Do we need an extra dimension? A pilot study on the use of three-dimensional anorectal manometry in children with functional constipation

Desiree F. Baaleman1,2,3 | Mana H. Vriesman1,2 | Marc A. Benninga2 | Neetu Bali1 | Karla H. Vaz1 | Desale Yacob1 | Carlo Di Lorenzo1 | Peter L. Lu1 | Ilan J. N. Koppen1,2

1Division of Pediatric Gastroenterology, Hepatology, and Nutrition, Department of Pediatrics, Nationwide Children’s Hospital, Columbus, Ohio, USA
2Department of Pediatric Gastroenterology and Nutrition, Emma Children’s Hospital, Amsterdam UMC, University of Amsterdam & VU University, Amsterdam, The Netherlands
3Gastroenterology and Hepatology, Amsterdam Gastroenterology Endocrinology Metabolism, Amsterdam UMC, Univ Amsterdam, Amsterdam, The Netherlands

Correspondence
Desiree F. Baaleman, Department of Pediatric Gastroenterology, Emma Children’s Hospital, Amsterdam UMC, University of Amsterdam, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands.
Email: d.f.baaleman@amsterdamumc.nl

Funding information
Desiree F. Baaleman received financial support from the Amsterdam Gastroenterology Endocrinology Metabolism (AGEM) research institute, the VSBfonds, and the Prins Bernhard Cultuurfonds with support from the Jadefonds to conduct this research

Abstract

Background: Recently, a new high-definition (or three-dimensional “3D”) high-resolution anorectal manometry (3D-ARM) catheter has been introduced. This catheter allows for a more detailed visualization of the anal canal. However, its clinical utility and tolerability in children with constipation are unknown. Our primary objective was to evaluate the agreement between findings from solid-state high-resolution anorectal manometry (HR-ARM) and 3D-ARM. Secondary objectives were to investigate if 3D-ARM has additional value over HR-ARM and to evaluate patient and provider experience.

Methods: Prospective pilot study including children (8–18 years of age) with functional constipation scheduled for anorectal manometry. Children underwent HR-ARM and 3D-ARM consecutively. We compared manometry results of both procedures and collected data on patient and provider experience via self-developed questionnaires.

Key Results: Data of ten patients were analyzed (60% female, median age 14.9 years). In the majority of patients, ARMs were performed awake (n = 8, 80%). In two patients, the recto-anal inhibitory reflex (RAIR) was visualized during HR-ARM but not during 3D-ARM. Anal canal resting pressures were significantly higher during 3D-ARM compared to HR-ARM (median 77 mmHg [IQR 59–94] vs. 69 mmHg [IQR 51–91], respectively, p = 0.037). No significant anatomical or muscular abnormalities were visualized during the 3D-ARM. The majority of children identified the 3D-ARM as the more unpleasant (5/7 [71%]) and more painful procedure (6/7 [86%]) and therefore preferred the HR-ARM (4/7 [57%]).

Conclusions & Inferences: In our patient sample, 3D-ARM was associated with more discomfort without providing more useful information and even resulted in an inconsistent visualization of the RAIR.

KEYWORDS
anorectal manometry, children, constipation, functional constipation
1 | INTRODUCTION

Functional constipation (FC) is a common disorder in children, with a worldwide pooled prevalence of 9.5%. It is characterized by infrequent, hard, large, and painful bowel movements and is often accompanied by fecal incontinence and abdominal pain. Children with FC are usually treated with behavioral interventions and oral laxatives but approximately one third of children remain symptomatic after 6–12 months of treatment. If conventional treatment fails, anorectal manometry (ARM) can be used to assess the neuromuscular function of the anorectal canal via a manometry catheter inserted in the rectum through the anus. ARM may be used to evaluate anal canal resting pressure, the presence of the recto-anal inhibitory reflex (RAIR) and defecation dynamics. The risk of not obtaining the results of the scheduled HR-ARM procedure. Moreover, since the 3D-ARM catheter has a larger diameter than the HR-ARM catheter, the 3D-ARM could theoretically dilate the anorectal canal if performed first, thereby affecting measurements of the consecutive HR-ARM.

