

Subtle errors of bladder wall thickness measurement have a significant impact on the calculation of ultrasound-estimated bladder weight. A pilot study

Vasileios I. Sakalis¹, Vasileios Sfiggas², Ioannis Vouros², Georgios Salpiggidis², Athanasios Papathanasiou², Apostolos Apostolidis³

¹Department of Urology, General Hospital of Thessaloniki, Agios Pavlos, ²Department of Urology, General Hospital of Thessaloniki, Hippokrateion, ³Department of Urology, 2nd University Hospital of Thessaloniki, Papageorgiou, Thessaloniki, Greece.

Abstract

Aims: Ultrasound-estimated bladder weight (UEBW), is an emerging diagnostic tool, which has been used in both males and females with lower urinary tract dysfunction. The currently acknowledged UEBW calculation methods rely on the accurate measurement of bladder wall thickness (BWT). We aim to identify if subtle errors in BWT measurement have a significant impact on UEBW calculations. **Materials and methods:** Twenty patients were randomly selected from an overactive bladder patient cohort. The primary endpoint was to identify the range of false BWT measurements outside which significant changes in UEBW calculation occur. We used the Kojima method and a semi-automatic 3-D model that is based on Chalana's principle. Measurements were performed using the correct BWT and a series of faulty calculations from +0.5 mm to -0.5 mm using steps of 0.05 mm from true BWT. The effect of a fixed 0.5 mm BWT error was checked in bladder volumes above and below 250 ml and in three UEBW groups (<35 gr; 36-50 gr; >51gr). **Results:** BWT measurement errors above 0.25 mm cause statistically significant changes in UEBW calculation when a 3-D model is used and errors above 0.15 mm when Kojima's method is used. At a fixed BWT error of 0.5 mm and bladder volume <250 ml, there is a 23.76% deviation from true UEBW, while at volumes >250 ml the deviation is 32.72%. The deviation is inversely proportional to the UEBW result, and heavier bladders deviate less. **Conclusions:** UEBW is a promising diagnostic tool, but small errors in BWT measurement might cause significant deviation from the true values. A 3-D calculation model appears to minimize such risks.

Keywords: ultrasound; bladder weight; bladder wall thickness; error

Introduction

Over the past decade, the interest for bladder wall thickness (BWT) and detrusor wall thickness (DWT) measurements has grown rapidly. Their potential use as add-ons to uroflowmetry and conventional ultrasonography, has initiated a quest for their diagnostic validity in

different types of lower urinary tract problems in both genders [1,2]. Even if formal standardization is still lacking, numerous studies have been published so far, using these modalities for diagnostic purposes and for the assessment of treatment efficacy. It has been proved that a urodynamic diagnosis of detrusor overactivity (DO) correlates well with BWT and DWT measurements [3-6]. A small study could not distinguish between DO and bladder outlet obstruction (BOO) in males [1]. A recent meta-analysis on non invasive diagnostic tests in males with lower urinary tract symptoms (LUTS), did not find any threshold or cut-off value that can be safely used [7].

The principle of BWT and DWT measurement is that muscle thickening should compensate the increased peripheral resistances, in a similar manner to the cardiac muscle, as a consequence of an abnormally high after-

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Corresponding author: Vasileios I. Sakalis MSc, FEBU, FRCS

Department of Urology, General Hospital of

Thessaloniki, Agios Pavlos,

161 Ethnikis Antistasis, Thessaloniki,

Greece, POB 551 34

Phone: +30 2313 304676, Mob: +30 6987 402020

E-mail: vsakkalis@hotmail.com

load [8,9]. Morphological studies have shown that the thickening is a dual effect of smooth muscle hypertrophy and collagen deposition [8]. Animal studies have demonstrated bladder wall hypertrophy and hence increased bladder weight following partially induced BOO, within as little as 2 weeks [10].

