Comparison of air-charged and water-filled catheters for use in cystometric assessment

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Meinen lieben Eltern und Großeltern

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Abbreviations

AFC	air-filled catheter
ACC	air-charged catheter
BOO	bladder outlet obstruction
CMG	cystometrogram
CRF	Clinical Review Form
CLPP	cough leak point pressure
DO	detrusor overactivity
ICS	International Continence Society
LOA	limits of agreement
MCC	maximum cystometric capacity
MUCP	maximum urethral closure pressure
Pves	vesical pressure
Pabd	abdominal pressure
Pabd-ACC	abdominal pressure measured by air-charged catheter
Pabd-WFC	abdominal pressure measured by water-filled catheter
Pdet	detrusor pressure
Pves-ACC	vesical pressure measured by air-charged catheter
Pves-WFC	vesical pressure measured by water-filled catheter
PVR	post-void residual
Qmax	maximum voiding flow
SD	standard deviation
UDS	urodynamics
VLPP	Valsalva leak point pressure
WFC	water-filled catheter

1. Introduction

1.1 What is urodynamics?

The definition of the term “urodynamics” (UDS) goes back to the mid-20th century when David Davis used it in presenting work on upper tract pressure and renal injury (Davis, 1954). In the early 60s, G. Enhorning was the first person using simultaneous bladder and rectal pressure measurement during filling and micturition (Enhorning, 1961).

Before introducing the urodynamic study into clinical practice, urologists made their diagnosis mainly based on symptoms and anatomic findings such as a) prostate enlargement, b) degree of a vaginal prolapse and c) bladder trabeculation. They were all demonstrated radiologically or cystoscopically. Understanding the function of the lower urinary tract as the underlying cause of bladder dysfunction drove leading clinicians to develop urodynamic investigations of bladder dysfunction. That was when the term of “functional urology” evolved. The urodynamic study was and is still the only way of objectively assessing the function of the lower urinary tract (Nitti, 2011). Its primary goal is to evaluate the function of the lower urinary tract, detecting and quantifying potential dysfunctions through simulating natural storage and voiding of urine (Almallah, 2000). Generally, the urodynamic study consists of different forms of assessments: uroflowmetry, cystometry, pressure/flow measurement and urethral pressure profile. Uroflowmetry is a fundamental test and an objective way of “observing” the act of micturition (Brown, 2013). Meanwhile, cystometry and pressure/flow measurement are well established methods of objectively assessing the function of bladder and bladder outlet. Basically, cystometry can be divided into two phases-filling phase and voiding phase. During filling phase, bladder sensations are normally recorded. The first sensation of bladder filling, first desire to void, strong desire to void, and any other events like detrusor overactivity (DO) and cough leak point pressure (CLPP) are also assessed (Figure 1). During voiding phase, the function of detrusor and urethra are assessed, especially in the diagnosis of bladder outlet obstruction (BOO), which is the golden standard for the surgery in men. Some nomograms have already been developed, for instance the ICS nomogram and the Schaefer nomogram, to quantify BOO. Particularly, the Schaefer nomogram divided the BOO into seven grades, and six grades for the assessment of detrusor

contractility during voiding.

For decades, videourodynamics has also played an important role in clinical practice, especially in patients with neurogenic diseases. The technique of obtaining fluoroscopic imaging during multichannel UDS was popularized in the United States by Tanagho (Tanagho, 1966) and in Europe by Turner-Warwick (Bates, 1970). Over the years, the value of adding functional and anatomical pictures to multichannel urodynamic studies has been described in various publications (Nitti, 1999; Webster, 1980; Mayo, 1979; Kuo, 2005).

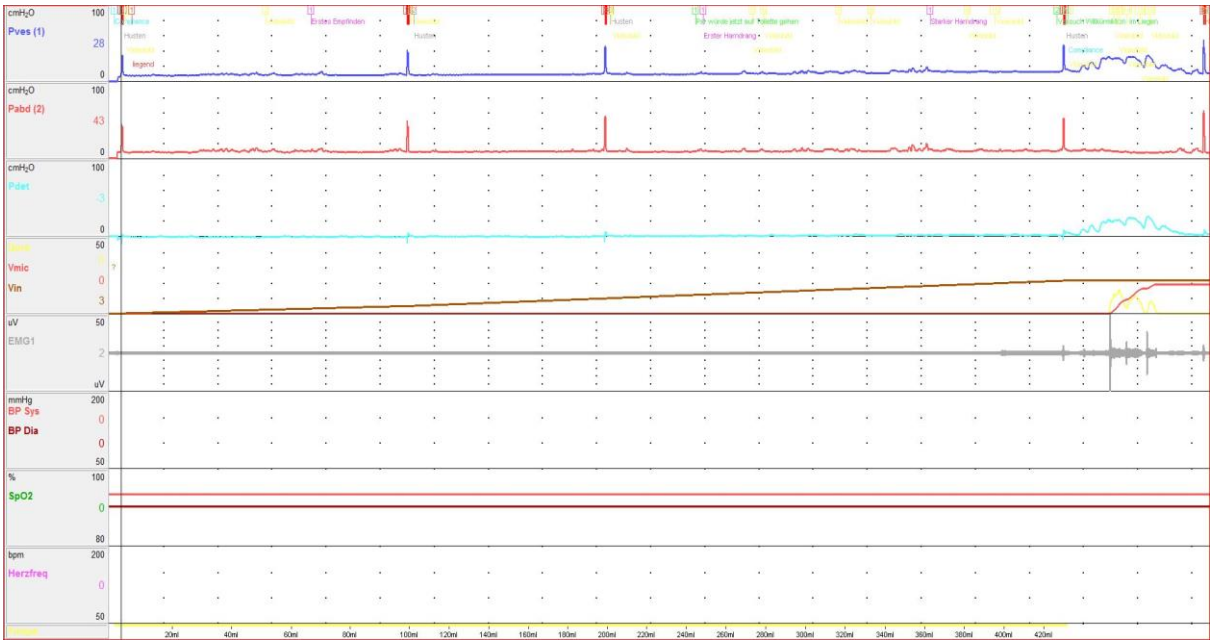

Fig.1: An example of normal cystometrogram. During filling phase, bladder sensations are recorded – first sensation of bladder filling, first desire to void, strong desire to void. Coughs are used to check quality of measurement.

1.2 Currently used catheter models

There are three main forms of catheters available on the market. These are water-filled catheter (WFC; Figure 2, 3), which is recommended by the ICS, air-filled catheter (AFC; Figure 4, 5) and microtip catheter (Figure 6).

a) Water-filled catheter

In clinical practice, UDS performed with WFC is called gold standard at present. This technique has been recommended by ICS for their use since 2002 (Schafer, 2002). During the examination, pressure is being transmitted through a column of water in

the tube to the external transducer (Valentini, 2013; Duckett, 2013; Zehnder, 2008). In preparation of the measurement, the transducer is leveled to the height of the upper rim of the symphysis pubis. With a continuous water column in the lumen of the catheter, the pressure at the transducer is the same as in the body at transducer level, regardless of the location of the catheter tip. However, if the patient changes his/her position, e.g. from lying to sitting position, the transducer should be moved vertically in order to keep the transducer and the upper rim of symphysis pubis at the same level. As this is the most mature technology, all advices of how to perform UDS are made based on the WFC system. However, the complexity of set-up of the examination is relevant and still prone to producing artefacts easily. In addition, intense training of involved staff is necessary. Consequently, new technologies are still needed.

Fig. 2: Water-filled cystometry / pressure flow catheter (Picture from Laborie).

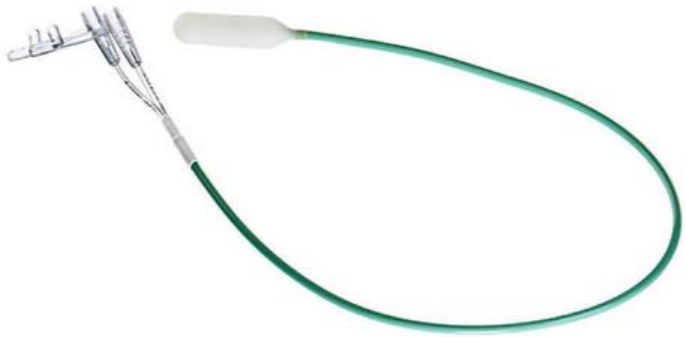

Fig. 3: Water-filled abdominal pressure catheter (Picture from Laborie).

b) Air-filled catheter

The air-filled catheter (AFC) was first introduced by Douglas James in the UK in 1970s (Abrams, 2017). However, this technology was scarcely used in urodynamic clinics in recent decades. This was also true after the T-Doc system was introduced in 1998, with a US patent (6 447 462) granted in 2000. In 2002, the Good Urodynamic Practices report was issued, which was developed based on the WFC measurement system, and has become a guideline for the urodynamic test for a dozen years. Since then, the WFC system has been regarded a golden standard in urodynamic measurement. On the contrary, few studies were performed for the testing of AFCs, no matter *in vitro* or *in vivo.* To the best of our knowledge, no such a guideline was ever published for AFCs. This made the situation of application of AFCs in daily clinical practice even worse despite having some advantages compared with WFCs. However, with increasing studies published in recent years related to AFCs, the focus turns back to it again. Although tested with a very low number of catheters, AFCs yielded highly repeatable results (R=0.9999) *in vitro* (Awada, 2015). In a recent performance study of AFCs, the results obtained by AFCs exhibited strong linearity and low hysteresis. In the frequency response test, the study also showed that AFCs were capable of recording fast urodynamic events such as coughs (Bruna, 2017). Based on these two *in vitro* studies, it suggests that the AFC is a reliable device and could meet the technical requirements for routine urodynamic examinations.

The AFC measurement system is relatively similar to the one with WFCs, which both have an external transducer. The most prominent difference is that the transmitting medium is air, not water. The hydrostatic pressure difference between the catheter tip and the transducer is negligible, because the weight of a column of air is negligible. As in a water-filled system, pressure has to be equalized to the atmospheric pressure (“to zero the system”) before every measurement. Unlike in the water-filled system, which takes the upper edge of the symphysis as the reference point, the reference point of the AFC system is the catheter tip itself. Therefore, the position of the catheter tip within the bladder plays a role when interpreting pressure data. In addition, air is easily compressible and might lead to damping during fast movements (high frequency movements, like coughs). Chamber researches have already substantiated this phenomenon *in vitro* (Cooper, 2011; Awada, 2015). The term “air-charged catheter” refers exclusively to the T-Doc system and is a protected

trademark.

Fig. 4: Air-charged cystometry / pressure flow catheter (Picture from Laborie).

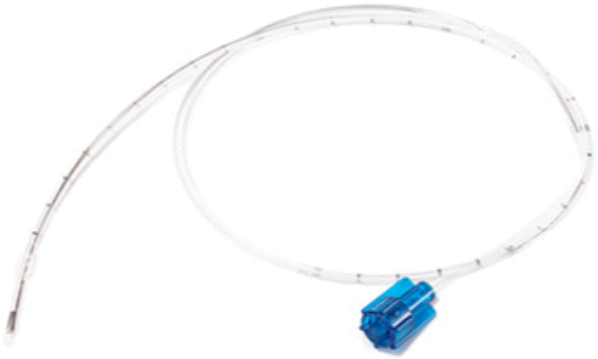

Fig. 5: Air-charged abdominal pressure catheter (Picture from Laborie).

c) Microtip catheter

In this set-up, a micro transducer is attached to the tip of the catheter. The pressure signal is directly collected by the transducer without medium transmission. With a high measurement bandwidth, it can record the high frequency events like coughs without damping or underdamping. However, these catheters are non-disposable and more expensive. These limit its use in clinical practice (Zehnder, 2008; Culligan, 2001; Versi, 1990; Brown, 1969). In addition, microtip catheters measure unidirectional, requiring accurate orientation of the pressure diaphragm. It has to be mentioned that the exact position of the catheter tip within the bladder and the relative position between the catheters are unknown. This makes it more difficult to interpret data obtained with this setting.

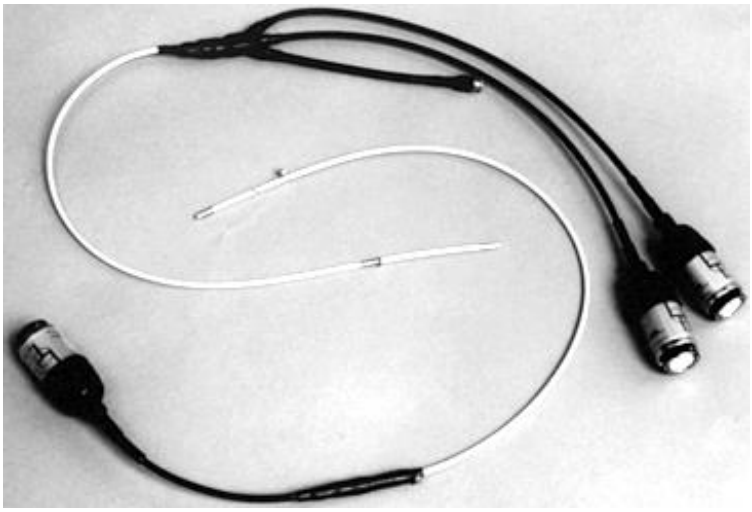

Fig. 6: Microtip cystometry and abdominal pressure catheter (Walters et al, 2015).

1.3. Comparative studies

a) Overview

There are eleven publications reporting results of comparative studies between WFCs, AFCs and microtip catheters (Cooper, 2011; Awada, 2015; Digesu, 2014; Gammie, 2016; Martin, 2012; Hundley, 2004; Hundley, 2006; Zehnder, 2008; Kuhn, 2007; Wang AC, 2002; Timothy, 2018, Table 1). Most of them were urethral pressure comparative studies. The majority of authors concluded that there were significant differences between different catheter technologies. Therefore, results obtained with one or the other system were not per se interchangeable. However, results of studies evaluating the same topic were controversial. Wang et al investigated 301 patients with genuine stress incontinence. They concluded that maximum urethral closure pressure (MUCP) readings obtained from water-filled double-lumen catheters were significantly higher than that from microtip catheters (Wang AC, 2002). Kuhn et al concluded that the mean water perfusion MUCP measurement resulted in significantly lower readings than MUCP readings using with microtip catheters (Kuhn, 2007). Zehnder et al indicated that AFCs gave higher readings than microtip catheters for MUCP at rest (mean difference 7.5 cm H_2O; Zehnder, 2008). On the other side, Martin et al reported that MUCP measured with AFCs was significantly lower than MUCP measured with the microtip catheter system (Martin, 2012).

b) Air-filled vs. water-filled catheter

Currently, standardized pressure values for diagnosis based on urodynamic testing

were developed using WFCs (Schafer, 2002; Rosier, 2010; Lose, 2002). This has been the golden standard in urodynamic measurement for decades. Nevertheless, there are still a lot of deficiencies in the WFC technology as mentioned before. Hence, developing a new reliable technology is necessary. However, this is time and cost consuming. What if any two out of the three available current technologies would be interchangeable, especially between WFCs and AFCs? If that would be the case, WFC's norm would be also applicable to the AFC system and overcome some deficiencies inherited in WFCs. A few studies were conducted in the past comparing cystometric pressure values between AFCs and WFCs (Cooper, 2011; Awada, 2015; Digesu, 2014; Gammie, 2016; Timothy, 2018). Of those five publications, three compared WFCs with AFCs in a clinical setting (Digesu, 2014; Gammie, 2016; Timothy, 2018). Two of them had a similar study design by using two simultaneous catheters assessing vesical pressure (Pves) and two simultaneous catheters assessing abdominal pressure (Pabd) (Digesu, 2014; Gammie, 2016). It is assumed that this setup could have led to an interference between catheters during measurement. Moreover, the presence of two catheters in the urethra could affect the pressure measurement at voiding and/or cough and Valsalva leak points. According to the recommendation from the International Continence Society (ICS), the urethral measurement catheter should be as thin as possible (Schafer, 2002). Therefore, a comparative study was conducted to assess the equivalency of the AFC and WFC pressure readings during cystometric assessment by using a dual-lumen catheter that could record air and water pressures simultaneously as recently reported by Timothy (Timothy, 2018). However, only Pves was assessed in their study, which is lack of clinical significance. In our study, the "single catheter" technology was also used. Because T-Doc catheters were used in this study, the term "air-charged catheters (ACCs)" was used in instead of "AFCs" in the following context.

