TOMUS

Urodynamics Testing Procedures for the TOMUS Trial

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I. Overview

Urodynamic studies (UDS) are commonly included in the pre-operative evaluation for women being considered for stress incontinence surgery. However, it is not clear whether the pre-operative utilization of urodynamics data affects surgical outcomes or post-operative management of voiding dysfunction. Justification for this practice varies between clinicians and includes:

1) Selecting the type of surgical procedure,
2) Excluding patients with mixed incontinence and detrusor overactivity from surgery,
3) Enabling surgeon to make intra-operative modifications of the procedure, and
4) Establishment of a baseline assessment of voiding function to better manage post-operative complications.

An important secondary aim of TOMUS is to systematically evaluate the clinical utility of pre-op UDS. Several important hypotheses related to UDS are described in the main TOMUS protocol (See TOMUS protocol Section B, page 8-9). These hypotheses will be tested through the collection and analyses of urodynamics data gathered pre-operatively and at the 12 month post-op study visit. If the patient requires surgical re-treatment for SUI or surgical treatment for voiding dysfunction prior to the 12 month visit, UDS will be conducted prior to the re-treatment surgery in lieu of UDS due at the 12 month post-op visit.

UDS data will be analyzed at study completion to ascertain whether certain UDS variables are predictive of clinical outcomes. UDS data will also be analyzed to evaluate changes in lower urinary tract function secondary to the TOMUS surgical procedures as well as to correlate with patient symptoms of voiding dysfunction, de novo urge symptoms and persistent urinary incontinence. UDS data will not be used for eligibility determination, as the surgeon must be blinded to UDS data. Furthermore, the UDS physician interpreters (NB: not the TOMUS surgeon) will be blinded as to which MUS procedure the patient is randomized to receive. Additionally, post-operative assessment of voiding dysfunction will be completed without use of UDS information. Once the diagnosis and treatment plan have been documented for the post-operative voiding dysfunction, the pre-operative UDS data will be unblinded. Changes in the treatment plan that may be made after review of the pre-operative UDS data will be documented in order to assess clinical utility of pre-operative UDS data in post-operative management decisions.

TOMUS UDS testing procedures (documented herein) are a modified version of the SISTEr UDS procedures. Substantive modifications included:

1) Addition of a urethral pressure profile (UPP) to measure maximum urethral closure pressure (MUCP) and functional urethral length (FUL);
2) Elimination of prolapse reduction maneuvers for patients with Stage III or IV anterior pelvic organ prolapse during filling cystometry; and,
3) Exclusion of EMG.

UDS completed on TOMUS subjects will be conducted for research purposes only as surgeons will be blinded to results of UDS throughout the study unless required for treatment of post-operative voiding dysfunction. Hence, signals for TOMUS subjects should not be placed in the clinical record. Furthermore, the surgeon must not complete his/her own UDS testing. Likewise, s/he must not review or interpret UDS for his/her own surgical study patients. UDS testing will be performed by a certified UDS tester; and signals will be de-identified prior to review and interpretation by a certified physician investigator (other than the surgeon) at the local site.

All women participating in the UITN study will undergo UDS in a standardized manner. The order of administration for UDS should be as follows...

- Non-Instrumented Uroflow (NIF)
- Urethral Pressure Profile (UPP)
- Filling Cystometry (CMG)
- Pressure Flow Study (PFS)

II. Quality Control (QC) Standards

Several QC testing standards have been established by the TOMUS UDS Working Group in an effort to minimize variability of UDS completion and interpretation across sites. Standards documented below are in keeping with several of the recommendations of the ICS Standardisation Committee of Good Urodynamic Practice published by Schafer and others (Schafer et. al. 2002).

A. Certification of Testers

As described, UDS testing must be performed by a clinician certified as a TOMUS UDS tester. Requirements for Tester certification are described below.

A.1. Certification requirements for SISTEr certified testers:

1. Currently registered / licensed to meet state requirements for clinicians completing UDS testing (e.g. MD, RN, NP, PA, other technician categories, etc.);
2. Currently certified as a SISTEr UDS tester;
3. Regularly and frequently performed UDS in the SISTEr trial including NIF, CMG and PFS;
4. Reviewed the final version of the TOMUS Protocol;
5. Reviewed the final version of the TOMUS UDS Testing Procedures;
6. Reviewed the TOMUS UDS testing standards detailed in the UDS QC Observation Checklist;
7. Reviewed the TOMUS UPP DVD;
8. Attended central training or reviewed UPP procedures and QC standards with a colleague that attended central training;
9. Discussed TOMUS UDS procedures and QC standards with a UITN Physician Investigator;
10. In tandem with a UITN physician investigator or certified tester, conducted a minimum of **3** UDS per TOMUS protocol:
11. Demonstrated compliance in the performance of UDS testing per the TOMUS protocol as observed by a UITN PI, Co-PI or authorized designee completing the UDS QC Observation Checklist; and,
12. Submitted an Attestation of Compliance for attainment of TOMUS UDS certification to the BCC.

