



# Prostate Biopsy and Targeted Therapy

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# Disclosure

- President and CEO 3DBiopsy LLC

# Biopsy Techniques 2016

- 12-core standard transrectal (TRUS)
  - 1.2 million/year
  - 3.3 million world-wide
- mpMRI guided transrectal
- Transperineal
  - template guided  $\pm$  mpMRI
  - 3D-mapping guided

# Current Biopsy/Treatment Algorithm

230,000  
newly  
diagnosed

20,000 GS  
8-10

210,000  
GS 6-7

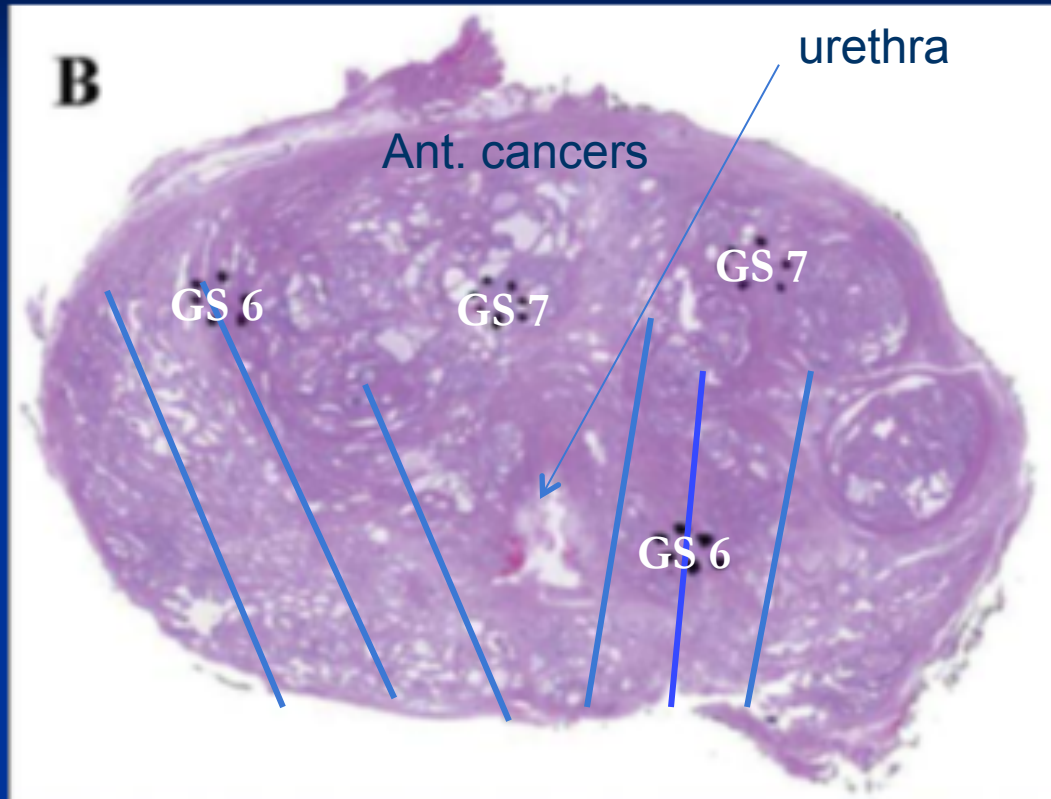
RP

RT

Surgery

RT

Surveillance  
Focal Therapy



# Pathologic Findings in Radical Prostatectomy Specimens From Patients Eligible for Active Surveillance With Highly Selective Criteria: A Multicenter Study

Jean-Baptiste Beauval, Guillaume Ploussard, Michel Soulié, Christian Pfister, Simon Van Agt, Sébastien Vincendeau, Sébastien Larue, Jérôme Rigaud, Nicolas Gaschignard, Morgan Rouprêt, Sarah Drouin, Mickael Peyromaure, Jean Alexandre Long, Francois Iborra, Guy Vallancien, Francois Rozet, Laurent Salomon, and Members of Committee of Cancerology of the French Association of Urology (CCAFU)

- Retrospective analysis of 10,785 consecutive radical prostatectomy performed in 10 university hospitals
- 919 patients fulfilled the following criteria:
  - T1c
  - PSA <10 ng/mL
  - 1 positive biopsy, tumor length <3 mm and Gleason score <7.
- Gleason score was upgraded in 34% of patients, including 1.2% Gleason score 8-9. Pathologic stages were pT2 in 87.3%, pT3 in 11.1%, and pT4 in 1.4% of cases. Extraprostatic extension was found in 12.5%.
- **Only 26% of patients had “insignificant” tumors.**

