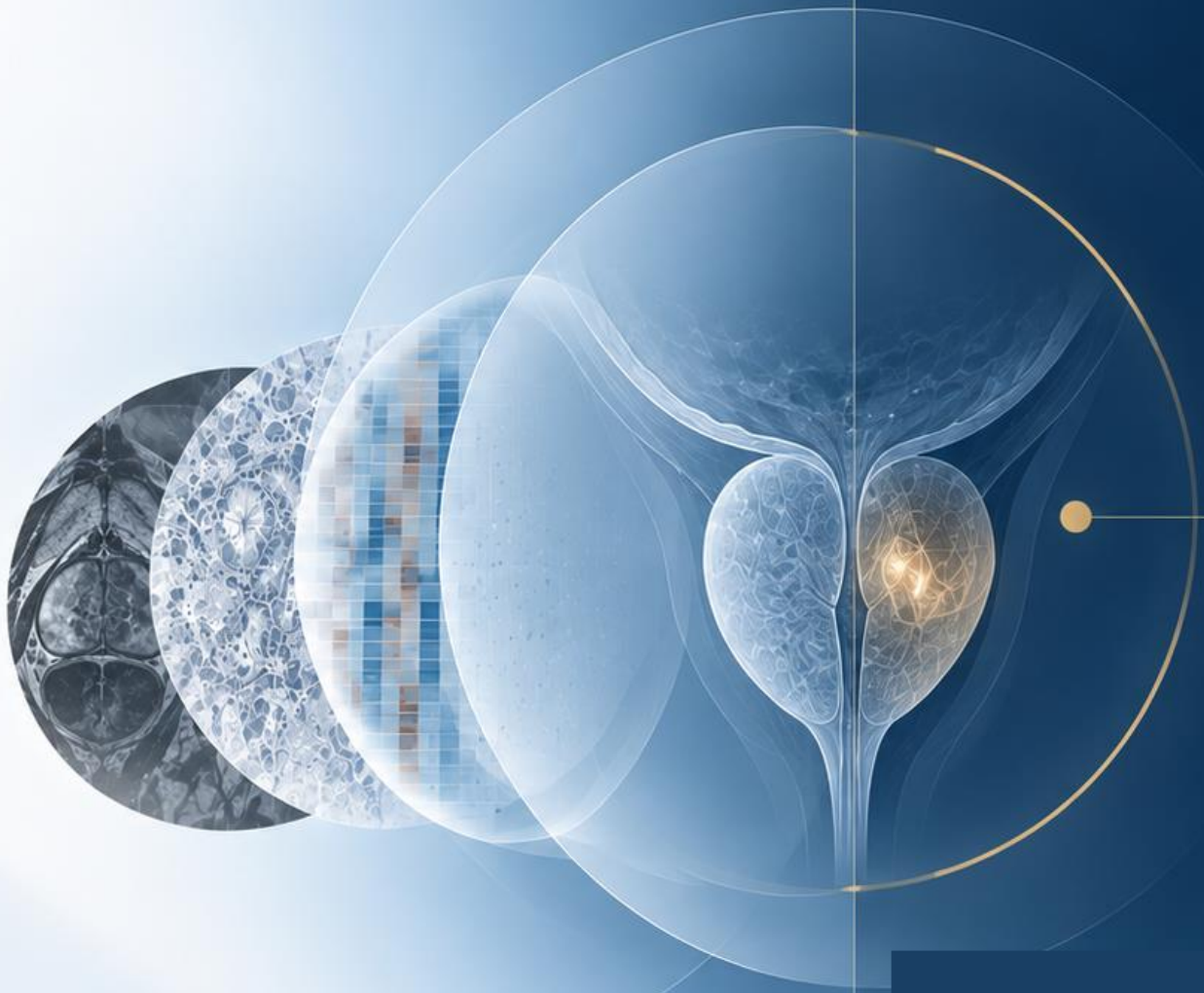
MRI
At 6 months

BIOPSY
At 12 months

I follow the St Vincent's / Australian pathway

Thank You

QUESTIONS & DISCUSSION



Dr. Ilan Gielchinsky
Urologic Oncologic Surgeon
Robotic Surgery | Minimally Invasive Surgery | Focal Therapy

Selected Bibliography

Optional backup slide

- EAU Guidelines on Prostate Cancer. 2026.
- AUA/ASTRO. Clinically Localized Prostate Cancer Guideline. 2022; amended 2026.
- NICE NG131. Prostate cancer: diagnosis and management.
- Eggener SE, et al. Molecular Biomarkers in Localized Prostate Cancer: ASCO Guideline. JCO 2020.
- Hamdy FC, et al. Fifteen-Year Outcomes after Monitoring, Surgery, or Radiotherapy. NEJM 2023.
- Newcomb LF, et al. Long-Term Outcomes Using Protocol-Directed Active Surveillance. JAMA 2024.
- Bokhorst LP, et al. A Decade of Active Surveillance in PRIAS. Eur Urol 2016.
- Tosoian JJ, et al. Development and Validation of an 18-Gene Urine Test. JAMA Oncol 2024.
- Lebastchi AH, et al. Surveillance Methodologies After Focal Therapy. Eur Urol 2020.
- Light A, et al. TARGET. Eur Urol 2024.
- Giganti F, et al. PI-FAB. Eur Urol Oncol 2023.
- Scheltema MJ, et al. Median 5-year outcomes of focal IRE. BJU Int 2023.
- Blazevski A, et al. Focal IRE outcomes. Eur Urol Oncol 2020.
- Lantz A, et al. PRIS randomized trial protocol. Eur Urol Open Sci 2023.