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High-resolution anal manometry: Repeatability, validation, and comparison with conventional manometry

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Abstract

Background: Accurate measurement of anal sphincter function is potentially of value in defining treatment of common pelvic floor disorders. The aim of this study was to establish repeatability and validate high-resolution anal manometry (HRAM) by comparison to conventional manometry (CM). Arising from this work would be definitive normal range data.

Methods: Eighty healthy volunteers (40 female) underwent a test-retest repeatability study. A 16-channel water-perfused HRAM catheter was compared to an 8-channel conventional catheter using a station pull-through technique.

Key Results: High-resolution anal manometry had similar precision to conventional manometry when measuring resting pressure (intraclass correlation coefficient [ICC] 0.73 vs 0.68, HRAM vs CM) and squeeze increment (ICC 0.90 vs 0.94, HRAM vs CM). HRAM measured resting pressures 10% lower than CM and squeeze pressure 27% higher than CM.

Conclusions and Inferences: High-resolution anal manometry is a valid technique with comparable precision to CM. HRAM measurements differ considerably to CM, and a new set of normal values must be used.

KEYWORDS
anorectal manometry, fecal incontinence, pelvic floor dysfunction, test validation

1 | INTRODUCTION

Fecal incontinence is a common condition with a prevalence of approximately 8%.[1] Anorectal manometry provides a quantitative measure of anorectal function and forms part of the recommended assessment.[2,3] The justification of its widespread use has been questioned due to its limited precision, accuracy, and ability to predict treatment outcome.[4-8] This contrasts the use of endoanal ultrasound which has become central in the decision-making process of patients with fecal incontinence.[9]

High-resolution manometry was first developed for the esophagus by Clouse in order to overcome the limitations of conventional manometry.[10] When applied to the esophagus, high-resolution manometry has been shown to be more easily interpreted,[11] provide enhanced information on esophageal physiology,[12] increase diagnostic accuracy,[13] and predict success of treatments.[14,15] High-resolution manometry provides simultaneous longitudinal pressure measurements enabling complete definition of the intraluminal pressure environment by incorporating three essential elements:

1. Multiple-channel catheters with finely spaced points of measurement
2. Interpolation techniques to accurately estimate pressure in between points of measurement
3. Topographical display methods

The net result of these factors is to permit simultaneous measurement of anal and rectal function. The ability of high-resolution manometry to fully define the anorectal pressure environment has the potential to overcome some of the limitations seen in conventional manometry. HRAM has been found to correlate well with conventional manometry with HRAM measuring resting and squeeze pressures significantly higher.[16-18] Furthermore, Carrington et al[19] found that by using new measures of anal sphincter function derived from HRAM, they were able to be more sensitive in distinguishing healthy women from women with fecal incontinence.

The aim of this study was to firstly establish the repeatability of HRAM. Secondly, we wished to validate HRAM by comparing its repeatability with conventional manometry in addition to defining normality for HRAM.

Key Points

- High-resolution anal manometry (HRAM) is now being used in the assessment of patients with fecal incontinence and evacuatory disorders following its successful application in esophageal manometry.
- This study aims to determine the repeatability of HRAM and compare its repeatability to conventional manometry (CM).
- We found HRAM to be a valid technique with comparable repeatability to CM.
- HRAM values differ significantly to CM, and new set of normal values must be used.
- We have presented normal ranges for water-perfused HRAM.

2 | MATERIALS AND METHODS

2.1 | Participants

Eighty healthy volunteers underwent a test-retest repeatability study. Participants were recruited by email, online notice boards, and advertisement in the local newspaper, with a payment of £100 to compensate for their time. Men and women over 18 years of age with normal anorectal function were included in the study. Healthy volunteers were excluded if they had a history of constipation, fecal incontinence, perianal sepsis, previous colonic, rectal or perianal surgery, inflammatory bowel disease, spinal injury, rectal prolapse, previous instrumental delivery, greater than second-degree obstetric perineal tear, or significant sphincter defect demonstrated on endoanal ultrasound. Previous instrumental delivery and greater than second-degree obstetric perineal tear were excluded to minimize the number of participants who underwent the repeated manometry testing and then had to be excluded due to subsequent sphincter defect in endoanal ultrasound. Endoanal ultrasound was not performed prior to manometry as this may alter the sphincter physiology, but performed directly after the repeated manometry tests allowing the study to be completed in one sitting. A full clinical history in addition to the following questionnaires was used to confirm absence of anorectal symptoms: Cleveland Clinic Incontinence[20]; St Mark's Incontinence[21]; Cleveland Clinic Constipation[22]; Constipation Severity Instrument[23]; and the modified Obstructive Defecation Score[24,25] (original out of 31 modified as used by Harris et al out of 24).