Comparison of different catheters	Provenance	Sample size	Characteristics
	Kuhn A et al 2007 Int Urogynecol J	18	Evaluated event: MUCP Reproducibility: WFC r=0.95 Microtip r=0.7-0.8 Measured pressure readdings: Mircotip catheter >WFC
	Alex C. Wang et al 2002	272	Evaluated event: MUCP Reproduciblity:

Microtip vs. water-filled catheter	BJOG		WFC r=0.91 Microtip catheter r=0.94 Measured pressure readings: Microtip catheter <WFC
	Hundley AF et al 2006 Int Urogynecol J	95	Evaluated events: Valsalva and Coughs (cystometry) Reproduciblity: WFC r=0.96-0.98 Microtip catheter r=0.99 Measured pressures readings: mircotip catheter>WFC
	Hundley AF et al 2004 Int Urogynecol J	Vitro study	Intravesical pressure recordings from microtip catheter and water-based systems are not interchangeable
Air-filled vs. microtip catheter	Pascal Zehnder et al 2008 Journal of Urology	64	Evaluated events: MUCP and FPL Reproducibility AFC r=0.9-0.97 Microtip catheter r=0.78-0.93 Measured pressure readings: AFC> microtip catheter
	Mueller Martin et al 2012 Ginekol Pol	122	Evaluated events: MUCP Measured pressure readings: AFC< microtip catheter
Air-filled vs. water-filled catheter	M.A. Cooper et al 2011 Neurourology and urodynamics	Vitro study	WFC-underdamped system ACC-overdamped System (when pressure>3.02Hz)
	Hassan K. Awada et al 2014 Neurourology and urodynamics	Vitro study	Developed a Formula from peak pressure of AFC to peak pressure of WFC value; Algorithm corrected 90% of peak pressure readings measured by ACCs
	G. Alessandro Digesu et al 2013 Int Urogynecol J	20	Cystometric simultaneous measurement Measured pressures readings: ACC>WFC Bland-Altman showed wide 95% LOA
	A. Gammie et al 2015 Neurourology and urodynamics	62	Cystometric simultaneous measurement The difference could reach up to 10 cm H_2O,even took the baseline pressure into account Measured pressure readings: ACC>WFC
	Timothy et al	50	Cystometric simultaneous

	2018 Neurourology and urodynamics		measurement with “single catheter” technology ACCs and WFCs showed similar pressure results and were consequently comparable

Tab. 1: List of publications: comparative studies of different catheter types

1.4 Objectives / Ethical Vote / Support

Primary Objective

1. To determine if the maximum pressure readings measured by WFC and ACC measurement systems, when the bladder was filled to 50 ml, 100 ml, 200 ml and maximum cystometric capacity (MCC) during urodynamic evaluations, were equivalent during Valsalva manoeuvres and coughs.

Secondary Objectives

1. To determine if the voiding pressure readings at maximum voiding flow (Qmax) and maximum pressure readings at DO, as measured by WFC and ACC measurement systems, were equivalent.
2. To determine if the resting pressure readings, as measured by WFC and ACC measurement systems, were equivalent.

Ethical Vote

A study proposal was submitted to the Ethics Commission of the Universitätsklinikum Bonn. An approval with the approval number 395/15 was granted in February 2016. The proposal and the approval were depicted in the Appendix 7.1 and 7.2, respectively.

Support

The study was funded and technically supported by Laborie Medical Technologies.

2. Material and Methods

2.1 Patient selection

Inclusion criteria

- Male and female patients (Adults, 21 years and older)
- Patients scheduled for urodynamic evaluation in clinical routine at the neurological rehabilitation center (Godeshoehe e.V.) in Bad Godesberg, Bonn.

Exclusion criteria

- Patients with clinical acute urinary tract infections (this did not include patients with asymptomatic bacteriuria).
- Patients who suffered from urethral stricture disease
- Patients who were pregnant
- Patients with an indwelling suprapubic catheter

Recruitment plan

The target number of enrolment was 25 patients. All enrolled patients were examined at one institution – the neurological rehabilitation center (Godeshöhe e.V.), Bonn. Patients were recruited via patient referrals. Since it was estimated to enroll two patients per week, 13 weeks were planned for recruitment. In accordance with the study protocol, the day of signing Informed Consent Form (ICF) was called the day of enrollment.

Informed consent process

The investigator (according to applicable regulatory requirements) or a person designated by the investigator and under the investigator's responsibility, has fully informed the patients of all pertinent aspects of the clinical trial, including that the trial was approved by the Ethics Commission.

Prior to a patient's participation in the clinical trial, the written ICF was signed by the patient and investigator. The name and personal patient data were added. Finally, a copy of the signed and dated written ICF was given to the patient. The ICF was depicted in the Appendix 7.3.

2.2 Materials in use

The following devices and equipment were utilized in each urodynamic study:

- Urodynamic processor and computer with urodynamic software (Solar Silver, Medical Measurement Systems, Enschede, Netherlands)
- Infusion transducer
- Pressure cuff
- Split perfusion line
- 60 ml male luer lock syringe
- 10-20 ml luer lock syringe (for abdominal line priming)
- Uroflowmeter
- Air-charged transducer cables: Pves (yellow) and Pabd (blue)
- 2 air-charged, single sensor bladder catheters (per patient), 7 Fr T-DOC® Stylet
- Channel 3- Smith Medical P4 pressure transducer plate and cable
- Channel 4- Smith Medical P4 pressure transducer plate and cable
- 2 water transducer cartridges with luer lock plug
- Urodynamics pump tubing infusion line
- 2x water pressure measurement tubing with 3-way stopcock
- 1000mL beaker
- 2x 1000mL bag sterile saline
- Lubricant, tape and gloves
- Any other supplies required for urodynamic studies

Equipment and disposables were provided by Laborie.

2.3 Assessment of T-Doc air-charged catheter measurement

Performance parameters

The performance parameters were as follows: vesical pressure measured by air-charged catheter system (Pves-ACC); vesical pressure measured by water-filled catheter system (Pves-WFC); abdominal pressure measured by air-charged catheter system (Pabd-ACC); abdominal pressure measured by water-filled catheter system (Pabd-WFC).

Safety parameters

Safety parameters were assessed through adverse events. Possible adverse events included:

- Hematuria
- Dysuria
- Urinary tract infection

Methods of assessment

The ACCs were used to measure Pves and Pabd for both air-charged and water-filled catheter systems.

Four transducers were used to assess and record vesical and abdominal pressure in each system. This was done by using a conventional urodynamic machine.

Safety was assessed based on any adverse events that were reported throughout the investigation.

Data Collection

Adverse events, device deficiencies, serious adverse events, and unanticipated adverse device effect were recorded in the Clinical Review Form (CRF; see Appendix 7.4).

2.4 Study procedure

Visit Schedule

Evaluation	Visit 1 = Day 1	Visit 2 = Day 2
Informed Consent	X	
Inclusion Criteria	X	
Exclusion Criteria	X	
Medical History	X	
Current Medication	X	
Pressure Measurement		X
Questionnaire for Operator		X

Preparation of the urodynamic study

A. Set-up of infusion line and urodynamic pump

The infusion line was positioned and the infusion transducer was connected to the system. Then the saline bag was spiked with the infusion line. The distal end of the infusion line was placed into a sterile beaker or held over a container. Drip chamber was gently squeezed until it was nearly half full and the line was flushed completely. Then the line shut was clamped with the roller clamp. Pump head was opened and compressible portion of tubing was positioned across the rollers from left to right.

B. Set-up of the perfusion line in abdominal pressure measurement

A constant drip perfusion pressure-cuff was set up. The settings were being kept in such a way that approximately one drop every two seconds ran through, creating a perfusion rate of 1-2 mL/min (20 drops = 1mL). Then the line was flushed, the tip of the measurement tubing remained sterile

C. Set-up of transducers

The transducer plates were mounted on the system's transducer mounting bracket with the ability for height adjustment to align with patient's symphysis pubis. Then the transducer cartridges were slid down until it 'clicked'. Air-charged transducers and cables were connected to channel 3 and 4. Water-filled transducers and cables were connected to channel 1 and 2.

D. Set-up of vesical pressure measurement line

The measurement tubing was attached to the bottom end of the water transducer cartridge and the distal tip was connected with the air-charged catheter through a three way stopcock (See figure 7a). Then the perfusion tubing was attached to the side port of the water measurement line (See figure 7a). The stopcock on the transducer was turned with the "OFF" handle positioned outward, then a syringe full of water on top was placed to flush if necessary (See figure 7b). After that, the perfusion was hooked up and the three way stopcock was turned so it was closed to the pump. The water pressure measurement line with saline was flushed through the water transducer to get all air bubbles out. The three way stopcock was turned to make the perfusion tubing and the catheter connected. The pump was started in order to get out all of the remaining air in the tubing. After that, the pump was stopped. The air-charged measurement line was connected to the air-charge cable and transducer (channel 3) in open position and zeroed to the atmosphere.

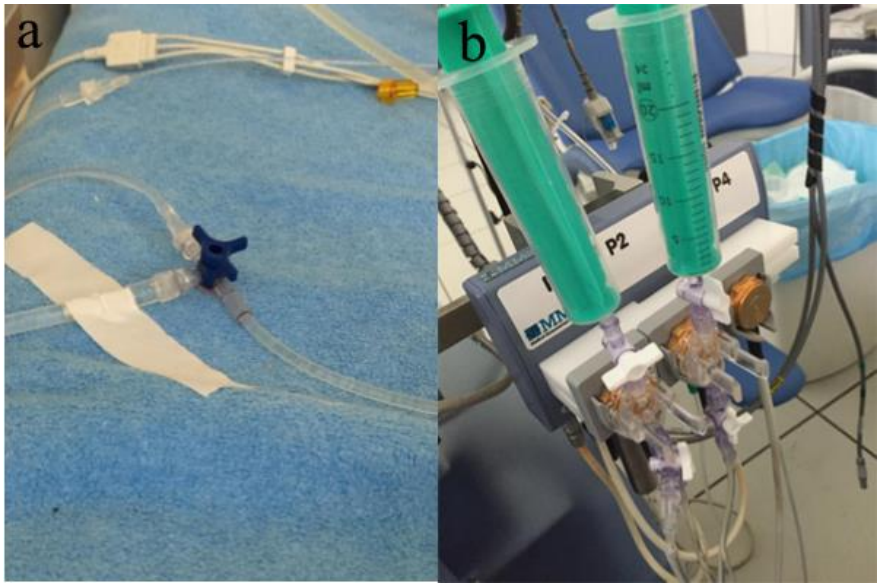

Fig. 7: Example of a completed set-up. a. A three way stopcock permitted the dual functionality; b. Transducers (P1-P4) and syringes

E. Set-up of abdominal pressure measurement line

The measurement tubing was attached to the bottom end of the water transducer cartridge and the distal tip was connected with the air-charged catheter through a three way stopcock. The slow rate perfusion tubing was attached to the side port of the water measurement line. Then the water pressure measurement line with saline was flushed through the water transducer to get all air bubbles out. Air-charged catheter was connected to the air transducer and cable (channel 4) in open position and zeroed to the atmosphere.

F. Preparation of equipment and software

The urodynamic system was turned on and the computer was booted. An empty 1000 mL graduated beaker was placed on the top of the uroflowmeter. The commode chair and funnel were placed on top of the uroflowmeter and beaker. It was confirmed that the beaker was positioned horizontally and centered on the platform and the funnel was not touching the beaker. Then urodynamic software was started. Patient data (name, gender, etc.) was registered. The patient was asked to enter the examination room and was explained what would happen during the procedure.

G. Calibration of catheters

At the beginning of each urodynamic test, both vesical and rectal ACCs were being calibrated using a column of distilled water at 0, 20 and 30 cm H_2O. The level was

measured from the center of each air-charged balloon to the surface of the water which represented level 0 (0 cm H_2O). The calibration of the water-filled transducers was performed using a ruler. The tip of each catheter was placed at the level of each transducer, which stood for level 0 (0 cm H_2O). Then the end of the catheter was raised to 20 and 30 cm above the transducer, which stood for a pressure of 20 and 30 cm H_2O.

Procedure of the urodynamic study

The patient was prepared in lying position or sitting position. The three way stopcock was turned to ensure that the T-Doc ACC was open to the pump (closed to the water transducer). Then the vesical catheter was inserted (In males, the catheter was advanced 8 cm plus the length of the penile shaft; in females, the catheter was advanced 8-10 cm into the urethra). The catheter was fixed with tapes loosely to the patient to keep it from falling out. It was ensured that water transducer was located at the height of the patient's symphysis pubis. After that, the vesical T-Doc ACC was charged. The stopcock was closed to the pump (open to the water transducer). The rectal catheter was inserted 10-15 cm deep and the stylet was removed. The rectal T-Doc ACC was charged. Both vesical and rectal measurement lines were primed using perfusion syringe. Then urodynamic recorder was started. The patient was asked to perform three times' Valsalva manoeuvres followed by three times' coughs to ensure that Pdet subtraction was within 5 cm H_2O. If not, the catheter was repositioned or the water channel was flushed to ensure baseline subtraction was correct. To start filling, the stopcock was opened to the pump (closed to the water transducer) and the pump was started. At every planned filled volume (50 ml, 100 ml, 200 ml, MCC), the pump was stopped and the stopcock was switched so that it was open to the water transducer. The patient was asked to perform three times' Valsalva manoeuvres followed by three times' coughs in sitting or lying position. Volume event was marked on tracing and actually filled volume was recorded in the CRF. To resume filling, the stopcock was opened to the pump (so it was closed to the water transducer). The patient bladder was filled to the capacity as normally indicated for standard UDS. Every sensation event and DO event was marked in the urodynamic software and recorded with the study time of an observed event in the CRF. When the MCC was reached, the pump was stopped. Permission to void was marked on tracing. The patient was asked to void into the volume measuring device and the start

time was recorded in the CRF. During this period, if the patient position was changed, the position of the transducer was also adjusted accordingly to keep patient's upper rim of the symphysis pubis and transducers always at the same level. At last, the urodynamic procedure was completed and concluded as normal. Any artefacts, patient or line movements were recorded in the CRF.

2.5. Statistical analysis

All statistical analyses were performed by using Medcalc statistical software version 15.6.1 (MedCalc Software bvba, Ostend, Belgium) and Microsoft excel 2013. Sample size was calculated based on a previous pilot study, the calculation was as follows:

A study of a continuous response variable from matched pairs of study subjects was planned. Prior data (COWACC study for Valsalva manoeuvre measurement at 200 ml, McKinney, 2015) indicated that the difference in the response of matched pairs was normally distributed with a standard deviation of 6 cm H_2O. If the true difference in the mean response of matched pairs is 4.1 cm H_2O, it would need to study 19 pairs of subjects to be able to reject the null hypothesis that this response difference was zero with probability (power) 0.8.

The Type I error probability associated with this test of this null hypothesis was 0.05. The equation for this was as follows:

$$N = \frac{\left(z_{\alpha/2} + z_{\beta}\right)^2 \sigma^2}{\left(\mu - \mu_0\right)^2}$$

here zα/2 is 1.96 for 0.05 and zβ was 0.842 for 80% power, σ was the standard deviation and μ-μ0 was the difference between the means. A correction factor was applied, resulting in a number of required subjects from 19. Additional 6 patients were included to prepare for procedural and data collection error. This added up to a total of 25 patients.

It was assumed that baseline pressure values would be different between WFC and ACC measurement systems (due to the different reference points used by the different technologies). A reasonable comparison of pressure readings can only be made between changes with respect to the baseline pressure value during

movements like Valsalva manoeuvres and coughs (Gammie, 2009). Pressure values changed from resting pressure of each filled volume (i.e. 50 ml, 100 ml, 200 ml) before each Valsalva manoeuvre and cough were used for comparisons. Other events, for instance, maximum pressure at DO and Pdet at maximum voiding flow (Qmax), “changed value” was used as well. For every suggested filled volume (i.e. 50 ml, 100 ml), the real filled volume was recorded (i.e.102 ml, 205 ml, 303 ml) and included the data within +/-10 cm H_2O at each suggested filled volume when doing following analyses. The “70% rule” proposed by Sullivan was used to screen the raw data during coughs, which cough signal quality was evaluated by comparing the measured height of the cough spikes on Pabd and Pves traces as: Grade A, a good cough signal (smaller spike 70–100% of the larger); Grade B, moderate cough signal (smaller spike 30–70% of the larger); Grade C, a poor cough signal (smaller spike 0–30% of the larger spike). Grade A was deemed to be acceptable, grade B and C unacceptable (Sullivan, 2003). Consequently, grade A cough signals were included in the following analysis. The same rule was applied to the quality control of Valsalva manoeuvres.

Correlations between the two methods during Valsalva manoeuvres and coughs were assessed by linear correlation plots. A paired sample t-test was used for the comparison of all the events. The Bland-Altman plot was used to assess the equivalency between the two measurements for repeated data and single measurement data (Bland, 1986; Bland, 2007). Null hypothesis was that pressure readings measured by WFC and ACC systems were equivalent. Results were presented as mean ± standard deviation (SD), $p<0.05$ was considered as statistically significant.