2 | MATERIALS AND METHODS

We conducted a pilot study from 2017 to 2020 including children (8–18 years of age) who were scheduled for ARM (either awake or under anesthesia) and had a diagnosis of FC according to Rome III criteria. We excluded children with insufficient proficiency of the English language and with neuromuscular disorders or any other systemic disease which could affect the sphincter function. The local Institutional Review Board approved the study protocol (IRB15-01136). Patients were invited to participate in the study and thus to undergo 3D-ARM in addition to the HR-ARM which was already indicated, by one of the investigators of the research team. All parents gave written consent and all children older than nine years of age provided assent. On the day of the procedures, after obtaining consent and assent, data were collected on the child's medical history, current symptoms, and treatment. After baseline data collection, children proceeded with both ARMs. Both ARMs were performed prior to any other procedure, including digital rectal examination. Since HR-ARM was the golden standard to evaluate anorectal function, we performed the HR-ARM first. Thus, children could still refrain from undergoing the second manometry without the risk of not obtaining the results of the scheduled HR-ARM procedure. Moreover, since the 3D-ARM catheter has a larger diameter than the HR-ARM catheter, the 3D-ARM could theoretically dilate the anorectal canal if performed first, thereby affecting measurements of the consecutive HR-ARM.

2.1 | Manometry protocol

HR-ARM studies were performed using a solid-state catheter (UniTip High Resolution Catheter, model number K12959-L5-1038-D from Unisensor AG) according to our institutional protocol. 3D-ARM was performed with a high-definition manometry probe (The ManoScan™ AR 3D probe from Medtronic). If possible, the ARMs were performed awake with the patient lying on their left side. For those unable to tolerate the ARMs awake, or patients who were already scheduled to undergo another procedure under anesthesia, the study was performed under general anesthesia in the supine position. All procedures included assessment of the resting pressure of the anal canal and involved incremental rectal balloon inflations to evaluate the presence of the RAIR. If the study was performed awake, rectal sensory thresholds during balloon inflations were assessed, as well as the evaluation of squeeze and push (or bear down) maneuvers. After the first ARM, the exact same protocol,
including a similar number and volume of incremental balloon inflations, was followed for the other ARM in order to accurately compare outcomes.

2.2 | Analysis of manometric data

After completion of both manometries the manometries were analyzed by a pediatric gastroenterologist specialized in gastrointestinal motility disorders. Analyses of manometric data of HR-ARM were performed using a commercially available manometric system (Solar GI HRM v9.1, Medical Measurement Systems (MMS), Enschede, the Netherlands). Analyses of manometric data of 3D-ARM were performed with the use of specialized software (Given Imaging, Duluth, GA). The anal canal resting pressure was calculated as the mean pressure during a resting period of at least 20 s. This was usually measured at the beginning of the study unless a child was very nervous at the beginning and a more accurate measurement could be obtained later during the study. A normal RAIR was defined as a drop of >15% in internal anal canal pressure during a balloon inflation. In addition to these outcomes, if the ARMs were performed awake, the child was asked to perform squeeze and push-maneuvers and to report levels of sensation, urge, and discomfort during balloon inflations. During the squeeze maneuver the child was asked to squeeze the anal canal as strongly as possible for a period of 20–30 s from which maximum squeeze pressure and squeeze duration were calculated. During the push test, the child was asked to bear down for 20–30 s as if to defecate, the pressures visualized during this maneuver could indicate if the child was able to adequately relax their pelvic floor while increasing abdominal pressure. Rectal sensation was evaluated during each balloon inflation and the minimal balloon volume at which children-reported sensation, urge, and discomfort were recorded.17 During the investigation, the duration of both procedures was tracked and documented.

2.3 | Child and investigator outcomes

Children who underwent both HR-ARM and 3D-ARM awake were asked to complete a questionnaire, asking them which procedure was more unpleasant, more painful, and which one they preferred. Immediately after both ARMs the investigator who performed the ARMs answered a questionnaire regarding both procedures. Two investigators performed the ARM procedures. This questionnaire included questions on ease of insertion of catheter on a 5-point Likert-scale (1 = very difficult, 5 = very easy); ease of visualization of anal canal on a 5-point Likert-scale (1 = very difficult, 5 = very easy); bleeding during or after the investigation (yes/no); time duration of investigation (from insertion until removal of catheter).

2.4 | Statistical analyses

Data were analyzed with the use of SPSS version 21.0 (SPSS Institute, Chicago, IL) and expressed as median and interquartile ranges or number and percentages. Since no previous data were available on the use of 3D-ARM in children when initiating this study, we were not able to perform a power analysis and this study...
was setup as a pilot study. We aimed to include a sample of 12 patients based on recommendations on the minimal sample size of pilot studies. However, inclusion of patients was difficult, as children were not eager to have an additional ARM performed and three included children eventually refused to undergo the second ARM. Furthermore, most included patients reported that the 3D-ARM was more painful. Therefore, we decided to terminate the study after including 10 patients. Wilcoxon signed rank test and McNemar change test were used to compare outcomes of the two ARMs (HR-ARM vs. 3D-ARM). * indicates p Value < 0.05.

