A comparison of function lumen imaging probe measurements of anal sphincter function in fecal incontinence

Alexander O’Connor¹,² | Donghua Liao³ | Asbjørn Mohr Drewes³,⁴ | Abhiram Sharma¹,² | Dipesh H. Vasant²,⁵ | John McLaughlin²,⁶ | Edward Kiff¹ | Karen Telford¹,²

¹Department of General Surgery, Wythenshawe Hospital, Manchester University NHS Foundation Trust, Manchester, UK
²Division of Diabetes, Endocrinology & Gastroenterology, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester Academic Health Sciences Centre, Manchester, UK
³Mech-Sense, Department of Gastroenterology and Hepatology, Aalborg University Hospital, Aalborg, Denmark
⁴Department of Clinical Medicine, Aalborg University, Aalborg, Denmark
⁵Neurogastroenterology Unit, Gastroenterology, Wythenshawe Hospital, Manchester University NHS Foundation Trust, Manchester, UK
⁶Department of Gastroenterology, Northern Care Alliance NHS Foundation Trust, Manchester, UK

Correspondence
Alexander O’Conner, The University of Manchester, Oxford Road, Manchester, UK. Email: alexander.oconnor@postgrad.manchester.ac.uk

Abstract

Background: The functional lumen imaging probe (FLIP) is a test of anal sphincter distensibility under evaluation by specialist centers. Two measurement protocols termed "stepwise" and "ramp" are used, risking a lack of standardization. This study aims to compare the performance of these protocols to establish if there are differences between them.

Methods: Patients with fecal incontinence were recruited and underwent measurement with both protocols at a tertiary pelvic floor referral unit. Differences in minimum diameter, FLIP bag pressure, and distensibility index (DI) at rest and during squeeze were calculated at various FLIP bag volumes.

Key Results: Twenty patients (19 female, mean age 61 [range: 38–78]) were included. The resting minimum diameter at 30 and 40 mL bag volumes were less in the stepwise protocol (mean bias: −0.55 mm and −1.18 mm, $p<0.05$) along with the DI at the same bag volumes (mean bias: −0.37 mm²/mmHg and −0.55 mm²/mmHg, $p<0.05$). There was also a trend towards greater bag pressures at 30 mL (mean bias: +2.08 mmHg, $p=0.114$) and 40 mL (mean bias: +2.81 mmHg, $p=0.129$) volumes in the stepwise protocol. There were no differences between protocols in measurements of minimum diameter, maximum bag pressure, or DI during voluntary squeeze ($p>0.05$).

Conclusion and Inferences: There are differences between the two commonly described FLIP measurement protocols at rest, although there are no differences in the assessment of squeeze function. Consensus agreement is required to agree the most appropriate FLIP measurement protocol in assessing anal sphincter function.

Keywords
anal sphincter, distensibility, fecal incontinence, functional lumen imaging probe, sphincter function
1 | INTRODUCTION

Fecal incontinence (FI) affects 8% of the adult population,1 with anal sphincter dysfunction considered a principal cause.2,3 High-resolution anorectal manometry (HRAM) with a fixed-diameter catheter is the investigation of choice for sphincter dysfunction.4 However, resistance to distension has been proposed as the main determinant of sphincter function5 leading to the development of tests of sphincter distensibility.6

The Functional lumen imaging probe (FLIP)7–9 measures distensibility of a sphincter during volume-controlled distension and has demonstrated utility in the investigation of FI.6,7,10 However, for research between units to be comparable, standardization of physiological measurements is crucial for the development of this technology to continue.11 Two FLIP measurement protocols termed “stepwise” and “ramp” have emerged from different specialist centers risking a lack of standardization. Using the stepwise protocol, authors have reported distensibility measurements at fixed bag volumes in patients with FI,12 and healthy controls.13 The ramp protocol, while also measuring parameters at the same fixed bag volumes, adds other measurements during opening and closing of the anal canal, which have clinical utility in the investigation of FI.13–15 These measurements at fixed bag volumes have never been compared between protocols meaning different studies cannot be combined or compared. This study aims to compare the performance of these two protocols in the same patients to establish if differences exist between them.

2 | MATERIALS AND METHODS

2.1 | Patient recruitment

Patients with FI were identified prospectively and provided written informed consent. FI severity was assessed with the Vaizey score16 and the impact on quality of life by the Manchester Health Questionnaire.17 Patients were excluded if they lacked cognitive capacity, were pregnant, or had a diagnosis of anorectal cancer or inflammatory bowel disease.

