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Characterization and correction of pressure drift in the ManoScan™ high-resolution manometry system: *In vitro* and *in vivo*

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Key Points

- The aim of this study was to provide critical in-depth analyses of the reported pressure drift in the ManoScan high-resolution manometry (HRM)™ system.
- Studies were performed *in vitro* and *in vivo*, and two correction methods – thermal compensation (TC) and interpolated thermal compensation (ITC) – were tested.
- Overall pressure drift varied both between studies ($p < 0.001$) and within sensors ($p < 0.001$).
- Drift resulted from thermal shock, an initial pressure change at intubation, and baseline drift, a linear drift over time ($R^2 > 0.96$).
- The substantial drift in the ManoScan™ HRM system is highly variable and not corrected via the standard operating instructions.

Abstract

Background *A substantial pressure drift in high-resolution manometry (HRM) has been reported; however, fundamental questions remain regarding the origin and management of this drift. The aim of this study was to provide critical in-depth analyses of ManoScan™ HRM drift in vitro and in vivo.* ***Methods*** *A total of sixteen 15-min studies and twelve 5-h studies were performed in a water bath at 37 °C at 4.0 cm depth (2.9 mmHg) with ESO and ESO Z catheters. Six 5-h in vitro studies were performed similarly at a depth of 9.0 cm (6.6 mmHg). Eight 15-min studies and nine 8-h in vivo studies were performed with healthy participants. Two correction methods – thermal compensation (TC) and interpolated thermal compensation (ITC) – were tested.* ***Key Results*** *Overall pressure drift varied both between studies ($p < 0.01$) and within sensors ($p < 0.01$). Drift resulted from thermal shock, an initial pressure change at intubation, and baseline drift, a linear drift over time ($R^2 > 0.96$). Contrary to previous reports, there was no correlation between drift and average ($r = -0.02$) or maximum pressure exposure ($r = -0.05$). Following data correction, ITC had the lowest median error but persisted with a maximum error of 2.5 mmHg (IQR = 3.0).* ***Conclusions & Inferences*** *The substantial drift in the ManoScan™ HRM system is highly variable and not corrected via the standard operating instructions. ITC has superior performance but requires communication with the manufacturer to enable this option. This has a substantial impact on clinical diagnosis, utility of existing normative data, and future research of HRM.*

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INTRODUCTION

A substantial pressure drift in the ManoScan™ high-resolution manometry (HRM) system has been reported, refuting the manufacturer's report that pressure uniformity remains within 2 mmHg for 4 h or less of recording.[1–3] Although it is well established that this drift is considerable, variable, and not corrected by standard operating instructions,[2,3] three fundamental questions remain insufficiently answered.

Firstly, what is the pattern of drift within and across studies? Although it is clear that drift is present, there are conflicting reports on the pattern of this drift. Robertson *et al.*[2] evaluated drift *in vitro*, using a water bath of known depth during 2-h recordings. The authors identified two components comprising pressure drift: a 'thermal effect', or an immediate change in pressure as the catheter temperature changes to body temperature at intubation, and a 'baseline drift', or linear drift across time. In one of their analyses, Babaei *et al.*[3] evaluated drift *in vivo* by monitoring the first pharyngeal sensor from a large dataset of 560 clinical studies recorded by six distinct HRM catheters. The authors simply reported that the pressure drift is 'variable throughout the recording even in the pharynx' (p. 283).

Secondly, what components contribute to drift? Although Robertson *et al.*[2] found the 'thermal effect' to result from temperature shock, they stated that 'baseline drift' is directly related to study duration, increasing with a linear trajectory. In contrast, Babaei *et al.*[3] concluded 'contrary to common perception, temperature, duration, and even peak pressure exposure are not the principal determinants of variable [pressure drift] across sensors of a clinical manometry study' (p. 283). They speculated that average pressure exposure on a sensor was the most influential factor in predicting pressure drift. However, the authors did not report if they removed drift from average pressure exposure before correlating the average pressure with drift. This has the potential to greatly bias results. Further, with an average recording duration of 35 min (±14 min), it is unclear if study durations were sufficient to reveal additional baseline drift.

Thirdly, how do the available correction methods operate and perform? Both articles reported that 'thermal compensation' (TC) does not sufficiently address the drift; however, neither study used the ManoView™ analysis software to apply TC. Additionally, Robertson *et al.*[2] replicated a second correction method (activated in the software following discussion with manufacturer), termed 'interpolated thermal compensation' (ITC) with a manual compensation algorithm. As above, the accuracy and generalizability of their manual replication of this secondary analysis method is unknown.

The aim of this study was to explore these three questions *in vitro* and *in vivo*, both in abbreviated and extended-length recordings. Although *in vitro* studies have been criticized in previous reports,[3] a controlled environment is robust for investigating system faults. This study is the first to analyze drift both *in vitro* and *in vivo*, as well as the first to evaluate correction methods using the ManoView™ analysis software. This is important for both clinical use and future research of HRM.

MATERIALS AND METHODS

Equipment

All HRM studies were completed using the ManoScan 360™ HRM system (Model A120) and combined ManoScan Z™ system (Model A200). Two catheters were tested as part of this protocol: (i) ManoScan™ ESO catheter (EPS0042) with 36 pressure sensors at 2.75 mm diameter and (ii) ManoScan™ ESO Z catheter (EAZ1523) containing 36 pressure sensors and 18 impedance channels at 4.2 mm diameter. Both catheters were free from defect and under warranty, with 169 and 33 uses for the ESO and ESO Z catheters, respectively. *In vivo* calibrations were routinely performed, and each recording session was preceded by calibration per standard operating instructions. Manosheath was not utilized.