Conventional manometry and high-resolution manometry were undertaken at one sitting by the same person with a 5-minute interval between each individual manometry test. We minimized order effect by changing the order with which the manometry tests were performed cycling through the six possible permutations ensuring each was equally represented and spread out during the study:

1. HRAM, HRAM, CM, CM
2. CM, CM, HRAM, HRAM
3. HRAM, CM, HRAM, CM
4. CM, HRAM, CM, HRAM
5. HRAM, CM, CM, HRAM
6. CM, HRAM, HRAM, CM

No enema or bowel preparation was used. The participants lay in the left lateral position.

Ethical approval for this study was granted by the National Hospital for Neurology and Neurosurgery Research Ethics Committee (reference number 10/H0716/8) and was performed between June 2010 and August 2011.

2.2 | Conventional manometry

Conventional manometry used a 4.9-mm-diameter water-perfused catheter with eight channels arranged radially 2 cm from the catheter tip perfused at 0.6 mL/min with a balloon attached at the tip to elicit the rectoanal inhibitory reflex (RAIR). The pressure was recorded in cmH_2O relative to atmospheric pressure. A standard station pull-through technique using 1-cm intervals was used for both resting and squeeze pressure measurements.[2] To elicit the RAIR, the catheter was inserted to the station of highest resting pressure. Rapid insufflation and desufflation of the balloon with 50 mL of air was performed by hand.

2.3 | High-resolution manometry

A custom 16-channel 4.4-mm-diameter water-perfused high-resolution manometry catheter was used. The intra-anal array consisted of 13 of the 16 channels, starting at 5 mm from the anal verge and at 5-mm intervals extending to 6.5 cm from the anal verge. The proximal channels were positioned posteriorly to optimally measure the action of puborectalis. There were two further rectal channels at either side of the balloon, with the final channel 15 cm distal to the anal verge measuring atmospheric pressure. Once the catheter was correctly positioned, it was secured in place using a clamp. The protocol consisted of a 5-minute accommodation phase prior to three cycles of 1-minute resting periods followed by a squeeze. The rectoanal inhibitory reflex (RAIR) was elicited with 50 mL.

2.4 | Endoanal ultrasound

A B-K Medical (Herlev, Denmark) 2050 three-dimensional endoanal ultrasound probe was used to establish internal and external sphincter integrity and absence of atrophy. The crystal frequency was set at 10 MHz. The participants were positioned supine for the examination. The studies were anonymized prior to assessment by a radiologist. Twelve participants (eight women) did not undergo endoanal ultrasound due to lack of availability of endoanal ultrasound machine.

2.5 | Data analysis

Custom programs were written in MATLAB (MathWorks, Natick, MA, USA) to perform automated analysis of HRAM and conventional manometry. In order to eliminate bias, the studies were anonymized and randomized prior to analysis. Using the MMS anorectal manometry measurement and analysis software (Medical Measurement Systems v8.19c, the Netherlands), each section of the study was divided into its component parts and exported into MATLAB. Blocked channels caused by debris introduced into narrow lumina used in HRAM were automatically identified and corrected for. The resulting dataset for each part of the protocol was analyzed as detailed below. Normal range data for HRAM are derived using the MATLAB program using the definitions consistent with those used in commercially available systems. Although a fully automated technique was developed and used, in each case the data produced were individually checked to ensure accuracy.

2.6 | Analyzing conventional manometry

The mean pressure from all eight channels was calculated for each station of the station pull-through. The highest pressure from each of the six stations was used as the resting pressure. The resting rectal pressure was calculated as the lowest pressure in the proximal 4 cm. The maximum pressure recorded from the mean of all eight channels was the squeeze pressure. The baseline pressure was the mean pressure from all eight channels in the first second. The squeeze increment was the pressure increase from baseline anal resting pressure immediately preceding squeeze maneuver. The functional anal canal length (FACL) was defined as the distance between the anal verge and the point at which the pressure exceeded 20% above rectal pressure.[26] The high-pressure zone length was defined as the length of sphincter that is >50% of maximum pressure.

The mean of the eight channels was calculated for each time point during the RAIR to form a single channel of data and analyzed as for HRAM.