2.2 | Functional lumen imaging probe

The EndoFLIP™ system (Medtronic®, MN, USA) uses a highly compliant 12 cm bag that fills with a conductive solution to a diameter of 25 mm (EF-325N catheter). Using impedance planimetry, the diameter of the bag is measured at 5 mm intervals over 8 cm. In combination with a pressure transducer, FLIP records diameter and pressure measurements.7

2.3 | Functional lumen imaging probe measurement protocols

There are two measurement protocols termed “ramp” and “stepwise” which have been highlighted in a recent review (Figure 1).9

Key points

1. There is no agreed measurement protocol for FLIP assessments of anal sphincter function.
2. Differences exist between the two commonly described (‘stepwise’ and ‘ramp’) measurement protocols.
3. The most relevant FLIP parameter and associated measurement protocol requires agreement through consensus.

With the ramp protocol, the FLIP bag fills at a rate of 40 mL/min to 10 mL twice, then to 20, 30, 40, and 50 mL. Between each filling volume, the bag is emptied. In the stepwise protocol, the bag is filled at the same rate from 0 to 50 mL in increments of 10 mL without deflation between steps. In each protocol, distension to a fixed bag volume is followed by 30s of iso-volumetric recording of resting parameters before the patient is asked to squeeze for 10s. The ramp and stepwise protocol last 13 and 7 min respectively unless the measurements are interrupted by the clinician.

Patients underwent measurement with both protocols in the order randomized by a statistician before recruitment. Between measurements, the catheter was removed, and 5 min elapsed.

2.4 | Analysis of the functional lumen imaging probe data

Data were analyzed using a customized MATLAB subroutine (R2022a, Mathworks, Natick, MA, USA) described previously.18 Resting measurements were recorded as the averaged bag pressure and minimum diameter over 10 s during the 30-s resting period. During squeeze assessment, the minimum diameter and corresponding maximum bag pressure were recorded. Cross-sectional area (CSA) was calculated from the corresponding diameter measurements. Distensibility index (DI) is calculated as minimum CSA/bag pressure.

2.5 | Statistical analysis

Statistical analysis was performed using SPSS Version 29.0 for Mac® (IBM, NY, USA). The mean differences (mean bias) and 95% confidence interval (95% CI) of the differences were calculated. A paired t-test was used, and statistical significance considered at p < 0.05 level.

2.6 | Ethical approval

This study received approval from the local research ethics committee (Greater Manchester West, UK Ref: 19/NW/0633) and was conducted according to the Declaration of Helsinki.
3 | RESULTS

Twenty patients with FI were included (Table 1). In one patient, distension to 50 mL during the ramp measurement was not tolerated.

3.1 | Resting assessment

Measurements obtained at bag volumes 30, 40 and 50 mL are presented in Table 2, with the mean bias calculated as stepwise protocol—ramp protocol. Results at 10 and 20 mL bag volumes are not presented as the anal canal remained closed in all patients. No significant differences were seen in measurements of bag pressure between protocols, although there was a trend towards higher bag pressures during stepwise assessment. There was a difference between the minimum diameter measurements at 30 and 40 mL bag volumes in the stepwise protocol, which were on average, 0.55 and 1.18 mm less than those measured during the ramp assessment ($p < 0.05$). There was a trend towards reduced minimum bag diameter measurements at 50 mL ($-1.00 \text{ mm} [95\% \text{ CI: } -2.20 \text{ to } -0.20]; p = 0.098$). Similarly with DI, measurements were lower during stepwise assessment at 30 and 40 mL ($p < 0.05$). However, once the bag reaches 50 mL, there was only a trend towards reduced measurements in the stepwise assessment (mean bias: $0.70 \text{ mm}^2/\text{mmHg} [95\% \text{ CI: } -1.60 \text{ to } -0.19]; p = 0.115$).

3.2 | Squeeze assessment

The data obtained at 30, 40, and 50 mL bag volume during squeeze is presented in Table 3. Data obtained at 10 and 20 mL is not presented as the anal canal remained closed in all patients. There were no significant differences in squeeze measurements obtained between the ramp or stepwise measurement protocol.

4 | DISCUSSION

This study aimed to investigate if there were differences in measurements between the stepwise and ramp FLIP protocols to...
establish if results from specialist centers could be combined and compared. However, it has demonstrated there are differences at rest with the minimum diameter and DI from the stepwise protocol less than the ramp protocol at 30 and 40 mL bag volumes. At 50 mL there remained a non-significant trend towards reduced minimum diameter and DI in the stepwise protocol. Furthermore, there was a trend towards greater resting bag pressures in the stepwise assessment. There were, however, no differences observed in measurements of squeeze function between the protocols.