The bladder wall appears on ultrasound (US) as a three-layered structure with the hypoechoic detrusor between the two hyperechoic layers that represent the mucosa and the serosa [1]. Various techniques have been proposed to measure BWT and DWT, using different approaches (transvaginal, transperineal or suprapubic), with different probes (3.5 MHz, 5 MHz, or 7.5 MHz) in either an empty bladder or in comfortable filling volumes [11]. The original approach in females measured BWT transvaginally at three areas with empty bladder, and the BWT was the average of these measurements [12]. In men, Oelke et al proposed a method using a 7.5 MHz probe suprapublically which measures anterior bladder wall thickness at 250 ml filling volume [13].

Ultrasound-estimated bladder weight (UEBW) concept has been advocated as a more reliable measure of bladder wall hypertrophy, because it can be calculated regardless of the degree of bladder filling. UEBW has been used as a diagnostic tool in males or females with LUTS, as a predictor of the outcome or as a monitoring tool [1].

Up to date, there are two methods for UEBW calculation. The Kojima method considers the bladder as a perfect sphere and calculates UEBW when bladder volume and BWT are known [14]. The Chalana method, which is an automatic measurement from 3-Dimensional (3-D) US, based on the calculation of bladder surface [3]. Although their principle of measurement differs, they both rely on an accurate BWT measurement. The majority of the relevant publications are based on Chalana's principle, which lacks formal standardization.

Cut-off values for BWT, DWT, and UEBW are not strictly set. None of the studies published so far have quantified the measurement error and how it influences the final values of the analysed parameters. In this pilot study, we aim to investigate if subtle errors of BWT measurement affect the UEBW calculation and to assess the level of the BWT error which does not produce statistically significant changes in UEBW.

Materials and methods

Patient sample

Twenty male patients were randomly selected from an overactive bladder patient cohort of more than one-hundred fully investigated patients with cysto-manometry and US studies, which were performed before and

after combined pharmacologic intervention with an alpha blocker (Tamsulosin) and an anticholinergic (Solifenacin). It is a homogenous group of patients, with marked storage-type LUTS (mainly urgency, possibly accompanied by micturition frequency, nocturia and/or urgency-associated incontinence), prostate volume >30 ml, postvoid residual <100 ml, prostate specific antigen <4 ng/ml, maximum flow rate >10 ml/sec, without neurological problems and free of urinary tract infections or urinary tract malignancies. We used the General Electronic Logic E9 ultrasound device, equipped with a 3.5 MHz and an 8.0 MHz transabdominal and a 7.5 MHz transrectal probes. All measurements were performed by two physicians and the results were the means of the two measurements. All patients gave their informed consent, according to the World Medical Association Declaration on Helsinki, revised in 2000, Edinburgh. The study was approved by the local Ethics Committee.

The primary endpoint of this study was to identify the arithmetic range of BWT measurements above which statistically significant changes in UEBW calculation occur. Secondary end-points were the comparison of subtle errors effect in different UEBW groups, in different volumes of the bladder filling and between the two available techniques. For this reason, we evaluated sequential calculations of UEBW, using false BWT values with an increment 0.05 mm above and below the true BWT value. We used the Kojima method or spheroidal model and a 3-D method which is based on Chalana's principle [3]. This 3-D method is a semi-automatic calculator of UEBW that allows the user to interfere with multiple parameters such as BWT, bladder volume and bladder surface.

Measurement of bladder wall thickness

BWT was measured suprapublically using the 8.0 MHz probe. This frequency can image pelvic organs with satisfactory resolution (<0.13 mm), including the anterior bladder wall even in obese individuals [13,15]. A single perpendicular focused image showing 2 hyperechoic lines, representing the mucosa and the adventitia, and a middle hypoechoic area representing the detrusor muscle were considered adequate (fig 1) [13]. According to the standardization of International Continence Society (ICS) on imaging, BWT represents the average of three measurements on the anterior bladder wall with the bladder filled at more than 50% of normal capacity or more than 250 ml [13,16]. False measurements of transversalis fascia echo or median umbilical ligament echo were avoided [13]. Since many of our subjects presented with small bladder volumes, the BWT was measured at the level of normal desire of bladder fullness.