A.2. Certification requirements for testers not previously certified in a UITN protocol:

1. Currently registered / licensed to meet state requirements for clinicians completing UDS testing (e.g. MD, RN, NP, PA, other technician categories, etc.);
2. Regularly and frequently performs UDS in their clinical practice;
3. Reviewed the final version of the TOMUS Protocol;
4. Reviewed the final version of the TOMUS UDS Testing Procedures;
5. Reviewed the TOMUS UDS testing standards detailed in the UDS QC Observation Checklist;
6. Reviewed the TOMUS MUCP DVD;
7. Attended central training or reviewed UPP procedures and QC standards with a colleague that attended central training;
8. Discussed TOMUS UDS procedures and QC standards with a UITN Physician Investigator;
9. In tandem with a UITN physician investigator or certified tester, conducted a minimum of **3** UDS per TOMUS protocol;

10. Demonstrated compliance in the performance of UDS testing per the TOMUS protocol as observed by a UITN PI, Co-PI or authorized designee completing the UDS QC Observation Checklist; and,
11. Submitted an Attestation of Compliance for attainment of TOMUS UDS certification to the BCC.

NOTE: Performance standards 10 and 11 cannot be completed on UITN subjects.

B. Maintenance of Certification Status through Re-certification

The Steering Committee has established a requirement for **annual** re-certification for most staff categories to prevent/minimize drift and maintain consistency across CTCs. UDS Testers must complete re-certification procedures annually.

C. Equipment and Supplies

All CTC use Laborie testing equipment and testing equipment are registered with the BCC. Flow and pressure transducer equipment must be checked every three months against calibration standards per manufacturer's equipment specifications. Calibrations must be completed when measures fall outside of the standards. Sites must keep a written log of the calibration checks completed including date performed and signature of the person completing the calibration check.

D Source Documentation Protections

Sites must develop and maintain, fail safe back–up procedures for the UDS electronic data to guard against loss or corruption of electronic UDS signals.

The electronic signals are considered the primary source document for the TOMUS UDS. Maintaining a "back up" copy of the UDS in electronic format protects the UDS research data in the event of inadvertent deletions, and/ or failure or corruption of the clinical UDS workstation.

Sites must make a copy of the patient's electronic UDS signals from the UDS clinical workstation and move the copy to a second restricted access study hard drive. Sites commonly store their copies on the UITN Data Manager's hard drive or on a shared project drive on an institutional network.

As a rule, site use a floppy disk or USB memory stick to move the signals from one hard drive to the other. Once the study has been transferred to the 'back up" location, the study can be deleted from the floppy or memory stick. These procedures are described in detail in the "Electronic UDS Signals Transfer Procedures".

Sites must submit a written description of their local back up procedure to the BCC and a BCC Monitor will review the electronic UDS back up folder at the time of the annual QC Site Visits.

E Central Repository

A UITN UDS central repository of electronic signals has been established at the Biostatistical Coordinating Center (BCC) for the purposes of QC central review (10% random re-review) and for secondary, tertiary, or ancillary studies that may be planned at a future date. Continence Treatment Centers (CTCs) must send an electronic copy of the signals to the UITN UDS central repository at the BCC on a routine basis. Electronic transfer procedures are described in the "Electronic UDS Signals Transfer Procedures".

F Procedures for Blinding Surgeons from UDS Data

To achieve TOMUS research aims, surgeons must be blinded from UDS test results. As such, the patient's TOMUS surgeon must not complete UDS testing, or review or interpret the patient's UDS signals. In addition, UDS signals must be methodically **de-identified** to maintain surgeons' blinding. A hard copy of the de-identified signals may be maintained in the patient's **research** file but hard copies of the signals must NOT be placed in the patient's medical

record. Sites must maintain the primary source document in electronic format on the local TOMUS project drive. De-identification procedures are described elsewhere.

UDS signals for TOMUS subjects MUST NOT be placed in the patient's clinical record.