Recent work with HRAM had addressed a lack of standardization which made comparisons between institutions impossible. However, while it is invariably the EF-325N catheter used in FLIP measurements of the anal sphincter, there is no such agreed measurement protocol with two currently reported in the literature. There is therefore a risk that if this technology becomes more widespread, institutions will adopt different practices hindering the generalizability of their findings.

The stepwise protocol has been used to describe the distensibility of the anal canal at fixed bag volumes. It can differentiate between patients with FI and healthy controls and is proposed as a complementary tool to HRAM. By contrast, the ramp protocol adds a dynamic assessment of the sphincter complex during inflation and deflation. Various additional parameters can be measured during opening–closing of the anal canal including the yield pressure and pressure-strain elastic modulus which have been used in the investigation of FI. The stepwise protocol is faster to perform at approximately 7 min, whilst the ramp protocol lasts approximately 13 min. The different results at the same bag volumes observed in this study may be a consequence of the unequal loading-unloading (inflation-deflation) process and prolonged measurement time in the ramp protocol. This changes the viscoelastic properties of the anal sphincter through preconditioning which can explain the increased diameter and DI measurements observed at rest in the ramp protocol. Additionally, given the length of the FLIP catheter (12 cm), a significant proportion remains in the lower rectum. This may activate the recto-anal inhibitory reflex to different extents between each protocol, which cannot be quantified with the current single bag catheter design.

**TABLE 1** Patient characteristics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number of patients (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (range)</td>
<td>60 (38–78)</td>
</tr>
<tr>
<td>Male/Female, n (%)</td>
<td>1 (5%)/19 (95%)</td>
</tr>
<tr>
<td>Obstetric History, n (%)</td>
<td></td>
</tr>
<tr>
<td>Parous†</td>
<td>18/19 (95%)</td>
</tr>
<tr>
<td>Vaginal delivery‡</td>
<td>18/18 (100%)</td>
</tr>
<tr>
<td>Caesarean Section‡</td>
<td>2/18 (11%)</td>
</tr>
<tr>
<td>Episiotomies or perineal tear‡</td>
<td>14/18 (79%)</td>
</tr>
<tr>
<td>Bowel function history, n (%)</td>
<td></td>
</tr>
<tr>
<td>Urge fecal incontinence</td>
<td>19 (95%)</td>
</tr>
<tr>
<td>Passive fecal incontinence</td>
<td>8 (40%)</td>
</tr>
<tr>
<td>Evacuation difficulties</td>
<td>9 (45%)</td>
</tr>
<tr>
<td>Previous treatments for bowel dysfunction, n (%)</td>
<td>7 (35%)</td>
</tr>
<tr>
<td>Trans-vaginal rectocele repair</td>
<td>4 (20%)</td>
</tr>
<tr>
<td>Percutaneous tibial nerve stimulation</td>
<td>3 (15%)</td>
</tr>
<tr>
<td>Trans-anal repair of mucosal prolapse</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Vaizey incontinence score, mean (SD)</td>
<td>13 (4)</td>
</tr>
<tr>
<td>Manchester Health Questionnaire, mean (SD)</td>
<td>426.41 (196.14)</td>
</tr>
</tbody>
</table>

Abbreviation: SD, standard deviation.
†Female only.
‡Percentage calculated from non-parous females only.
§Percentage calculated from females with vaginal deliveries only.

**TABLE 2** A summary of the differences between resting measurements obtained at 30, 40, and 50 mL bag volumes between a ramp and stepwise FLIP measurement protocol.

