Title

High Resolution Anal Manometry: Repeatability, Validation and Comparison with Conventional Manometry

Running Title

Repeatability of High Resolution Anal Manometry

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Keywords

Anorectal manometry
Test validation
Pelvic floor dysfunction
Faecal incontinence

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 Anorectal Manometry (HRAM) by comparison to conventional manometry (CM). Arising from this work would be definitive normal range data.

Methods

80 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

HRAM 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 & Inferences

HRAM 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.

Introduction

Faecal 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[3;4]. The justification of its widespread use has been questioned due to its limited precision, accuracy and ability to predict treatment outcome[5-9]. This contrasts the use of endoanal ultrasound which has become central in the decision making process of patients with faecal incontinence[10].

High resolution manometry was first developed for the esophagus by Clouse in order to overcome the limitations of conventional manometry[11]. When applied to the esophagus, high resolution manometry has been shown to be more easily interpreted [12], provide enhanced information on esophageal physiology [13], increase diagnostic accuracy [14] and predict success of treatments [15;16]. 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 nett 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[17-19]. Furthermore, Carrington et al 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 faecal incontinence[20].

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.

Materials and Methods

Participants

80 healthy volunteers underwent a test-retest repeatability study. Participants were recruited by email, online notice boards and by 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, faecal 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 minimise 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 were used to confirm absence of anorectal symptoms: Cleveland Clinic Incontinence; St Mark’s incontinence; Cleveland Clinic Constipation; Constipation Severity Index; and the Obstructive Defecation Index.

Conventional and high resolution manometry was undertaken at one sitting by the same person with a five minute interval between each individual manometry test. We minimised order effect by changing the order with which the manometry tests were performed cycling through the six possible permutations:

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. There was a five minute interval in between studies.

Ethical approval for this study was granted by the National Hospital for Neurology and Neurosurgery research ethics committee (reference number 10/H0716/8)

Conventional Manometry

Conventional manometry used a 4.9mm diameter water perfused catheter with eight channels arranged radially 2cm from the catheter tip perfused at $0.6 ml min^{-1}$ 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 1cm intervals was used for both resting and squeeze pressure measurements[3]. To elicit the RAIR the catheter was inserted to the station of highest resting pressure. Rapid insufflation and desufflation of the balloon with 50mls of air was performed by hand.

High Resolution Manometry

A custom 16 channel 4.4mm diameter water perfused high resolution manometry catheter was used. The intra-anal array consisted of 13 of the 16 channels, starting at 5mm from the anal verge and at 5mm intervals extending to 6.5cm from the anal verge. The proximal channels were positioned posteriorly to optimally measure the action of puborectalis. There were two further rectal channels either side of the balloon, with the final channel 15cm 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 five minute accommodation phase prior to three cycles of one minute resting periods followed by a squeeze. Then, additional measures of external sphincter function were assessed with a five second squeeze, cough test, valsalva manoeuvre and forcefully exhaling into a sphygmomanometer to a pressure of 50mmHg. The rectoanal inhibitory reflex (RAIR) was elicited with 50mls.

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 anonymised prior to assessment by a radiologist. 12 participants (8 women) did not undergo endoanal ultrasound due to lack of availability of endoanal ultrasound machine.

Data Analysis

Custom programs were written in MATLAB (Mathworks, Naticks, MA) to perform automated analysis of HRAM and conventional manometry. In order to eliminate bias the studies were anonymised and randomised prior to analysis. Using the MMS anorectal manometry measurement and analysis software (Medical Measurement Systems v8.19c, 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 analysed 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 was individually checked to ensure accuracy.

Analysing 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. 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[21]. The high pressure zone length was defined as the length of sphincter that is greater than 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 analysed as for HRAM.

Analysing High Resolution Anorectal 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 neighbouring channels excluding the distal 2.5cm. 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[21]. The high pressure zone length was defined as the length of sphincter that is greater than 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 [22;23]. 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.

Statistical Analysis

We used methods as described by Bland-Altman to determine repeatability and displayed this data on Bland-Altman plots[24]. Two statistical methods were used to calculate repeatability. The intra-class 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 is 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 be 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. 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, US).

Results

Table 1 summarises the demographics and median questionnaire scores of the 80 healthy volunteers There was no significant difference in the age between the males and females (p = 0.22 Wilcoxon rank-sum test).23 females were nulliparous and 17 were parous. The median number of children amongst 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.