G Standards for Signals (AKA: tracings, graphs, recorder output)

1. **Graph scaling**: In keeping with recommendation of the ICS Standardisation Committee of Good Urodynamic Practice (Schafer, et. al. 2002), the scaling of the signals will be standardized across centers. Urodynamic quality control is dependent on the Tester's ability to recognize patterns, and the recognition of patterns is improved by standard scaling of the signals:

   a) Graph scaling for the NIF signals is standardized as follows:

   One millimeter will equal 1 s on the x-axis for both Flow and Volume; and on the y-axis, 1mm will equal 1ml/s for Flow and 1 mm will equal 10 ml for Volume.

   b) Graph scaling for the UPP signal is standardized as follows:

   One millimeter equals one second on the x-axis.

   c) Graph scaling for the CMG and PFS signal is standardized as follows:

   *A minimum scaling for pressures will be set at **50**cm H_2O per cm; **25**ml/s per cm for Flow; and **1**min per **3**cm for the time axis.*

   d) For all study signals, the scales for the **x-axis** and the **y-axis** must be clearly indicated.

2. **Channel Order** for signal configurations is standardized as follows:

   a) NIF: Flow on the top followed by volume.

   b) UPP: pura on the top followed by pves then pclo.

   c) CMG and PFS: Flow on top followed by volume, pves, pabd, pdet and VH_2O last.

3. **Annotation**: UDS signals must be annotated in accordance with required annotations listed on Attachment B.

H. Interpretation of the UDS and completing the UITN Data Form

A UITN Physician Investigator certified as a TOMUS UDS Reviewer, will complete the review and interpretation of the signals and complete the TOMUS data form (F305). As previously described, surgeon must remain blinded from their TOMUS patient's UDS test results. Therefore, surgeons must not conduct UDS testing or review or interpret UDS signals for their own TOMUS patients. Circumstances to the contrary must be reported as protocol violations.

I Repeating Tests

Testers should examine signals prior to removal of the catheters to determine if any study must be repeated. Repeat testing is warranted in the following circumstances:

- Repeat the NIF if the voided volume is <150mL. The patient can either be mechanically filled or one can wait for spontaneous filling. As long as the repeated NIF is performed with the patient uncatheterized and with a full or near full bladder volume, prior instrumentation should have no effect on the results of this free flow study.
- The PFS should be repeated if catheters fall out or if there is evidence that the catheters were not functioning properly during the voiding phase.

  Repeat testing with prolapse reduction will not be performed for patients with Stage III or IV prolapse.

II. Urodynamics Testing Procedures

A. Overview

Patients should be instructed to arrive for the UDS testing with a full bladder in preparation for non-instrumented uroflowmetry (NIF) followed by catheterization for a post-void residual (PVR) and a dipstick urinalysis of the catheterized specimen. If the dipstick urinalysis is within normal limits, urethral pressure profile measurements (UPP) will be performed followed by filling cystometry (CMG) and a pressure flow study (PFS).

B. Non-Instrumented Uroflowmetry (NIF)

B.1 Instruments and Materials

- UITN registered Laborie uroflowmeter, recorder and printer
- TOMUS UDS Worksheet (optional)

B.2. Procedure

Every reasonable effort should be made to conduct the NIF with a full or near full bladder. Patients should be strongly encouraged to drink a sufficient amount of fluid prior to the start of testing to minimize the need to repeat the NIF.

1. The scale should be set to zero prior to the start of each patient's study.

2. With a full bladder before any instrumentation, the patient will void into the uroflowmeter while in a sitting position. The patient should be provided ample privacy for the void.

3. Record the time-flow curve using the Laborie urodynamic recorder. Parameters to be measured include maximum flow rate, mean flow rate, time to maximum flow and voided volume.

4. After the void, catheterize the patient and measure the PVR. The catheter type and size used to perform this PVR can be determined by each individual CTC.

5. An immediate dipstick urinalysis should be performed on the catheterized specimen. If suggestive of infection, the instrumented study should be deferred until after successful treatment of the infection.

If the voided volume (VV) is <150 ml, a non-instrumented uroflow should be repeated at another time, e.g. at the end of the PFS after a mechanical refill.

B.4 Data Points for the NIF

The following data points must be recorded for the NIF:

- Qmax = Maximum flow rate (ml/sec)
- Qmean = Mean flow rate (ml/sec)
- Time to maximum flow (sec)

- Voided volume (ml)
- Post void residual (PVR)
- Flow pattern using ICS definitions (continuous, smooth; continuous, fluctuating; intermittent)

C. Urethral Pressure Profile

A major change in the UDS protocol for TOMUS is the addition of a static urethral pressure profile to obtain maximum urethral closure pressure (MUCP) measurements and Functional Urethral Length (FUL). The set-up and testing procedures are listed below in sequential order.