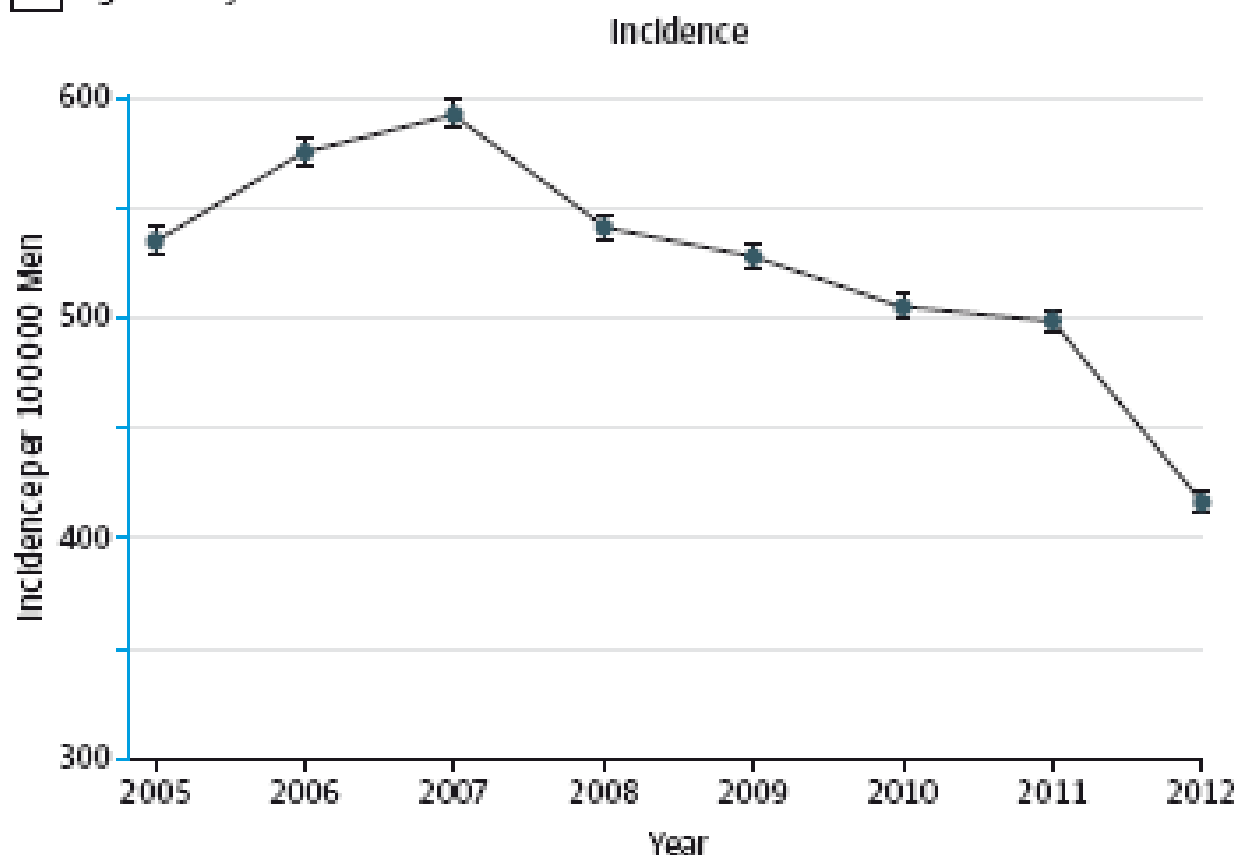
# The Playing Field Has Changed

- When TRUS biopsy introduced cancers were larger and detectable by both DRE and TRUS
- Today lesions are very small or located in regions that are not discoverable by DRE or TRUS
- This has resulted in the 12-core biopsy being a “semi-blind” procedure.
- Re-biopsy using the same technology does not yield better results

# Prostate Cancer Incidence and PSA Testing Patterns in Relation to USPSTF Screening Recommendations

Ahmedin Jemal, DVM, PhD; Stacey A. Fedewa, MPH; Jiemin Ma, PhD; Rebecca Siegel, MPH;  
Chun Chieh Lin, PhD; Otis Brawley, MD; Elizabeth M. Ward, PhD

**A** Aged  $\geq 50$  y



Screening rates ↓  
10% 2005-2008  
18% 2010-2013



The Centers for Medicare & Medicaid Services (CMS) seeks stakeholder comments on the following clinical quality measure under development:

**Title:** Non-Recommended PSA-Based Screening

**Description:** The percentage of adult men who were screened unnecessarily for prostate cancer using a prostate-specific antigen (PSA)-based screening test

## *Prostate Testing Should Be Up to the Patient*

Wednesday, December 2, 2015

That the U.S. Preventive Services Task Force states that PSA causes “more harm than good” is an unfortunate byproduct of the success of PSA. However, the problem isn’t PSA but the biopsy technique used to diagnosis prostate cancer. The solution to this problem is to improve the biopsy test. Investigators are having

NELSON N. STONE, M.D.  
*New York*

# Biopsy Approaches

- mpMRI
  - Only identify index lesion and hemi-ablate
- TPMB
  - Ablate individual lesions-targeted focal therapy

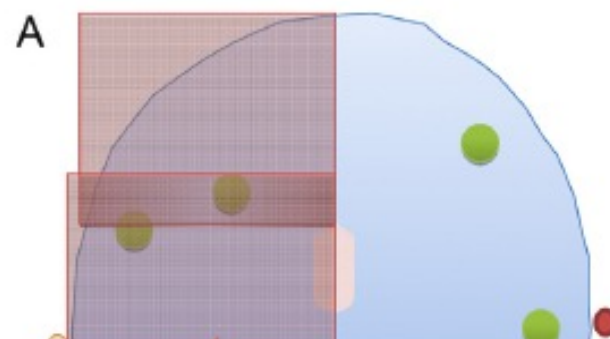
# Focal Ablation Targeted to the Index Lesion in Multifocal Localised Prostate Cancer: a Prospective Development Study

Hashim U. Ahmed<sup>a,b,†,\*</sup>, Louise Dickinson<sup>a,b,†</sup>, Susan Charman<sup>c,d</sup>, Shraddha Weir<sup>b</sup>, Neil McCartan<sup>b</sup>, Richard G. Hindley<sup>e</sup>, Alex Freeman<sup>f</sup>, Alex P. Kirkham<sup>g</sup>, Mahua Sahu<sup>b</sup>, Rebecca Scott<sup>a</sup>, Clare Allen<sup>g</sup>, Jan Van der Meulen<sup>c,d</sup>, Mark Emberton<sup>a,b</sup>

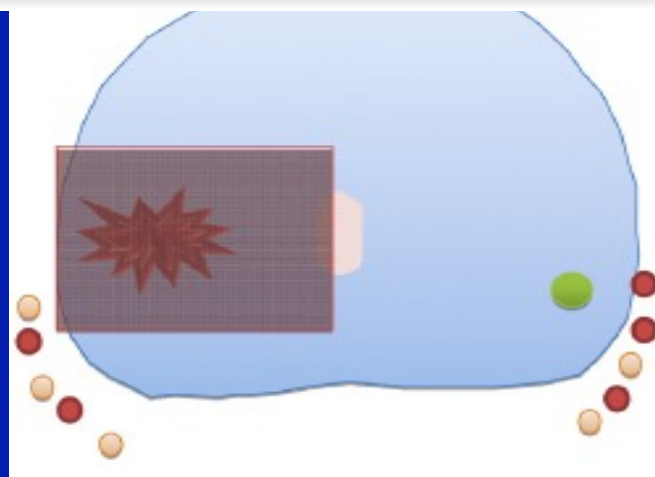
Men with localised low-risk ( $n = 7$ ), intermediate-risk ( $n = 47$ ), and high-risk ( $n = 2$ ) prostate adenocarcinoma  
Total  $n = 56$