Procedure

Eight 15-min and nine 8-h *in vivo* studies were performed with healthy participants using the ESO catheter. Ethical approval was obtained from the local institutional review board with informed consent obtained prior to commencement of data collection. The participants ranged in age from 21 to 52 years old (mean = 32.3 years). No participant reported a history of dysphagia, neurologic disorder, or muscular impairment. No participant reported use of any medications that might have affected swallowing or sleep. For the 15-min *in vivo* studies, data were collected on volitional and spontaneous swallowing, with five cued dry swallows and five 10 mL thin liquid bolus swallows in 15 min (in addition to spontaneous swallowing generated by the participant). Data for the extended-length studies were collected overnight. The catheter was placed transnasally using a routine protocol.[4] As this research study investigated pharyngeal rather than esophageal swallowing, sensor 1 was located just inside the naris. The participant was assisted to achieve a comfortable position in bed following catheter insertion and was allowed to sleep. The researchers monitored the participant through observation of manometric recordings throughout the night and viewed via remote access to the HRM system. Approximately 8-h from intubation, the catheter was removed from the nasopharynx.

Eight 15-min and six 5-h *in vitro* studies were performed in a water bath at 37 °C at a depth of 4.0 cm (equivalent to 2.9 mmHg). These short and long duration *in vitro* studies were replicated with both the ESO and ESO Z catheters, for a total of sixteen 15-min studies and twelve 5-h studies at a depth of 4.0 cm. An additional six 5-h studies were completed with the ESO Z catheter at an increased depth of 9.0 cm (equivalent to 6.6 mmHg). All 5-h *in vitro* studies included a 2-min initial 37 °C water bath, after which the catheter was held aloft in room-temperature air for 30 s, prior to reimmersion into the 37 °C water bath for the 5-h recording period. The temperature of the water bath was maintained with a digital immersion circulator and manually confirmed by the researchers with an external digital thermometer each hour.

Compensation methods

The manufacturer provides a standard TC method in the analysis software. TC is a single-step process where the user applies the correction method at a manually selected time point following extubation (while the catheter remains at body temperature, but with no external pressure applied). The recorded pressure on each sensor at this time point immediately post-extubation is then subtracted from the entire recording from each respective sensor. The manufacturer recommends applying TC to all studies prior to analysis.

Interpolated thermal compensation, a compensation method developed to compensate for longer duration studies, is not enabled by default in the software and requires manufacturer intervention for use. Interpolated thermal compensation is executed by selecting two time points with no external pressure applied, one at the beginning and one at the end of the study, which are set to 0 mmHg. Per the application note, drift between these two points is then corrected with a linear interpolation.[1] To achieve this, it is necessary to prepare a water bath at 37 °C. At the beginning of the recording, the catheter is immersed in this water bath for a period of 2 min. The catheter is then removed and held aloft at room-temperature air with no external pressure applied. Following this, intubation is performed. At the end of the study, the user records extubation, as done for the TC method. Thus, pressure is continually recorded from the point of immersion in the initial water bath to extubation at completion of the study. A two-step process in the ManoView™ software environment is used to compensate the data. First, TC is applied at the user-selected time point at catheter removal from the initial 2-min water bath to remove any thermal effects. Then, ITC is applied at the user-selected time point immediately following extubation at the end of the study to correct for drift.

Data analysis

Pattern of drift To investigate the first question regarding the pattern of drift within and across studies, only the extended-duration studies were evaluated. Raw data from the *in vivo* studies were exported and plotted using commercial software (MATLAB R2014a; The MathWorks Inc., Natick, MA, USA, 2014). A best-fit line approach was utilized to allow filtering of swallowing-related pressure from overall pressure recording during the extended duration *in vivo* studies. This best-fit line was generated for each sensor from a time point 2 min from the start of the study (when any thermal effect would be stabilized[1]) to 2 min from the end of the study (prior to extubation). A median across 10 samples at each time point was used to ensure the point selected was representative of recorded pressure at the start and end of the study. Baseline drift per hour was then calculated by subtracting the first point (median of 10 samples) of the best-fit line from the last point (median of 10 samples) and dividing by study length in hours. Thermal effect was estimated by subtracting the total baseline drift from the last point, with any residual pressure constituting a thermal effect.

The controlled 5-h *in vitro* studies were evaluated in a two-step manner. First, raw pressure data after catheter removal from the 2-min water bath were analyzed to evaluate thermal effects. The time point for analysis was manually selected and corresponded to the time of removal of the catheter from the water bath, leaving the catheter at 37 °C but with no external pressure applied (as specified in the user manual[1]). Any incident pressure above zero was attributed to a thermal effect. Then, these pressures were corrected using the first step of the ITC process on the standard ManoView™ software. Similar to *in vivo* studies, a best-fit line was generated to calculate baseline drift per hour. Additionally, linearity of baseline drift was evaluated for goodness of fit, comparing results to the best-fit line.

Non-parametric statistics were necessary due to the highly non-normal distributions of the pressure readings data (Shapiro–Wilk test, $p < 0.01$). A median was calculated to represent overall drift, baseline drift per hour, and thermal effect for each study. This comprised a median across the 36 sensors for each individual study. Maximum drift per hour and interquartile range (IQR) were also calculated. Kruskal–Wallis H tests were used to evaluate the variability across sensors and studies. A Wilcoxon signed-rank test was used to compare thermal effect and baseline drift per hour, respectively, between *in vivo* and *in vitro* data. Of note, sensor 27 in the ESO catheter was found to have values consistent with extreme outliers in the extended-duration studies. This sensor was removed from analyses but reported separately when applicable (Table 2).

Origin of drift A Pearson's product-moment correlation coefficient was used to analyze the relationship between thermal effect and baseline drift per hour. With regard to the *in vivo* studies, mean and maximum pressures on each sensor were calculated for the 15-min studies. Pearson's product-moment correlation coefficients were again used to analyze the relationships between average and maximum pressure exposure with overall drift, both before and after correction. A Wilcoxon signed-rank test was used to compare overall drift, thermal effect, and baseline drift per hour, respectively, between the low (4 cm water) and high (9 cm water) depth studies.