NOTE: in the event that there is any vaginal prolapse at or past 0 cm during the UPP portion of the study,

a) The prolapse should be manually reduced to its normal anatomic position (without the aid of any intravaginal foreign bodies) and UPP testing should be attempted. Since patient will be in supine position, it is unlikely the prolapse will recur.
b) If the prolapse does recur after manual reduction, even while in the supine position, the UDS tester may reduce the prolapse again with whatever measure customarily used. Careful attention must be paid to ensure that the reduction device is not adjacent to the urethra.

C.1 Instruments and Materials

- 7Fr Laborie triple lumen water perfusion catheter
- UPP puller
- IV bag of normal saline or sterile water (1000mL)
- Infusion cuff
- non vented administration set
- pressure tubing
- appropriate caps
- external pressure transducers

C.2. UPP Set-Up Procedures:

1. Put the IV bag inside the infusion cuff and slip the hanger cord through the IV bag hanger hole so the weight of the bag is supported by the cuff. Hang the cuff with the bag inside it.

2. Using the non vented administration set, close the roller clamp and spike the bag.
   Inflate the cuff to 200-250 mm Hg, and then close the stopcock to the cuff to maintain pressure. Check the pressure periodically to maintain pressure between 200- 250 mm Hg.

3. Connect the male LL coming from the administration set to the female end of the uniflow flush device (30 ml/hour) and close the adjacent capped male LL with a pressure- withstanding LL plug. <u>The cap that is on the device will not hold pressure.</u>

4. Connect the flow restrictor portion of the uniflow flush device to the female LL underside of the Nova Dome.

5. Connect the pressure tubing to the upper male LL side of the Nova Dome and attach this tubing to the catheter.

   NOTE: The fluid path enters the Nova Dome from the bottom to allow the infused water to flush all the air from the transducer. This looks "backwards" from the other two Nova Domes.

6. The entire pura system can be flushed by opening the rollerball (near the infusion bag) and squeezing together the yellow arms of the flow restrictor. If necessary, this should be done before the catheter is

inserted. When properly functioning, there should be a slow drip from the end of the tubing or the urethral hole in the catheter (if attached to the catheter).

C.3. UPP Testing Procedure

1. After the NIF, position the patient on the exam table, UDS chair, or birthing chair, in the supine or supine lithotomy position with her head elevated slightly for comfort. The urethra should be approximately parallel to the floor.

2. Insert the 7Fr. triple lumen catheter so that both pressure apertures are **in** the bladder.
    a. Cap the infusion port on the catheter to prevent leakage of fluid.
    b. Attach the pves pressure tubing to the pves port of the catheter.
    c. Attach the pura pressure tubing to the pura port of the catheter.

3. Position the urodynamic puller securely near the urethral meatus and attach the catheter to the puller.

4. Ensure that the roller ball is open near the infusion bag. There should be a slow dripping from the chamber.

5. Open the measuring systems so that both pura and pves are measuring the pressure in the bladder. Ensure that the catheter is sufficiently inserted so that both the vesical aperture and the urethral aperture are **in** the bladder. (The catheter should be inserted at least 10 cm from the distal end). Have the patient cough and Valsalva with the UPP test running and look for concordant signals in both pura and pves signals. Troubleshoot, flush either or both lines, if signals are not concordant. Fluid can be added to the bladder thru the pura tubing, the pves tubing, or the infusion port with a syringe attached temporarily. Add fluid through the pressure lines or fluid line as needed.

6. Once both signals demonstrate proper functioning in the bladder, **zero both pressure systems in the bladder simultaneously.**

    NOTE: This is different than the CMG/PFS protocol. The outcome measure for UPP is a subtracted measure that is dependent on both pressure systems starting at equal values. CMG /PFS studies will still be zeroed to atmosphere.

7. Complete three withdrawals at a puller speed of 1 mm/sec with urethral aperture directed laterally. Stop the puller prior to complete withdrawal of the catheter from the bladder. The puller should be stopped and then reversed as soon as the urethral aperture is seen at the urethral meatus. At this point, the urethral pressure is often recording a negative value since the systems were zeroed in the bladder.

    NOTE: pura may become negative at this point.