Absence of any cancer on both sides,  
 $n$  (%; 95% CI)

Index lesion focal therapy using transrectal HIFU  
Total  $n = 56$

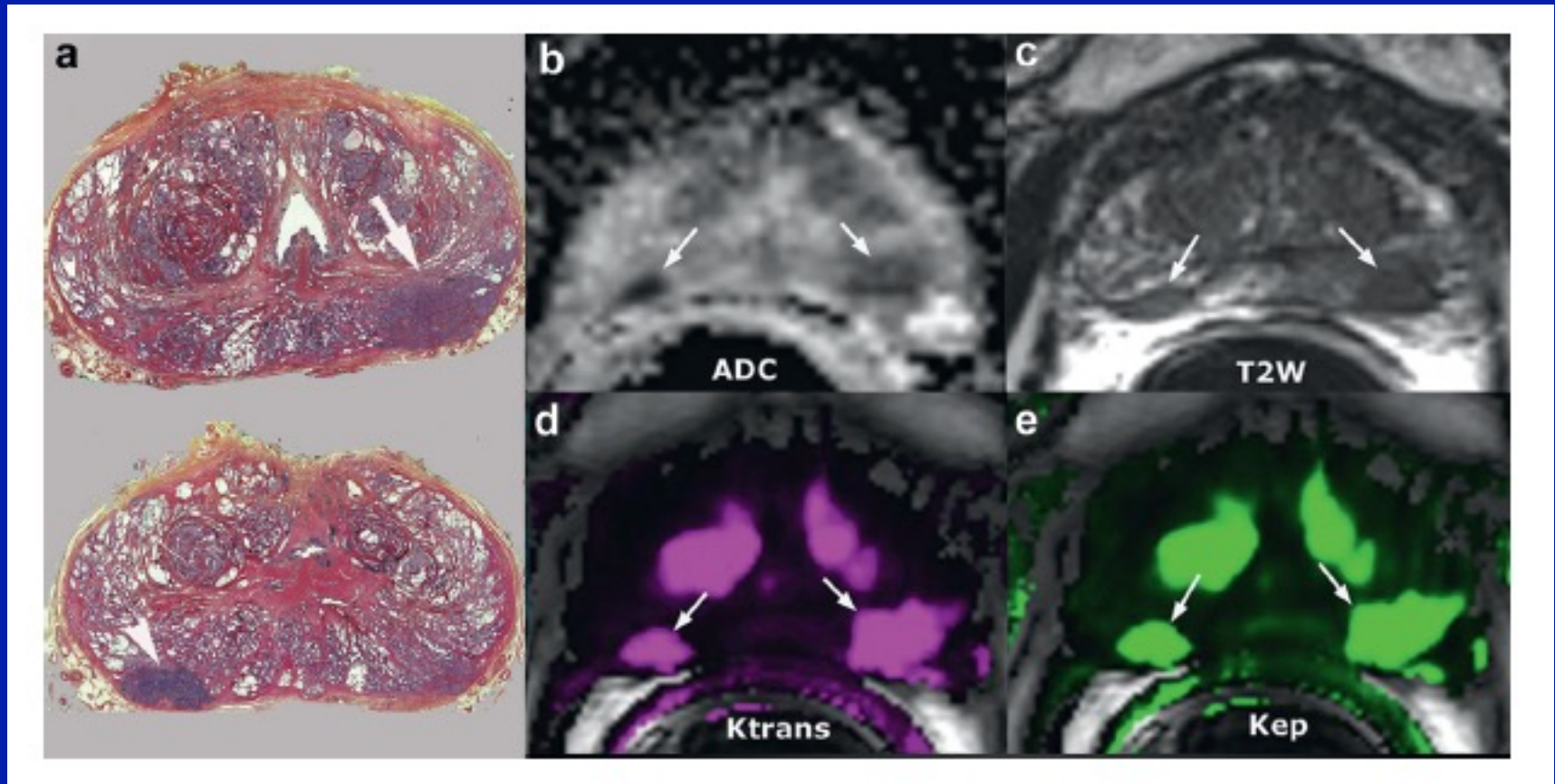


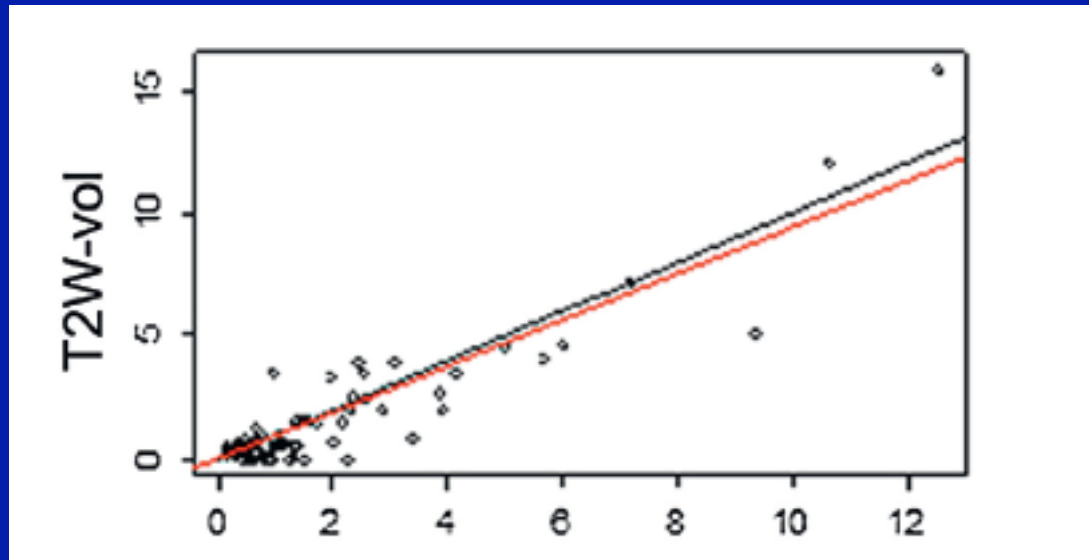
30/52 (57.7; 43.2-71.3)



# Tumor Target Volume for Focal Therapy of Prostate Cancer—Does Multiparametric Magnetic Resonance Imaging Allow for a Reliable Estimation?