3. Results

3.1 Demographics

A total of 25 patients (9 male and 16 female) with a mean age of 43.3 years (range 21-62 years) were recruited from April to August 2016. Most patients were investigated in a sitting position except that 9 patients were investigated in lying position. The urodynamic diagnoses were as follows: 5 patients had neurogenic detrusor overactivity, 6 had neurogenic detrusor underactivity, 3 patients had bladder hypersensitivity, 2 patients had idiopathic detrusor underactivity, 3 patients had idiopathic detrusor overactivity, 4 patients had both neurogenic detrusor overactivity and detrusor sphincter dyssynergia, 2 patients did not show any pathological findings. One of the patients presented with an episode of automatic dysreflexia with high blood pressure. The infusion pump had to be stopped at 335mL before maximum capacity was reached. The data from this patient was included in the analysis. There were no fatal and any other adverse events. A full study example was displayed in Figure 8.

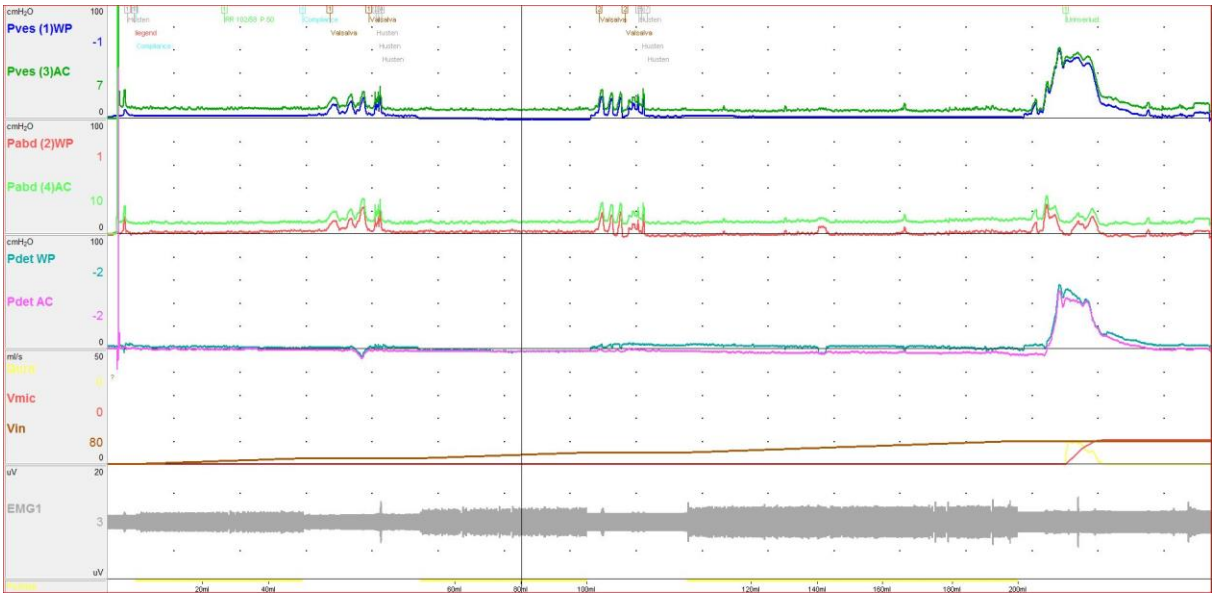

Fig. 8: Urodynamics with simultaneous ACC and WFC measurement. Blue and red lines represent vesical pressure measured by water-filled system and abdominal pressure measured by water-filled system, respectively. Dark green and light green represent vesical pressure measured by air-charged system and abdominal pressure measured by air-charged system, respectively. During filling phase, the Pves-WFC line is closed through a three way stopcock until Valsalva manoeuvres and coughs.

3.2 Quality control

Four tests were excluded after measurement. Two tests were due to poor abdominal pressure measurement with unknown reasons for both systems. One test was due to losing active signals of Pabd-ACC measurement halfway. Another test was due to the consistent low Pabd measurement in water-filled system during Valsalva manoeuvres and coughs. They all could not be settled by either adjusting catheter position or flushing the catheter. Ultimately, 21 patients were included in our analysis. There were 250 and 301 paired raw data collected during Valsalva manoeuvre and cough pressure measurement, respectively. After quality control by the “70% rule”, 213 (85.5%) and 225 (90%) data showed a good quality (Grade A) in WFC and ACC measurement systems during Valsalva manoeuvres, respectively. Meanwhile, 205 (68.1%) and 282 (93.7%) data were Grade A in WFC and ACC measurement systems during coughs (Table 2). Finally, 204 and 190 paired data were used for the comparison at Valsalva manoeuvres and coughs, respectively.

Quality control	**Valsalva manoeuvre**		**Cough**	
	WFC	ACC	WFC	ACC
All (n)	250	250	301	301
Grade A (%)	213 (85.2%)	225 (90%)	205 (68.1%)	282 (93.7%)
Grade B (%)	35 (14%)	21 (8.4%)	81(26.9%)	17 (5.6%)
Grade C (%)	2 (0.8%）	4 (1.6%)	15(5%)	2 (0.7%)

Tab. 2: Grade A, smaller peak pressure >0.7 larger; Grade B, smaller peak pressure >0.3 and <0.7 larger; Grade C, smaller peak pressure <0.3 larger

3.3 Comparison in Valsalva manoeuvres and coughs between WFC and ACC measurements

3.3.1 Linear correlation plot

A strong correlation was observed between the two measurement systems in Pves (R^2=0.988) and Pabd (R^2=0.968) at Valsalva manoeuvres; Pves (R^2=0.972) and Pabd (R^2=0.943) at coughs, respectively. The results were presented in Figure 9, 10.

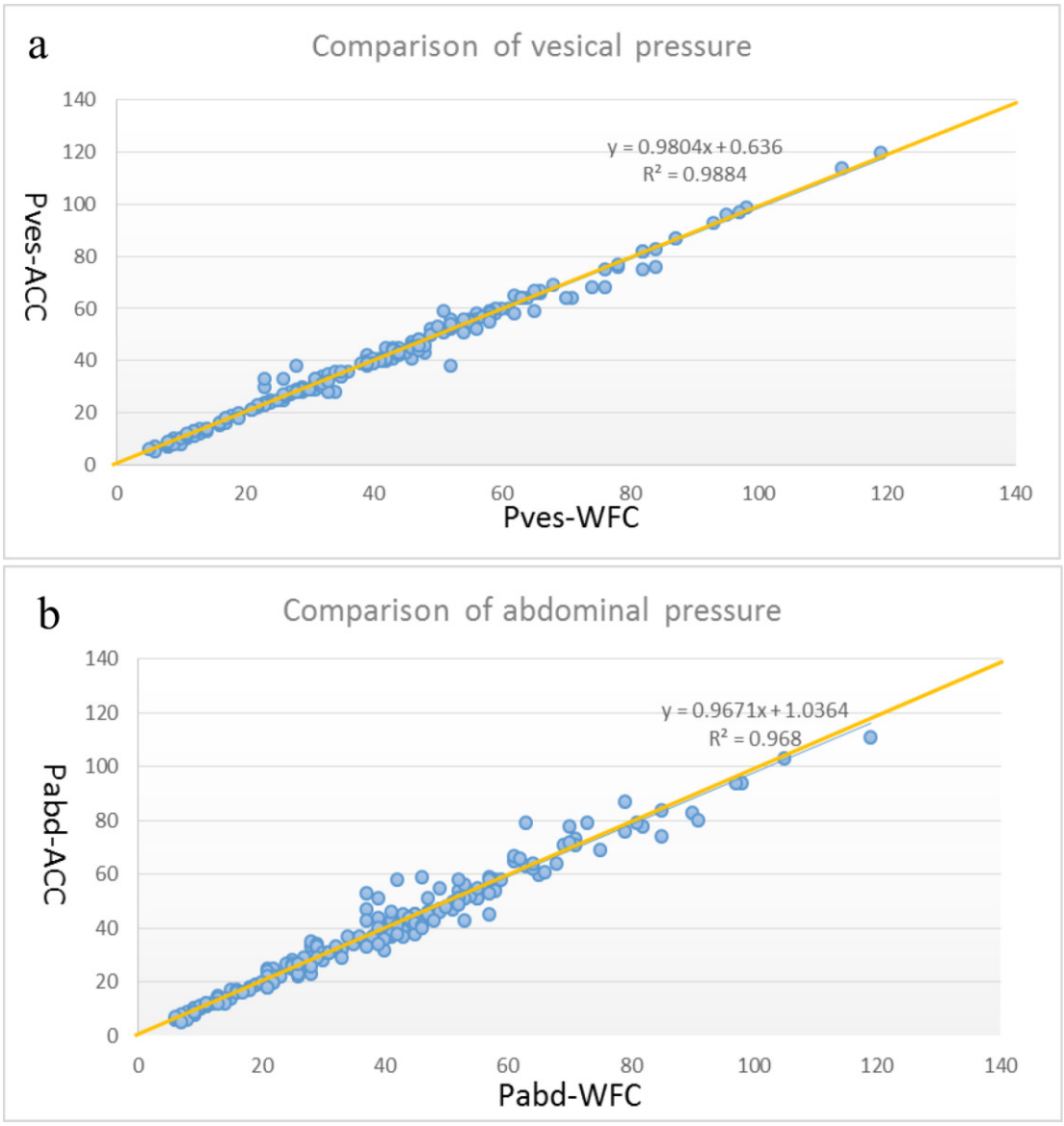

Fig. 9: a. Correlation of Pves-ACC and Pves-WFC at Valsalva manoeuvres; b. Correlation of Pabd-ACC and Pabd-WFC at Valsalva manoeuvres. Yellow line represents X=Y, blue line represents trend line.

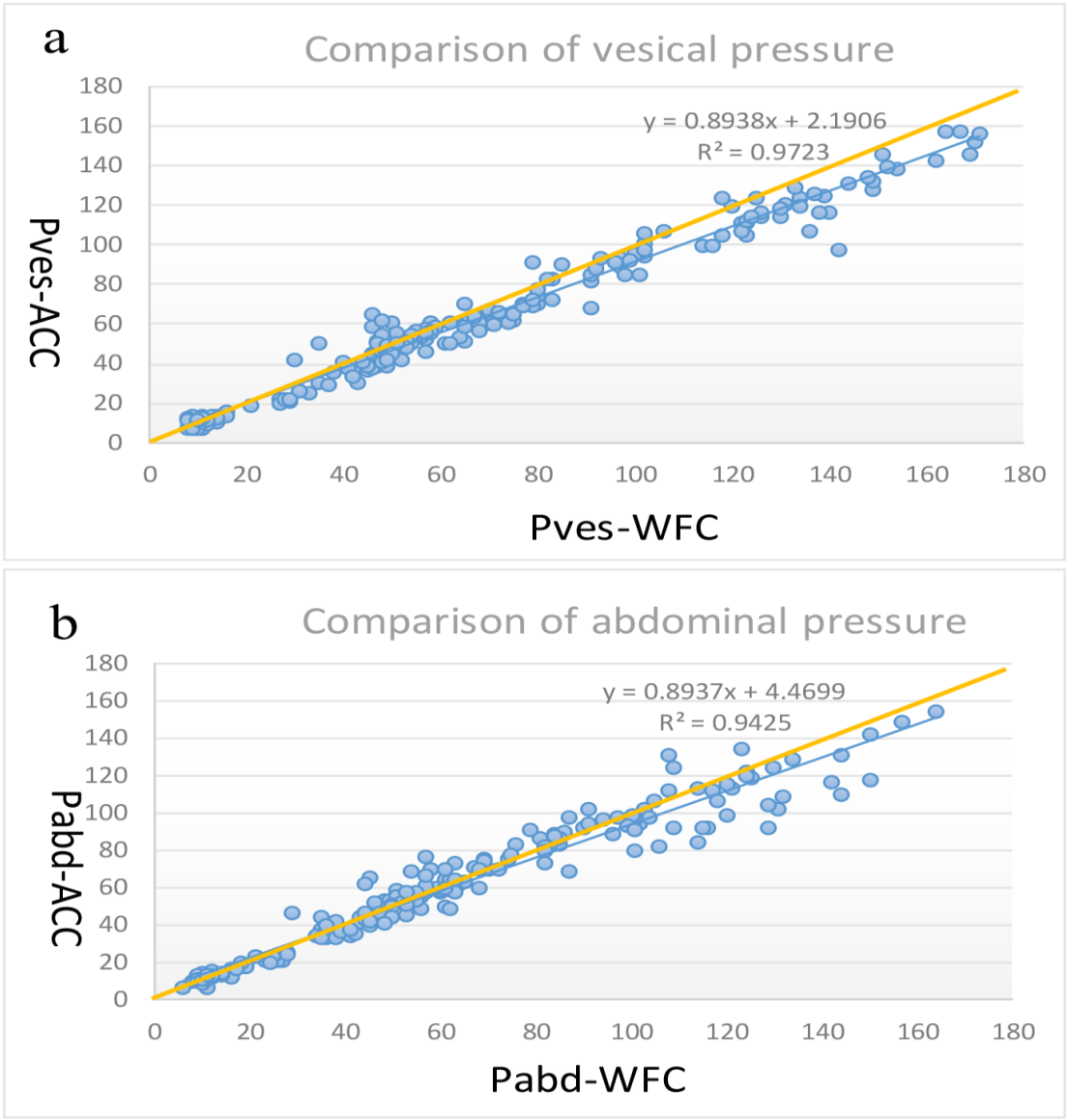

Fig. 10: a. Correlation of Pves-ACC and Pves-WFC at coughs; b. Correlation of Pabd-ACC and Pabd-WFC at coughs.

3.3.2 Paired sample t-test

There was no statistically significant difference between the two methods regarding Pves (P=0.43), Pabd (P=0.51) and Pdet (P=0.85) at Valsalva manoeuvres. However, there was a significant difference for all parameters at coughs (P<0.001). Details were depicted in Table 3.

	Number of paired data	WFC mean (SD) in cmH_20	ACC mean (SD) in cmH_20	Paired t test P-value
Maximum Pves at Valsalva	204	39.44 (23.34)	39.31 (23.02)	0.43
Maximum Pabd at Valsalva	204	38.11 (22.04)	37.93 (21.70)	0.51
Maximum Pdet at Valsalva	204	1.65 (3.39)	1.72 (3.85)	0.85
Maximum Pves at Cough	190	69.65 (43.25)	64.59 (39.21)	<0.001
Maximum Pabd at Cough	190	63.01 (38.67)	60.71 (35.66)	<0.001
Maximum Pdet at Cough	190	6.83 (7.82)	3.89 (9.44)	<0.001

Tab. 3: Comparison of pressure changes in Pves, Pabd, Pdet at Valsalva manoeuvres and coughs.

3.3.3 Bland-Altman plot

The Bland-Altman plots showed that paired difference in Pves, Pabd and Pdet measurement at Valsalva manoeuvres could reach up to 5.2 cm H_2O, 8.1 cm H_2O and 10.6 cm H_2O, respectively. Whereas, it could reach up to 20.0 cm H_2O, 19.5 cm H_2O, 20.1 cm H_2O in Pves, Pabd and Pdet measurement at coughs, respectively. The results were displayed in Figure 11 and 12.