8. Reverse the puller until both apertures are back in the bladder. **The two pressure measurements should be within 3 cm H_20 equivalence. If not, re-zero both pressure systems in the bladder before the next withdrawal.** Have the patient cough before the start of every UPP pull to document agreement in the pressure measuring systems. Troubleshoot, flush either or both lines, if signals are not concordant

9. At the end of the third pull, reverse the puller so that the catheter is well within the bladder, disconnect the catheter from the puller, and securely tape the catheter to the perineum and leg in preparation for the filling CMG. Disconnect the urethral pressure tubing from the catheter and cap the pura port. Close the roller ball near the infusion bag to prevent continued leaking from the pura tubing.

10. Introduce a short 10-14 French female catheter alongside the 7Fr triple lumen catheter to empty the bladder before the start of filling cystometry.

11. Review the UPP signal and determine if the "UPP start" and/or "UPP stop" annotations are correctly placed. Move annotations as necessary. To obtain an accurate calculated FUL measurement the "UPP start" annotation should be placed at the start (inflection point) of the pclo signal as soon as the signal starts to increase above baseline. The "UPP stop" annotation should be placed at the end of the signal when the pressure is decreasing and pclosure = pclosure at UPP start.

    Do not move "UPP pull start" and/or "UPP pull stop" annotations.

C.4 Data Points for the UPP

Three separate maximum urethral closing pressure (MUCP) measurements and functional urethral length (FUL) measurements will be recorded on the UPP event summary:

- **MUCP** =. MUCP is measured as centimeters of water (i.e. cmH_2O) and is labeled "Peak Pclo" on the UPP summary.
- **FUL** is the length of the urethra measured in millimeter (mm) along which urethral pressure exceeds bladder pressure. It is labeled "length" on the UPP summary. FUL **is not** the "length of the continence zone" on the UPP summary.

D. Filling Cystometrogram (CMG)

D.1 Instruments and Materials

- The registered UITN multi-channel urodynamics recorder
- External pressure transducers
- Fluid-filled column type urodynamics tubing
- 7French triple lumen transurethral catheter
- A standard manufactured rectal balloon catheter

A fluid column-type urodynamics catheter is required by protocol, no other types of electronic or light sensing catheters are allowed. The urodynamics catheter used for UPP, CMG and PFS must be triple lumen, 7French catheter to satisfy the UPP testing requirements.

Intravesical pressure (pves), intra-abdominal pressure (pabd), and subtracted detrusor pressure (pdet) should be continuously recorded on a multichannel urodynamics recorder throughout the conduct of the CMG. Flow rate and volume should also be continuously recorded.

D.2 Procedure

1. The triple lumen 7French catheter placed intravesically for the UPP study will remain in place to monitor bladder pressure during the filling CMG.

2. With the patient still in the supine position, place the rectal balloon catheter in the rectum and securely tape the catheter to the perineum and leg. One of the standard manufactured rectal balloon catheters should be used.

3. When both catheters are placed and securely taped, assist the patient to a freestanding, weight bearing position.

4. Position the patient to permit direct observation of the urethral meatus during Valsalva maneuvers. If necessary, the patient may be positioned with one foot on a footstool to permit direct observation of the urethral meatus. If a footstool is used, be certain the patient is safe and weight bearing on both feet and that the external transducers remain positioned at the upper level of the symphysis pubis.

5. Position the external transducers at the upper level of the symphysis pubis.

6. Simultaneously zero the pves and pabd catheters to atmospheric pressure by opening stopcocks.

7. Instruct the patient to cough to assess proper placement of the catheters and to document the dynamic response of the pressure channels.

   NOTE: The pves and pabd signals should demonstrate symmetric cough transmission and pdet should be between 0 and 5 cm/H_2O at this time. If pdet is a negative number or >5 cm/H_2O, perform trouble shooting measures, e.g. check for air bubbles, re-evaluate the position of the catheters, flush the catheters, re-zero to atmosphere, etc. Excessive rectal balloon filling may cause abnormally high Pabd readings and the balloon volume may need to be adjusted. Filling should not commence until pabd and pves pressure signals document the dynamic response of the pressure channels and the pdet is between 0 and 5 cm/H_2O. (Both the CMG and PFS will be considered implausible if pdet is outside a -5 to +10 cm/H_2O range at CMG baseline.)

8. Document the baseline with an annotation on the signal.

9. Fill the bladder with room temperature saline or sterile water at a rate of 50 mL/min.

10. At a bladder volume of 100 mL, instruct the patient to cough and reassess proper placement and function of the catheters and transducers (**annotate this cough on the signal**). Look for the dynamic response of the pressure channels. If pressures channels do not track at this time, repeat troubleshooting measures.

11. Bladder Sensation Parameters: Three bladder sensation parameters must be measured during the CMG. The patient should be instructed to report when she has the sensation of 1) first desire to void, 2) strong desire to void, and 3) a sensation of maximum cystometric capacity, using the following standardized definitions/descriptions.