F. Cornud,\* Gaby Khoury, Naim Bouazza, Frederic Beuvon, Michael Peyromaure, Thierry Flam, Marc Zerbib, Paul Legmann and Nicolas B. Delongchamps





	slope [IC95]	p-value	correlation coefficient	r <sup>2</sup>
T2W volume	0.94 [0.87-1.01]	0.12	0.88	0.84
DW volume	1.05 [0.98-1.13]	0.16	0.90	0.85
DCE volume	0.65 [0.55-0.76]	<10 <sup>-4</sup>	0.62	0.48

Underestimation in 43/87 (49%) by mean of 0.56 cc (0.005-2.84)

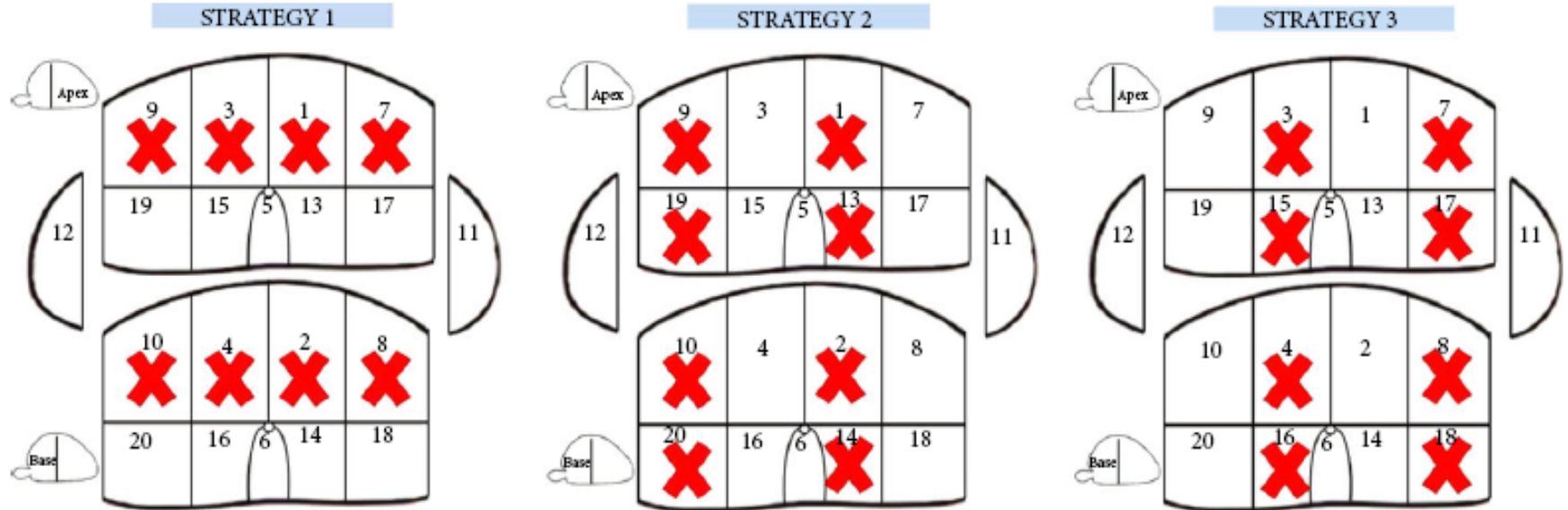
# Transperineal Template-Guided Prostate Biopsy and TFT



# Transperineal template prostate-mapping biopsies: an evaluation of different protocols in the detection of clinically significant prostate cancer

Massimo Valerio\*<sup>†‡</sup>, Chukwuemeka Anele\*<sup>†</sup>, Susan C. Charman<sup>§</sup>, Jan van der Meulen<sup>§</sup>, Alex Freeman<sup>¶</sup>, Charles Jameson<sup>¶</sup>, Paras B. Singh\*\*<sup>†</sup>, Mark Emberton\*<sup>†</sup> and Hashim U. Ahmed\*<sup>†</sup>

Fig. 2 Visual representation of the three strategies simulating reported variations of 5-mm TPM.



N=391

Average number cores 46

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	Strategy 1	Strategy 2	Strategy 3
Sensitivity (95% CI), %	78 (73–84)	85 (80–90)	84 (79–89)
NPV (95% CI), %	73 (67–80)	80 (74–86)	79 (72–84)



# How important is it to *know* all the pathology in the prostate?

## ■ Crawford et al at AUA 2016

- RP stage was pT2a/b in 4 (16%), pT2c in 13 (52%) and pT3 in 8 (32%). The 2 patients with low volume disease on RP each had 1 core GS 6 with TPMB.
- TPMB correctly identified 100% of the RP patients.

## ■ Skouteris et al

- Urinary tract infections are 5x more common in TRUS biopsy compared to TPMB
- Urinary retention occurred in 7.4% of TPMB and was associated with older age and increased prostate size.