<table>
<thead>
<tr>
<th>FLIP measured parameter (n=20)</th>
<th>Mean (SD) stepwise</th>
<th>Mean (SD) ramp</th>
<th>Mean difference (bias) (stepwise—ramp)</th>
<th>95% CI of bias</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bag pressure at 30 mL, mmHg</td>
<td>26.00 (6.75)</td>
<td>23.92 (6.91)</td>
<td>2.08</td>
<td>−0.54 to 4.71</td>
<td>0.114</td>
</tr>
<tr>
<td>Bag pressure at 40 mL, mmHg</td>
<td>44.69 (10.08)</td>
<td>41.87 (9.30)</td>
<td>2.81</td>
<td>−0.89 to 6.52</td>
<td>0.129</td>
</tr>
<tr>
<td>Bag pressure at 50 mL, mmHg†</td>
<td>58.92 (10.24)</td>
<td>56.34 (10.66)</td>
<td>2.84</td>
<td>−1.31 to 7.00</td>
<td>0.168</td>
</tr>
<tr>
<td>Minimum diameter at 30 mL, mm</td>
<td>5.25 (0.86)</td>
<td>5.81 (1.37)</td>
<td>−0.55</td>
<td>0.09 to −0.12</td>
<td>0.016</td>
</tr>
<tr>
<td>Minimum diameter at 40 mL, mm</td>
<td>8.53 (2.49)</td>
<td>9.27 (2.88)</td>
<td>−1.18</td>
<td>0.18 to −0.57</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Minimum diameter at 50 mL, mm²</td>
<td>14.52 (2.25)</td>
<td>15.27 (3.78)</td>
<td>−0.70</td>
<td>2.20 to 0.20</td>
<td>0.098</td>
</tr>
<tr>
<td>DI at 30 mL, mm²/mmHg</td>
<td>0.90 (0.38)</td>
<td>1.27 (0.80)</td>
<td>−0.37</td>
<td>−0.64 to −0.09</td>
<td>0.012</td>
</tr>
<tr>
<td>DI at 40 mL, mm²/mmHg</td>
<td>1.55 (1.10)</td>
<td>2.11 (1.42)</td>
<td>−0.55</td>
<td>−0.94 to −0.16</td>
<td>0.008</td>
</tr>
<tr>
<td>DI at 50 mL, mm²/mmHg</td>
<td>3.17 (1.65)</td>
<td>3.76 (2.24)</td>
<td>−0.70</td>
<td>−1.60 to 0.19</td>
<td>0.115</td>
</tr>
</tbody>
</table>

Abbreviations: DI, distensibility index; FLIP, functional lumen imaging probe; SD, standard deviation.
†Data from 19 patients used for analysis.
*Paired t-test, significance at p < 0.05 level.
Bold indicates significance at p < 0.05 level.
This study has highlighted differences in resting measurements between the two FLIP protocols. Patients were measured with both protocols on the same day, with the order randomized, making each patient their own control to improve the validity of the findings. However, it is limited to 20 patients and whilst the results here highlight differences between these protocols at rest, their clinical significance in the investigation or management of FI requires consideration. Further work is required to define the role of FLIP and to agree, through consensus, the most appropriate distension protocol. Specifically, if the ramp protocol offers additional diagnostic value over simply the measurements of fixed bag volumes with the stepwise protocol.

While the contributions of each component of the anal sphincter complex to each FLIP measurement are yet to be determined, these small differences in diameter at rest are likely overcome by the greater force of contraction from striated muscle, leaving no differences between squeeze measurements (Table 3).

This study has highlighted differences in resting measurements between the two FLIP protocols. Patients were measured with both protocols on the same day, with the order randomized, making each patient their own control to improve the validity of the findings. However, it is limited to 20 patients and whilst the results here highlight differences between these protocols at rest, their clinical significance in the investigation or management of FI requires consideration. Further work is required to define the role of FLIP and to agree, through consensus, the most appropriate distension protocol. Specifically, if the ramp protocol offers additional diagnostic value over simply the measurements of fixed bag volumes with the stepwise protocol.

### 5 CONCLUSION

When comparing the ramp and stepwise FLIP protocols there are differences at rest. The reason for this is likely differences in tissue preconditioning between the protocols. The most relevant FLIP parameter and associated measurement protocol requires agreement through consensus.

### AUTHOR CONTRIBUTIONS

AOC, DL, EK, AS and KT designed the study. AOC and DL undertook data acquisition. AOC, DL, EK, AS and KT were involved in data analysis and interpretation. AOC, EK, AS and DHV assisted in drafting the initial manuscript. AMD, AS, DHV, JM, EK and KT supervised the project and the preparation of the manuscript. All authors provided critical revision of the manuscript, were involved in intellectual discussion, approve the final version of the manuscript, and agree to be accountable for all aspects of the work.

### ACKNOWLEDGMENTS

The authors wish to acknowledge The Royal College of Surgeons of England for supporting this study.

### FUNDING INFORMATION

No specific sources of funding were obtained for this study.

### CONFLICT OF INTEREST STATEMENT

The authors wish to declare no competing interests related to the content of this manuscript.

### DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

### ORCID

Alexander O’Connor [https://orcid.org/0000-0002-3964-9152](https://orcid.org/0000-0002-3964-9152)

Donghua Liao [https://orcid.org/0000-0003-3908-6537](https://orcid.org/0000-0003-3908-6537)

### REFERENCES


---