Correction methods Finally, TC was applied using the ManoView™ analysis software for the 15-min studies, and both TC and ITC were applied to the 5-h *in vitro* studies based on methods specified in the user manuals.[1,5] Performance of correction methods were evaluated from the *in vitro* water bath recordings as this allows direct comparisons from the corrected pressure readings to the known pressure applied, namely 2.9 mmHg. For the 15-min *in vitro* studies, the error was calculated by subtracting 2.9 mmHg from the recorded pressure at each sample across the 15-min period. Next, a median was taken from these results to represent the study error in its entirety. Then, from the raw data, TC was applied, and medians were re-computed with the same method to compare error of this compensation method to the raw data. A similar method was utilized for the extended-duration studies. The error was calculated by subtracting 2.9 from the recorded pressure at each sample across the 5-h period. Median error over time was then calculated by generating the median of all the sample errors across 30 min, 2 h, 4 h, and at the end of the study, respectively. The median error of the raw data was then

compared with the error resulting following application of TC or ITC.

RESULTS

Pattern of drift

Consistent with a previous report,[2] results suggest two individual components contribute to overall pressure drift, namely a thermal effect and baseline drift. Thermal effect is evidenced by a substantially altered pressure reading at the onset of the study, while baseline drift is noted by an increasing pressure reading with time. Importantly, thermal effect and baseline drift are superimposed on intraluminal pressure, which can only be estimated *in vivo*. This contrasts with *in vitro* studies that have a known, controllable pressure to which you can directly compare measurement error against. Plots of raw *in vitro* data from example ESO and ESO Z studies depicting thermal effect and baseline drift are available for review in Figs S1 and S2. *In vitro*, there was evidence of an overall drift in pressure that varied substantially both between studies (15-min studies, $\chi^2(7) = 122.9$, $p < 0.01$; extended-duration studies, $\chi^2(5) = 13.4$, $p = 0.02$) and within sensors (ESO catheter, $\chi^2(35) = 75.2$, $p < 0.01$; ESO Z catheter, $\chi^2(35) = 96.8$, $p < 0.01$) over trials.

Thermal effect When investigating the thermal effect in further detail, marked variability in both *in vivo* and *in vitro* recordings were revealed, as detailed in Tables 1A and B, respectively. The median across sensors was derived and then analyzed for a total study median. Wilcoxon signed-rank test revealed differences in thermal effect between *in vitro* and *in vivo* studies ($Z = -4.34$, $p < 0.001$).

Fig. 1 depicts the variability across sensors (*x*-axis) and pressure medians across studies (*y*-axis) for the *in vivo* (Fig. 1A) and *in vitro* (Fig. 1B) studies, respectively.

Baseline drift Evaluation of median, maximum, and interquartile range of baseline drift per hour across *in vivo* and *in vitro* studies is summarized in Table 2A and B. A median was taken across sensors and then summarized for a total study median. Wilcoxon signed-rank test revealed no significant differences in thermal effect between *in vitro* and *in vivo* studies ($Z = -1.02$, $p = 0.33$).

Linearity was calculated *in vitro* for each sensor and then averaged across studies in a summary statistic. Baseline drift was found to be linear within a given sensor and trial ($R^2 = 0.96$). Linearity was similarly high with both the ESO ($R^2 = 0.96$) and ESO Z catheters ($R^2 = 0.93$). Similar to the thermal effect, Fig. 2 depicts the median variability across each sensor (*x*-axis) and pressure medians across *in vivo* and *in vitro* studies (*y*-axis), respectively.

The relative contributions of thermal effect and baseline drift per hour to overall pressure drift for the 5-h *in vitro* studies were investigated. At the beginning of the study, thermal effect contributes to the majority of the overall drift for both the ESO and ESO Z catheters. However, with increasing study duration, baseline drift per hour comprises over 75% of the overall drift by the end of the study due to its linearly increasing properties.

Origin of drift

There was no correlation between thermal effect and baseline drift for the ESO catheter ($r = -0.02$) or ESO Z catheter ($r = 0.13$). The magnitude of the thermal effect and the slope of the linear baseline drift per hour appear to be unpredictable and highly variable.

Replication of the Babaei *et al.*[3] analyses were undertaken to investigate the relationship between overall drift and average pressure exposure on a sensor during a recording. Using non-corrected data, a high correlation was found between mean pressure exposure during the 15-min *in vivo* study with overall pressure

Table 1 (A) Thermal effect across *in vivo* studies using the ESO catheter (mmHg). (B) Thermal effect across *in vitro* studies, using ESO and ESO Z catheters (mmHg)

(A)		Study 1	Study 2	Study 3	Study 4	Study 5	Study 6	Study 7	Study 8
ESO catheter	Median (IQR)	−4.1 (3.9)	−1.2 (8.4)	−13.3 (8.6)	−12.4 (13.5)	2.5 (18.1)	−11.5 (9.7)	−2.6 (11.0)	−5.7 (11.3)
	Maximum	8.43	11.9	4.7	6.4	55.3	19.7	104.5	20.1

(B)		Study 1	Study 2	Study 3	Study 4	Study 5	Study 6
ESO catheter	Median (IQR)	4.4 (3.2)	−5.3 (10.3)	−0.1 (6.7)	−0.6 (5.6)	−1.7 (1.5)	−2.0 (1.6)
	Maximum	16.6	11.2	25.9	2.9	−0.3	3.3
ESO Z catheter	Median (IQR)	3.4 (3.9)	−2.1 (2.3)	−6.0 (1.4)	1.6 (1.9)	2.9 (3.6)	−1.5 (1.8)
	Maximum	28.3	10.8	−3.1	7.5	11.2	1.3