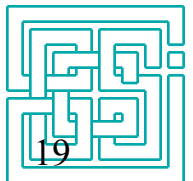
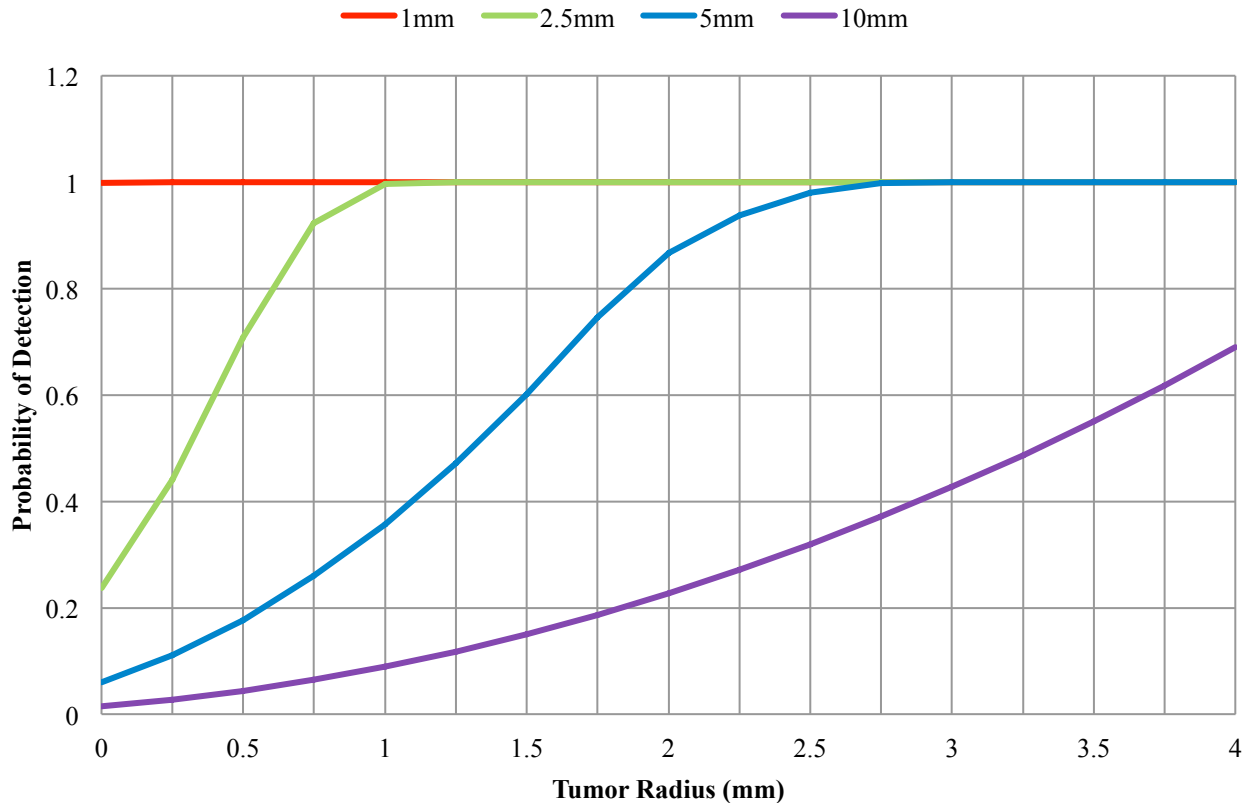
# Inadequacy of Current Technology

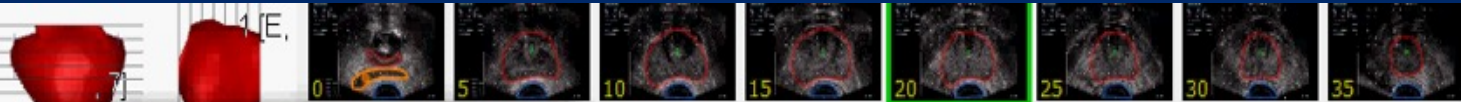
- Biopsy needles designed >30 years ago with limited core size and length
- No software that provides real-time tracking, representation and recall
- Procurement and registry of pathology is time consuming and error prone

# Probability of Detection vs. Tumor Radius

(Grid sizes (mm) = 1, 2.5, 5, 10 – 15 gauge needle)

## Probability of Detection vs. Tumor Radius





**Biopsy Site Editor**

ID: 1

Probe Angle: -12.1 deg

Location (X,Y):  Snap

Start Depth (Z): 2.49 L

Length: 1.7L

Tumor 1		Tumor 2	
Gleason Value	1	Gleason Value	1
Gleason Start	0%	Gleason Start	100%
Gleason End	0%	Gleason End	100%

Preview

Length inside Prostate: 1.70 cm

Biopsy Taken (go to next biopsy site)

Overlapping Sites: 18  
 Min Overlap: 0.01 cm 1%  
 Max Overlap: 0.17 cm 10%  
 Avg Overlap: 0.05 cm 3%

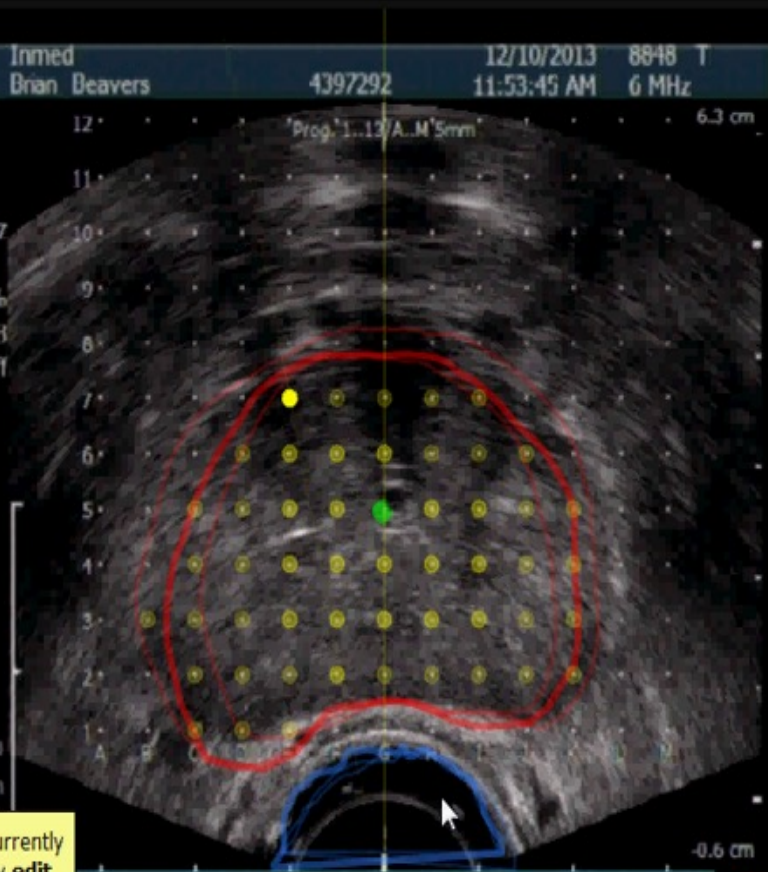
Inmed Brian Deavers 4397292 12/10/2013 11:53:45 AM 8848 T 6 MHz