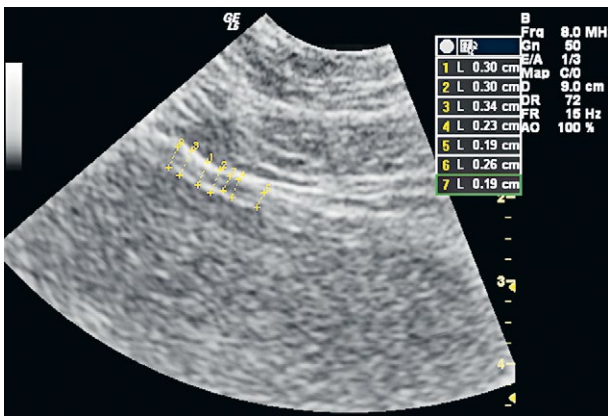


Fig 1. Ultrasonographic image of bladder wall using an 8.0 MHz probe and measurement of bladder wall thickness (measurements 1-3) and detrusor wall thickness (measurements 4-7).

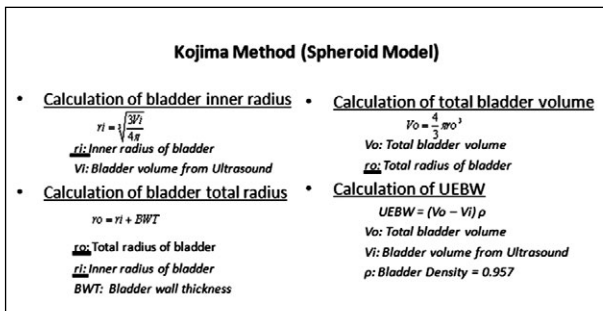


Fig 2. The mathematical calculations of spheroidal model of Kojima.

Measurement of ultrasound estimated bladder weight by the Kojima method

On the assumption that the bladder is a perfect sphere, Kojima et al estimated bladder weight when volume and BWT are known [14]. The respective calculations in our patient sample are shown in figure 2.

Measurement of ultrasound estimated bladder weight using the 3-D bladder Model based on Chalana’s principle

According to the ICS subcommittee on imaging standardisation, ‘the most accurate technique for measuring the volume of an irregular object is the step sectioning and integration of the area on each side’ [1]. This step-sectioning or planimetric volumetric approach was first described by Watanabe et al in 1982 [17]. It involves the volume calculation of each separate slice and the total volume of the organ under evaluation, results from the sum of each separate volumetry. The technique is implemented in various measurements, such as volume measurements of the urinary bladder, prostate gland, renal parenchyma, and the cardiac left ventricle from ultrasound images.

A 3.5 MHz probe was used to acquire images for further analysis. The probe was placed 2 cm above pubis symphysis and the bladder was scanned from the bladder neck to the dome to obtain parallel images by a step of 8 mm, using a stabilization stepper (Accucare by Multi-purpose Workstation) designed for transperineal template biopsies, which has been modified to hold the convex probe as well. This distance was selected to reduce the investigation time and patient’s discomfort. A smaller step size would lead to a larger amount of images, increase the investigation time, and potentially be negatively influenced by the subject’s movements, while a larger step size would reduce the available information. The series of planimetric images were saved in DICOM format for further analysis.

For each bladder section image, the inner bladder contour was manually delineated and segmented. Considering the step length (8 mm), a small cylinder was triangulated for every section/step using MATLAB R2012a (Matrix Laboratory, Mathworks) and using C++ computing language a 3D model was developed [18]. The bladder surface area (BSA) was calculated by adding the triangulated surface area of each cylinder. The UEBW was calculated from the following formula $UEBW = BSA \times BWT \times \rho$, where ρ is the density of the bladder [14].