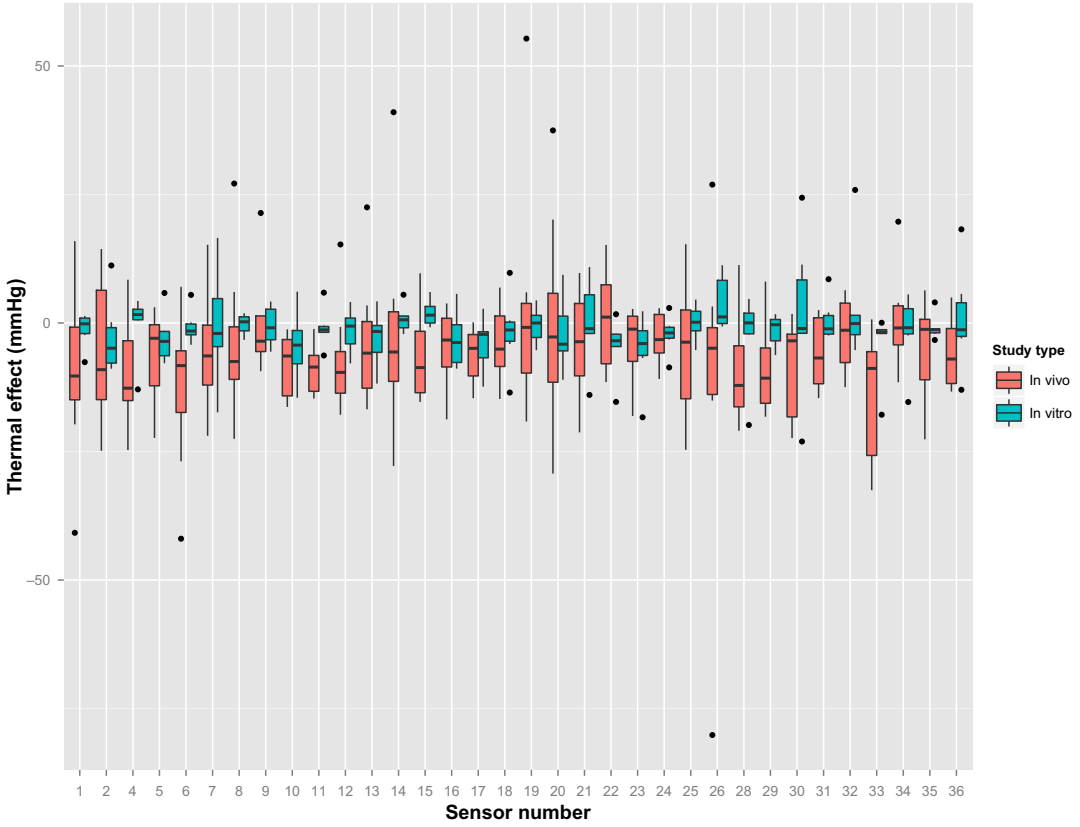

Figure 1 The box plot represents variability of the thermal effect across sensors over *in vivo* and *in vitro* studies. The line represents the median, the box represents the interquartile range (25th and 75th percentiles), and the whiskers represent the range.

Table 2 (A) Baseline drift per hour across *in vivo* studies using the ESO catheter (mmHg/hour). (B) Baseline drift per hour across *in vitro* studies, using ESO and ESO Z catheters (mmHg/hour)

(A)		Study 1	Study 2	Study 3	Study 4	Study 5	Study 6	Study 7	Study 8
ESO catheter	Median (IQR)	3.0 (0.9)	2.6 (1.1)	2.3 (1.4)	1.7 (1.0)	3.5 (1.7)	2.9 (1.7)	2.8 (1.6)	2.9 (1.6)
	Maximum	19.2	20.4	21.6	18.7	7.5	9.9	5.4	5.6

(B)		Study 1	Study 2	Study 3	Study 4	Study 5	Study 6
ESO catheter	Median (IQR)	3.2 (1.3)	3.8 (2.2)	3.1 (1.1)	2.1 (1.1)	2.2 (1.1)	2.0 (1.2)
	Maximum	6.6*	7.7*	6.5*	5.5	5.5	4.9
ESO Z catheter	Median (IQR)	3.7 (1.9)	3.1 (2.8)	3.8 (2.0)	4.0 (3.2)	4.0 (3.6)	4.4 (4.0)
	Maximum	5.9*	6.3*	7.8*	7.5	8.3	9.3

*If sensor 27 is included, the maximum baseline drift for the ESO catheter becomes 55.7, 65.6, and 90.6 across the three studies.

drift ($r = 0.93$, $p < 0.01$) and a moderate relationship between peak pressure exposure during a 15-min study with overall pressure drift ($r = 0.51$, $p < 0.01$). Importantly, however, when the data were corrected by applying TC, as recommended by the manufacturer, the relationships between overall drift and mean pressure exposure ($r = -0.02$, $p = 0.69$) as well as drift and maximum pressure exposure ($r = -0.05$, $p = 0.39$) disappeared.

A comparison of data with the catheter submerged at two depths was completed to further assess the influence of average pressure exposure and development of overall drift, thermal effects, and baseline drift per hour, respectively. Table 3 summarizes the median drift (and IQR) across the drifting subcategories for the two depths.