2.7 | Analyzing high-resolution anal manometry

The virtual e-sleeve pressure is defined as the highest pressure in any channel at each time point. The virtual e-sleeve pressure was used to determine resting pressure, squeeze pressure, squeeze increment, maximum cough pressure, maximum cough increment, and RAIR measurements. Rectal pressure was defined as the mean of the lowest two neighboring channels excluding the distal 2.5 cm. The FACL was defined as the distance between the anal verge and the point at which the pressure exceeded 20% above rectal pressure.[26] The high-pressure zone length was defined as the length of sphincter that is >50% of maximum pressure. The start of the RAIR was defined as the point at which the pressure decreased below two standard deviations of the mean baseline pressure immediately prior to the RAIR. The end of the RAIR was defined as the point when the pressure was restored to two thirds of the baseline pressure from the minimum pressure.[27,28] The maximum reduction in pressure was the difference between the mean baseline pressure and the minimum pressure during the RAIR. The maximum percentage reduction was the maximum pressure reduction expressed as a percentage of the baseline pressure.

2.8 | Statistical analysis

We used methods as described by Bland-Altman to determine repeatability and displayed these data on Bland-Altman plots.[29] Two statistical methods were used to calculate repeatability. The intraclass correlation coefficient (ICC) calculates repeatability by comparing the differences between pairs of measurements with the overall difference between all measurements where one denotes perfect agreement. The ICC was included as it is useful when comparing the repeatability of two methods as it takes into account the overall difference in measurements, thereby reducing the reliance on equal variance. The mean difference between first and second measurements (mean bias) was calculated and the Wilcoxon rank-sum test used to test for order effects. The standard deviation of the differences between the first and repeated test was then calculated. The repeatability coefficient is double the standard deviation of the differences between the repeated measurements. The repeatability coefficient was included as it is clinically useful as approximately 95% of repeated measurements should fall within the ± repeatability coefficient range.

In order to demonstrate our findings were invariant to the order in which they were performed, we compared the measurements and repeatability of measurements between the six groups in whom tests were performed in a different order (as listed in the Participants section). To enable this comparison, repeatability was calculated in each individual for resting pressure and squeeze increment pressure. ICC or repeatability coefficient cannot be used on an individual basis; therefore, individual repeatability was calculated by the difference between the two tests divided by the mean of the two tests. The measurements and repeatability of measurements were compared in the six groups using the Kruskal-Wallis test.

The normal ranges were calculated for males and females using HRAM. The normal ranges were expressed as 5th and 95th percentiles reducing the influence of outliers and the reliance on the data being normally distributed. SPSS was used for statistical analysis (version 20, IBM, New York, USA).

3 | RESULTS

Table 1 summarizes the demographics and median questionnaire scores of the 80 healthy volunteers. There were no significant difference in the age between the males and females ($P = 0.22$ Wilcoxon rank-sum test). Twenty-three females were nulliparous, and 17 were parous. The median number of children among the parous population was 2 with a range of one to four. Sixty-eight of the 80 (85%) healthy volunteers underwent 3D EAUS. There were no individuals with sphincter injury or atrophy identified.

3.1 | Test-retest repeatability

Table 2 displays the repeatability for HRAM and conventional manometry using two measures of repeatability. Using intraclass correlation coefficient as the measure of repeatability, we found similar repeatability for HRAM and CM when measuring resting pressure (ICC 0.73 vs 0.68) and when measuring squeeze pressure increment (ICC 0.94 vs 0.90). The distribution of the differences between the first and repeated tests was tested for normality using the Shapiro-Wilk test for HRAM and CM measuring resting pressure. There was no significant difference to the normal distribution validating the use of mean bias and repeatability coefficient (HRAM resting $P = 0.18$, CM resting $P = 0.31$). Figure 1 is the Bland-Altman plot comparing repeatability of conventional manometry and HRAM for resting pressure and squeeze increment. For both methods, squeeze pressure measurements were more repeatable than resting pressure measurements and RAIR measurement lacked repeatability. The mean bias for resting pressure using HRAM was +3.2 cmH_2O ($P = 0.06$; Wilcoxon signed rank test) and +1.1 cmH_2O for CM ($P = 0.49$; Wilcoxon signed rank test). The mean bias for squeeze increment using HRAM was +4.5 cmH_2O ($P = 0.79$; Wilcoxon signed rank test) and +5.7 cmH_2O for CM ($P = 0.08$; Wilcoxon signed rank test). There was therefore no significant difference in the initial and repeated tests.

Repeatability was invariant to order in which the tests were performed as there were no significant differences between the six groups (the six different permutations of performing the two tests twice) when measuring repeatability of resting pressure or squeeze increment when using HRAM or CM (HRAM resting $P = 0.986$, CM resting $P = 0.332$, HRAM squeeze $P = 0.865$, CM resting $P = 0.690$; Kruskal-Wallis test). In addition, we have demonstrated that there was no significant differences in resting pressure and squeeze increment pressures between the same six groups (HRAM resting $P = 0.257$, CM resting $P = 0.542$, HRAM squeeze $P = 0.206$, CM resting $P = 0.162$; Kruskal-Wallis test).