Details of the comparison processing

For each patient, we calculated the true UEBW, based on the true BWT measurement, using both techniques Kojima’s and 3D model. Then, 20 additional false UEBW measurements were performed using incorrect BWT measurements at 0.05 mm step apart from the true BWT, 10 of them with a positive increment up to + 0.5 mm and another 10 with a negative step down to -0.5 mm. At the end, each patient had 21 UEBW calculations using the Kojima method and 21 UEBW calculations using the 3-D model. The Kojima and 3-D simulations were automated on MATLAB (Matrix Laboratory, Mathworks) [18]. Mean percentage deviation from true UEBW calculation was assessed.

Each patient was then allocated to one of three groups based on UEBW: Group I (UEBW up to 35 gr), Group II (UEBW 36 – 50 gr), and Group III (UEBW more than 51 gr). The mean percentage deviation was calculated for each group. In addition, the patients were allocated to two groups, based on the initial bladder volume (Group 1: Bladder Volume <250 ml, Group 2: Bladder Volume >250 ml).

Statistical analysis

The statistical analysis was performed using SPSS 20.0 (IBM Corporation). Intragroup variability was assessed by t-test and intergroup variability by Mann-Whitney test. A baseline value was considered as the

true UEBW calculation, when the true BWT was used. Statistical significance was set at $p < 0.05$ values.

Results

The baseline characteristics of the study group are shown in table I. Mean bladder volume at examination was 242.17 ml (range 100-528 ml). Using sequential calculations of UEBW with incorrect BWT measurements with a 0.05 mm increment step from true BWT, we found that errors up to 0.2 mm in BWT measurement do not cause significant changes in the 3-D calculation of UEBW. An error of 0.25 mm or more, leads to a statistically significant difference ($p < 0.001$) from the true value of UEBW, with a mean difference of 4.08%. It seems that the range of error in BWT measurement to avoid incorrect UEBW measurements is from -0.2 mm to +0.2 mm. Using the Kojima method, incorrect BWT measurements from 0.15 mm above or below the true BWT produce significantly different UEBW results (table II).

Table III, compares the mean percentage deviations from true UEBW measurement (baseline) in different UEBW groups, when there is error in the BWT measurement at 0.5 mm. Both groups show that deviation is inversely proportional to the UEBW value and heavier bladders tend to deviate less. 3-D UEBW calculation deviates less compared to the Kojima method but both

are statistically significantly different from baseline ($p < 0.05$). At the extreme values, the heaviest bladder weighed 115.73 gr, with the 3-D model showing a mean deviation of 17.54%, an increment deviation of 7.89% and a decrement deviation of 8.74%. On the other extreme, the lightest bladder weighed 22.42 gr, with the 3-D model showing a mean deviation of 32.25%, an increment deviation of 14.52% and a decrement deviation of 17.65%.

Table I. Baseline characteristics of the study group

	Mean (range)
Age (years)	70.25(49-85)
Bladder volume (ml)	242.17(100-528)
BWT (mm)	3.065(1.4-5.2)
DWT (mm)	1.735(0.7-3.825)
UEBW Kojima (gr)	53.32(29.3-125.70)
UEBW 3-D (gr)	47.74(22.4-115.7)
Volume prostate (ml)	38.34(30-83.9)
PSA (ng/ml)	2.19(0.2-4.0)
Uroflow (ml/sec)	13.26(10-24)
BOOI	63.88(12-164.8)
BCI	134.97(63-218)
IPSS	21.16(9-28)

BWT: Bladder wall Thickness; DWT: Detrusor wall thickness; UEBW: Ultrasound-estimated bladder weight; PSA: Prostate Specific Antigen; BOOI: Bladder outlet obstruction index; BCI: Bladder contractility Index; IPSS: International prostate symptoms score

Table II. Comparison of the mean percentage deviation based on the arithmetic deviation from the true BWT.