A Wilcoxon signed-rank test revealed significant differences between the two depths for overall drift

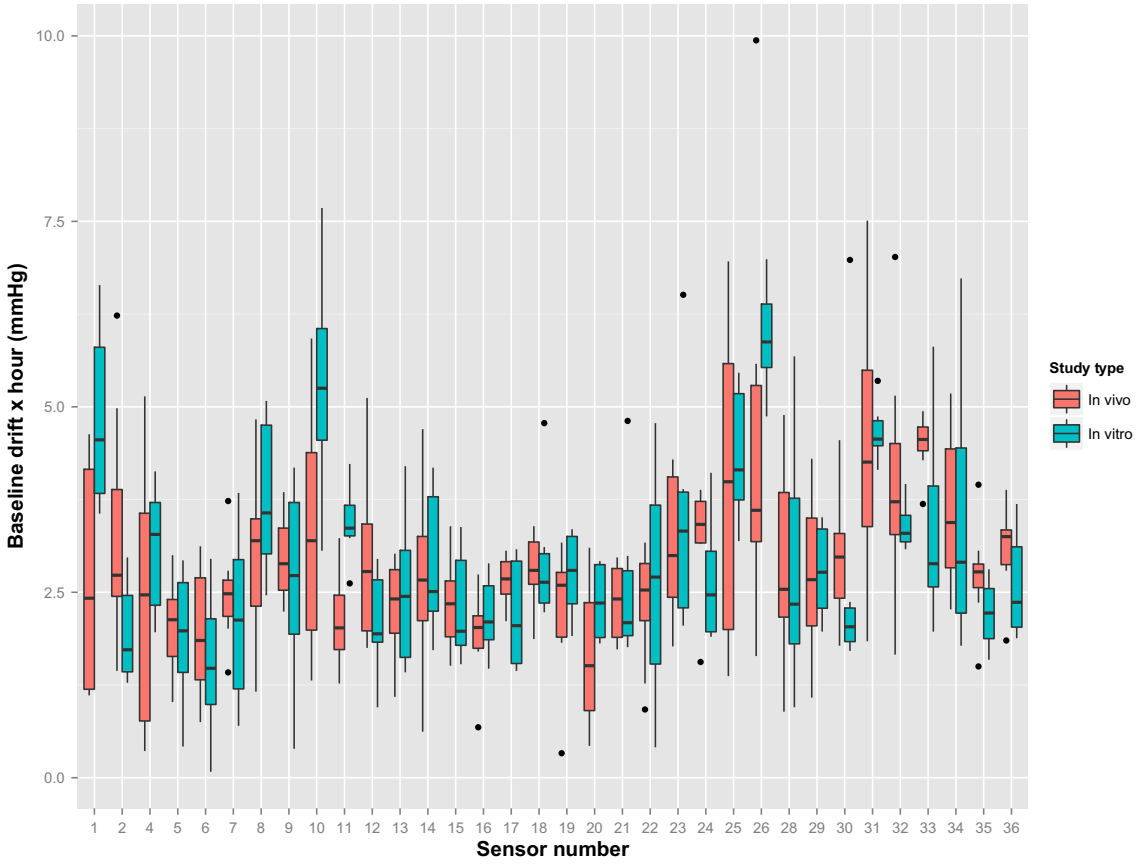

Figure 2 The box plot represents variability of the baseline drift per hour across sensors in the *in vivo* and *in vitro* studies.

($p < 0.01$) and baseline drift per hour ($p < 0.01$), but no significant differences were found between the two depths for median thermal effect ($p = 0.65$). The comparisons of thermal effect and baseline drift per hour are represented in Figs 3 and 4, respectively. The median thermal effect is close to zero due to the frequent occurrence of both negative and positive values across the two depths.

Table 3 Pressure contribution to an overall error across two depths

	2.9 mmHg (4.0 cm depth)	6.6 mmHg (9.0 cm depth)	Significance
Median baseline drift (IQR) (mmHg/h)	*3.7 (0.7)*	*4.2 (0.6)*	$p < 0.01$
Median thermal effect (IQR) (mmHg)	−0.1 (4.6)	−0.2 (1.0)	$p = 0.65$
Median total drift (IQR) (mmHg/hour)	20.9 (4.8)	20.7 (4.5)	$p < 0.01$

Correction methods

For the 15-min *in vitro* studies, the median error of the raw data was 3.4 (IQR = 0.8) for the ESO catheter and 3.6 (IQR = 0.5) for the ESO Z catheter. Following correction with TC, the median error reduced to 2.7 (IQR = 0.7) for the ESO catheter and 3.3 (IQR = 0.5) for the ESO Z catheter. ITC was not tested for the 15-min studies as it is intended for extended-duration studies. However, both correction methods were analyzed in the extended-duration studies; a summary of the median error following correction by TC and ITC is summarized in Table 4. In this table, the extended-duration studies are segmented into four time periods for evaluation of measurement error over time. As the correction methods were applied to correct substantial drift at the end of extended-duration studies, performance of the correction methods at the shorter time points cannot be generalized to shorter duration studies. Short duration studies (<30 min) have substantially less baseline drift and therefore react differently to compensation than the extended-duration studies.