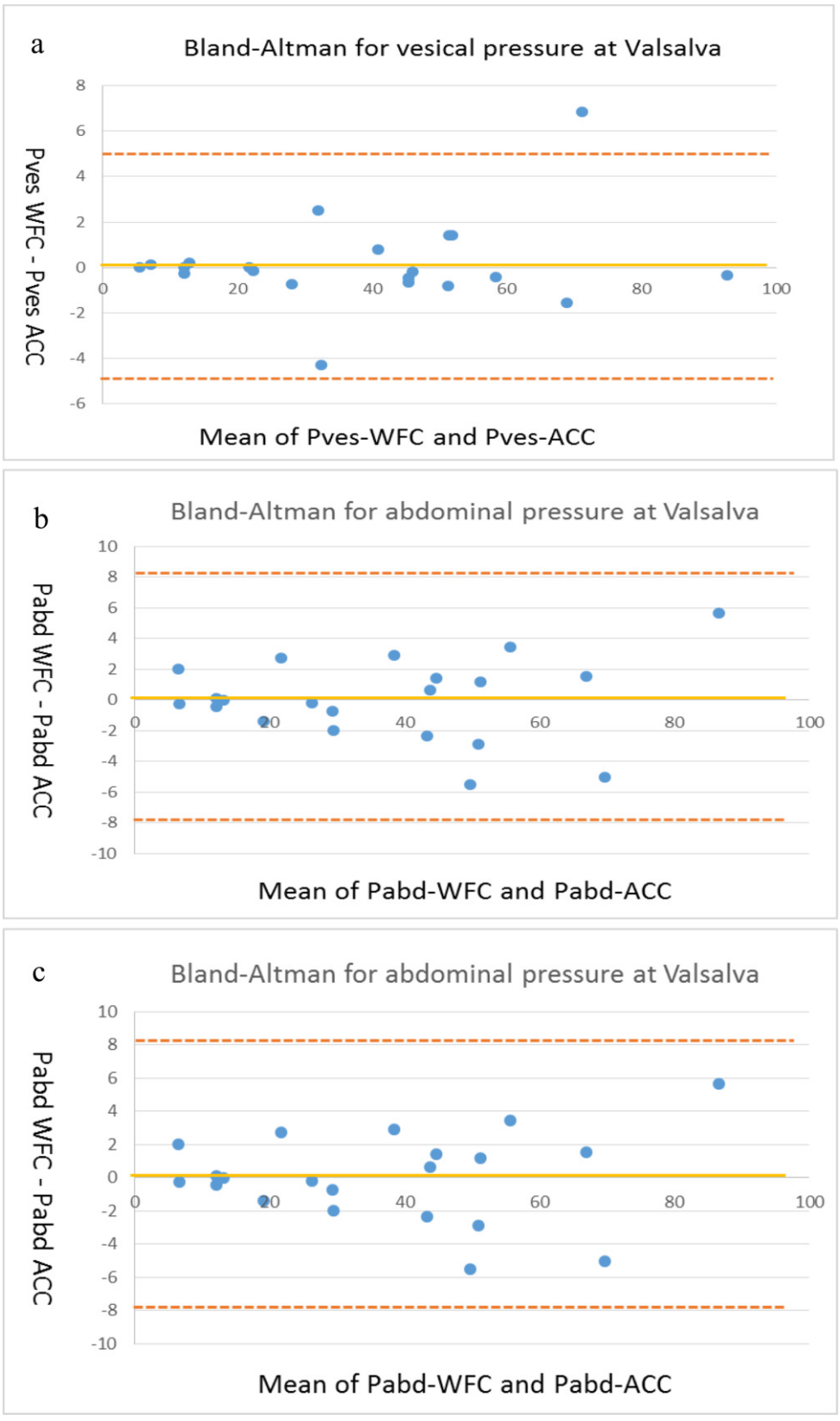

Fig. 11: Bland-Altman plots for repeated measurements at Valsalva manoeuvres. a. The 95% limits of agreement are -4.9 to 5.2 cm H_2O (mean=0.16, SD=2.58), b. The 95% limits of agreement are -8.0 to 8.1 cm H_2O (mean=-0.04, SD=4.09), c. The 95% limits of agreement are -10.6 to 10.4 cm H_2O (mean=0.12, SD=5.37).

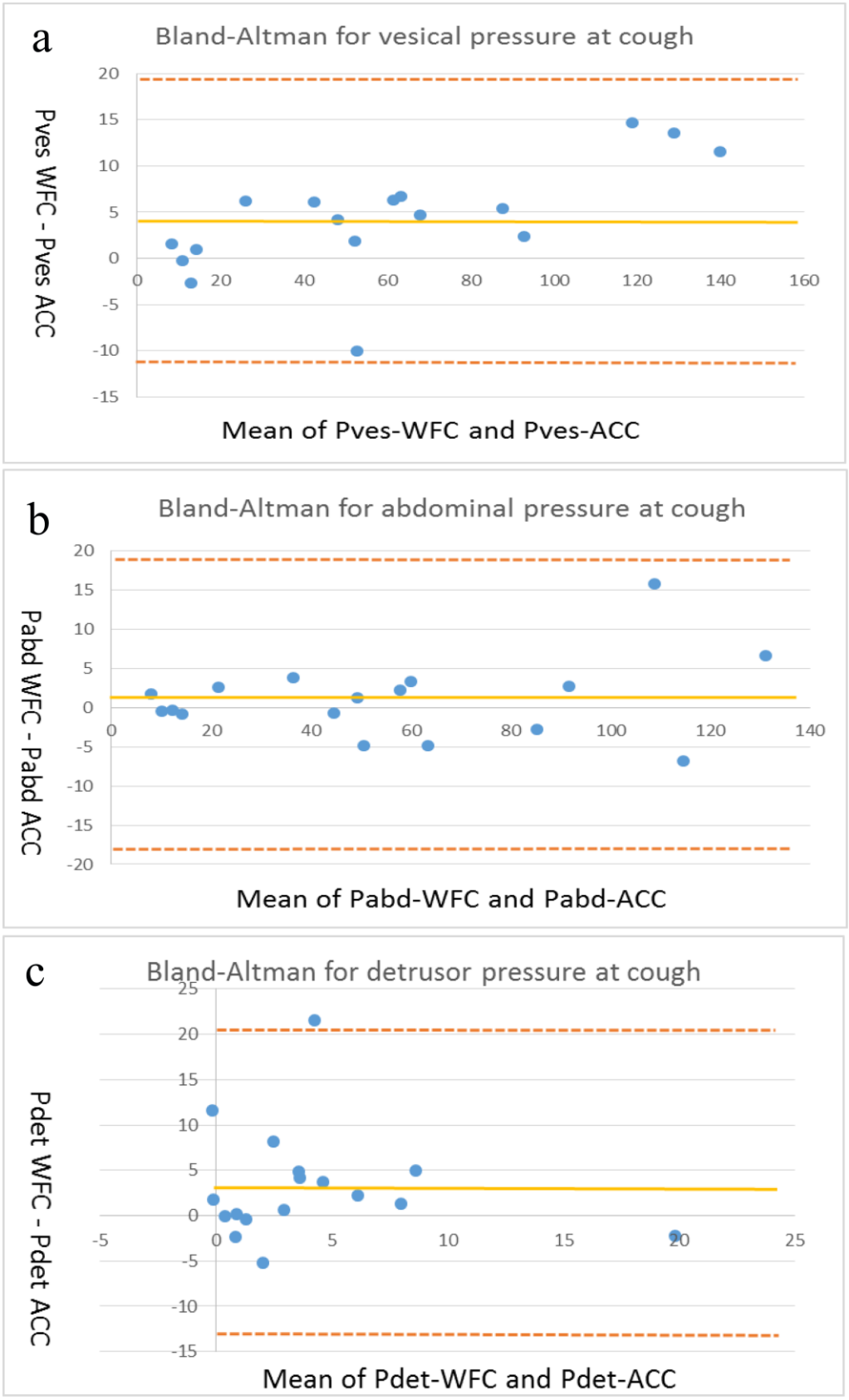

Fig. 12: Bland-Altman plots for repeated measurements at coughs. a. The 95% limits of agreement are -11.4 to 20.0 cm H_2O (mean=4.30, SD=8.00), b. The 95% limits of agreement are -17.3 to 19.5 cm H_2O (mean=1.08, SD=9.40), c. The 95% limits of agreement are -13.7 to 20.1 cm H_2O (mean=3.22, SD=8.61).

3.3.4 Comparison between WFC and ACC measurement at each filled volume in Valsalva manoeuvres

Data was also analyzed by applying t-test to the comparison at different filled volumes. There were no statistically significant differences at each filled volume in Valsalva manoeuvres, except for the comparison at 200±10 ml in Pves and Pdet measurement, which showed a significant difference between the two systems (P=0.0007 and 0.03, respectively). The results were displayed in Figure 13 and Table 4.

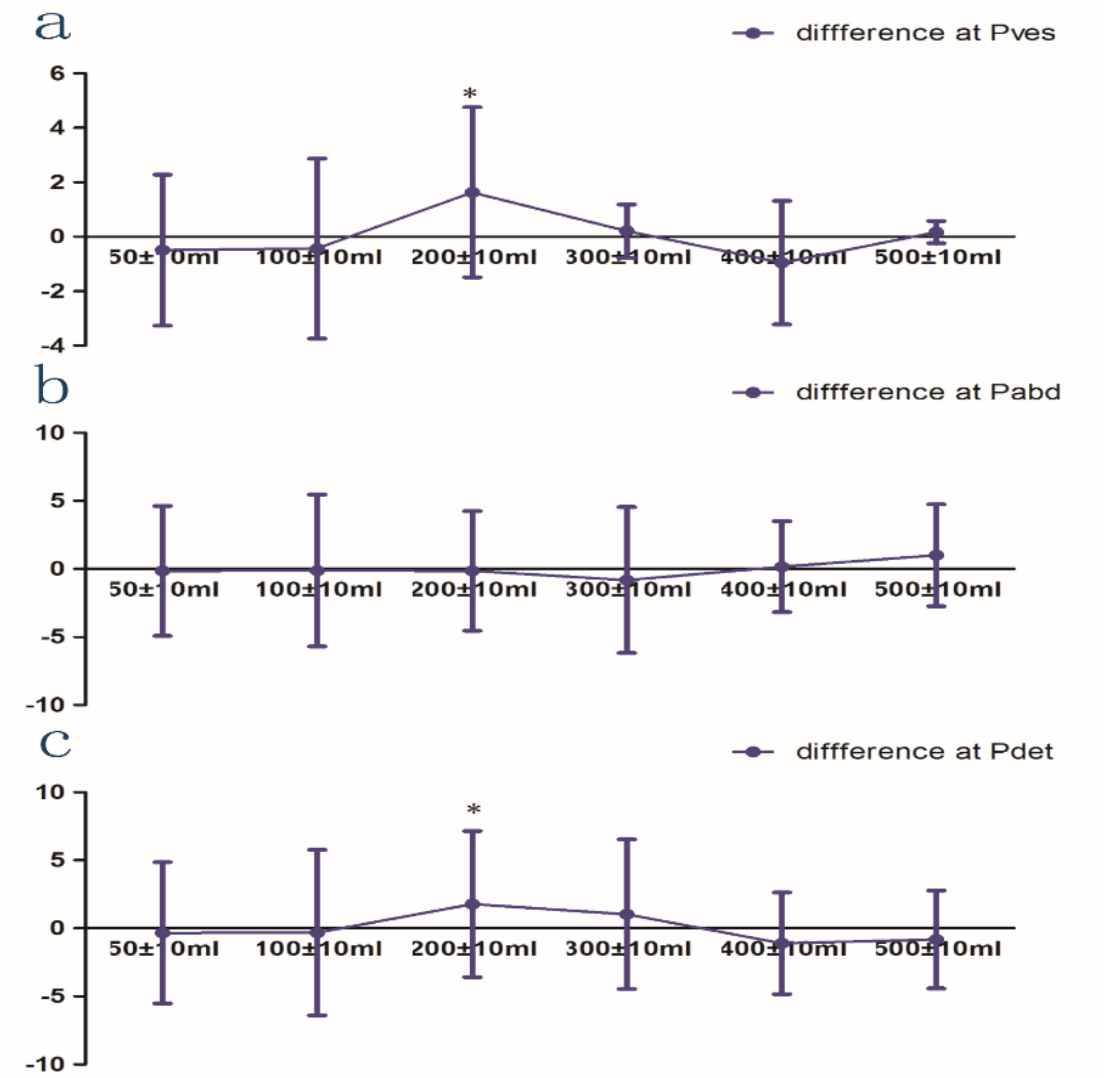

Fig. 13: Comparison between WFC and ACC measurement at each filled volume in Valsalva manoeuvres. *p<0.05

Recording point	Number of data	Difference at Pves (SD)	Difference at Pabd (SD)	Difference at Pdet (SD)
		T test P-value	T test P-value	T test P-value
50±10ml volume	57	-0.49 (2.78) 0.18	-0.15 (4.78) 0.81	-0.34 (5.19) 0.62
100±10ml volume	69	-0.43 (3.31) 0.28	-0.12 (5.58) 0.86	-0.32 (6.08) 0.66
200±10ml volume	48	1.63 (3.12) <0.001	-0.16 (4.39) 0.82	1.77 (5.37) 0.03
300±10ml volume	34	0.21 (0.98) 0.23	-0.82 (5.36) 0.38	1.03 (5.49) 0.28
400±10ml volume	19	-0.95 (2.27) 0.09	0.16 (3.34) 0.84	-1.11 (3.74) 0.21
500±10ml volume	6	0.17 (0.41) 0.36	1.00 (3.74) 0.54	-0.83 (3.60) 0.60

Tab. 4: Comparison between WFC and ACC measurement at six different filled volumes in Valsalva manoeuvres.

In contrast, in the Pves measurement, there were significant differences at 50 ±10 ml to 400±10 ml between the two systems. Significant differences were also shown at 200±10 ml and 300±10 ml in Pabd measurement; In Pdet measurement, differences at 50±10 ml, 400±10 ml and 500±10 ml were statistically significant. The results were displayed in Figure 14 and Table 5.

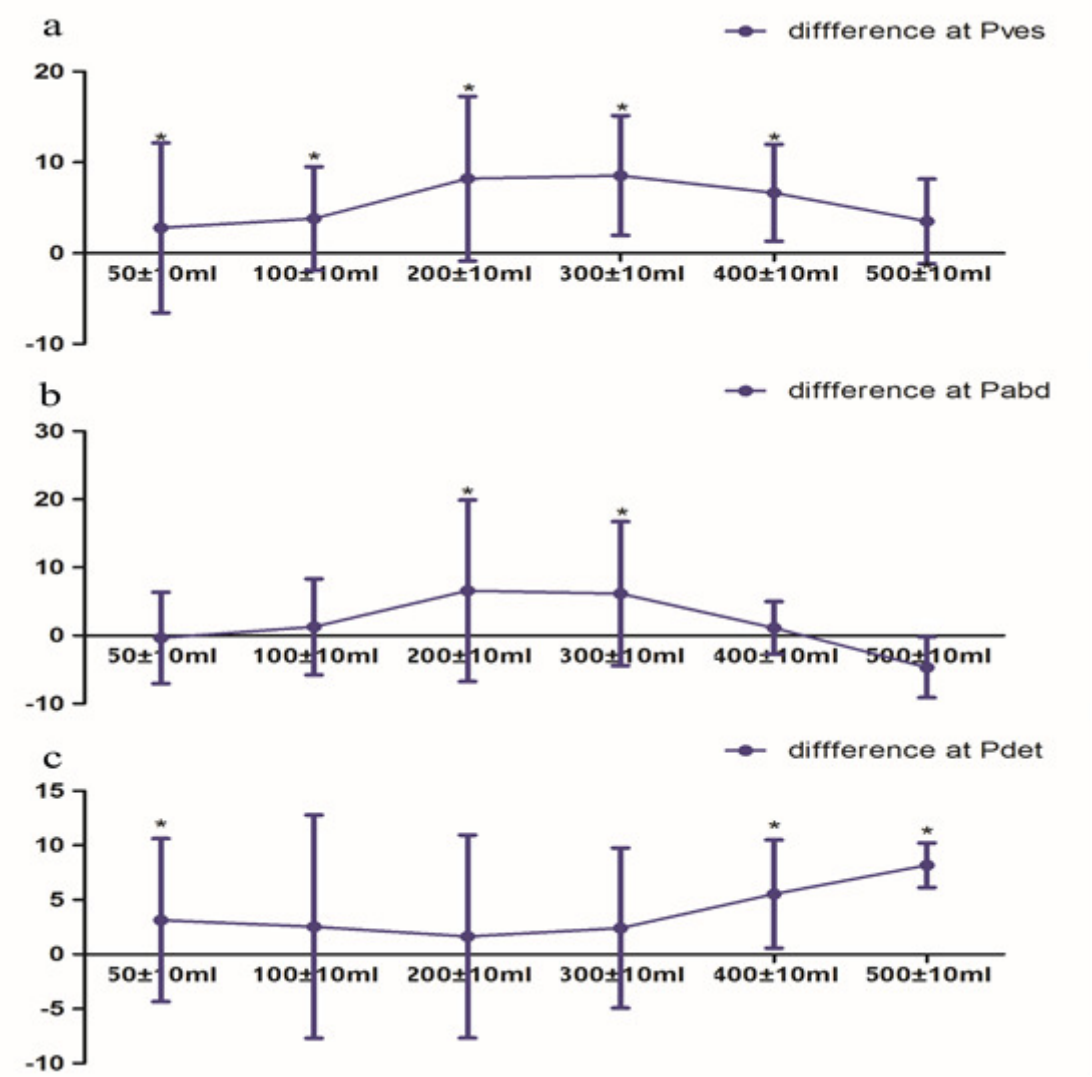

Fig. 14: Comparison between WFC and ACC measurement at six different filled volumes in coughs. *p<0.05

Recording point	Number of paired data	Difference at Pves (SD)	Difference at Pabd (SD)	Difference at Pdet (SD)
		T test P-value	T test P-value	T test P-value
50±10ml volume	49	2.78 (9.35) 0.04	-0.36 (6.70) 0.70	3.14 (7.48) <0.01
100±10ml volume	48	3.81 (5.70) <0.001	1.27 (7.04) 0.22	2.54 (10.24) 0.09
200±10ml volume	35	8.20 (9.06) <0.001	6.57 (13.31) <0.001	1.63 (9.31) 0.31
300±10ml volume	29	8.55 (6.58) <0.001	6.14 (10.56) <0.01	2.41 (7.34) 0.08
400±10ml volume	17	6.65 (5.33) <0.001	1.12 (3.85) 0.25	5.53 (4.96) <0.001
500±10ml volume	6	3.50 (4.42) 0.11	-4.67 (4.46) 0.05	8.17 (2.04) <0.001

Tab. 5: Comparison between WFC and ACC measurement at six different filled volumes in coughs.