MI: 1.80 < 1.80  
 TIS: 0.7 < 4.0  
 Res / Hz 1/24 Hz  
 General  
 Gain 61 %  
 Dyn. Range 79 dB  
 Harmonic Off

Enable Outlining

Changing outlines is currently disabled to more easily edit

-0.6 cm





17 mm specimen  
obtained with standard,  
fixed-length needle



60 mm specimen  
obtained with 3DIG Biopsy Needle

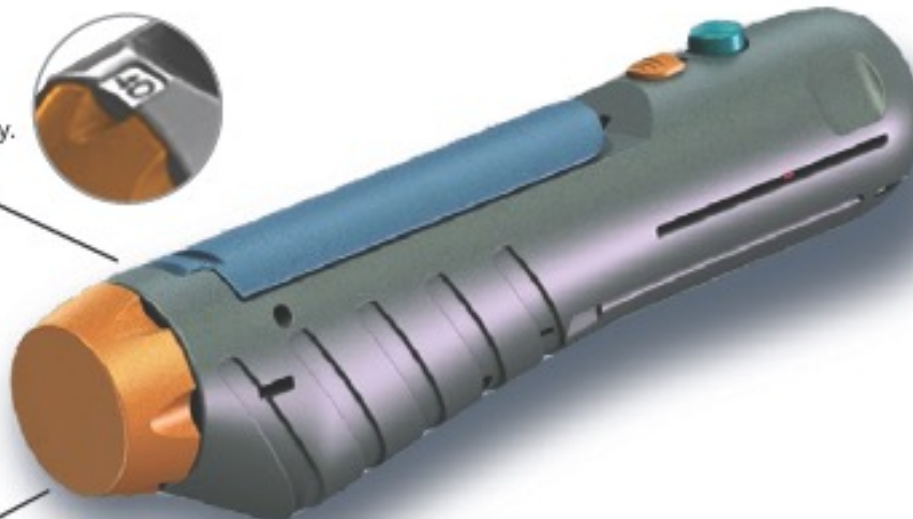


Biopsy Counter displays individual sample numbers.

Indicator Window displays length of biopsy.




















Adjustable Dial sets length of specimen.



Service Indicator Display.



# Previous Workflow

Day	One	Two	Three	Three
Location	Histopathology Lab	Operating Room	Gross Dissection Room	Histopathology Lab
Participants		    		
Touchpoint		 	    	 
Action	<p><b>Kit Creation</b></p> <ul style="list-style-type: none"> <li>Input Patient info</li> <li>Print labels</li> <li>Cut Media</li> <li>Sterilize Media</li> </ul>	<p><b>Table Setup (~2 hours)</b></p> <p><b>Prostate Biopsy Procedure</b></p> <ul style="list-style-type: none"> <li>Doctor yells Site location</li> <li>Nurse labels Formalin Vial</li> <li>Doctor takes Biopsy</li> <li>Hands Gun to Nurse</li> <li><b>Nurse rolls Biopsy onto Media</b></li> <li>Hands second Gun to Doctor</li> <li><b>Second Nurse dyes distal end of Biopsy</b></li> <li>Second Nurse places Media+Biopsy into Formalin Vial</li> <li>Second Nurse places Vial into Styrofoam Tray</li> </ul> <p>Repeat above for all Biopsy Samples</p> <p><b>Samples soak in Formalin Vials</b></p> <p>They soak from 6-72 hours (Avg ~12hrs)</p>	<p><b>Table Setup</b></p> <p><b>Tissue Gross Dissection</b></p> <ul style="list-style-type: none"> <li>Remove single Vial from Styrofoam Tray</li> <li><b>Inspect sponge, removing any found Biopsy</b></li> <li><b>Remove any Biopsy floating in Formalin</b></li> <li>Measure length</li> <li><b>Use Swab to dye entire top of Biopsy</b></li> <li><b>Blot off extra dye with lint-less lab wipe</b></li> <li><b>Pick up dyed Biopsy and put into acetic acid bath</b></li> <li>Soak Biopsy in glacial acetic acid to set dye</li> <li><b>Pick up dyed Biopsy and put into Cassette</b></li> <li>(3 Biopsies per Cassette, Dyed 3 different colors)</li> <li>Put single Biopsy Sponge into Cassette</li> <li>Place Cassette into Cassette Rack</li> <li>Input data into computer</li> </ul> <p>Repeat above for until Cassette Rack is full</p> <p>Place Cassette Rack, with lid, into Tissue Processor</p> <p>Rack may include more than one procedure's Cassettes</p> <p><b>Tissue Processing</b></p> <p>Rack can be held in Tissue Processor for up to 72 hours</p>	<p><b>Tissue Embedding</b></p> <ul style="list-style-type: none"> <li>Rack is placed into Tissue Embedder compartment</li> <li>Media+Biopsy taken out of Cassette (Placed on Tissue Embedder)</li> <li>Embedding Mold slightly filled with Paraffin Wax</li> <li><b>Biopsy placed into bottom of Embedding Mold</b></li> <li><b>Use metal tamper to gently press Biopsy flat</b></li> <li>Cassette (without lid) is placed on Embedding Mold</li> <li>Embedding Mold filled with Paraffin Wax (No large bubbles allowed)</li> <li>Mold removed once cooled and hardened</li> <li>Repeat above for each Cassette</li> </ul> <p><b>Tissue Microtomy</b></p> <ul style="list-style-type: none"> <li>Mold is clamped onto Microtome (Squared off)</li> <li>Sum cuts are taken and placed into water bath</li> <li>Sliced strips are broken apart with Tweezers</li> <li>Slices are placed on slide</li> <li>Repeat above for each Mold</li> </ul> <p><b>Routine H&amp;E Staining</b></p> <p>Coverslipping Station</p>