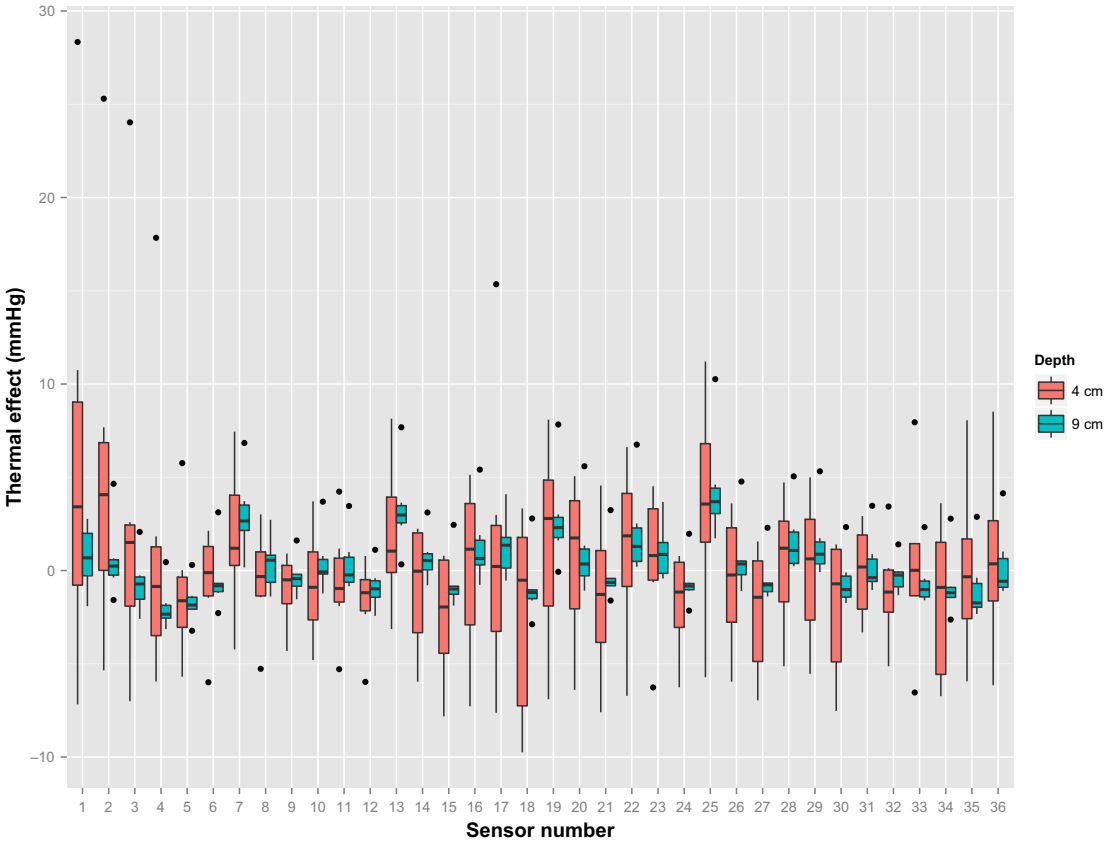

Figure 3 The box plot represents variability of the thermal effect across sensors in two depths.

As seen in Table 4, the non-corrected data have increasing median errors over time across studies. This contrasts to the findings of TC, where median error reduces as study duration increases. This is due to the design of TC, as this correction simply shifts the error to the beginning of the study. However, ITC is able to correct the extended-duration data with the lowest residual median error due to the two-point correction method. These principles are visually represented in Fig. 5, a schematic depicting the extended-duration correction profiles for TC and ITC from the non-corrected data.

Lastly, an analysis was undertaken to investigate accuracy of ITC when no initial TC is applied, as clinical and research users report a desire to perform ITC without the initial 2-min water bath for efficiency and retrospective application of this compensation. As depicted in Fig. S3, visual analysis of ITC as a single-step compensation (without the initial 2-min water bath) does not correct the thermal effect and inverts the slope of the baseline drift. Both steps of the ITC method are critical for optimized performance of this compensation.

DISCUSSION

This study is the first to evaluate pressure drift and correction methods in the ManoScan™ HRM system *in vitro* and *in vivo*. The influence of this overall pressure drift refutes manufacturer report that pressure uniformity remains within 2 mmHg for 4 h or less of recording.[1–3] Further, overall drift was found to significantly vary between sensors and studies and is not corrected via the standard operating instructions utilizing ManoView™ software.

Pattern of drift

This study confirms that overall drift comprises a thermal effect – a variable reaction secondary to rapid temperature change stabilizing after 2 minutes[1] – and baseline drift – a linear drift increasing with time.[2] This thermal effect and baseline drift per hour are physiologically implausible, as it is unlikely that the human body would have variable and extreme positive and negative pressure readings at intubation, increasing in amplitude throughout the study. Study duration