3.4 Comparison between WFC and ACC systems at each filled volume, DO and pressure at Qmax in resting pressure measurement

3.4.1 Student's t-test

Except in the comparison at initial resting pressure (P<0.01) and maximum pressure at DO (P<0.01), no statistically significant differences were found in all other clinical events between the two systems. The results were presented in Table 6.

Recording point at which pdet read	Number of paired data	WFC mean (SD) in cm H_20	ACC mean (SD) in cm H_20	Paired t test P-value
Resting, 50±10ml volume	21	0.86 (2.76)	-1.29 (4.74)	0.08
Resting, 100±10ml volume	20	2.05 (3.03)	-0.85 (5.40)	0.06
Resting, 200±10ml volume	17	2.65 (3.77)	0.94 (5.85)	0.32
Resting, 300±10ml volume	14	3.14 (3.32)	-0.50 (5.89)	0.07
Maximum cystometric capacity	21	4.05 (4.04)	0.76 (5.78)	0.06
Pressure at Qmax	18	38.28 (27.28)	39.00 (28.02)	0.60
Maximum pressure at DO	22	40.05 (29.81)	37.45 (30.47)	<0.01
Initial resting pressure	21	1.10 (2.77)	-2.67 (5.23)	<0.01
Resting pressure after voiding	10	4.00 (4.06)	2.80 (7.13)	0.49

Tab. 6: Comparison of the two measurement systems in Pdet values at different points of the test.

3.4.2 Comparison in resting Pves and Pabd at each filled volume

The Student t-test was also used to compare the two systems in resting Pves and Pabd at each filled volume. Significant differences in Pves were documented at 50±10ml (P<0.01), 100±10ml (P=0.01) and 200±10ml (P=0.04; Figure 15 and Table 7). On the other hand, statistically significant differences were observed at 50±10ml (P<0.01) and 100±10ml (P<0.01) in resting Pabd measurements between WFC and ACC systems (Figure 16 and Table 8).

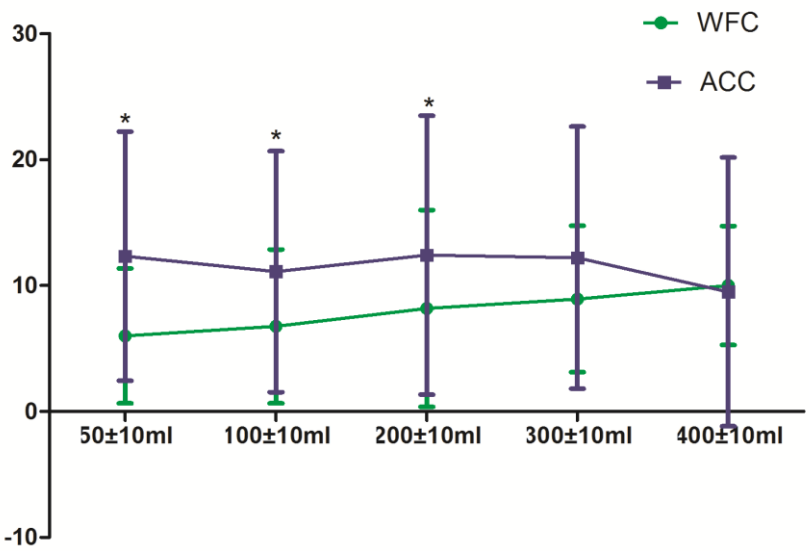

Fig. 15: Comparison in resting Pves at each filled volume between WFC and ACC measurement.

Recording point at which Pves read	Number of data	WFC mean (SD) in cm H_2O	ACC mean (SD) in cm H_2O	T test P-value
Resting, 50±10ml volume	21	6.00 (5.45)	12.33 (9.88)	<0.01
Resting, 100±10ml volume	20	6.75 (6.11)	11.10 (9.57)	0.01
Resting, 200±10ml volume	17	8.18 (7.82)	12.41 (11.07)	0.04
Resting, 300±10ml volume	14	8.93 (5.82)	12.21 (10.41)	0.18
Resting, 400±10ml volume	6	10.00 (4.73)	9.5 (10.67)	0.90

Tab. 7: Comparison between WFC and ACC measurement in resting Pves at five different filled volumes.

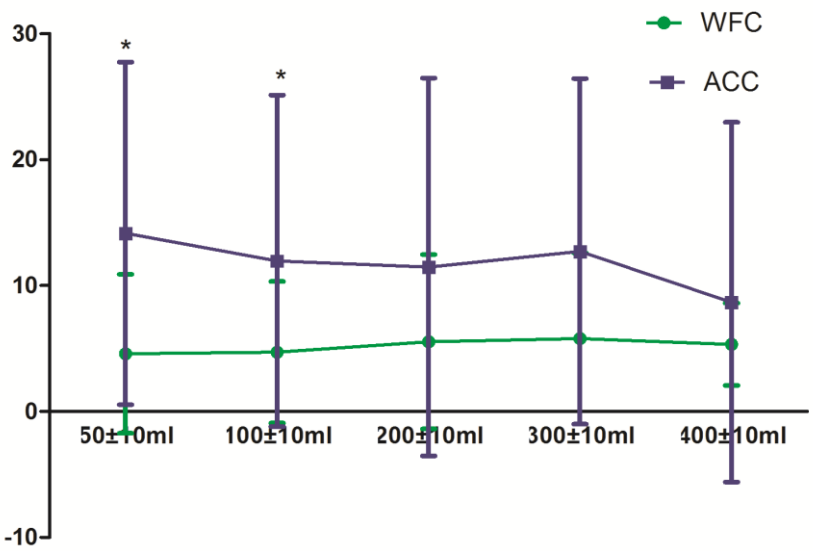

Fig. 16: Comparison in resting Pabd at each filled volume between WFC and ACC measurements. *p<0.05

Recording point at which Pabd read	Number of data	WFC mean(SD) in cm H_2O	WACC mean(SD) in cm H_2O	T test P-value
Resting, 50±10ml volume	21	4.57 (6.31)	14.14 (13.60)	<0.01
Resting, 100±10ml volume	20	4.70 (5.62)	11.95 (13.16)	<0.01
Resting, 200±10ml volume	17	5.53 (6.92)	11.47 (15.00)	0.07
Resting, 300±10ml volume	14	5.79 (6.80)	12.71 (13.73)	0.07
Resting, 400±10ml volume	6	5.33 (3.27)	8.67 (14.28)	0.59

Tab. 8: Comparison between WFC and ACC measurement in resting Pabd at five different filled volumes.

3.4.3 Bland-Altman plot

The Bland-Altman plots were also plotted for the resting Pdet at each filled volume and other urodynamic events (DO and pressure at Qmax). The narrowest pressure difference interval was observed in the comparison of maximum Pdet at DO, which limits of agreement (LOA) was -3.2-8.4 cm H_2O. Whereas, the widest pressure difference interval was observed in the comparison of resting Pdet at maximum cystometric capacity (LOA, -11.5-18 cm H_2O), which means the difference between the two measurement modalities could reach up to 18 cm H_2O in the resting Pdet measurement. The specified results were depicted in Figure 17.

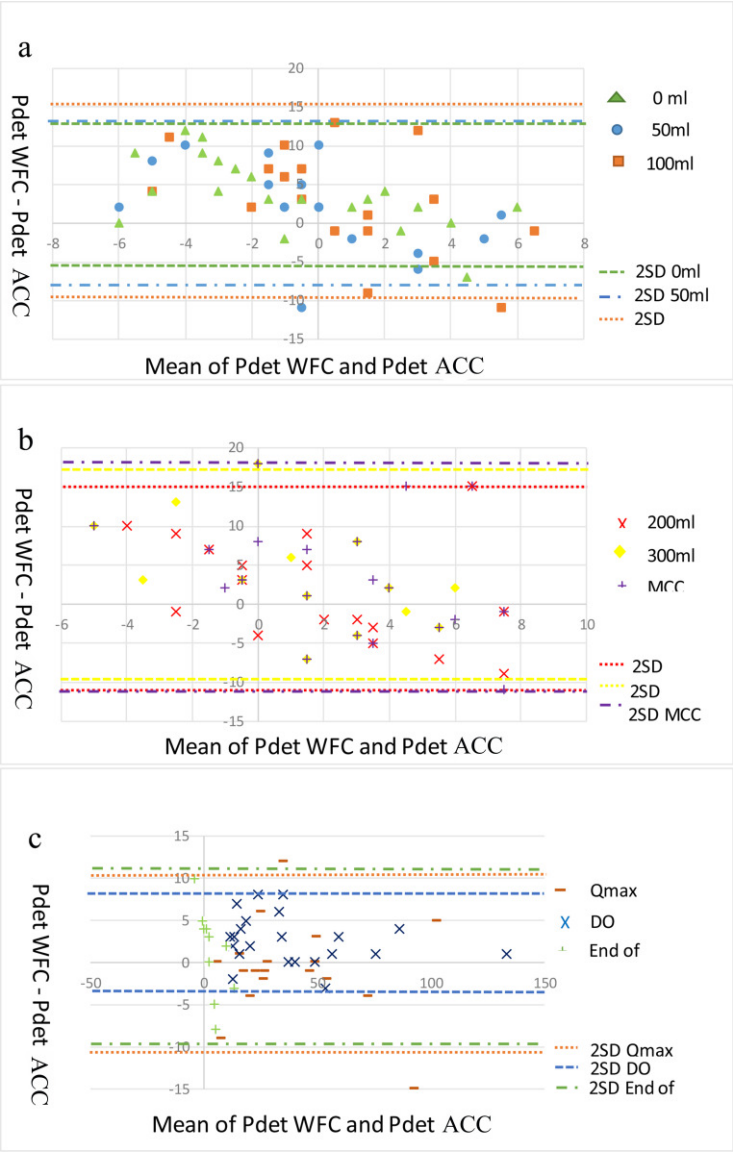

Fig. 17: Bland-Altman plots. Evaluation of equivalency between Pdet-WFC and Pdet-ACC at the start of filling, 50±10ml, 100± 10ml, 200±10ml, 300±10ml, end of voiding and MCC in resting pressure measurement (from graph a to c), at Qmax and DO pressure measurement (graph c).

3.4.4 Comparison in different positions at each filled volume

Student t-test was used to compare the resting Pdet between lying and sitting position at each filled volume. There were no statistically significant differences between lying and sitting positions, no matter in WFC or ACC measurement. Although not statistically significant, there was a visual difference at each filled volume in air-charged system, which patients in lying position obtained lower pressure readings than patients in sitting position, and the readings tended to be negative in lying positions. The specific results were depicted in Figure 18, 19 and Table 9, 10.

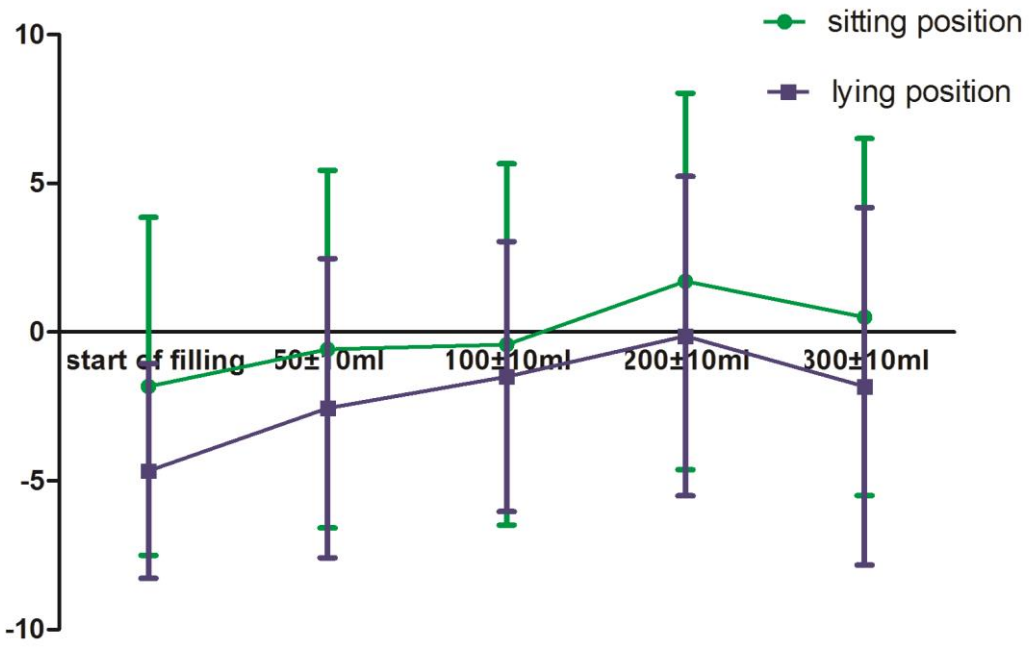

Fig. 18: Comparison of resting Pdet readings between sitting and lying positions at each filled volume in air-charged system.

Recording point at which pdet read	Number of data (sitting/lying)	ACC sitting mean (SD) in cm H_2O	ACC lying mean (SD) in cm H_2O	T test P-value
Initial resting pressure	12/9	-1.83 (5.68)	-4.67 (3.61)	0.21
Resting, 50±10ml volume	12/9	-0.58 (6.01)	-2.56 (5.03)	0.44
Resting, 100±10ml volume	12/8	-0.42 (6.07)	-1.50 (4.54)	0.67
Resting, 200±10ml volume	10/7	1.70 (6.33)	-0.14 (5.37)	0.54
Resting, 300±10ml volume	8/6	0.50 (6.00)	-1.83 (6.01)	0.49

Tab. 9: Comparison of resting Pdet readings between sitting and lying positions at each filled volume in air-charged system.

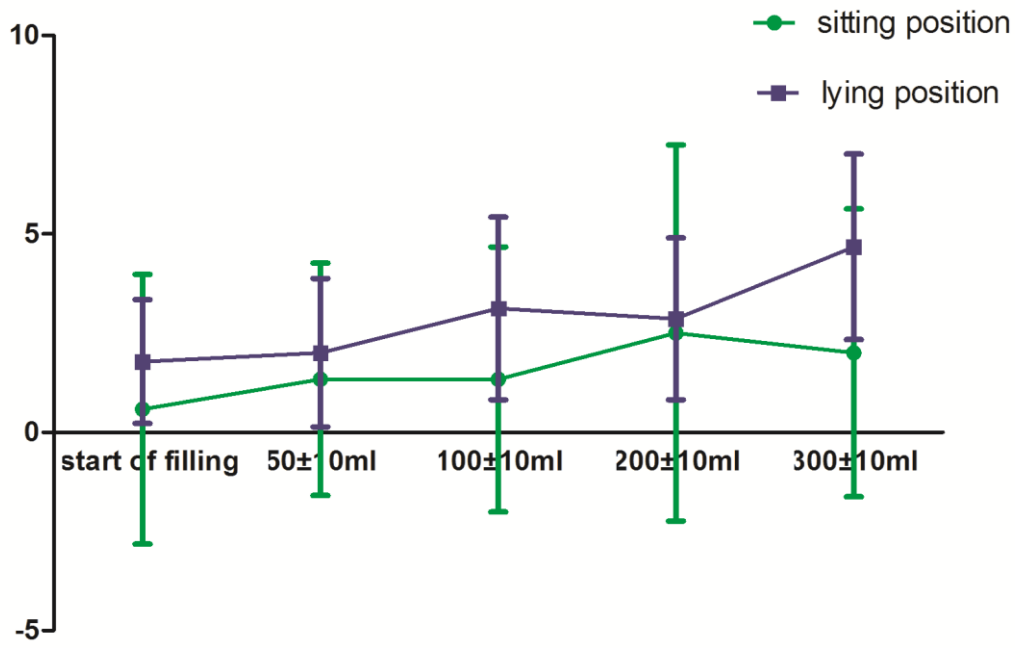

Fig. 19: Comparison of resting Pdet readings between sitting and lying positions at each filled volume in water-filled system.

Recording point at which pdet read	Data points (sitting/lying)	WFC sitting mean (SD) in cm H_2O	WFC lying mean (SD) in cm H_2O	T test P-value
Initial resting pressure	12/9	0.58 (3.40)	1.78 (1.56)	0.30
Resting, 50±10ml volume	12/9	1.33 (2.93)	2.00 (1.87)	0.56
Resting, 100±10ml volume	12/8	1.33 (3.34)	3.12 (2.30)	0.20
Resting, 200±10ml volume	10/7	2.50 (4.74)	2.86 (2.04)	0.85
Resting, 300±10ml volume	8/6	2.00 (3.63)	4.67 (2.34)	0.14

Tab. 10: Comparison of resting Pdet readings between sitting and lying positions at each filled volume in water-filled system.