    First Desire to Void: When filling commences, instruct the patient that you need to know when she has a *first desire to void.* This is defined as "the feeling, during filling, that would lead the patient to pass urine at the next convenient moment, but voiding can be delayed if necessary". Tell the patient:

    "*If you are watching TV, tell me when you would go to the bathroom at the next commercial*."

    Strong Desire to Void: After this milestone is reached, instruct the patient that you need to know when she has a s*trong desire to void.* This is defined as "a persistent desire to void without the fear of leakage." Tell the patient:

    "*Tell me when you can't wait for the next commercial."*

    Maximum Cystometric Capacity: After this milestone is reached, proceed to *maximum cystometric capacity (MCC)* which is defined as "the volume at which the patient feels she can no longer delay micturition". Tell the patient:

    "*I need to know how much your bladder can hold. Let me know when you can't take any more in your bladder."*

12. Obtain Three Valsalva Leak Point Pressure (VLPP) measurements

    a) IMPORTANT NOTES:

    - Three VLPP values will be obtained to ensure test precision and evaluate reproducibility. (A mean value for VLPP will be calculated in analyses at the BCC.) In the event that leakage cannot be reproduced with three Valsalva maneuvers, despite careful coaching, two VLPP values will be accepted.
    - To accurately determine VLPP, Testers must directly observe the urethral meatus for urine leakage coincidental with Valsalva maneuvers.
    - A slow Valsalva maneuver is best for accurate VLPP measurements. To coach the patient to perform Valsalva maneuvers correctly, instruct her to bear down slowly, incrementally increasing her effort until leakage occurs or the maximum amount of straining is reached.
    - Tell the patient that you will say, "Stop pushing," as soon as you observe urine leakage and teach her to relax the instant she hears your instruction.
    - Testers may employ various strategies to permit direct observation for urine leakage while simultaneously annotating the signals including.

      i) Proper patient positioning including use of a footstool as described in D.2.4 above.

      ii) Patient coaching: Patient teaching should be completed prior to the start of testing. If the patient is able to complete Valsalva maneuvers properly and relax when she hears the Tester's instruction to, "Stop pushing", the annotation for the VLPP can be marked at the maximum point of the Valsalva spike on the signals.

      iii) Two-person exam: An assistant may annotate the signals on the directive of the primary Tester as s/he completes the observation.

iv) Use of a remote keypad device: A remote keypad device may be used to allow the Tester to annotate the signals when she observes leakage from a location distant from the computer keyboard.

b) LPP Testing Procedures

- **S**top the infusion at **200 mL** and perform Valsalva maneuvers as described above. If leakage is observed, repeat Valsalva maneuvers two more times to obtain 3 VLPPs at the 200 mL volume, record/annotate the VLPP measures on the signals. Resume infusion to determine MCC.
- If leakage is not observed at the 200 mL volume, resume infusion and repeat Valsalva maneuvers at each 100 ml increment until leakage is observed or MCC is reached. When leakage is observed, determine the VLPP values per the procedures described above, and then resume infusion to MCC.
- If the patient reaches MCC without demonstrating leakage with Valsalva at or prior to MCC, instruct her to cough maximally and observe for urine leakage. Record the presence or absence of urodynamic stress incontinence at MCC, and then proceed to the PFS.
- Regardless of the volume at which the patient leaks, the bladder volume at first desire to void, strong desire to void, and MCC must be measured and annotated on the signals.
- The **Pves** and **Pabd at MCC** should also be annotated on the signals.
- All critical data points should be annotated on the signals.
- If micturition occurs or a large volume (>100ml) of fluid is otherwise lost during the performance of the CMG, the test should be re-started after completely emptying the bladder to ensure accurate bladder volumes.

D4. Procedures for patients with anterior prolapse Stage III or IV

CMG testing will performed without reduction on all patients in the TOMUS trial. CMG testing should not be repeated with reduction for patients with Stage III or IV anterior prolapse.