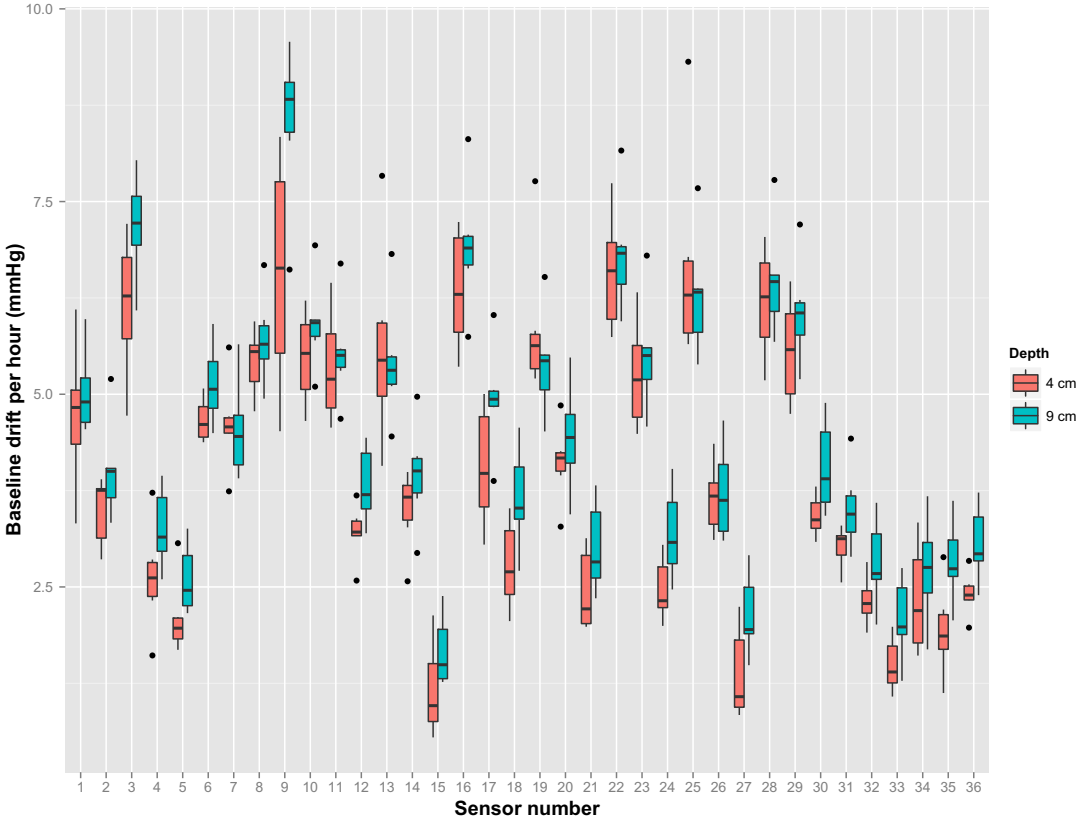

Figure 4 The box plot represents variability of the baseline drift per hour across in two depths.

Table 4 Median error (IQR) across extended duration *in vitro* studies evaluating the correction methods as compared with non-corrected data (mmHg)

	Non-corrected	TC	ITC
ESO catheter			
30 min	4.2 (0.9)	14.5 (3.3)	2.3 (2.5)
2 h	3.9 (0.8)	13.2 (2.7)	2.5 (3.0)
4 h	4.5 (1.8)	11.5 (2.2)	2.4 (3.1)
End of study	5.2 (2.3)	10.3 (2.0)	2.4 (3.0)
ESO Z catheter			
30 min	3.0 (1.4)	17.5 (3.2)	1.8 (0.5)
2 h	6.0 (2.5)	13.1 (2.7)	2.6 (0. 2)
4 h	9.0 (6.3)	9.6 (3.3)	2.5 (1.0)
End of study	10.6 (7.0)	9.6 (3.2)	2.2 (1.1)

has a direct impact on overall pressure reading due to the constancy of the baseline drift, with pressure readings increasing with time in all circumstances but with different sensors having different rates of baseline drift per hour. This contrasts with the findings of Babaei *et al.*,[3] who reported that drift is likely non-linear. In their analyses, they utilize a pharyngeal sensor (e.g., sensor 1) as a baseline measure to track overall pressure drift, arguing this sensor is 'recording in a compartment in equilibrium with atmospheric pressure' (p. 297). Although pharyngeal sensors are surrounded by atmospheric pressure at rest, the pharynx is a moving structure that can fluctuate throughout the recording due to extraneous movement associated with breathing and speech. Measurement may also be influenced by catheter positioning (e.g., resting against lateral pharyngeal wall). Due to these constraints, reliance on *in vitro* studies, rather than pharyngeal sensors, for confirmation of patterns of drift against a known baseline is critical. Thus, as the pattern of drift consisting of a thermal effect and subsequent baseline drift was easily replicated from previous reports,[2] and is evident *in vivo*, results support overall drift being comprised these two interacting elements.

Origin of drift

With regard to what elements contribute to drift, debate exists as to whether drift results from temperature and duration or average pressure exposure during a study. As stated previously, Babaei

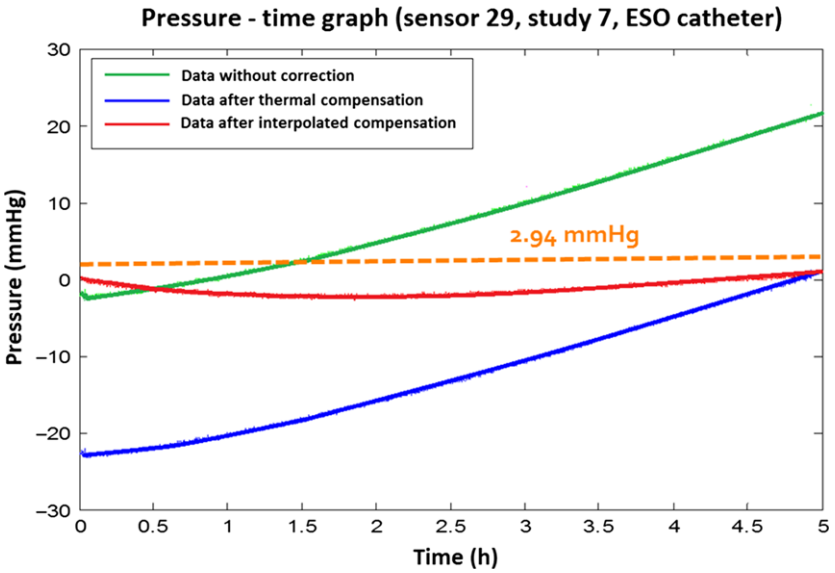

Figure 5 Comparison of correction methods using a single example sensor, with pressure-time graph showing non-corrected data, thermal compensated data, and interpolated thermal compensated data against the referent dashed line of actual pressure exposure (2.9 mmHg).