Results: Test-Retest Repeatability

Table 2 displays the repeatability for HRAM and conventional manometry using three measures of repeatability. Using Intra-class 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 +1.1cmH_2O for CM (p=0.49 Wilcoxon signed rank test). The mean bias for squeeze increment using HRAM was +4.5cmH_2O (p=0.79 Wilcoxon signed rank test) and +5.7cmH_2O for CM (p =0.08 Wilcoxon signed rank test). There was no significant difference in the initial and repeated tests indicating there were no significant order effects.

Results: Defining Normality

Table 3 summarises 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 is not normally distributed and is 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 tended to have a higher pressures and longer high pressure zones and functional anal canals for all measurements during rest, squeeze, cough and 5 second squeeze.

Results: Comparing HRAM and Conventional Manometry

Conventional manometry and HRAM were well correlated when measuring resting pressure and squeeze increment (correlation 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 11.5cmH_2O lower than conventional manometry and a mean of 42.5 cmH_2O higher for squeeze increment.

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[25]. 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 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[26]. Similarly we found quantifying the RAIR, functional anal canal lengths, 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 summarises the study results for repeatability test re-test anorectal physiology studies. The repeatability results in this study for 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 38cmH_2O to 42cmH_2O, with our study at the lower limit of this range. The range of repeatability coefficients for squeeze pressure was from 35 to 87cmH_2O with our study measuring 58cmH_2O. Eckhardt et al [27] 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 25mmsec^{-1} puller Schizas et al found the intraclass correlation coefficient was 0.97 for resting pressure and 0.99 for squeeze pressure[28]. This is substantially more repeatable than the 0.68 and 0.94 we obtained for conventional station pull through vector volume, and more repeatable than Otto et al with a 8 channel set up with an ICC of 0.6-0.7 for resting pressure and 0.75-0.79 for squeeze pressure[29]. This may in part be explained by the time interval between tests with the mechanical puller technique being approximately 30 seconds, 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[30]. Repeatability coefficients were not specifically quoted in the text. However, using the Bland-Altman plots the repeatability coefficients were approximately 14cmH_2O and 82cmH_2O for resting pressure and squeeze pressure respectively. This was more repeatable than we calculated for HRAM with repeatability coefficients of 32cmH_2O for resting and 98cmH_2O for squeeze increment pressure. Chakraborty et al reported on the repeatability of 3D HRAM in patients with faecal incontinence who were in the placebo arm of a therapeutic study[31]. 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 (143cmH_2O vs 98cmH_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 versus unidirectional pressure measurements and the resulting increase in the total number of pressure measurements means 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 summarises publications of normal ranges for HRAM [26;32]. 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 comparible study is by Rasijeff et al who performed water perfused HRAM on 60 healthy volunteers and established similar normal values[33]. One difference was the lower limit of normal for squeeze increment was higher in our study for both male and female (76 vs 36cmH_2O for female and 143 vs 49cmH_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% / 11.5cmH_2O) and squeeze increment higher than CM (27% / 42.5cmH_2O). In contradiction to our study, Jones et al found that solid state high resolution manometry measured resting pressures higher than conventional water perfused manometry[17]. HRAM measured squeeze pressure 27% higher than conventional manometry which is comparable to the findings of Jones et al. Rasijeff et al 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[33]. 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 in a short time interval. We tried to minimise the effect of this by cycling through the six permutations of repeated HRAM and CM measurements as outlined in the methods. Finally, a custom made HRAM catheter and MATLAB program was used and the normal values are specific for this setup, although a 6 cm, 5mm 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, this 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

J M Gosling – none declared, Dr Andrew Plumb – none declared, Prof Stuart A Taylor – none declared, Mr Richard Cohen – none declared, Dr Anton V Emmanuel – None declared,

Author Contribution

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

Key Points

- High resolution anal manometry (HRAM) is now being used in the assessment of patients with faecal 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

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Tables

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 Index (median)	0/73	5.5/73

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 secs	19 secs
	Max Reduction in Pressure	0.43	0.52	35 cmH_2O	35 cmH_2O
	Max Percentage reduction	0.54	0.28	30%	36%

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)
5 second Squeeze Measurements		
Maximum Pressure (cmH_2O)	364.5 (240.5-590.3)	233.0 (160.8-381.0)
Maximum Increase in pressure (cmH_2O)	283.8 (132.9-506.1)	152.0 (65.1-260.7)
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 (5^{th} and 95^{th} Percentile).