### RESULTS

Twenty patients with FC were approached for recruitment of which fourteen were enrolled in our study protocol, see Figure 2. Of those fourteen, three declined to proceed with the second manometry after the first one, and one could not proceed with 3D-ARM due to technical difficulties. Therefore, data of ten patients were analyzed (60% female, median age 14.9 years, IQR 13.0–16.4).

#### 3.1 Anorectal manometry findings

The majority of patients had their ARMs performed awake (n = 8, 80%). The indication for the ARMs in these eight patients was to evaluate for the presence of pelvic floor dyssynergia. Two patients had their ARMs performed under general anesthesia. In one patient the ARMs were combined with the placement of a colon manometry catheter under general anesthesia. The other patient has an autism spectrum disorder and was not deemed to tolerate an ARM awake. The indication for the ARMs under general anesthesia was to evaluate for the presence of the RAIR and to measure anal canal resting pressure. In one patient 3D-ARM was performed first because of the preference of the child. Measurement results of both ARMs are shown in Table 1. In two patients (20%)

| Procedure awake, n (%) | HR-ARM | 3D-ARM | p Value |
|------------------------|--------|--------|---------|
| Duration of procedure in minutes, median (IQR) | 11 (9–13) | 12 (9–13) | 0.953 |
| Resting pressure in mmHg, median (IQR) | 69 (51–91) | 77 (59–94) | 0.037 * |
| Recto-anal inhibitory reflex (RAIR) present, n (%) | 10 (100%) | 8 (80%) | 0.500 |
| Balloon volume to trigger RAIR, median (IQR) | 30 (10–50) | 20 (10–30) | 0.414 |
| Maximum squeeze pressure in mmHg, median (IQR) | 132 (118–137) | 127 (118–164) | 0.889 |
| Duration squeeze in seconds, median (IQR) | 11 (4.3–12) | 20 (10–24) | 0.050 |
| Abnormal push test, n (%) | 5 (63%) | 5 (63%) | 1.000 |
| Balloon volume at first sensation in ml, median (IQR) | 15 (10–50) | 10 (10–30) | 0.465 |
| Balloon volume with urge sensation in ml, median (IQR) | 30 (15–75) | 50 (20–60) | 0.785 |
| Balloon volume with discomfort in ml, median (IQR) | 105 (55–150) | 90 (50–120) | 0.157 |

* indicates p Value < 0.05.
the RAIR was only visualized during HR-ARM and not during subsequent 3D-ARM. Anal canal resting pressure was higher during 3D-ARM (median 77 mmHg [IQR 59–94] vs. 69 mmHg [IQR 51–91], p = 0.037). Although maximum squeeze pressure did not differ between ARMS, there was a trend towards a longer squeeze duration during 3D-ARM (median 20 s [IQR 10–24] vs. 11 s [IQR 4.3–12], p = 0.050). There were no statistically significant differences between other ARM outcomes. During evaluation of the 3D-ARM results, no significant anatomical or muscular abnormalities were observed.

3.2 | Child reported manometry experience

Seven children answered questions about their experience during both ARMs, two underwent both procedures under general anesthesia, and one did not complete the questionnaire. As shown in Table 2, the majority of children found the 3D-ARM the more unpleasant procedure (5/7 [71%]), and more painful procedure (6/7 [86%]), resulting in the majority of children preferring the HR-ARM (4/7 [57%]). Reasons for the preference for the HR-ARM included: “3D was more painful,” “it felt smaller,” “it felt less painful and like it wasn’t pushed up further.” Two children (29%) preferred the 3D-ARM. Reasons for preferring the 3D-ARM included: “it felt shorter, beginning was more painful but got better as it went on”, “3D was easier to squeeze”. One child (14%) had no preference for either one of the procedures.

3.3 | Investigator reported outcomes

Data on provider experience was available for eight children, see Table 2. On a 5-point Likert scale ranging from 1 (very difficult) to 5 (very easy), insertion of the 3D-ARM catheter was deemed significantly more difficult compared to insertion of the HR-ARM catheter (median 3 [IQR 1.5–3.5] vs. 4 [IQR 3–4.5], p = 0.038). The perceived ease of visualization of the anal canal did not significantly differ between procedures. In one child blood was seen on the catheter after removal of both the HR-ARM and 3D-ARM catheters, and in one child blood was seen on the catheter only after removal of the 3D-ARM. In both children, the HR-ARM was performed first.