Nurse/Histologist brings Kit to OR

Histologist brings Vial trays to Gross Dissection Room

Cassette Rack is moved from to Embedding Center

## Notes

## Key



1 Touchpoint



Nurse



Doctor



Software Guy



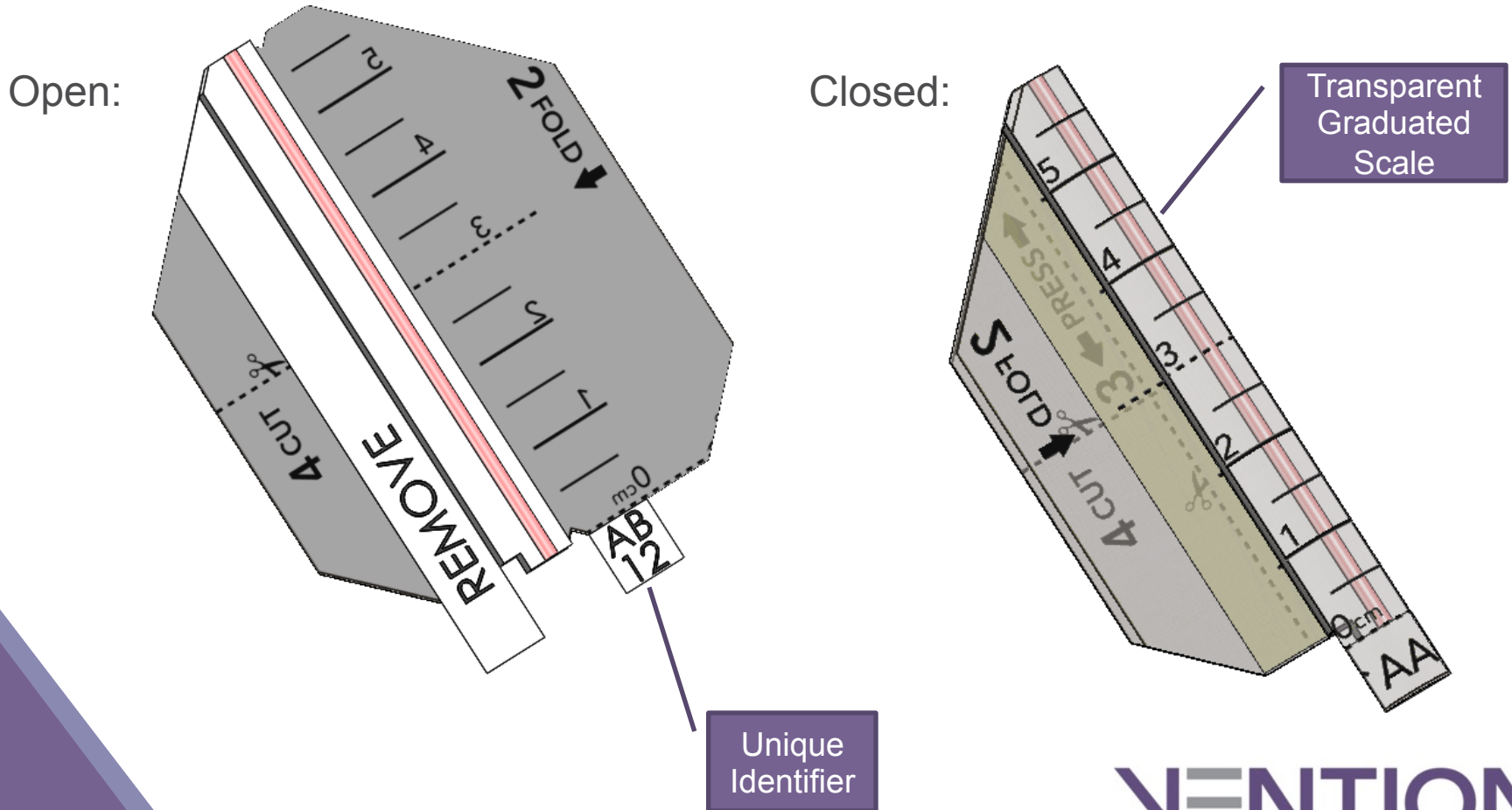
Histopathologist



Anesthesiologist

# The Biopsy Carrier Concept

A Biopsy Carrier that stays with tissue sample from the OR to the pathology slide.

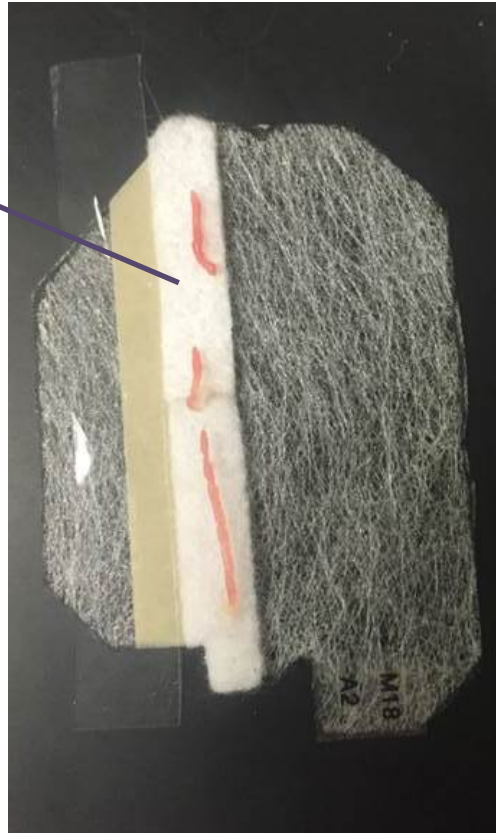


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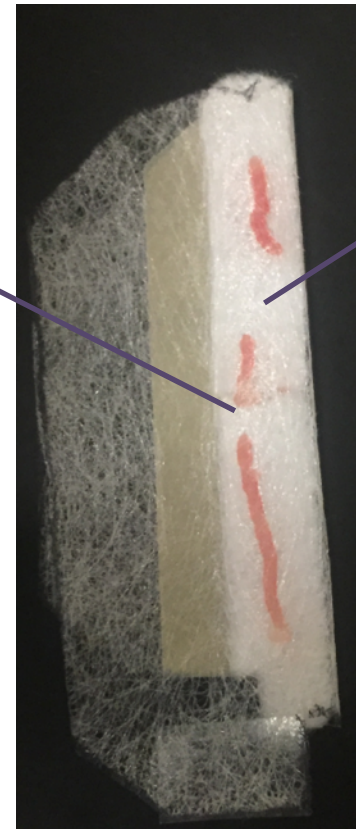
# A Biopsy Carrier Prototype