D.5 CMG Data Points

The following data points must be recorded or calculated for the CMG:

- Pves at CMG baseline (cm/H_2O)
- Pabd at CMG baseline (cm/H_2O)
- Bladder volume at first desire to void (ml)
- Bladder volume at strong desire to void (ml)
- Bladder volume at which VLPPs obtained (ml)
- VLPP measurements [Three measures preferred, two are required.]
  [NOTE: The VLPP measure is the absolute pressure above zero atmospheric
- Bladder volume at MCC (ml)
- Pves at MCC (cm/H_2O)
- Pabd at MCC (cm/H_2O)
- Urodynamic stress incontinence (yes /no)
- Detrusor overactivity (yes or no)
  - Volume at each occurrence (ml)
  - Detrusor overactivity incontinence (yes or no)
- Bladder compliance
  [MCC/ (Pves at MCC - Pves at baseline)]
- Mean of VLPP values
  [Mean Pves = (Pves 1 + Pves 2 + Pves 3) / 3] or [mean Pves = (Pves 1 + Pves 2) / 2]

E. Pressure Flow Study (PFS)

IMPORTANT NOTES:

- The PFS should be completed at MCC. If for any reason the bladder must be re-filled to complete the PFS, re-fill the patient to her MCC or a volume equivalent to a full or near full bladder volume.
- Patients must sit to void for the PFS. If the patient remains standing for any reason, annotate this on the signals and report it as required as a protocol deviation.
- Testers should review signals closely at the start of the PFS for plausibility and validity. Look for:
  a. Properly functioning pves and pabd signals;
  b. pdet > -5 and within 15 cm of the pdet value at MCC, i.e. it should be nearly the same as the pdet value at MCC; and
  c. Pves and pabd signals which are 70% concordant for the prevoid cough.

Troubleshoot the system if these conditions aren't met This includes but is not limited to adjustment of catheter positions, flushing the lines and checking for line occlusions **If these measures fail to resolve problem, re-zeroing to atmosphere before the void is acceptable and recommended**. Annotate the re-zeroing on the signals.

E.1 Procedures

1. Instruct the patient to sit on the urochair.

Before the void:

2. Reposition the external transducers to the upper level of the symphysis pubis.

3. Instruct the patient to cough to reassess proper placement and functioning of the catheters.
   - Look for the dynamic response of the pressure channels. Trouble-shoot as necessary.
   - Annotate the position change, the transducer adjustment and the cough on the signals.

4. Establish a clear PFS baseline: Establishment of stable baseline pressures (for approximately 10 seconds) prior to the start of the void is critical to reliable interpretation of the PFS.
   - Tell the patient not to void until instructed to do so.
   - Annotate the PFS baseline on the signals.

5. Instruct the patient to void. The patient may use her own personal method of reducing her pelvic organ prolapse in order to void.

After the void:

6. At the end of the void, instruct the patient to cough to confirm that catheters were in place throughout the voiding phase.
   - Annotate the post-void cough on the signals.

   NOTE: Data will not be recorded on the TOMUS data form without evidence on the signal that catheters were in place and functioning at Qmax.

7. Prior to removal of the catheters, determine if any study should be repeated. Repeat testing is warranted in the following circumstances:
   - Repeat the NIF if the voided volume was <150mL

- Repeat the PFS if catheters fell out during the void or if there is evidence that the catheters were not functioning properly during the voiding phase.

8. If either the NIF or the PFS must be repeated, re-fill the patient to her MCC or a volume equivalent to a full or near full bladder volume. Ideally, there will be <100ml difference between the bladder volumes at which the valid NIF and PFS are performed.

E.2 Data Points

The following data points will be captured for the PFS:

- Cough maneuver at the start of the study (yes / no)
- Maximum flow rate (ml/sec)
- Pves at PFS baseline (cm/H_2O)
- Pabd at PFS baseline(cm/H_2O)
- Pdet at PFS baseline (cm/H_2O)
- Pves at maximum flow (cm/H_2O)
- Pabd at maximum flow (cm/H_2O)
- Pdet at maximum flow (cm/H_2O)
- Time to maximum flow (sec)
- Voided volume (ml)
- Voiding mechanism (detrusor, abdominal, mixed, other)
- Cough maneuver at the end of the study (yes / no)
- Calculated PVR determined after Pressure Flow Study (ml)

Appendix A: TOMUS UDS Worksheet

UDS WORKSHEET FOR TOMUS

TOMUS PATIENT ID #:_____	
UDS TESTER ID: _____	DATE TESTS COMPLTETED:_____/_____/_____

NIF NIF EQUIPMENT ID#: __ __ __ / __ __ __ __		
QMAX: _____ mL/sec	QMEAN: _____mL/sec	TIME TO MAX FLOW: _____ sec
VOIDED VOLUME: _____mL	PVR: _____ mL	UA: WBC -- +
FLOW PATTERN: CONTINUOUS, SMOOTH	CONTINUOUS, FLUCTUATING	INTERMITTENT

NOTES:

MUCP	MUCP	FUL
1st pull	_____cm/H_2O	_____mm
2nd pull	_____cm/H_2O	_____mm
3rd pull	_____cm/H_2O	_____mm

NOTES:

CYSTOMETROGRAM (CMG)	TRIAL 1	TRIAL 2 (if necessary)
CMG EQUIPMENT ID#:	__ __ __ / __ __ __ __	__ __ __ / __ __ __ __
POSITION:	STANDING OTHER*	STANDING OTHER *
CATHETER DIAMETER:	_____Fr	_____Fr
P ves @ BASELINE:	_____cm/H_2O	_____cm/H_2O
P abd @ BASELINE:	_____cm/H_2O	_____cm/H_2O
FILL RATE:	_____ mL / min	_____ mL / min
STAGE III or IV PROLAPSE?	YES NO	
BLADDER VOLUMES		
1ST DESIRE:	_____ mL	_____ mL
STRONG DESIRE:	_____ mL	_____ mL

CMG continued	TRIAL 1			TRIAL 2 (if necessary)		
LEAK with VALSALVA	Valsalva 1	Valsalva 2	Valsalva 3	Valsalva 1	Valsalva 2	Valsalva 3
VLPP / Pves @ 200 mL						
VLPP / Pves @ 300 mL						
VLPP / Pves @ _____ mL						
BLADDER VOLUME @ MCC	_____ mL			_____ mL		
LEAK W / COUGH @ MCC?	YES NO N/A			YES NO N/A		
P ves @ MCC:	_____ cm/H_2O			_____ cm/H_2O		
P abd @ MCC:	_____ cm/H_2O			_____ cm/H_2O		

DETRUSOR OVERACTIVITY?	YES NO		YES NO	
	IF YES….		IF YES….	
	AT WHAT VOLUME?	LEAK?	AT WHAT VOLUME?	LEAK?
	1. VOLUME: _____ mL	YES NO	1. VOLUME: _____ mL	YES NO
	2. VOLUME: _____ mL	YES NO	2. VOLUME: _____ mL	YES NO
	3. VOLUME: _____ mL	YES NO	3. VOLUME: _____ mL	YES NO

NOTES: _____

_____

PRESSURE FLOW STUDY (PFS)	VOID 1	VOID 2 (REPEAT IF NEEDED)
PFS EQUIPMENT ID#:	PFS ID#: __ __ __ / __ __ __ __	PFS ID#: __ __ __ / __ __ __ __
SITTING PRE VOID COUGH?	YES NO	YES NO
Q MAX (MAX FLOW RATE):	_____ mL/sec	_____ mL/sec
Pves @ QMAX:	_____ cm/H_2O	_____ cm/H_2O
Pabd @ QMAX:	_____ cm/H_2O	_____ cm/H_2O
Pdet @ QMAX:	_____ cm/H_2O	_____ cm/H_2O
TIME TO MAX FLOW:	_____ sec	_____ sec
VOLUME VOIDED:	_____ mL	_____ mL
POST VOID COUGH:	YES NO	YES NO
PVR:	_____ ml	_____ ml

NOTES: _____

_____

Appendix B: Standard Annotations for UDS

Non-Instrumented Uroflowmetry (NIF):

- Uroflow Voiding Start
- Max. Flow
- Uroflow Voiding Stop
- Artifact

Urethral Pressure Profile (UPP)

- MUCP (peak marked automatically)
- UPP start
- UPP stop

Cystometrogram (CMG):

- Patient Standing
- CMG Baseline (Pves & Pabd at baseline)
- CMG Start (start of infusion)
- Cough at 100 ml
- First Desire
- Strong Desire
- Prolapse Reduced (if applicable)
- Valsalva No Leak
- Valsalva Leak (VLPP)
- MCC (Pves, Pabd, & volume)
- Cough at MCC-Leak
- Cough at MCC-No Leak
- Detrusor Overactivity-Leak
- Detrusor Overactivity-No Leak
- CMG Stop (stop of infusion)

Pressure Flow Study (PFS):

- Change to Sitting Position (position change)
- Patient Standing
- Transducers adjusted
- Pre-void Cough
- PFS baseline
- PFS Voiding Start
- Max Flow (Pves, Pabd, & Pdet)
- PFS Voiding Stop
- Post-void Cough

Misc. Terms:

- Unable to Void
- Pves Cath. Fell Out
- Pabd Cath. Fell Out
- Bladder Refilled
- Void
- Artifact
- Laughing
- Cough
- Pves Cath. Flushed
- Pabd Cath. Flushed
- Pves Cath. Adjusted
- Pabd Cath. Adjusted