Table 4 Table summarising test re-test repeatability studies of anorectal manometry.

Study	n	Sex	Age	Participants	Manometric Technique	Protocol	Statistical Method	Interval Between Tests	Inter or intra-observer	Resting pressure			Squeeze Pressure		
										Bias	2SD	CV	Bias	2SD	CV
Ryhammer et al [34]	58	F	45-58	Healthy volunteers	Single lumen Water perfused	MRP:2mm/s CPT x3. MSP: single station at point of MRP.	Bland Altman	99 days	Intra	+2.2	38cmH_2O	22%	-1.0	35cm H_2O	33
Bharucha et al[35]	19	F	24-40	Healthy volunteers	Water perfused 4 lumen radial	MRP: SPT MSP: SPT	Bland Altman	168 days	Inter and intra	-0.4	/	Intra 27% Inter 41%	+4.4	/	Intra 24% Inter 35%
Rogers et al[36]	16	M & F	50.7 (mean)	Symptomatic (FI, AP, Cons)	Micro-balloon	MRP: SPT MSP: SPT	Bland Altman	20 days	Inter	-10	42cmH_2O	/	-9	65cmH_2O	/
Bollard et al[37]	24		62 (median)	Incontinent	Dual Channel solid state catheter		Bland-Altman	0 days	intra	/	38cmH_2O	/	/	47cmH_2O	
Mitchell et al[38]	26	M & F	40-75	Symptomatic	Micro-balloon	MRP:SPT MSP:SPT	Bland-Altman	37 days	Inter and intra	1.3	40cm H_2O	/	8.7	86.7cm H_2O	
Coss-Adame et al[30]	16	M & F	21-62	Healthy Volunteers	3D HRAM 256 channel		Bland-Altman	14 days	/	≈0*	≈14*cm H_2O		≈2*	≈82*cm H_2O	
Chakraborty et al [39]	21	F	57+/-11	Incontinent	3D HRAM 256 channel		Bland-Altman	0 days	Intra		≈+31*/-45* cm H_2O			≈143* cm H_2O	
Gosling et al	80	M & F	19-68	Healthy volunteers	8 channel water perfused	MRP: SPT MSP: SPT	Bland Altman	0 days	Intra	+1	38cm H_2O	/	+6	60.0cmH_2O	/
Gosling et al	80	M & F	19-68	Healthy volunteers	16+1 water perfused HRAM		Bland Altman	0 days	Intra	-10	32cmH_2O	/	-9	98cmH_2O	/

2SD: 2xStandard deviation of differences (Repeatability coefficient), CV: Coefficient of variation (SD/(mean of two measurements) MRP: Maximal Resting Pressure MSP: Maximum squeeze pressure CPT: Continuous pull through technique SPT : Station pull through at 1cm increments FI: Faecal incontinence AP: Anal pain Cons: Constipation

*Numbers taken from Bland-Altman Plot actual numbers not quoted

Table 5 Table summarising 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[32]	62	Solid state	10	<50 (30)	92-152	31-154	10th 90th percentile
				>50 (32)	49-124	38-232	
Li 2013[40]	110	Solid State	256	F (46)	81.4+/- 3.0	227.6*+/- 11.4*	Mean+/- SEM
				M (64)	83.3+/- 2.9	264.8*+/- 9.4*	
Lee 2014[41]	54	Solid State	23	F (27)	44 (33-57)	27 (16-38)	Median (IQR)
				M (27)	63 (53-76)	75 (56-105)	
Carrington 2014[42]	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[30]	78	Solid State	256	F (42)	76 (97-110)	278* (253-305*)	Mean (95% CI of the mean)
				M(36)	122 (113-131)	362* (333-390*)	
Mion 2016[43]	46	Solid state	256	F (36)	101 (92-110)	245* (222-269)	Mean (95% CI of the mean)
				M (10)	105 (88-122)	371* (325-419)	
Prichard 2017[44]	30	Solid State		F(30)	129 (106-137)	162(102-194)	Median (IQR)
Rasijeff 2017[33]	60	Solid State	8	F (40)	35-128	48-447	5th 95th Percentile
				M (20)	67-159	86-731	
	60	Water Pefused	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	

*Squeeze pressure rather than squeeze increment

M Male, F Female, N Nuliparous, P Parous