	Mean (SD) Kojima	P value	Mean (SD) Planimetry	P value
BWT - 0.5	43.42 (19.87)	0.001	39.58 (18.57)	0.001
BWT - 0.45	44.40 (20.01)	0.001	40.23 (18.74)	0.001
BWT - 0.4	44.54 (20.69)	0.001	41.21 (18.86)	0.001
BWT - 0.35	45.88 (20.25)	0.001	41.56 (18.74)	0.001
BWT - 0.3	47.37 (20.45)	0.001	42.84 (19.17)	0.001
BWT - 0.25	48.36 (20.61)	0.001	43.66 (19.33)	0.001
BWT - 0.2	49.37 (20.77)	0.001	44.48 (19.49)	0.059
BWT - 0.15	50.35 (20.94)	0.001	45.29 (19.66)	0.092
BWT - 0.1	51.35 (21.10)	0.291	46.11(19.84)	0.388
BWT - 0.05	52.79 (21.25)	0.678	46.93 (20.02)	0.548
True BWT	53.36 (21.46)	-	47.74 (20.20)	-
BWT + 0.05	52.81 (22.38)	0.724	48.56 (20.39)	0.467
BWT + 0.1	55.37 (21.82)	0.342	49.37 (20.58)	0.201
BWT + 0.15	55.24 (21.15)	0.001	49.69 (21.16)	0.112
BWT + 0.2	57.39 (22.21)	0.001	51.00 (20.98)	0.081
BWT + 0.25	58.41 (22.41)	0.001	51.83 (21.18)	0.001
BWT + 0.3	59.43 (22.61)	0.001	52.64 (21.39)	0.001
BWT + 0.35	60.45 (22.81)	0.001	53.46 (21.60)	0.001
BWT + 0.4	61.48 (23.02)	0.001	54.67 (21.82)	0.001
BWT + 0.45	63.00 (23.15)	0.001	55.09 (22.04)	0.001
BWT + 0.5	63.48 (23.44)	0.001	55.31 (22.48)	0.001

BWT: Bladder wall thickness (mm), SD: Standard Deviation

There is a statistically significant difference in the mean deviation when bladder volume is considered. Table IV, shows the comparison for volumes up to 250 ml and 250 ml or more when there is an error in BWT at 0.5 mm. It appears that deviation is proportional to filling volumes. Mean percentage deviation from true UEBW measurement at 0.5 mm BWT error was 23.76% in bladder volumes less than 250 ml and 32.72% in bladder volumes higher than 250 ml. Both changes were significantly different from baseline ($p < 0.01$).

Discussions

This study has shown that subtle changes of BWT measurement may significantly affect UEBW calculation. Both techniques used showed a significant ($p < 0.001$) deviation from baseline in UEBW calculation, when a BWT error from the true value is 0.25 mm or more for the 3-D calculation and 0.15 mm or more for the Kojima method. We thus assume that subtle errors up to 0.15 mm are ‘safe’ and do not cause statistical significant changes in UEBW calculation with either method. As expected, Kojima’s spheroidal method is more sensitive to small BWT changes when compared to the 3-D method due to the volume formula effect that raises BWT measurement to the third power [6].

We have also demonstrated that thicker and heavier bladders tend to deviate less from true values. This is due

to the percentage changes, since an error of 0.5 mm in BWT measurement of a 5 mm-thick wall represents a 10% deviation while the same error in a 2 mm thick wall represents a 25% deviation. Table III shows that a 0.5 mm error in BWT causes 27.89% deviation in a heavy bladder with UEBW >51 gr, while the same error causes 33.6% deviation in a light bladder weighing <35 gr. These deviations are proportional with smaller errors. At 0.5 mm BWT error there is 12.55% deviation in UEBW >51 gr and 15.11% deviation in UEBW <35 gr.