TABLE 1 Table demonstrating demographics, number who underwent EAUS, and questionnaire results of healthy volunteers

	Male	Female
Number	40	40
Age (median (range))	30 (19-68)	32 (19-62)
Number who underwent EAUS	36 (90%)	32 (80%)
Cleveland clinic incontinence score (median)	0/20	0/20
St Mark's incontinence (median)	0/24	0/24
Cleveland clinic constipation (median)	1/30	2/30
Obstructed defecation score (median)	1/24	2/24
Constipation severity instrument (median)	0/73	5.5/73

3.2 | Defining normality

Table 3 summarizes the normal ranges for commonly used physiological parameters as calculated from 40 males and 40 females using the MATLAB program with definitions as described in the methods section. The data are not normally distributed and are presented as median with 5th and 95th percentiles which serve as normal ranges. Although there is a large overlap in the normal ranges for males and females, males have a significantly higher squeeze increment using HRAM and conventional manometry ($P = 0.0004$, HRAM; $P < 0.0001$, conventional, Wilcoxon rank-sum test).

3.3 | Comparing HRAM and conventional manometry

Conventional manometry and HRAM were well correlated when measuring resting pressure and squeeze increment (correlation

TABLE 2 Table displaying the test-retest repeatability of HRAM and conventional manometry for commonly used measurements taken during the resting, squeeze, and RAIR periods

	ICC		Repeatability coefficient	
	Conv	HRAM	Conv	HRAM
Resting period				
Resting pressure (cmH_2O)	0.68	0.73	38 cmH_2O	32 cmH_2O
Resting rectal pressure (cmH_2O)	0.84	0.74	9.6 cmH_2O	5.7 cmH_2O
FACL (mm)	0.42	0.63	16 mm	13 mm
HPZL (mm)	0.34	0.45	16 mm	14 mm
Squeeze period				
Max squeeze pressure	0.95	0.92	58 cmH_2O	92 cmH_2O
Squeeze increment	0.94	0.90	60 cmH_2O	99 cmH_2O
FACL	0.52	0.69	12 mm	13 mm
HPZL	0.54	0.53	12 mm	13 mm
RAIR				
RAIR duration	0.55	0.16	13 s	19 s
Max reduction in pressure	0.43	0.52	35 cmH_2O	35 cmH_2O
Max percentage reduction	0.54	0.28	30%	36%