4. Discussion

The introduction of the ACC has aroused tremendous interest among urodynamicists due to some advantages compared with the WFC. For instance, the ACC evades interference by air-bubbles as it contains weightless air column as the conductive medium during urodynamic measurement. In addition, due to its narrower frequency bandwidth compared to the WFC, it is much easier to set up an air-charged system correctly than a water-filled one. The ACC could avoid high frequency artefacts, such as tube knocks (Cooper, 2011). Consequently, there are less system related pitfalls. With the advantages listed above, researchers keep exploring the possibility of using the ACC as an alternative measurement tool to the WFC. However, urodynamic measurement using the WFC has still to be regarded as gold standard at present.

To date, two basic studies testing performance of the T-Doc ACC in vitro have been published. The focus in those publications was on their frequency response. Air dampens fast changes in pressure (e.g., coughs) and thus can be considered an over-damped system. On the contrary, water is an underdamped medium. Its resonant frequency sometimes results in magnified pressure changes. Cooper et al. conducted a test of both ACCs and WFCs, placed simultaneously in a pressure chamber, using standard engineering tests such as the transient step test and the frequency sweep test. These tests showed that T-Doc ACCs acted as a low-pass filter with a cut-off point at 3 Hz. In contrast, the WFC was a second order underdamped system and as such, had a broad resonance frequency of approximately 10 Hz, amplifying the signal from frequencies approximately 5 Hz to approximately 15 Hz and attenuating signals above 15 Hz (Cooper, 2011). However, this only matters in the case that these frequencies are clinically relevant. Thind et al. assessed the frequency spectrum of cough tests in six healthy volunteers, four men and two women. They found that 99% of pressure signals during coughs occurred at frequencies of 9 Hz or less (Thind, 1994). In an analysis of 131 consecutive pairs of urodynamic measurements during voiding, Kranse and van Mastrigt showed that most of the signal power occurred at frequencies less than 1 Hz (Kranse, 2003). This indicates that ACCs are capable of recording bladder pressure during voiding accurately, but T-Doc ACCs would likely attenuate the bladder pressure (i.e., record a lower bladder pressure than actual pressure) during coughs, since the cough is a high frequency event. WFCs can also record bladder pressure during voiding precisely, but in contrast to ACCs, it might possibly amplify the bladder pressure

during cough tests (Awada, 2015; Digesu, 2014). Another chamber test was conducted by Awada et al. who simultaneously tested T-Doc ACC and WFC pressure measurement systems in a pressure chamber with pressure signals consisting of systematic variations on bladder pressure during coughs and Valsalva manoeuvres (Awada, 2015). The ACCs undervalued the pressure events lasting less than 0.5 s, for example coughs, which lasted approximately 0.2–0.25 s. In comparison, Valsalva manoeuvre was a pressure event that lasted 1–2 s. Awada et al. also developed an algorithm to convert bladder pressure during cough and Valsalva tests, which was mainly for coughs. Whereas, it was nearly the same of pressure values detected by ACCs and WFCs during Valsalva manoeuvres (Awada, 2015). The algorithm was able to correct 90% of maximum pressures measured by the T-Doc ACCs. Would this algorithm be useful in clinical practice? This is clearly debatable. It is well known that most of the clinical relevant events are slow movements (low frequency). There are few high frequency events occurring during urodynamic measurement. Moreover, all of those were just *in vitro* studies, which did not take physiological factors into account. Therefore, the experiment should be continued *in vivo* in future research.

Three clinical peer-reviewed articles have been published up to now. Digesu et al used the individual ACC and WFC to study Pves, Pabd and Pdet in 20 women. Pressure measurements from ACCs were overall higher than pressure measurements from WFCs. Despite presenting higher pressure values, only Pabd showed a significant difference between methods. It was also highlighted that the difference between the two catheter systems was bigger in the rectum than that in the bladder, suggesting a physiological, rather than a physical reason for their results (Digesu, 2014). Gammie et al recruited 62 patients in their study. It was demonstrated that the measurements obtained by ACCs and WFCs were not significantly different during filling and at maximum flow during voiding, but the values could differ by up to 10 cm H_2O even with taking the start value into account. They also concluded that if the ACC would be used, care must be taken to compensate for any Pdet variations that occur during patient movement (Gammie, 2016). In a recent publication, Timothy et al used the “single catheter” technology, which simultaneously recorded the WFC and the ACC measurement readings using a single Tdoc-ACC. Pressure readings were recorded with WFC and ACC systems in 50 women. Valsalva manoeuvres, coughs and other urodynamic events were evaluated. However, in their study, the “single catheter” technology was only applied to the

comparison of Pves and no Pabd comparison data was accessible, which resulted in a lack of usefulness in clinical practice.

Comparing to previous clinical studies, the herein reported study was conducted in a neurological rehabilitation center, most patients (15/25) had neurogenic abnormalities. Both females (n=16) and males (n=9) were included in this study, whereas, only females were evaluated in previous studies. This indicates that the present study is more comprehensive in terms of demographics. Another distinct difference, compared to the previous studies, is the “single catheter” technology was applied to both Pves and Pabd measurement in this clinical research. A single T-Doc catheter was used to simultaneously record the pressure readings measured by the air-charged system and water-filled system in case of the cross-talk between two catheters in one lumen. Although it is an innovative and favorable method, some problems occurred in this research should be noted.

The primary goal of this study was to assess the equivalency between WFC and ACC systems at Valsalva manoeuvres and coughs. After quality control, >85% raw data was obtained with good quality (Grade A) in Valsalva manoeuvres for both systems. In cough pressure measurement, about 30% raw data was revealed moderate or bad quality (Grade B and C) with use of the WFC system. When it comes to specific measurements, the Pabd-WFCs were very low or with a deformative shape during coughs in some subjects or some episodes of measurement. It was assumed that the rectal catheter’s orifice might have interacted with rectal mucosa during fast movements in some cases, and therefore being blocked or partially blocked, even with the presence of a continuous low rate perfusion (Figure 20 and 21).

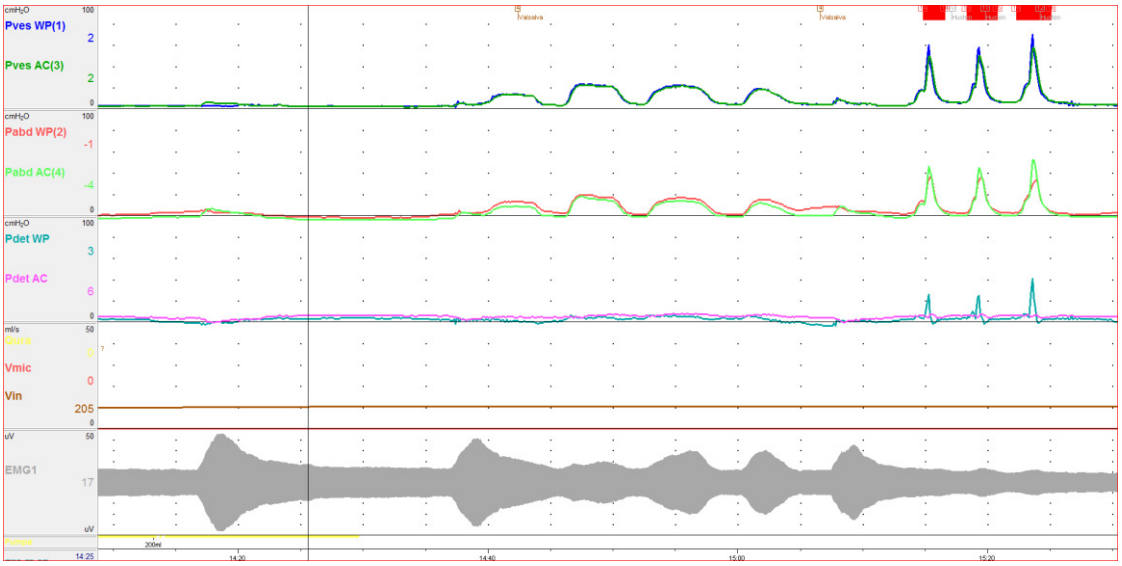

Fig. 20: An example of low pressure values in Pabd-WFC measurement during coughs.

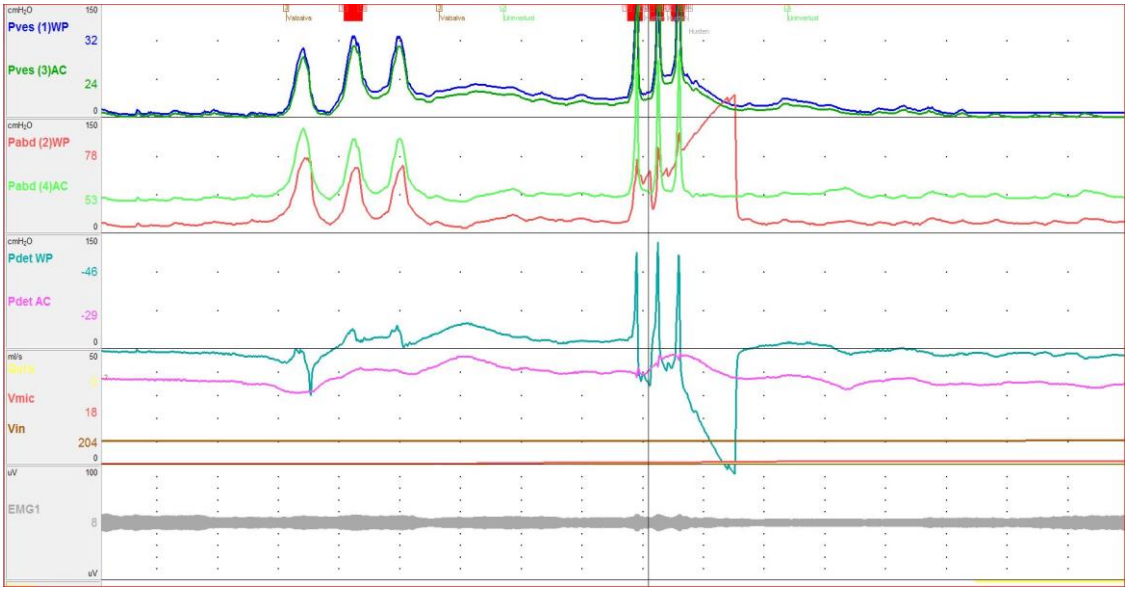

Fig. 21: An example of deformative shapes in Pabd-WFC measurement.

On linear correlation plots, a high correlation was observed between the two methods during Valsalva manoeuvres and coughs. This is accorded with the newly published article, which also showed a good correlation between the two measurements (Timothy, 2018). It seemed that they correlated better at Valsalva manoeuvres than at coughs (R^2=0.988 vs 0.972 at Pves; R^2=0.968 vs 0.943 at Pabd). In the cough test, the ACC tracings showed damped response in the Pves and Pabd measurement, especially in Pves measurement. That verified the results shown by the bench test from Cooper et al and Awada et al, which concluded that the ACC system appeared to be overdamped when performing high frequency (fast) movements, and showing a

slower response to change in pressures when compared to WFC system (Cooper, 2011; Awada, 2014).

When the results from paired sample t-test were considered, no statistically significant differences were found at Valsalva manoeuvres (p=0.43, p=0.51 p=0.85 for Pves, Pabd and Pdet respectively) between the two measurements. Mean values were nearly the same between the two measurements at Valsalva manoeuvres (39.44±23.34 cm H_2O vs 39.31 ±23.02 cm H_2O for Pves; 38.11±22.04 cm H_2O vs 37.93±21.70 cm H_2O for Pabd; 1.65 ±3.39 cm H_2O vs 1.72 ±3.85 cm H_2O for Pdet). In contrast, there was a significant difference between the two measurements at coughs (all p<0.001 for Pves, Pabd and Pdet respectively). Mean values seemed to be higher in WFC measurements than in ACC measurements (69.65±43.25 cm H_2O vs 64.59±39.21 cm H_2O for Pves; 63.01±38.67 cm H_2O vs 60.71±35.66 cm H_2O for Pabd; 6.83 ±7.82 cm H_2O vs 3.89±9.44 cm H_2O for Pdet). However, the maximum pressure difference between the two mean values is about 5 cm H_2O, it seems that it is lack of clinical meaning. In the previous clinic research, a significant difference between the two methods at Valsalva manoeuvres (P<0.001) was shown. In addition, the mean value of Pves-WFC was higher than the mean value of Pdet-ACC (0.9±7.0 cm H_2O vs 4.3±5.9 cm H_2O) in their study. On the contrary, although not statistically significant (P=0.221), a higher Pdet mean value was shown in ACC measurements than in WFC measurements at coughs (7.5±17.5 cm H_2O vs 4.0±17.9 cm H_2O; Gammie, 2016). In comparison, this study showed a similar mean value between the two measurements in Pdet at Valsalva manoeuvres (1.65±3.39 cm H_2O vs 1.72±3.85 cm H_2O), and higher Pdet mean value in WFC measurements than that in ACC measurements (6.83±7.82 cm H_2O vs 3.89±9.44 cm H_2O, P<0.001). The different results between the present study and the previous study might be due to different study design and varied set-ups. However, it appears that results from this study are closer to previous *in vitro* researches.

When Bland-Altman plots were performed, obvious differences between the two approaches were noticed. During Valsalva manoeuvres, the difference could reach up to 5.2 cm H_2O for Pves and 8.1 cm H_2O for Pabd, respectively. While in coughing, the discrepancy could be 20 cm H_2O for Pves and 19.5 cm H_2O for Pabd, respectively. This was comparable with two previous clinical studies reporting that pressure readings between air-charged and water-filled system were not directly

interchangeable (Digesu, 2014; Gammie, 2016). However, a 5.2 cm H_2O pressure difference between ACC and WFC measurement systems in Pves at Valsalva manoeuvres seems to be more acceptable in clinical practice. In the newly published article, although they stated that WFC and ACC systems were equally responsive even at coughs, the maximum difference could reach up to nearly 20 cm H_2O in Pves measurement between the two methods from Bland-Altman plots assessment. What's more, the methodology seems not correct used in their study for drawing the Bland-Altman plots, which should be taken an individual with repeated data for drawing the Bland-Altman plots (Bland, 2007).

The differences between WFC and ACC measurements by dividing it into different filled volume categories were also analyzed. Results showed a significant difference between the two different systems at 200ml±10ml in Pves measurement at Valsalva manoeuvres. The average difference was less than 2 cm H_2O, it seemed that this was clinically insignificant. The same way was applied to coughs. A statistically significant difference between the two measurements at 50±10ml, 100±10ml, 200±10ml, 300±10ml and 400±10ml in Pves, and at 200±10ml, 300±10ml in Pabd were documented, the maximum average difference was about 9 cm H_2O, indicating the two measurement methods had a larger pressure difference during coughs compared with that during Valsalva manoeuvres.

When other urodynamic events were compared, no statistically significant differences were found in all events between the two systems except in the comparison at initial resting pressure ($P<0.01$) and maximum pressure at DO ($P<0.01$). The resting Pdet recordings of WFC system were all positive, but negative for most resting Pdet recordings of ACC system. Pdet recordings seemed to be numerically bigger in the WFC system than in the ACC system, except in the comparison of pressure at Qmax, which the "changed values" were compared. One plausible explanation was probably due to relatively lower position on most occasions for rectal catheters and consequently higher static pressure was registered on rectal ACCs than on vesical ACCs, resting Pdet recordings could be negative in an ACC measurement. This also suggested that the relative catheters' position, between vesical and rectal catheters, might play an important role in the baseline pressure recordings in ACC measurement. From the Bland-Altman plots for each indication, the narrowest pressure difference interval was observed in the comparison of maximum Pdet at DO,

which LOA was -3.2-8.4 cm H_2O. Whereas, the widest pressure difference interval was observed in the comparison of resting Pdet at maximum cystometric capacity (LOA, -11.5-18 cm H_2O), which means the difference between the two measurement modalities could reach up to 18 cm H_2O in the resting Pdet measurement. What's more, at the start of the infusion in cystometric assessment, the LOA was -5.2-12.7 cm H_2O, which indicated the resting Pdet could reach up to 12.7 cm H_2O in the beginning. That confirmed the results from the previous research, which also stated that the pressure discrepancy could be up to about 10 cm H_2O between recordings from WFCs and ACCs at the start of urodynamic measurement (Gammie, 2016). Therefore, when using the air-charged system for diagnosis or evaluation with the water-filled system's cut-off values being applied, the corresponding baseline compensation should be considered as suggested by Gammie et al (Gammie, 2016). In the comparison of DO and Qmax, the "changed values" were used. On the other hand, the raw data were used in the comparison of resting Pdet at each filled volume. It indicated that although the influence of the baseline physiological reasons had been excluded when comparing the two measurements, it still showed some differences between the two systems. When comparing resting pressure data by diving them into different filled volume categories, it was shown that the average resting pressure reading at each filled volume was overall higher in ACC (Figure 16 and 17) than WFC measurements, except for the comparison at 400ml±10ml in Pves measurement, which showed a comparable average pressure readings between the two measurements. Because only 6 paired data was included in that comparison, the result should be treated cautiously. It coincided with the results from another previous clinical research, which also showed ACCs registered higher pressure recordings than WFCs (Digesu, 2014).