et al.[3] concluded that 'pressure drift preferentially affects esophageal high-pressure zones, and strongly correlates with "average pressure exposure" of a sensor during manometry' (p. 277). They speculated that average pressure exposure on a sensor is the most influential factor contributing to pressure drifts, while other recording parameters, such as duration, only explain a small proportion of overall drift. However, there are notable limitations in their analyses and subsequent conclusions. Firstly, with an average recording duration of 35 min (± 14 min), it is unclear if their study durations were sufficient to reveal additional drifting components (e.g., baseline drift). Secondly, if average pressure exposure during a study most accurately predicts pressure drift, it is unclear why sensors evaluated *in vitro* would have variable pressure drift. *In vitro*, sensors can be placed in a 37 °C water bath with constant pressure by keeping sensors at a fixed depth. Thus, all sensors *in vitro* were exposed to the same average pressure. Therefore, variable pressure drift despite equal average pressure exposure directly negates the possibility of average pressure exposure being the principal determinant of pressure drift. Finally, the authors do not report whether they performed TC prior to calculating average pressure exposure to a sensor. If compensation is not applied, then average pressure exposure to a sensor would be calculated including pressure drift, artificially inflating the average pressure exposure for sensors that coincidentally had higher rates of pressure drift. In replication, our findings support this notion. Although a significant correlation was found between pressure drift and non-corrected data, once the data were corrected based on manufacturer recommendations, relationships between pressure drift and average pressure exposure ($r = -0.02$) and between pressure drift and maximum pressure exposure ($r = -0.05$) disappeared. The high correlation reported by Babaei *et al.*,[3] replicated above without correction, is likely due to correlating pressure readings that were non-corrected (e.g., still containing drift inherent in the reading) with the drift itself. It is clear that average pressure exposure is not a primary mediator of pressure drift when the data are corrected based on manufacturer recommendations. Nevertheless, when comparing data derived from the two depths, significant differences were found in baseline drift per hour and overall pressure drift for extended-duration studies. Increased pressure may modulate the gradient (e.g., slope) of the baseline drift per hour, but further investigation is needed to explore this possibility. Due to the highly variable nature of the data with an inclination toward significant outliers, it is important to balance these significant findings by comparing medians and interquartile ranges, which are closely overlapped, and the non-significant difference of thermal effect between the two depths. These results support the substantial role of temperature and duration in modulating overall pressure drift, replicated from previous reports[2] and evidenced *in vivo*.

Correction methods

With regard to correction methods, this is the first study to trial available correction methods via standard operating instructions employing ManoView™ software. Previous studies evaluated the theory of the TC and ITC correction methods using self-generated software. However, the applicability and generalizability of these custom programs are not known and direct testing of the system based correction methods is necessary.

Findings support previous research[2,3] that documents the standard TC process does not correct the error associated with the drift, but simply reallocates the error to the beginning of the study. In shorter duration studies, the median error associated with correcting the drift with TC was greater than manufacturer statements that pressure uniformity remains within 2 mmHg for 4 h or less of recording.[1] For extended-duration studies, TC performs even more poorly, with median errors greater than 7.4 mmHg.

In contrast, ITC, with its two-step linear interpolation correction method, is able to correct the error associated with baseline drift, even in extended-duration studies. However, the user has to be aware of this option to be able to pursue its activation in the software, as ITC is not reported in the ManoScan™ or ManoView™ user manuals. Once requested by name, the manufacturer has to intervene in order to enable this software option. Nevertheless, ITC was found to be the most effective correction method with corrected values having an error roughly within the stated pressure uniformity measure of 2 mmHg. Although this method is superior, it is more time-consuming, requiring the user to record a 2-min water bath at 37 °C prior to recording the study. Further, since this 2-min water bath is required in order to apply ITC appropriately, previously collected data cannot be retrospectively corrected using ITC by the software (Fig. S3).

Limitations

Further work is needed to determine the electromechanical mechanisms of HRM sensors which lead to pressure drift. Previous publications have speculated that the catheter design may lend itself to deformation due to an air gap within the sensing membrane from a rigid surface of a metallic inner electrode.[3,6] With different metals in use, such as copper, the variable distortions following temperature shock at intubation may play a critical role in generating pressure drift. Although analog signals often have some level of baseline drift, how or why this baseline drift is variable across studies and between sensors is not known. Further investigation by the manufacturer is needed to understand the development of drift as a result of the intrinsic nature of the catheter. The current study investigates pressure drift in two discrete catheters. As there is notable variability both between sensors and across catheters, ongoing research investigating a greater number of catheters is warranted. Additionally, it is unclear how additional compensations, such as the weekly ManoScan™ *in vivo* compensation, are interacting with pressure drift and the related compensation methods. Lastly, the extended duration *in vivo* studies were conducted at night to encourage participants to sleep with the catheter *in situ*. Although participants reported sleeping during the study subjectively, it is unknown if participants were engaging in behaviors (e.g., snoring, restlessness) that may have affected recordings due to the extended nature of the study.

CONCLUSIONS

The substantial drift in the ManoScan™ HRM system is highly variable across sensors and studies and is not corrected via standard operating instructions. This drift can have a substantial impact in clinical diagnosis and research. For example, when evaluating function of the upper esophageal sphincter (UES), normative data indicate that average nadir UES pressure of −4 mmHg has a narrow standard deviation of only 7 mmHg.[7] With a possible pressure drift of 6.5 mmHg in 15 min, caution is needed when interpreting acquired data and forming subsequent diagnoses. The standard TC process did not correct the error associated with the drift. Interpolated thermal compensation is able to correct the error associated with baseline drift but requires communication with the manufacturer to enable this option. Overall pressure drift can have a substantial impact in clinical diagnosis and research of pharyngeal and esophageal function, and caution should be taken when referencing previously reported normative data. Further research is indicated to evaluate if this measurement error is an inherent feature of other HRM measurement systems across manufacturers, and thus pervasive across this technology.

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CONFLICTS OF INTEREST

The authors have no competing interests.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of this article at the publisher's web site:

Figure S1 This pressure-time graph plots raw *in vitro* data using the ESO catheter. Measured pressure should equal 2.94 mmHg. However, note the variability in the y-intercept at time zero reflecting thermal effect and the increasing baseline drift with time.

Figure S2 This pressure-time graph plots raw *in vitro* data using the ESO Z catheter. Measured pressure should equal 2.94 mmHg. However, note the variability in the y-intercept at time zero reflecting thermal effect and the increasing baseline drift with time.

Figure S3 Similar to Fig. 5, this figure depicts correction methods, where actual pressure exposure should be 2.94 mmHg. This graph includes correction with the ITC method and ITC method when used without the initial TC point (one-step analysis rather than the two-step analysis). Note the marked residual error when using ITC in this non-standard method.