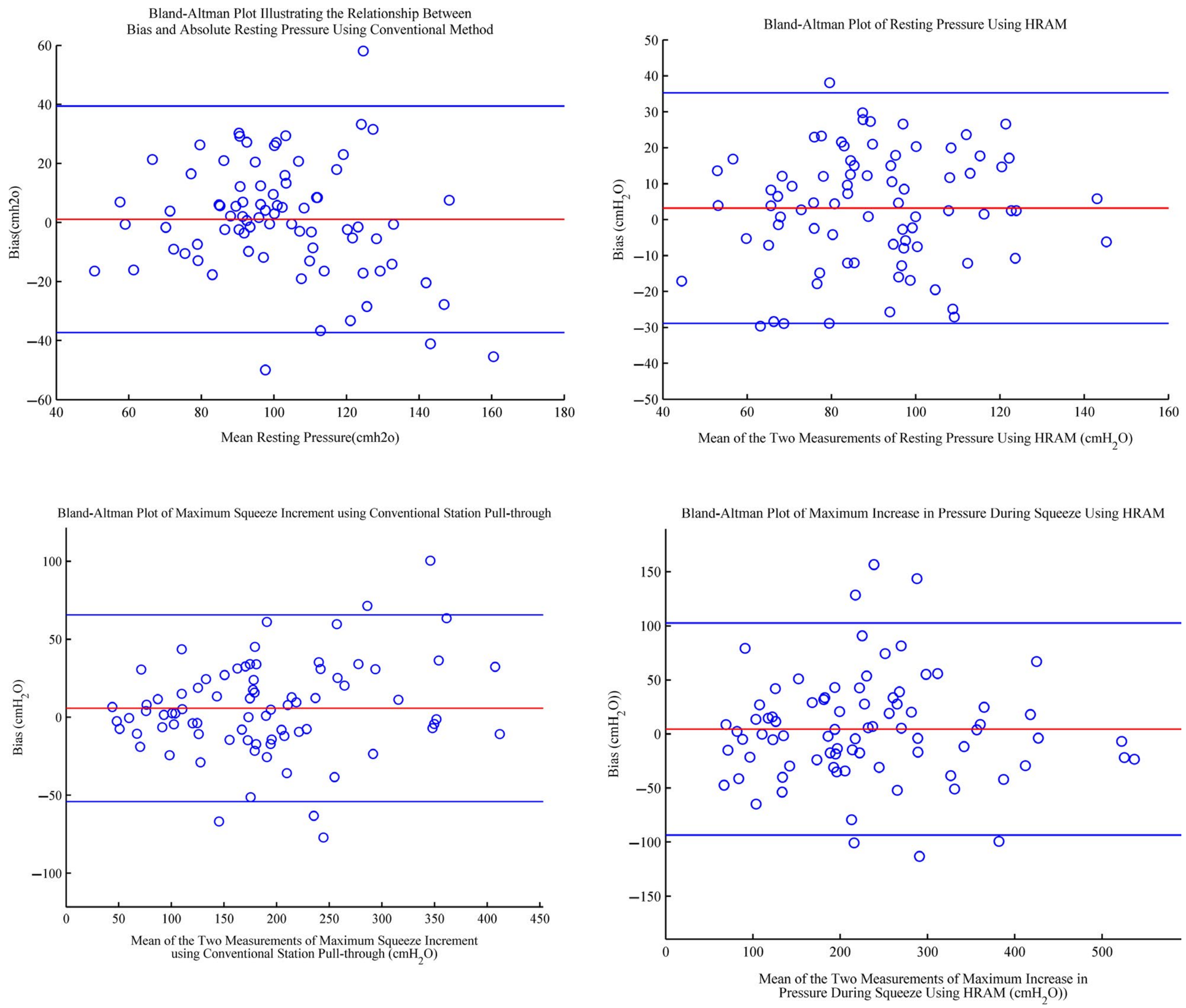

FIGURE 1 Bland-Altman plot demonstrating the repeatability of HRAM and conventional manometry for resting and squeeze increment. The *x*-axis represents the mean of paired measurements, and the *y*-axis represents the difference between the paired measurements. The horizontal red line is the mean difference between the paired measurements. The horizontal blue line represents 2 standard deviations of the differences. The blue line therefore indicates the limits of repeatability. The graphs demonstrate that repeatability is similar for both conventional manometry and HRAM

coefficient 0.76 and 0.91, respectively). HRAM measured resting pressure 10% lower than conventional manometry. However, HRAM measured squeeze increment 27% higher than conventional manometry. Figure 2 is a Bland-Altman plot comparing measurements from HRAM and conventional manometry, with HRAM measuring resting pressure a mean of 11.5 cmH_2O lower than conventional manometry and a mean of 42.5 cmH_2O higher for squeeze increment.

4 | DISCUSSION

Precision is a fundamental prerequisite of a physiological measurement. Imprecision would preclude improvements in the accuracy of diagnostic accuracy and ability to subclassify abnormalities akin to the Chicago classification for high-resolution esophageal manometry.[30] This study provides a key step in the justification of using HRAM by determining its repeatability. We found HRAM had similar repeatability to CM in measuring resting and squeeze increment pressure. Carrington et al[31] found that residual push pressure, maximum rectal push pressure, and endurance squeeze duration had such a wide variation in health that they are unlikely to have diagnostic utility. Similarly, we found quantifying the RAIR, functional anal canal lengths, and high-pressure zone lengths had poor repeatability raising questions on their diagnostic utility.

Comparing repeatability studies is challenging due to methodological heterogeneity, specifically the time interval between studies and whether the same person performed the tests. Repeatability is also calculated using a wide variety of statistical methods. Table 4 summarizes the study results for repeatability test-retest anorectal physiology studies. The repeatability results in this study for

TABLE 3 Normal ranges of commonly used parameters using high-resolution anal manometry calculated using MATLAB program with definitions described in methods

	HRAM	
	Male	Female
Resting period measurements		
Resting pressure (cmH_2O)	94.0 (64.4-133.3)	83.8 (53.0-122.4)
Rectal pressure (cmH_2O)	7.9 (2.1-17.8)	5.3 (1.8-14.6)
Functional anal canal length (mm)	37.9 (28.9-49.8)	34.8 (20.0-43.1)
High-pressure zone length (mm)	25.7 (15.7-34.6)	20.3 (10.3-30.4)
Squeeze period measurements		
Maximum pressure (cmH_2O)	368.8 (235.25-604.9)	240.4 (159.9-376.6)
Maximum squeeze increment (cmH_2O)	284.7 (142.7-523.9)	166.6 (76.4-262.8)
High-pressure zone length (mm)	23.5 (14.0-35.1)	19.3 (11.1-26.7)
Cough period measurements		
Maximum pressure (cmH_2O)	238.3 (125.8-416.3)	171.2 (111.1-288.0)
Maximum cough increment (cmH_2O)	138.4 (46.0-310.8)	86.3 (26.7-190.5)
RAIR measurements		
Absolute pressure decrease (cmH_2O)	55.9 (25.3-87.3)	50.5 (18.6-91.9)
Percentage decrease (%)	81.5 (58.0-92.0)	80.7 (51.4-93.4)
Duration (secs)	19.6 (9.3-33.7)	19.4 (11.8-36.4)

Median (5th and 95th Percentile).

