

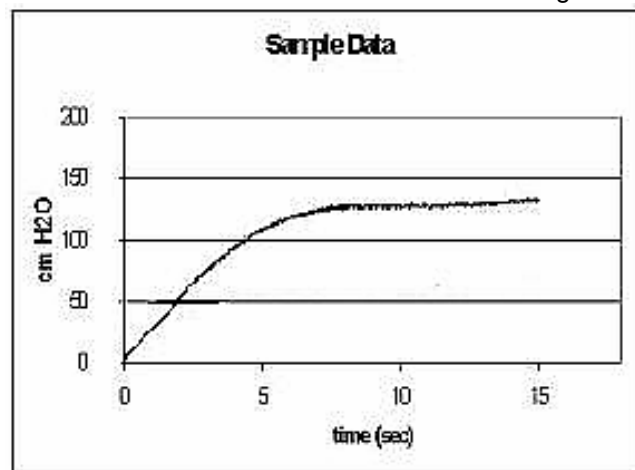
PROOF OF CONCEPT STUDIES OF THE URETHRAL RETRO-RESISTANCE PRESSURE: RESULTS OF PRELIMINARY BENCH, ANIMATE, AND EARLY HUMAN STUDIES USING A MONITORR™ PROTOTYPE

Hypothesis / aims of study

Using bench, animate and human models, the aims of the proof of concept were 1) to establish that the Urethral Retro-resistance Pressure (URP) is a measurement of the pressure required to achieve and maintain an open sphincter 2) to determine whether the device can provide a consistent pressure measurement with an identifiable and interpretable waveform.

Study design, materials and methods

This proof of concept was to be established using the URP measurement in the bench and porcine model and in women with stress urinary incontinence (SUI). A meatal plug was inserted approximately 5 mm into the urethral meatus. The prototype device infused sterile normal saline at a constant flow rate into the urethra against a closed sphincter for a period of 15 seconds. The device displayed the pressure required to open the sphincter. The curve plateau represented the pressure at which the open sphincter is maintained (Figure below). This method (URP) eliminated the need for a urethral catheter thereby avoiding the introduction of a catheter-induced artifact during the measurement.



Bench testing was performed to assess the URP waveform and to evaluate the reproducibility of the URP measurement using an adjustable NIST certified pressure gage (artificial sphincter) to test seven prototype units.

The porcine model was used to 1) examine the URP waveform, 2) compare retrograde and antegrade URP measurements, 3) visualize the opening of the urethral sphincter corresponding with the onset of URP plateau, and 4) evaluate the consistency of the URP measurement. The Yucatan porcine model was examined according to Institutional Animal Care and Use Committee (IACUC) guidelines. Two URP measurements were performed in the standard retrograde fashion. Using a laparoscope, a view was obtained inside the bladder and dye was injected via the meatal plug as the URP measurement was observed. The infusion of dye was filmed as it entered the bladder while simultaneously observing the URP waveform. After careful entry into the bladder, two URP measurements were obtained in an antegrade fashion at the bladder neck.

In women with SUI, we sought to evaluate the within-subject variation of the URP measurement at a single visit, the effect of baseline covariates on the URP measurement, and the overall distribution of the URP measurement within the total study population.

All centres received ethics committee or institutional review board approval. One hundred fifty (150) consenting women with SUI were evaluated at seven centers. After emptying the patient's bladder, at least three URP measurements were obtained on each patient at a single visit.

Results

In bench testing, the mean URP measurement was within 1.24 cm H₂O of the designated pressure gage setting. Additionally, the URP waveform was consistently similar to the graph as shown above. In porcine studies, a direct relationship between fluid entering the bladder and the onset of the URP plateau was confirmed visually on laparoscopy. The mean retrograde URP measurement was 21cmH₂O and the mean antegrade URP measurement was 25 cmH₂O. The within-porcine model standard deviation of (retrograde) URP was 1.79 cmH₂O. In women with SUI, the mean age was 57 years and the mean body mass index (BMI) was 28.4. The URP values were normally distributed. The mean URP was 101 cmH₂O. The mean within-subject standard deviation of URP was 5.45 ± 8.31 . Age and menopausal status had a statistically significant effect on URP ($p < 0.001$ and $p = 0.0019$ respectively).

Interpretation of results

Using a MoniTorr™ prototype, URP was found to be a consistent measurement in the bench, porcine and human models. We were able to visualize via laparoscopy that the opening of the urethral sphincter corresponded with the onset of the URP plateau. Antegrade and retrograde URP measurements in the porcine model were similar. Increasing age and postmenopausal status resulted in lower URP measurements.

Concluding message

The URP measurement was consistent and interpretable in bench, porcine and human models. Although these results are from a MoniTorr prototype, the proof of concept for the URP measurement has been achieved.

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