Bladder filling volumes affect also the true UEBW. Oelke et al found that BWT is stable at filling volumes 250 ml to 400 ml [11]. Therefore, any deviation from baseline measurements could be attributed to volume changes. The Kojima method is affected by volume changes as one gathers by its calculation formula. The 3-D method is affected less, since it uses the triangulated bladder surface area. Yet, subtle changes (0.5 mm) in BWT measurement cause a 32.72% deviation from the true UEBW value when the 3-D method is applied in volumes higher than 250mls and 23.76% deviation at volumes less than 250 ml. These changes are significant from baseline ($p = 0.017$ and $p = 0.024$ respectively).

Automatic measurement systems have several advantages [19]. They are user-friendly, hand-held devices, typically used by non-specialized individuals, and reduce the need for sophisticated calculations. It should be noted that the vast majority of studies including UEBW are on

Table III. Comparison of the mean percentage deviation in different groups based on bladder weight (Group I UEBW up to 35gr; Group II UEBW 36-50 gr; Group III UEBW more than 51 gr), with an error of BWT measurement at 0.5 mm.

		Group I (n=6)	Group II (n=8)	Group III (n=6)
Kojima	MPD (range)	39.1* (30.71-53.65)	33.46* (27.85 -38.47)	28.71* (21.56-46.52)
	SD	8.87	4.43	10.64
	MPD increment	17.86*	15.27*	13.1*
	MPD decrement	22.49*	18.32*	15.57*
3D model	MPD (range)	33.59* (26.32-52.63)	31.64* (25.64-37.03)	25.22* (15.6-45.45)
	SD	10.86	4.78	12.53
	MPD increment	15.11*	14.24*	10.81\$
	MPD decrement	19.01*	17.32*	14.12\$

* $p < 0.01$ from True UEBW calculation; \$ $p = 0.035$ from True UEBW calculation; n- number of patients; BWT: Bladder Wall thickness; UEBW: Ultrasound Estimated Bladder weight; SD: standard deviation; MPD: mean percentage deviation (%)

Table IV. Comparison of the mean percentage deviation in UEBW calculation based on bladder volume with an error in BWT measurement at 0.5 mm

		Bladder Volume	
		<250 ml (n=12)	>250 ml (n=8)
Range (min – max)		80 – 240 ml	260 – 528 ml
Kojima	MPD (range)	27.01* (21.56-33.47)	35.76* (19.40-53.64)
3D model	MPD (range)	23.76* (15.61-32.26)	32.72* (17.54-52.63)

* $p < 0.01$ from True UEBW calculation; MPD: mean percentage deviation (%); BWT: Bladder Wall thickness; UEBW: Ultrasound Estimated Bladder weight, n- number of patients

Bladder Scan Verathon system. According to the official manual, Bladder scan can measure bladders filled from 100 to 300 ml and BWT from 1 to 4 mm, thus excluding patients with a thicker bladder wall as well as those with very small or very large bladder capacity as for example in detrusor overactivity patients. A disadvantage is the use of a 3.5 MHz probe which does not have adequate discriminative penetration. These issues were raised by Oelke et al, in their comparison of a hand measurement to the automatic measurements of BWT [19]. We can add to this knowledge that BWT needs to be carefully assessed to have a true UEBW measurement that can be safely reproduced.

The strengths of this study include the homogeneous sample of subjects and the simulation on these measurements with two different techniques that are widely used in the literature. A limitation, is that we did not use the prototype BladderScan machine, since it was impossible to run multiple faulty values for a single patient. Instead, we developed a semi-automatic model for this purpose that is based on the same principle, serving the purpose of this study.

Conclusion

Results of this pilot study suggest that UEBW could become a useful tool for diagnostic and monitoring purposes in patients with LUTS, especially in patients with overactive bladder syndrome, since their thicker bladder walls and their small bladder capacity minimize the risk for inaccurate measurements. The impact of subtle changes in BWT measurement at the level of 0.2mm for 3-D calculation and at level 0.1mm for Kojima calculation of UEBW should be considered.

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Conflict of interest: none

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