Although not statistically significant, it also indicated that resting Pdet for each filled volume seemed to be lower in the lying position than that in the sitting position, and tended to be negative in the lying position (Figure 19). As the reference point in the air-charged system is the catheter itself, the relative position between rectal and vesical catheters plays a role. A lower position yielded relatively higher hydrostatic pressure readings (Gammie, 2014), which led the rectal ACC registered higher pressure readings than the vesical ACC in the lying position, and consequently caused relatively negative readings in Pdet. The different baseline readings at each filled volume in lying position could be attributed to the influence of the filling.

However, we cannot draw a conclusion about that due to small population size and heterogeneity between subjects. This should be looked after in future studies.

There are some limitations should be noted in this study. First, an open catheter with perfusion for abdominal pressure measurement was used. Although, a low flow rate continuous perfusion was used during tests in case of blockage, it could not be ensured that there was no interaction between the catheter and the rectal mucosa during movements, which might result in an increased number of outliers. However, by using the “70% rule” proposed by Sullivan and manual inspection, only data with good quality were included in this study. Second, the difference in diagnostics was not compared when using the different systems, so how the difference in pressures could affect clinical diagnostics was unknown. Third, the sample size might be a limiting factor for some comparisons, for instance coughs, performed in this study.
Despite using changed values from baseline for the comparison of primary events, differences were still found in some patients. This was especially true in Pabd measurements. We have not figured out the specific reasons, but it is assumed that this is due to how the balloon interacts with vesical or rectal mucosa. This has to be kept in mind in future comparative studies while settings for Pabd measurements are developed. Future studies should concentrate on establishing typical value ranges for ACC systems. This requires a larger number of included cases in future clinical studies.

5. Summary

The aim of this study was to determine whether the air-charged and water-filled pressure readings were equivalent. A single catheter system, the commercially available 7-Fr T-Doc air-charged catheter, was tested in different scenarios (like during Valsalva and cough manoeuvres). With this catheter model, simultaneous readings of water and air pressures within the bladder could be achieved. Then the filling and voiding data recordings were compared to each other. The paired-data points of these events were evaluated using the paired t-test, Bland-Altman plots and linear correlation methods, respectively.

25 patients were recruited and examined, 21 patients were included for analysis in the end. Both sets of the system showed a good correlation at Valsalva manoeuvres (R^2=0.988, 0.972 for vesical and abdominal pressure respectively) and coughs (R^2=0.968, 0.943 for vesical and abdominal pressure respectively). Paired t-test of detrusor pressure (Pdet) showed that there was no statistically significant difference between the two measurements at Valsalva manoeuvres (p=0.85), at initial resting pressure (p=0.13), at 50±10ml resting pressure (p=0.16) and at voiding pressure at maximum flow (Qmax; p=0.51).

However, Bland-Altman plots indicated values of a given patient between the two methods could reach up to 5.2 cm H_2O and 8.1 cm H_2O in vesical and abdominal pressure measurement respectively at Valsalva manoeuvres, to 20 cm H_2O and 19.5 cm H_2O in vesical and abdominal pressure measurement respectively at coughs. Paired data, in other urodynamic events, also showed similar discrepancies between the two systems.

ACC and WFC might be interchangeable for some urodynamic parameters like Pves and Pabd at Valsalva manoeuvres, but not for fast changing pressure signals like coughs. Studies focusing ACCs are still lacking. Missing data from such studies is the main reason why ACCs currently cannot replace WFCs in conventional UDS (Abrams, 2017). However, based on data reported in this thesis, it appears that the catheter systems are equivalent when it comes to diagnosis based on patterns, like for diagnosis of urinary stress incontinence and DO. In case accurate pressure values are needed - like for diagnosis of BOO and calculation of bladder compliance - ACCs appear to be inferior compared to WFCs based on current guidelines.

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7. Appendix:

7.1Ethical proposal

Antrag an die Ethik-Kommission der Medizinischen Fakultät der Rheinischen Friedrich-Wilhelms-Universität Bonn

Evaluation der urodynamischen Messergebnisse mit besonderem Fokus auf die Vergleichbarkeit der luft- bzw. wassergefüllten Messkatheter-Befüllung

A. FORMALES

1. Bezeichnung des Vorhabens

Evaluation der urodynamischen Messergebnisse mit besonderem Fokus auf die Vergleichbarkeit der luft- bzw. wassergefüllten Messkatheter-Befüllung.

2. Verantwortlicher Leiter (Projektleiter; eigenhändige Unterschrift; Leiter der Studie kann nur ein qualifizierter Wissenschaftler sein, der bei klinischen Studien Arzt sein muss)

a) Verantwortlicher Leiter im hiesigen Prüfzentrum

Univ. - Prof. Dr. med. Ruth Kirschner-Hermanns,
Neuro-Urologischer Schwerpunkt der Klinik und Poliklinik für Urologie des UKB

b) Bei Multizenterstudien: Leiter der Klinischen Studie in Deutschland

entfällt

3. Art und Zahl der Prüfstellen bzw. beteiligte Ärzte

Univ. - Prof. Dr. med. Ruth Kirschner-Hermanns
Dr. Ruth Tabaza
Michael Kowollik
Dr. Anette Kohler
Neuro-Urologischer Schwerpunkt der Klinik und Poliklinik für Urologie des UKB 2

4. Kostenträger

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Karmeliterhöfe, Karmeliterstr. 10, 52064 Aachen
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IBAN: DE84390500001071554677, SWIFT: AACSDE33
Amtsgericht Aachen, Vereinsregisternr. 4357, Steuernr. 201/5909/4635

5. Wurde schon ein Antrag gleichen Inhaltes bei einer anderen Ethik-Kommission gestellt?

Nein

B. UNTERSUCHUNGSBESCHREIBUNG

1. Wissenschaftliche Beschreibung des Vorhabens

Durch eine Erweiterung unserer klinischen Routine wollen wir neben der Verwendung von wassergefüllten Kathetern auch „Luftkatheter“(air-charged T-Doc-Katheter) etablieren. Beide Verfahren sind von der internationalen und der Deutschen Kontinenzgesellschaft anerkannte Messverfahren.

Um unseren internen Qualitätsstandards überprüfen zu können, wollen wir Messungen mit einem zugelassenen, dualen Kathetersystem durchführen, welches die Befüllung über Wasser und den air-charged Ballon zulässt.

Unsere generierten Vergleichsdaten wollen wir, neben unserer klinischer Bewertung, ebenfalls der

Firma Laborie/MMS entgeltlich zur Verfügung stellen.
Die Patientendaten werden pseudonymiert übermittelt und bei Veröffentlichung anonymisiert dargestellt.

2. Vorlage des Prüfplans

2.1. Studiendesign

Beobachtungsstudie

2.2. Patienten

Alle Patienten, die in der Neuro-Urologie des Universitätsklinikums der Universitätsklinik Bonn und in der Neuro-Urologie des Rehabilitationsklink eine im Rahmen der routinemäßig durchgeführten klinischen Untersuchung eine urodynamische bzw. videourodynamische Untersuchung bekommen.
Eine urodynamische Untersuchung beinhaltet nach den Richtlinien der Internationalen Continence Society (ICS) einen freien Uroflow, einschließlich einer Restharnuntersuchung (zumeist durch Ultraschall), eine Zystometrie in der Füll- und in der Miktionsphase, als auch eine Urethradruckprofilmessung als Durchzugsmessung und/oder als kontinuierliche Messung während der zystometrischen Füllungsphase.
Die so ermittelten Patientendaten werden in einer Datenbank gespeichert, deren Software von der Firma MMS entwickelt wurde, welche Teil der urodynamischen Messeinheit ist. Nur die Beschäftigten der Neuro-Urologie haben im Rahmen ihrer klinischen Tätigkeit Zugang zu den Patientendaten hat.
Die für die klinische Studie wichtigen Daten werden zusätzlich in pseudonymisierter Form gespeichert, ausgewertet und gegebenenfalls weitergegeben.
Pseudonymisiert bedeutet, dass keine Angaben von Namen oder Initialen verwendet werden, sondern nur ein Nummern- und/oder Buchstabencode, evtl. mit Angabe des Geburtsjahres.
Die Daten sind gegen unbefugten Zugriff gesichert. Eine Entschlüsselung erfolgt nur unter den vom Gesetz vorgeschriebenen Voraussetzungen.
Im Rahmen einer Pilotstudie sollen Datensätze von 25 Patienten erfasst und pesudonymisiert weitergegeben werden.

2.3. Messvariablen

Wie in den Standards der ICS 2002 festgelegt

3. Vorgesehene Gesamtdauer

5 Jahre

4. Probandenauswahl (z.B. Ein- und Ausschlusskriterien)

4.1. Einschlusskriterien

- einwilligungsfähige, volljährige Patienten mit Blasenfunktionsstörung, die in der klinischen Routine urodynamisch vermessen werden

4.2. Ausschlusskriterien

• Patienten mit Harnwegsinfekten, die eine urodynamische Evaluation nicht zulassen
• Patienten die eine urodynamischen Evaluation ablehnen, bzw. der wissenschaftlichen Auswertungen ihrer Daten nicht zustimmen.
• Nichteinwilligungsfähige Patienten
• Minderjährige Patienten

5. Art der Prüfung (bei Arzneimitteln: Phase)

Diagnostische Beobachtungsstudie

6. Finden folgende Bestimmungen Anwendung?

a) Arzneimittelgesetz? **entfällt**

b) Medizinproduktegesetz? **entfällt**

c) Strahlenschutzgesetz? **entfällt**

d) Röntgenverordnung? **entfällt**

e) Medizingeräte-Verordnung? **entfällt**

7. Welche Vorprüfungen sind durchgeführt worden?

Evaluation von Urethradruckprofilmessungen wurden seit 2011 im Kontinenzzentrum Aachen an der RWTH Aachen durchgeführt und teilweise publiziert.

8. Pharmakologisch-toxikologische Prüfung:

a) durchgeführt?

b) Ergebnisse hinterlegt bei zuständiger Bundesbehörde?

c) Zusammenfassung der für die Durchführung der klinischen Überprüfung wesentlichen Ergebnisse

entfällt

9. Mögliche Komplikationen und/oder Risiken

Während der urodynamischen Evaluation bestehen durch die Katheterisierung Risiken der Entwicklung von Harnwegsinfekten. Bei Patienten mit hohem Querschnitt besteht darüber hinaus ein Risiko der autonomen Dysregulation. Die Indikation zur videourodynamischen Untersuchung wird allein nach klinischen Maßgaben gestellt.

10. Risiko-Nutzen-Abwägung

Die Indikation zur urodynamischen Evaluierung wird allein nach klinischen Kriterien gefällt – weder die Erfassung der Daten, noch die Evaluation der Daten hat weder einen Einfluss auf die Indikation noch auf die Therapieentscheidung.

11. Zwischenauswertung und Abbruchkriterien

entfällt

12. Form und Inhalt der Probandenversicherung

Nicht notwendig, weil die Untersuchungen und das Blasentraining klinisch indiziert sind und Patienten aus der Routineuntersuchung rekrutiert werden. Eine Probandenversicherung wird nicht gesondert abgeschlossen. Bei verschuldensabhängigen Zwischenfällen sind die Patienten über die übliche Haftpflicht des Hauses versichert. Eine Wegeunfallversicherung ist nicht zutreffend.

Bonn, den

Univ.-Prof. Dr. med. Ruth Kirschner-Hermanns
Neuro-Urologie
Klinik und Poliklinik für Urologie des UKB 6

Literatur

Abrams P, Cardozo L, Fall M, Griffiths D, Rosier P, Ulmsten U, van Kerrebroeck P, Victor A, Wein A. The standardisation of terminology of lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. In: Am J Obstet Gynecol. 2002 Jul;187(1):116-26.PMID: 12114899

Werner Schäfer,* Paul Abrams, Limin Liao, Anders Mattiasson, Francesco Pesce, Anders Spangberg, Arthur M. Sterling, Norman R. Zinner und Philip van Kerrebroeck Good Urodynamic Practices: Uroflowmetry, Filling Cystometry, and Pressure-Flow Studies Neurourology and Urodynamics 21:261-274 (2002)

7.2 Ethical approval

Rheinische Friedrich-Wilhelms-Universität

Medizinische Fakultät

Ethik–Kommission

53127 Bonn, den 13.01.16
Sigmund-Freud-Str. 25
Biomedizinisches Zentrum
Zimmer 2G 029

Prof. Dr. med. Kurt Racké
Vorsitzender

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KRa/MB

Ethik-Kommission - Medizinische Fakultät Bonn
Biomedizinisches Zentrum, Sigmund-Freud-Str. 25, 53127 Bonn

Frau
Prof. Dr. Ruth Kirschner-Hermanns
Urologische Klinik
Universitätsklinikum Bonn
Sigmund-Freud-Straße 25
53105 Bonn / durch Boten

Lfd. Nr. 395/15
Bitte stets angeben!

Betr.: **Ihr Antrag an die Ethik-Kommission**
Antragsteller: **Prof. Dr. Ruth Kirschner-Hermanns**
Studientitel: **Evaluation der urodynamischen Messergebnisse mit besonderem Fokus auf die Vergleichbarkeit der luft- und wassergefüllten Messkatheter-Befüllung**
Sponsor: **Förderverein zur Kontinenzforschung und Kontinenzaufklärung e.V.**

- **Checkliste/Antrag**
- **Patienteninformation und Einverständniserklärung**

Sehr geehrte Frau Kollegin Kirschner-Hermanns,

die Ethik-Kommission für klinische Versuche am Menschen und epidemiologische Forschung mit personenbezogenen Daten der Medizinischen Fakultät der Rheinischen Friedrich-Wilhelms-Universität Bonn ist nach Beratung des o.g. Antrags auf ihrer Sitzung am 06.01.2016 zu dem Beschluss gekommen, gegen die o.g. Studie keine grundsätzlichen berufsethischen oder berufsrechtlichen Bedenken zu erheben.

Vor einer abschließenden Bewertung bittet die Ethik-Kommission um Klärung bzw. Berücksichtigung folgender Punkte und um Zusendung entsprechend geänderter Unterlagen in markierter, einfacher Form.

1) Im Prüfplan wird dargelegt, dass „alle Patienten……," bei denen eine urodynamische Diagnostik durchgeführt werden soll, in die Studie eingeschlossen werden sollen. Hier ist klarzustellen, dass nur einwilligungsfähige volljährige Patienten eingeschlossen werden,

da nicht erkennbar ist, dass ein Einschluss nicht-einwilligungsfähiger Patienten für das Erreichen des Studienziels erforderlich ist.

2) Es müsste eine Informationsschrift erstellt werden, die diesen Namen auch verdient.
3) Es ist geplant, Datensätze an mögliche Kooperationspartner weiterzugeben. Hier müsste sowohl im Prüfplan als auch in der Informationsschrift beschrieben werden, wie (pseudonymisiert oder vollständig anonymisiert) diese weitergegeben werden sollen. Für die Weitergabe personenbezogener (pseudonymisierter) Daten müsste eine entsprechende Zustimmung mit der Datenschutzerklärung eingeholte werden. Die Einwilligungserklärung/Datenschutzerklärung sollte in Anlehnung an den Mustertext des Arbeitskreises für MPG-Studien formuliert werden.

Mit freundlichen Grüßen

[redacted]

Prof. Dr. K. Racké
Vorsitzender der Ethik-Kommission

Nachfolgend sind die Mitglieder der Ethik-Kommission aufgeführt, die den o. g. Antrag auf ihrer Sitzung am 06.01.2016 beraten haben:

Herr Prof. Dr. Ch. Putensen, Arzt für Anästhesiologie
Herr Prof. Dr. I. Schmidt-Wolf, Arzt für Innere Medizin
Herr Prof. Dr. H. Bönisch, Fachpharmakologe, Fachapotheker für Arzneimittelinformation
Frau Dr. A. Pralong, Medizinethikerin
Herr Prof. Dr. H.-U. Paeffgen, Jurist
Herr Dr. S. Garbe, Arzt für Radiologie
Frau L. Beste, Patientenvertreterin
Prof. Dr. K. Racké, Arzt f. Pharmakologie und Toxikologie, Vors. der Ethik-Kommission

7.3 Informed Consent Form

Patienteninformation und Einwilligungserklärung zur Teilnahme an der Studie:

Evaluation der urodynamischen Messergebnisse mit besonderem Fokus auf die Vergleichbarkeit der luft- bzw. wassergefüllten Messkatheter-Befüllung

Sehr geehrte Patientin, sehr geehrter Patient,

wir möchten Sie fragen, ob Sie bereit sind, an der nachfolgend beschriebenen klinischen Studie teilzunehmen.