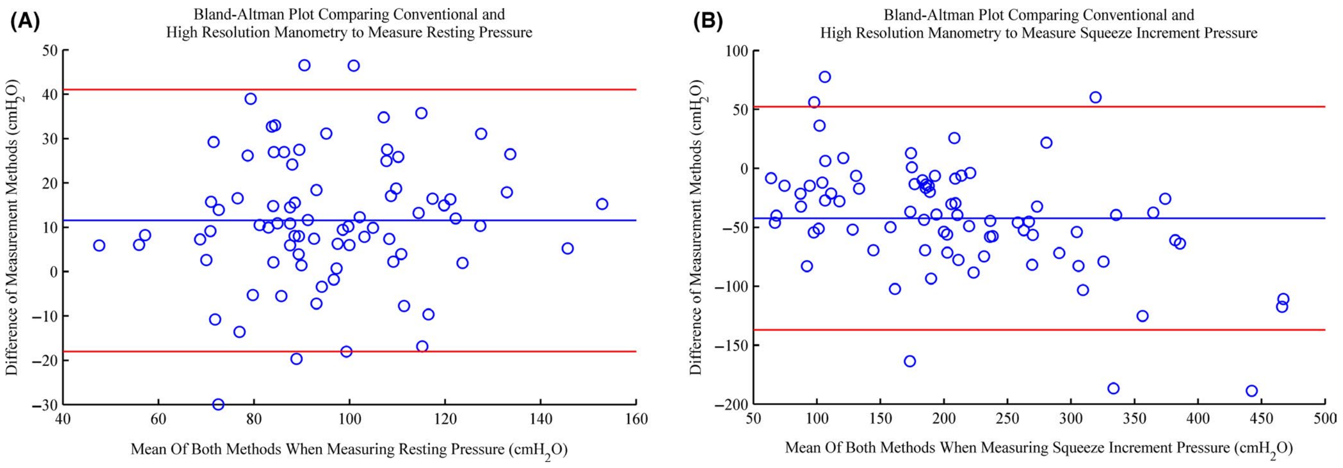

FIGURE 2 A, Resting Pressure: the Bland-Altman plot demonstrates that HRAM measured resting pressure a mean of 11.5 cmH_2O lower than CM. B, Squeeze Pressure: The Bland-Altman plot demonstrates that HRAM measured squeeze increment a mean of 42.5 cmH_2O higher than resting pressure. There is no relationship between the differences and the absolute values

conventional station pull-through manometry are consistent with those seen in previous studies. The range of the repeatability coefficients for resting pressure across the studies was from 38 to 42 cmH_2O, with our study at the lower limit of this range. The range of repeatability coefficients for squeeze pressure was from 35 to 87 cmH_2O with our study measuring 58 cmH_2O. Eckhardt et al[32] found the correlation coefficient for the first and second measurements of resting pressure was 0.97 for station pull-through and 0.99 using continuous pull-through but the repeatability coefficient was not calculated. Using the 25 mm/s puller, Schizas et al[33] found the intraclass correlation coefficient was 0.97 for resting pressure and 0.99 for squeeze pressure. This is substantially more repeatable than the 0.68 and 0.94 we obtained for conventional station pull-through manometry, and more repeatable than Otto et al[34] with a 8-channel setup with an ICC of 0.6-0.7 for resting pressure and 0.75-0.79 for squeeze pressure. This may in part be explained by the time interval between tests with the mechanical puller technique being approximately 30 seconds, in our study 15-60 minutes, and in the Otto et al study of up to 2 weeks. Coss-Adame performed a repeatability study on 16 healthy volunteers using a 3D HRAM with a 2-week interval.[35] Repeatability coefficients were not specifically quoted in the text. However, using the Bland-Altman plots the repeatability coefficients were approximately 14 and 82 cmH_2O for resting pressure and squeeze pressure, respectively. This was more repeatable

TABLE 4 Table summarizing test-retest repeatability studies of anorectal manometry