4 | DISCUSSION

In this study, 3D-ARM rendered higher anal canal resting pressure values compared to HR-ARM. Also, our results suggest that it may be more difficult to visualize the RAIR with 3D-ARM compared to the HR-ARM. Most children preferred the HR-ARM because the 3D-ARM catheter was larger and according to some children led to a more painful procedure. However, because of the larger diameter of the 3D-ARM catheter, it may be easier for patients to squeeze (as mentioned by one of our participants), which is supported by our results on squeeze duration during the 3D-ARM procedure.

Other studies evaluating the agreement between HR-ARM and 3D-ARM have reported various differences between both methods. Studies exploring the effect of ARM catheter diameter size found that larger catheter diameters are associated with an increase in both resting and maximum squeeze pressure. It has been proposed that this is the result of an increase in the sarcomere length of the external anal sphincter, assuming the external anal sphincter operates on the ascending limb of the length–tension curve. In other words, during the normal resting phase the external anal sphincter is tonically contracted, operating at a relatively short sarcomere length. When the sphincter is dilated or stretched, its sarcomere length increases, resulting in an increase in muscle capacity. This theory is supported by results from a study including 201 adults with ano-rectal disorders who underwent both conventional water-perfused ARM and 3D-ARM, where 3D-ARM rendered higher resting pressures. Another possible explanation for the higher resting pressures measured during 3D-ARM may be the discomfort experienced by the patients. More discomfort due to the larger diameter of the 3D-ARM catheter may make it more difficult for patients to relax. To our knowledge, only one study by Chakraborty et al. specifically evaluated the agreement between HR-ARM and 3D-ARM findings. Contrary to other findings, Chakraborty’s study, including 25 adult women with fecal incontinence, found higher resting pressures during HR-ARM compared to 3D-ARM (mean 64 ± 18 mmHg vs. 49 ± 19 mmHg, p < 0.001). Chakraborty et al. hypothesized that this may be the result of transformer hardware or software issues. However, another explanation may be that the external anal sphincter of participants in their population may not operate on the
ascending limb of the length-tension curve. An increase in diameter beyond the peak muscle capacity may then result in a decrease in muscle tension, as was seen in one of the previous studies which explored the effect of probe diameter on the anal canal pressure of 10 healthy women.20 Unlike our study results, Chakraborty et al. described that 25 adult woman had a higher squeeze pressure during 3D-ARM compared to HR-ARM (mean 21 ± 10 mmHg vs. 13 ± 7 mmHg, p < 0.05).21 The higher squeeze pressure found by Chakraborty et al., and the longer squeeze duration found in our study are likely the result of patients being able to sense and contract their muscles better around the larger and more rigid 3D-ARM catheter.

In two children we were unable to visualize the RAIR during 3D-ARM using the same study protocol as was used during HR-ARM. In both children, the HR-ARM was performed first. It is unclear why the RAIR was not visualized during 3D-ARM using the same balloon volume as during HR-ARM. The higher anal canal resting pressure during the 3D-ARM have may have obscured the visualization of the RAIR, as the absolute decrease in pressure may have been relatively small, although no other study has described this before.

The clinical utility of the 3D-ARM in children with FC is currently being evaluated. In adults, 3D-ARM has demonstrated its safety and clinical utility. A study including 221 3D-ARM studies reported that its clinical advantage over HR-ARM is the possibility to visualize puborectalis function and identify focal muscular defects.22 However, quantitative metrics of these outcomes are not yet available, resulting in relative low inter-observer agreements reported in this study. Another study in adults reports that 3D-ARM may be used to differentiate different types of dyssynergic defecation which may be useful to predict biofeedback outcomes in adults.23 Although in children the clinical benefit of biofeedback has not been shown,24 differentiation of dyssynergic defecation subtypes may facilitate the identification of patients in whom biofeedback may be effective.25 Although this may seem promising, an important limitation of the use of 3D-ARM to evaluate dyssynergic defecation is the position of the child. With the large, rigid (and expensive) 3D-ARM catheter, it is safer for a child to be in a left lateral position while trying to push-out the catheter. However, studies have shown that defecation is best evaluated in an upright position.25 Moreover, a recent systematic review concluded that the overall role of ARM in evaluating dyssynergic defecation seems limited.26 Therefore the usefulness of 3D-ARM in children may be limited to cases in which there is a suspicion of anatomical malformations, anatomical defects, or complications after anorectal surgery. Future studies may evaluate if in these cases the 3D visualization provides useful additional information compared to the HR-ARM, or other imaging studies.

Another aspect which should be taken into consideration is the costs of both procedures. For the 3D-ARM, we used the ManoScan AR 3D catheter which costs 26,500 USD. The balloon for each 3D-ARM procedure costs around 38 USD. For the HR-ARM, we used the AR Catheter Model #K12959-L5-1038-D, which costs 13,500 USD. The balloon for each HR-ARM procedure costs around 22 USD. In conclusion, the costs of 3D-ARM are higher than the costs of HR-ARM, when assuming that the same manometry system is used and the catheters are equally durable.