Ihre Teilnahme an dieser klinischen Studie ist freiwillig. Sie werden in diese Studie also nur dann einbezogen, wenn Sie dazu schriftlich Ihre Einwilligung erklären. Sofern Sie nicht an der klinischen Studie teilnehmen oder später aus ihr ausscheiden möchten, erwachsen Ihnen daraus keine Nachteile.

Sie wurden bereits auf die geplante Studie angesprochen. Der nachfolgende Text soll Ihnen die Ziele und den Ablauf erläutern. Anschließend wird ein Prüfarzt das Aufklärungsgespräch mit Ihnen führen. Bitte zögern Sie nicht, alle Punkte anzusprechen, die Ihnen unklar sind. Sie werden danach ausreichend Bedenkzeit erhalten, um über Ihre Teilnahme zu entscheiden.

1. Warum wird diese Prüfung durchgeführt?

Bislang hat man bei Ihrer Erkrankung in Deutschland zumeist einen Wasser-gefüllten Messkatheter für urodynamische Messungen verwendet. Weltweit werden urodynamischen Messung auch mittels eines Miniatur mit Luft-gefülltem Ballon (2,67 mm Durchmesser), einem sogenannten ‚air-charged Messkatheter' durchgeführt. Dieser Messkatheter, der weltweit verwendet und auch in Deutschland zugelassen ist, kann auch zur herkömmlichen Messung mit Wasser verwandt werden.

Im Rahmen dieser Studie wird ein sogenannter ‚air-charged'- Messkatheter verwendet, der Messung mit Luft oder Wasser ermöglicht. Mit dieser Studie erhoffen wir uns, die Qualität der Messmethode des ‚air-charged Messkatheters mit dem der ‚Wasser-Messung' als Gold-Standard der International Continence Gesellschaft' der verschiedenen Messmethoden zu vergleichen.

2. Erhalte ich das Prüfprodukt auf jeden Fall?

Bei jedem Studienteilnehmer wird der Air-charged T-Doc Messkatheter eingesetzt und urodynamische Blasendruckmessungen nach Standard der Internationalen Kontinenzgesellschaft durchgeführt.

3. Wie ist der Ablauf der Studie und was muss ich bei Teilnahme beachten?

Sie kommen für diese Studie nur dann in Frage, wenn ihre Beschwerden eine Untersuchung der Blasenfunktion mittels urodynamischer Messung notwendig machen. Bei Ihnen wird die Messung im Rahmen der klinischen Routine also nur durchgeführt, wenn die behandelnden Ärzte diese als notwendig erachten.
Der verwendete Messkatheter enthält zwei Kanäle, ein Luft- und ein Wasser-gefüllten, sodass während der Messung mittels Schalter/mechanischem Element zwischen beiden Messmethoden gewechselt werden kann. Eine erneute Katheterisierung ist deswegen nicht nötig.

4. Welchen persönlichen Nutzen habe ich von der Teilnahme an der Studie?

Sie werden durch die Teilnahme an dieser Studie außer einer ärztlichen Untersuchung voraussichtlich keinen persönlichen Gesundheitsnutzen haben. Die Ergebnisse der Studie können aber möglicherweise dazu beitragen, die Behandlung von Blasenfunktionsstörungen zukünftig besser beurteilen zu können.

5. Welche Risiken sind mit der Teilnahme an der Studie verbunden?

Die Anwendung des air-charged T-doc Messkatheter führt zu keinen besonderen Risiken.
Bitte teilen Sie den Mitarbeitern der Prüfstelle *alle* Beschwerden, Erkrankungen oder Verletzungen mit, die im Verlauf der klinischen Prüfung auftreten. Falls diese schwerwiegend sind, teilen Sie den Mitarbeitern der Prüfstelle diese bitte umgehend mit, ggf. telefonisch.

6. Welche anderen Behandlungsmöglichkeiten gibt es außerhalb der Studie?

Zur Beurteilung Ihrer Erkrankung stehen auch die folgenden Möglichkeiten zur Verfügung:
Messung mittels Wasser-gefüllten Messkatheters.

7. Wer darf an dieser klinischen Studie nicht teilnehmen?

An dieser klinischen Studie dürfen Sie nicht teilnehmen, wenn Sie gleichzeitig an anderen klinischen Prüfungen oder anderen klinischen Forschungsprojekten teilnehmen oder vor kurzem teilgenommen haben. Zudem muss eine urodynamische Messung induziert sein.

8. Entstehen für mich Kosten durch die Teilnahme an der klinischen Studie? Erhalte ich eine Aufwandsentschädigung?

Durch Ihre Teilnahme an dieser klinischen Studie entstehen für Sie keine zusätzlichen Kosten.

Für Ihre Teilnahme an dieser klinischen Studie erhalten Sie keine Aufwandsentschädigung.

9. Bin ich während der klinischen Studie versichert?

Da bei dieser Studie zwei etablierte Messverfahren verglichen werden und kein erhöhtes Risiko vorliegt, wird keine Patientenversicherung abgeschlossen. Es greift die allgemeine Haftpflichtversicherung des Hauses zur Durchführung der urodynamischen Messung.

10. Werden mir neue Erkenntnisse während der klinischen Studie mitgeteilt?

Sie werden über neue Erkenntnisse, die in Bezug auf diese klinische Studie bekannt werden und die für Ihre Bereitschaft zur weiteren Teilnahme wesentlich sein können, informiert. Auf dieser Basis können Sie dann Ihre Entscheidung zur weiteren Teilnahme an dieser klinischen Studie überdenken.

11. Wer entscheidet, ob ich aus der klinischen Prüfung ausscheide?

Sie können jederzeit, auch ohne Angabe von Gründen, Ihre Teilnahme beenden, ohne dass Ihnen dadurch irgendwelche Nachteile bei Ihrer medizinischen Behandlung entstehen.

Unter gewissen Umständen ist es aber auch möglich, dass der Prüfarzt oder der Sponsor entscheidet, Ihre Teilnahme an der klinischen Studie vorzeitig zu beenden, ohne dass Sie auf die Entscheidung Einfluss haben. Die Gründe hierfür können z. B. sein:

- Ihre weitere Teilnahme an der klinischen Studie ist ärztlich nicht mehr vertretbar;
- es wird die gesamte klinische Studie abgebrochen.

Sofern Sie sich dazu entschließen, vorzeitig aus der klinischen Studie auszuscheiden, oder Ihre Teilnahme aus einem anderen der genannten Gründe vorzeitig beendet wird, ist es für Ihre eigene Sicherheit wichtig, dass Sie sich einer empfohlenen abschließenden Kontrolluntersuchung unterziehen.

Der Prüfarzt wird mit Ihnen besprechen, wie und wo Ihre weitere Behandlung stattfindet.

12. Was geschieht mit meinen Daten?

Während der klinischen Prüfung werden medizinische Befunde und persönliche Informationen von Ihnen erhoben und in der Prüfstelle in Ihrer persönlichen Akte niedergeschrieben oder elektronisch gespeichert. Die für die klinische Studie wichtigen Daten werden zusätzlich in pseudonymisierter Form gespeichert, ausgewertet und gegebenenfalls weitergegeben.

Pseudonymisiert bedeutet, dass keine Angaben von Namen oder Initialen verwendet werden, sondern nur ein Nummern- und/oder Buchstabencode, evtl. mit Angabe des Geburtsjahres.

Die Daten sind gegen unbefugten Zugriff gesichert. Eine Entschlüsselung erfolgt nur unter den vom Gesetz vorgeschriebenen Voraussetzungen.

Die gesetzlichen Bestimmungen enthalten nähere Vorgaben für den erforderlichen Umfang der Einwilligung in die Datenerhebung und -verwendung. **Einzelheiten, insbesondere zur Möglichkeit eines Widerrufs, entnehmen Sie bitte der Einwilligungserklärung, die im Anschluss an diese Patienteninformation abgedruckt ist.**

13. Was geschieht mit meinen Aufnahmen mit bildgebenden Verfahren?

Die Aufnahmen mit bildgebenden Verfahren werden nach Abschluss der Prüfung in folgender Weise aufbewahrt:
Die Daten werden für zehn Jahre pseudonymisiert in den Räumen der Neuro-Urologie archiviert.

14. An wen wende ich mich bei weiteren Fragen?

Beratungsgespräche am Studienzentrum

Sie haben stets die Gelegenheit zu weiteren Beratungsgesprächen mit dem auf Seite 1 genannten oder einem anderen Prüfarzt, um weitere Fragen im Zusammenhang mit der klinischen Prüfung zu klären. Auch Fragen, die Ihre Rechte und Pflichten als Patient und Teilnehmer an der klinischen Studie betreffen, werden gerne beantwortet.

Einwilligungserklärung zur Teilnahme an der Studie

Evaluation der urodynamischen Messergebnisse mit besonderem Fokus auf die Vergleichbarkeit der luft- bzw. wassergefüllten Messkatheter-Befüllung

Einwilligungserklärung

.....
Name des Patienten in Druckbuchstaben

geb. am ..... Teilnehmer-Nr. .....

Ich bin in einem persönlichen Gespräch durch den Prüfarzt

.....
Name der Ärztin / des Arztes

ausführlich und verständlich über das Prüfprodukt und die Vergleichstherapie sowie über Wesen, Bedeutung, Risiken und Tragweite der klinischen Prüfung aufgeklärt worden. Ich habe darüber hinaus den Text der Patienteninformation sowie die hier nachfolgend abgedruckte Datenschutzerklärung gelesen und verstanden. Ich hatte die Gelegenheit, mit dem Prüfarzt über die Durchführung der klinischen Prüfung zu sprechen. Alle meine Fragen wurden zufrieden stellend beantwortet.

Möglichkeit zur Dokumentation zusätzlicher Fragen seitens des Patienten oder sonstiger Aspekte des Aufklärungsgesprächs:

Ich hatte ausreichend Zeit, mich zu entscheiden.

Mir ist bekannt, dass ich jederzeit und ohne Angabe von Gründen meine Einwilligung zur Teilnahme an der Prüfung zurückziehen kann (mündlich oder schriftlich), ohne dass mir daraus Nachteile für meine medizinische Behandlung entstehen.

Datenschutz:

Mir ist bekannt, dass bei dieser klinischen Prüfung personenbezogene Daten, insbesondere medizinische Befunde über mich erhoben, gespeichert und ausgewertet werden sollen. Die Verwendung der Angaben über meine Gesundheit erfolgt nach gesetzlichen Bestimmungen und setzt vor der Teilnahme an der klinischen Prüfung folgende freiwillig abgegebene Einwilligungserklärung voraus, das heißt ohne die nachfolgende Einwilligung kann ich nicht an der klinischen Prüfung teilnehmen.

1. Ich erkläre mich damit einverstanden, dass im Rahmen dieser klinischen Prüfung personenbezogene Daten, insbesondere Angaben über meine Gesundheit, über mich erhoben und in Papierform sowie auf elektronischen Datenträgern im interdisziplinären Kontinenz- und Beckenbodenzentrum, Bonn aufgezeichnet werden. Soweit erforderlich, dürfen die erhobenen Daten pseudonymisiert (verschlüsselt) weitergegeben werden:
   a) an Laborie/MMS, den Auftraggeber oder eine von diesem beauftragte Stelle zum Zwecke der wissenschaftlichen Auswertung,
   b) im Falle unerwünschter Ereignisse: an Laborie/MMS, den Auftraggeber und die zuständige Landesbehörde.

2. Außerdem erkläre ich mich damit einverstanden, dass autorisierte und zur Verschwiegenheit verpflichtete Beauftragte des Auftraggebers sowie die zuständigen Überwachungsbehörden in meine beim Prüfarzt vorhandenen personenbezogenen Daten, insbesondere meine Gesundheitsdaten, Einsicht nehmen, soweit dies für die Überprüfung der ordnungsgemäßen Durchführung der Studie notwendig ist. Für diese Maßnahme entbinde ich den Prüfarzt von der ärztlichen Schweigepflicht.

3. Ich bin darüber aufgeklärt worden, dass ich jederzeit die Teilnahme an der klinischen Studie beenden kann. Beim Widerruf meiner Einwilligung, an der Studie teilzunehmen, habe ich das Recht, die Löschung aller meiner bis dahin gespeicherten personenbezogenen Daten zu verlangen.

4. Ich erkläre mich damit einverstanden, dass meine Daten nach Beendigung oder Abbruch der Prüfung mindestens zehn Jahre aufbewahrt werden. Danach werden meine personenbezogenen Daten gelöscht, soweit nicht gesetzliche, satzungsmäßige oder vertragliche Aufbewahrungsfristen entgegenstehen *(vertraglich vereinbarte Fristen müssen hier genannt werden)*.

5. Ich bin damit einverstanden, dass mein Hausarzt

   .....
   Name

   über meine Teilnahme an der klinischen Prüfung informiert wird (falls nicht gewünscht, bitte streichen).

Ich erkläre mich bereit,an der oben genannten klinischen Studie freiwillig teilzunehmen.

Ein Exemplar der Patienten-Information und –Einwilligung habe ich erhalten. Ein Exemplar verbleibt im Prüfzentrum.

.....
Name des Patienten in Druckbuchstaben

....
Datum Unterschrift des **Patienten**

Ich habe das Aufklärungsgespräch geführt und die Einwilligung des Patienten eingeholt.

.....
Name des Prüfarztes/der Prüfärztin in Druckbuchstaben

....
Datum Unterschrift des aufklärenden **Prüfarztes/der Prüfärztin**

7.4 Clinic Review Form (CRF)

Visit 01/02	SITE-SUBJECT ID
	Bonn-_ _ _

SUBJECT INFORMATION

SUBJECT SEX (tick box)	MALE		FEMALE	
SUBJECT AGE AT TIME OF CONSENT				

INCLUSION CRITERIA

PATIENT NORMALLY INDICATER FOR URODYNAMICS EVALUATION? (tick box)	YES		NO	
ADULT PATIENT, 21 years or older				

EXCLUSION CRITERIA

PATIENT SUFFERS FROM BLADDER INFECTIONS (NOT INCLUSDING PATIENTS WITH ASYMPTOMATIC BACTERURIA, PROPHYLAXIS WITH AN ANTIBIOTIC IS AT THE DISRETION OF THE PHYSICIAN)? (tick box)	YES		NO	
PATIENT SUFFERS FROM STRICTURES IN THE URETHRA? (tick box)	YES		NO	
PATIENT IS PREGNANT	YES		NO	
PATIENT REQUIRES SUPRAPUBIC CATHETER	YES		NO	

VISIT DETAILS

DATE OF INFORMED CONSENT		DATE OF VISIT 1	

NOTES-Relevant treatments and ALL medications

DATE OF VISIT 2			(DD/MM/YYYY)	
HAS THE SUBJECT HAD A CHANGE IN MEDICATION? (tick box)	YES		NO	

INITIAL UROFLOW

FILE NAME OF URFLOW TRACING	
FILE NAME OF URFLOW DATA EXPORT	
PVR VOLUME(ml)	

CYSTOMETROGRAM (CMG)

All volume to be entered in mL. Time observed refers to the study time on the tracing

FILE NAME OF CMG TRACING	
FILE NAME OF CMG DATA EXPORT	

QUALITY CONTROL CHECKS

DO 3 COUGHS AND VALSALVA SHOW PDET SUBTRACTION WITHIN 5CM H_2O (tick box)	YES		NO	

PLANNED VOLUME RECORDINGS FOR RESTING, COUGH AND VALSALVA MEASUREMENTS

Approximate Volume(mL)	Actual Volume (mL)	NOTES(indicate if not marked on tracing
50		
200		
MBC		

CLINICAL IMPRESSIONS

DETRUSOR OVERACTIVITY		
	Time Observed	
FIRST SENATION		
FIRST URGENCY		
CAPACITY		

VOIDING PRESSURE STUDY

VPS			
	Study Time	Any Readjustments Made	Comments (indicate if not marked on tracing)
Start of VPS (Permission to Void)			

PATIENT/PRESSURE LINE MOVEMENT (ACTIFACTS)			
Description	Time Observed	Channel (s)	Any Readjustments Made

NOTES

DETAILS OF ANY ERRORS/PROBLEMS/DEVIATIONS (please describe)

PERSONNEL COMPLETING CRF	PRINT NAME		DATE	
	SIGATURE			

This form has been reviewed for accuracy and completeness				
PRINCIPLE INVESTIGATR	PRINT NAME		DATE	
	SIGNATURE			
SPONSOR (Laborie)	PRINT NAME		DATE	
	SIGNATURE			

8. Acknowledgement

My sincere gratitude to all of you. Without you, this work would not have been possible:

Prof. Dr. med. Ruth Kirschner-Hermanns

Dr. med. Michael Kowollik

Dr. med. Ruth Tabaza

Dr. Maximilian Schwan

Dr. Bruna M. Couri

Dr. rer. medic. Nadine Leistner

Tania Löhr

Antje Freund

Petra Wennemann

Veronica Ciolfi