Study	n	Sex	Age	Participants	Manometric technique	Protocol	Statistical method	Interval between tests (d)	Inter- or intra-observer	Resting pressure			Squeeze pressure		
										Bias	2SD	CV	Bias	2SD	CV
Ryhammer et al[39]	58	F	45-58	Healthy volunteers	Single-lumen water-perfused	MRP: 2 mm/s CPT ×3. MSP: single station at point of MRP.	Bland-Altman	99	Intra	+2.2	38 cmH_2O	22%	−1.0	35 cmH_2O	33
Bharucha et al[40]	19	F	24-40	Healthy volunteers	Water-perfused 4-lumen radial	MRP: SPT MSP: SPT	Bland-Altman	168	Inter and intra	−0.4	/	Intra 27% Inter 41%	+4.4	/	Intra 24% Inter 35%
Rogers et al[41]	16	M&F	50.7 (mean)	Symptomatic (FI, AP, Cons)	Micro-balloon	MRP: SPT MSP: SPT	Bland-Altman	20	Inter	−10	42 cmH_2O	/	−9	65 cmH_2O	/
Bollard et al[42]	24		62 (median)	Incontinent	Dual-channel solid-state catheter		Bland-Altman	0	Intra	/	38 cmH_2O	/	/	47 cmH_2O	
Mitchell et al[43]	26	M&F	40-75	Symptomatic	Micro-balloon	MRP:SPT MSP:SPT	Bland-Altman	37	Inter and intra	1.3	40 cmH_2O	/	8.7	86.7 cmH_2O	
Coss-Adame et al[35]	16	M&F	21-62	Healthy volunteers	3D HRAM 256 channel		Bland-Altman	14	/	≈0[a]	≈14[a] cmH_2O		≈2[a]	≈82[a] cmH_2O	
Chakraborty et al[36]	21	F	57 ± 11	Incontinent	3D HRAM 256 channel		Bland-Altman	0	Intra		≈+31[a]/−45[a] cmH_2O			≈143[a] cmH_2O	
Gosling et al	80	M&F	19-68	Healthy volunteers	8-channel water-perfused	MRP: SPT MSP: SPT	Bland-Altman	0	Intra	+1	38 cmH_2O	/	+6	60.0 cmH_2O	/
Gosling et al	80	M&F	19-68	Healthy volunteers	16 + 1 water-perfused HRAM		Bland-Altman	0	Intra	−10	32 cmH_2O	/	−9	98 cmH_2O	/

2SD, 2 × Standard deviation of differences (Repeatability coefficient); AP, anal pain; Cons, Constipation; CPT, continuous pull-through technique; CV, coefficient of variation (SD/(mean of two measurements)); FI, fecal incontinence; MRP, maximal resting pressure; MSP, maximum squeeze pressure; SPT, station pull-through at 1-cm increments.
[a]Numbers taken from Bland-Altman Plot actual numbers not quoted.

TABLE 5 Table summarizing studies of normal ranges for HRAM

Author	n	Solid state/ Water perfused	Number of channels	Age/Parity (n)	Resting pressure (cmH_2O)	Squeeze increment (cmH_2O)	
Noelting 2012[37]	62	Solid state	10	<50 (30)	92-152	31-154	10th 90th Percentile
				>50 (32)	49-124	38-232	
Li 2013[44]	110	Solid state	256	F (46)	81.4 ± 3.0	227.6[a] ± 11.4[a]	Mean ± SEM
				M (64)	83.3 ± 2.9	264.8[a] ± 9.4[a]	
Lee 2014[45]	54	Solid state	23	F (27)	44 (33-57)	27 (16-38)	Median (IQR)
				M (27)	63 (53-76)	75 (56-105)	
Carrington 2014[31]	115	Solid state	12	N (34)	64-150	44-336	5th 95th Percentile
				P (62)	42-136	33-315	
				M (19)	52-155	54-498	
Coss-Adame 2015[35]	78	Solid state	256	F (42)	76 (97-110)	278[a] (253-305[a])	Mean (95% CI of the mean)
				M (36)	122 (113-131)	362[a] (333-390[a])	
Mion 2016[46]	46	Solid state	256	F (36)	101 (92-110)	245[a] (222-269)	Mean (95% CI of the mean)
				M (10)	105 (88-122)	371[a] (325-419)	
Prichard 2017[47]	30	Solid state		F (30)	129 (106-137)	162 (102-194)	Median (IQR)
Rasijeff 2017[38]	60	Solid state	8	F (40)	35-128	48-447	5th 95th Percentile
				M (20)	67-159	86-731	
	60	Water perfused	10	F (40)	46-137	36-256	
				M (20)	54-158	49-415	
Gosling (current study)	80	Water perfused	16	F (40)	53-122	76-263	5th 95th Percentile
				M (40)	64-133	143-524	

F, female; M, male; N, nulliparous; P, parous.
[a]Squeeze pressure rather than squeeze increment.