Open:



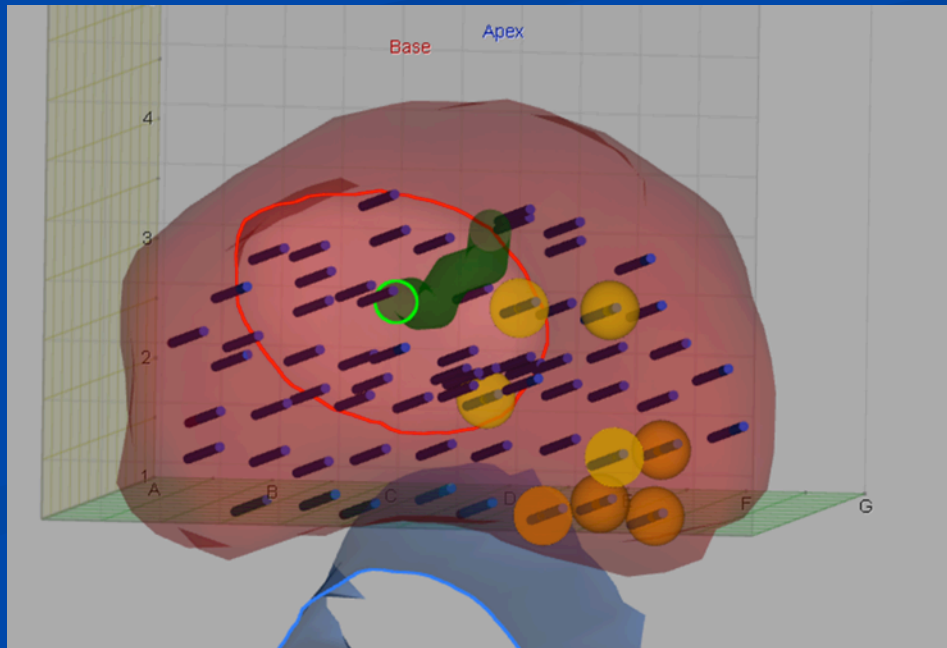
Non-woven material grabs tissue

Closed:



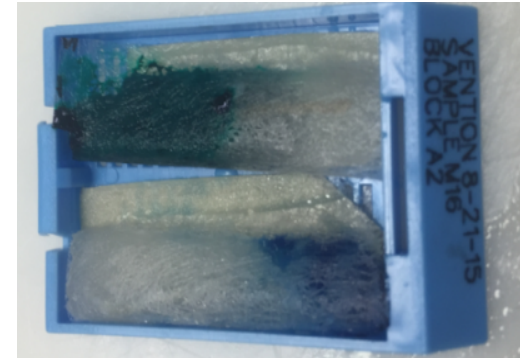
The carrier is able to be processed, embeddable and sliced on microtome

Backer material is transparent and retains sample



# In the Histology Lab

10. Dye tissue with tissue marking ink.  
This indicates distal and proximal ends

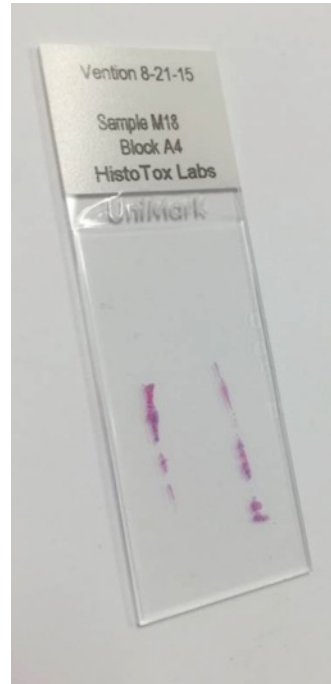


11. Run cassettes through standard  
tissue processing

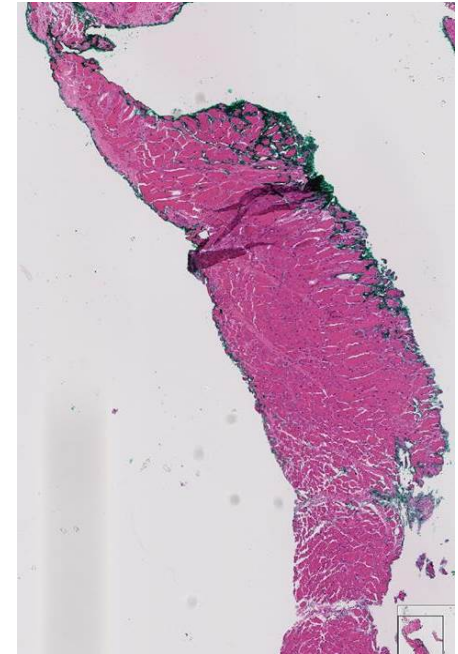


# In the Histology Lab

14. Run slides through standard H&E staining and cover slip



15. Slide is ready to analyze!



# Conclusions

- Selection of surveillance candidates can be improved with mpMRI targeted biopsies or TPMB
- Targeted focal therapy (TFT) requires precise location of ALL significant lesions and THEN a roadmap for treatment planning
- The jury is out as to whether some or all lesions need treatment
- Proof of success (lesion eradication) remains elusive.

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