Boundary Detection Pugh Matrix Research:
Objective: Evaluate 5 different boundary detection modalities

	Impedance	Infrared	Ultrasound elastography	Stiffness	Internal Pressure Sensing	Standard: Laparoscopic Palpation
Mm Resolution	1	0	1	1	1	0
Compatible with Surgical Robotics	1	1	0	1	1	0
Setup and Measurement Time	1	1	1	0	1	0
Undistorted by surrounding tissues	0	0	0	0	1	0
Total	**3**	**2**	**2**	**2**	**4**	**0**

The first problem that needs to be overcome for our solution is to identify the location of the boundary between the two different tissues.

The rhabdosphincter structure is the tube shape of the urethra surrounded by two layers of muscle. The inner layer of longitudinal muscle is the lissosphincter and the outer layer of muscle wrapped in rings around the urethra is the rhabdosphincter.

The prostate is a significantly more complex organ. The transitional zone is immediately surrounding the prostatic urethra is a mix of glandular cells and smooth muscle cells. The outer layers of the prostate contain more of the glandular, prostatic fluid secreting cells.

Given the stark differences in cell types between the two structures there may be a vast number of macroscopically measurable differences between the two. We examined 5 different measurement modalities: Impedance measurement, infrared light detection, ultrasound elastography, stiffness measurement, and internal pressure sensing. Our results are summarized in the Pugh Matrix above and expanded upon in the research below.

<u>Impedance Measurement</u>

The basis of this technology is the detection of the resistance of the tissue in much the same way that a stud finder measures the differences in the wall to locate the boards in the wall.

Edge detection- This is used to determine the first point at which a change occurs between two interfaces. In our case the best way to perform this would be to pass the device towards the boundary once and then from the other side once. This would allow you to place the center line twice and the difference between the two should be able to give you a small range within which to cut.

Alternative- Bipolar needle measurement

This method detects the impedance present between two electrodes positioned on a needle tip. This is different from monopolar measurement which uses a reference placed at the surface of the given tissue. Bipolar is generally considered to be more accurate.

Ideally you could stick the needle into the tissue in many different places and you could map out a rough boundary of where the cut location should be.

- Downside: It wouldn't allow you to determine the precise location only a relatively rough guide based upon how close to the correct line you place the needle.

It's possible that you could extrapolate this more generally and place two electrodes a little bit further apart. This would allow you to measure differences over a range of tissue. But you would need to set these a fixed distance apart to be reasonable. At this point this basically becomes an edge detector similar to above.

This technology has the potential to have a very high resolution as the impedance measurements would likely be accomplished using a bipolar needle detection system. This technology could also leverage a combination of an internal and external probe in order to obtain the impedance difference over the larger bulk of tissue between the two instead of only at the tip of a needle. Depending upon the kind of impedance measurement this could be significantly distorted by other tissues that remain at the surface and are not cleared away adequately by the surgeon.

<u>Infrared Light Detection</u>

The basis of this technology is the application of near infrared light onto the surface of the urethra/sphincter and prostate. This light potentially allows the surgeon to observe the differences between the two different structures.

This technology borrows its general idea from a technology called Accuvein where NIR light is shined at the arm and the veins stand out in stark contrast. This is because of the differences in the absorbance of the NIR light between the deoxygenated hemoglobin in the blood and the rest of the surrounding tissue.

Another added benefit for this technology is the recent development of NIR dyes that are being applied to the treatment of prostate cancer. These dyes are intended to preferentially stain the cancerous tissue to guide surgery.

If this could be applied to the surgical field then it could potentially overcome the need for a separate boundary identification tool as it could remain in place during the actual cutting.

This technology however also has a large number of unknowns. It would be difficult to test outside of the body because it is difficult to determine exactly what part or property of each tissue causes it to absorb the light preferentially. As a result it is difficult to say whether there is a significant enough difference between the tissues to actually identify the boundary. Finally, this technology would also be very prone to noise from the surrounding tissues like fat or fascia which are cleared away during the surgery.

<u>Ultrasound Elastography</u>

The basis of this technology is the excitation of a tissue with acoustic waves and the detection of the reflected acoustic waves. The idea is that tissues with different stiffnesses will reflect the acoustic waves differently.

- A high frequency probe is used to generate an acoustic radiation force within the tissue, causing local tissue displacements. The probe can switch to an imaging mode to such that these displacements are tracked as they correspond to the dissipation of acoustic energy depending on the mechanical properties.
    - In ARFI, the push region is tracked the tissue reverts to its pre-pushed state
    - In shear wave elastography, shear waves are generated by the acoustic radiation force, propagating outwards from the focal point. The higher the velocity, the greater the shear modulus

This measurement method is able to achieve sub millimeter level resolution and also has a significant body of research backing it up. However, the probe is potentially prohibitively expensive and would need to be significantly modified in order to fit into the laparoscopic surgical method. Also, given that this is a technology that is somewhat beyond our skillset it would be difficult to prototype.

Stiffness Measurement

The basis of this technology is that the relatively elastic urethra/sphincter structure will feel significantly different than the much firmer prostate gland.

- Biological tissues such as the prostate do not behave in a purely linear elastic manner instead they behave in a viscoelastic manner – related to the proportions of viscous and elastic tissue that make up the specific tissue.
- Current prostate elastic theory states that the epithelial tissue predominantly composed of acini (water filled glands) act in a viscous manner whereas the stromal (predominantly elastic smooth muscle) component acts in an elastic manner.
- Applying the current viscoelastic model to other tissues we would expect the bladder and rhabdosphincter (predominantly composed of muscle) to behave more elastically (have lower amplitude ratio (AR), mean ratio (MR)) in comparison to prostatic tissue.

This measurement modality has the inherent appeal of an obvious macroscopic difference between the tissues. There are technologies that exist in this area already although as of yet they have not been able to achieve the resolution that is required for our application. During the surgery the surgeon needs to resect a significant amount of fat and fascia from around the prostate and the urethra and this is an other significant source of potential error in the stiffness measurement.

Internal Pressure Sensing

This method varies widely from all of the previous methods because it focuses around the detection of the boundary from the inside of the urethra rather than outside within the surgical field. It would involve the application of pressure or some kind of force outwards from a probe in the urethra to evaluate the stiffness differences between the two structures.

One benefit of this system is that it would leverage an already significant body of work that has gone into the development of balloon based catheters. These catheters are used in a variety of procedures from electrical stimulation and ablation in the heart to cystography and injection therapy in urologic applications. The idea behind this device would be to place force sensors on the balloon of the catheter which would be selectively inflated and deflated with a controlled volume in order to examine the stiffness of the surrounding tissues. With multiple force sensors we would be able to identify the precise location to cut down to the desired millimeter resolution.