than we calculated for HRAM with repeatability coefficients of 32 cmH_2O for resting and 98 cmH_2O for squeeze increment pressure. Chakraborty et al[36] reported on the repeatability of 3D HRAM in patients with fecal incontinence who were in the placebo arm of a therapeutic study. The manometry was repeated on the same day, and again, the repeatability coefficient was not specifically quoted in the text, but approximating from the Bland-Altman plots, the repeatability was similar to this study for resting pressure but less repeatable for squeeze pressure (143 vs 98 cmH_2O squeeze increment, Chakraborty vs this study). Solid-state HRAM catheters such as those used in Coss-Adame et al and Chakraborty et al's studies employ multiple pressure sensors at each level providing circumferential pressure measurements. This is in contrast to water-perfused systems which have a single or unidirectional pressure measurement at each level. Circumferential vs unidirectional pressure measurements and the resulting increase in the total number of pressure measurements mean that solid-state HRAM systems have the attributes that could potentially translate into superior precision over the water-perfused HRAM system used in this study.

Table 5 summarizes publications of normal ranges for HRAM.[31,37] Making direct comparisons in the normal range data is hampered by differences in the statistical definitions of normality, the different manometric techniques, and variations in protocols. The most comparable study is by Rasijeff et al[38] who performed water-perfused HRAM on 60 healthy volunteers and established similar normal values. One difference was the lower limit of normal for squeeze increment was higher in our study for both male and female (76 vs 36 cmH_2O for female and 143 vs 49 cmH_2O for male, this study vs Rasijeff).

Comparing absolute values from HRAM and CM, we found that HRAM measured resting pressure lower than CM (10%/11.5 cmH_2O) and squeeze increment higher than CM (27%/42.5 cmH_2O). In contradiction to our study, Jones et al[16] found that solid-state high-resolution manometry measured resting pressures higher than conventional water-perfused manometry. HRAM measured squeeze pressure 27% higher than conventional manometry which is comparable to the findings of Jones et al Rasijeff et al[38] compared solid-state with water-perfused HRAM and found no difference in resting pressure; however, squeeze pressure measurements were significantly higher when using solid-state HRAM. Therefore, normal ranges for CM cannot be applied to HRAM and studies using CM and HRAM cannot be compared without adjustments. This is especially important to highlight as departments transition from CM to HRAM.

Rather than measuring existing indices more precisely, justification of the use of HRAM over CM therefore lies in displaying additional information not provided by conventional manometry. Specifically, its ability to simultaneously measure anal and rectal pressure gives insight into the coordination of anal and rectal pressures that conventional manometry does not provide. Further studies are needed to determine whether this additional information translates into clinical benefit.

Limitations of the study include 15% of participants not having an EAUS to establish sphincter integrity. However, we used a rigorous battery of questionnaire assessments to ensure that patients had no anorectal symptoms. Secondly, as the primary aim was to establish the repeatability, the normal ranges for HRAM and CM will be affected by having studies repeated within a short time interval. We tried to minimize the effect of this by cycling through the six permutations of repeated HRAM and CM measurements as outlined in the methods. Although the order of the tests was not randomized, cycling through each order ensured each of the 6 permutations was equally represented and spread out during the study. The studies were then anonymized and randomized prior to analysis to avoid bias in the interpretation and analysis stage. Finally, a custom-made HRAM catheter and MATLAB program were used and the normal values are specific for this setup, although a 6-cm, 5-mm-spaced intra-anal array is a common configuration for water-perfused HRAM and definitions used to derive the normal values are consistent with commercially available software.

We have quantified the repeatability of HRAM and CM. HRAM had similar repeatability to conventional manometry for resting and squeeze pressure and therefore validates the use of HRAM. The repeatability coefficient provides limits of agreement which places anorectal physiology measurement into context with regards to precision. As well as being clinically relevant, these data can be used for sample size calculations for future longitudinal studies using conventional and high-resolution manometry. Additionally, by comparing the absolute pressures obtained from HRAM and conventional manometry we found that HRAM measures resting pressure 10% lower than conventional manometry and 27% higher for squeeze increment highlighting the importance of using separate reference ranges which we have provided for HRAM and CM in males and females.

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DISCLOSURE

JM Gosling, Dr Andrew Plumb, Prof Stuart A Taylor, Mr Richard Cohen, and Dr Anton V Emmanuel have none to declare.

AUTHOR CONTRIBUTION

JMG prepared the ethical approval, performed the manometry studies, collected the data, analyzed the data, and wrote and edited manuscript; AP collected and analyzed the data; SAT collected and analyzed the data, and assisted with the protocol design; RC edited the manuscript and assisted with the protocol design; and AVE was study's principal investigator, conceived the study design, assisted with the ethical approval, analyzed the data, and edited the manuscript.

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