Strengths of our study include the prospective nature of the study, the consecutive performance of both ARM procedures, enabling a head-to-head comparison, and the evaluation of investigator and patient experience. The use of the exact same ARM protocol, including the number and volume of incremental balloon inflations for each patient may be considered both a strength and a limitation. It may be considered a strength as it results in a reliable comparison of patient experience, if one of the ARMs would have taken a lot longer, this could have affected the patient preference. However, it may also be considered a limitation, as in a few patients, the RAIR was not visualized during 3D-ARM which may have not been the case if we would have used higher balloon volumes. Other limitations of our study include the small and relatively older patient sample, limiting the generalizability of our findings. The larger size of the 3D-probe limits its use in newborns and infants, and the fact that school age children and adolescents found it more uncomfortable may suggest that younger children may find it more painful. Also, since the majority of patients had the 3D-ARM performed last, their experience during the HR-ARM may have biased their expectations of the 3D-ARM.

In conclusion, results of this pilot study indicate that the use of 3D-ARM in children without known anatomical abnormalities may not be preferable. In a select (post-surgical) patient population, use of the 3D-ARM may provide more information. However, in a child with intractable functional constipation, use of the 3D-ARM may cause more discomfort without providing more useful information.

ACKNOWLEDGMENTS
We would like to acknowledge the invaluable assistance of Roberta Chaney, RN and Charmaign Albright, RN in performing the manometry studies and completing the research project.

CONFLICT OF INTEREST
Authors have no conflict of interest to declare relating to the content of this article.

AUTHOR CONTRIBUTIONS
MAB, DY, CDL, and IJNK were involved in design of the work. DFB, MHV, and PLL contributed to acquisition and analysis of data. DFB contributed to analysis of data. DFB, MHV, MAB, NB, KHV, DY, CDL, and PLL contributed to interpretation of data. DFB and UNK drafted the initial manuscript. MHV, MAB, NB, KHV, DY, and CDL critically revised the manuscript for important intellectual content. All authors made substantial contributions to the work, approved the final version of the manuscript as submitted, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

DISCLOSURE
No competing interests declared.
REFERENCES
1. Koppen IJN, Vriesman MH, Saps M, et al. Prevalence of functional defecation disorders in children: a systematic review and meta-analysis. J Pediatr Gastroenterol Nutr. 2018;198(121-130):e126.
2. Dehghani SM, Kulouee N, Honar N, Imanieh MH, Haghighat A, Jafari M, et al. Anxiety associated with high-resolution anorectal manometry: a comparative study on a large patient population with anorectal disorders. Neurogastroenterol Motil. 2018;67(3):322-327.
3. Lamparyk K, Mahajan L, Debeljak A, Steffen R. Anxiety associated with high-resolution anorectal manometry in pediatric patients and parents. J Pediatr Gastroenterol Nutr. 2017;65(5):e98-e100.
4. Banasiuk M, Banaszek M, Dziekiewicz M, M. An ANMS-NASPGHAN consensus document on anorectal and colonic manometry in children. Neurogastroenterol Motil. 2017;29(1):8.
5. Meinds RJ, Trzpis M, Broens PMA. Anorectal manometry may reduce the number of rectal suction biopsy procedures needed to diagnose hirschsprung disease. J Pediatr Gastroenterol Nutr. 2018;67(3):322-327.
6. Basilo G, Bharucha AE. High-resolution anorectal manometry: an expensive hobby or worth every penny? Neurogastroenterol Motil. 2017;29(8):12.
7. van der Plas RN, Benninga MA, Büller HA, et al. Biofeedback training in treatment of childhood constipation: a randomised controlled study. Lancet. 1996;348(9030):776-780.
8. Rao SSC, Kavlock R, Rao S. Influence of body position and stool characteristics on defecation in humans. Off J Am Coll Gastroenterol. 2006;101(12):2790-2796.
9. Andrianjafy C, Luciano L, Loundou A, Bouvier M, Vitton V. Three-dimensional high-resolution anorectal manometry to diagnose dyssynergic defecation: systematic review and meta-analysis of diagnostic test accuracy. Neurogastroenterol Motil. 2021;33:e14137.

How to cite this article: Baaleman DF, Vriesman MH, Benninga MA, et al. Do we need an extra dimension? A pilot study on the use of three-dimensional anorectal manometry in children with functional constipation. Neurogastroenterology & Motility. 2022;34:e14370. doi:10.1111/nmo.14370