EQUINE VETERINARY JOURNAL
Equine vet. J. (2008) **40** (6) 584-588
doi: 10.2746/042516408X313643

Intra-articular stabilisation of the equine cricoarytenoid joint

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Keywords: horse; laryngoplasty; cement; cricoarytenoid joint

Summary

Reasons for performing study: **The success of laryngoplasty is limited by abduction loss in the early post operative period.**

Objective: **To determine the efficacy of polymethylmethacrylate (PMMA) in stabilising the cricoarytenoid joint (CAJ) and reducing the force on the laryngoplasty suture.**

Hypothesis: **Injection into the cricoarytenoid joint resists the forces produced by physiological laryngeal air flows and pressures thereby reducing the force experienced by the laryngoplasty suture.**

Methods: **Ten cadaver larynges were collected at necropsy and PMMA was injected into one CAJ at selected random. Each larynx was subjected to physiological conditions with with constant (static) or cycling (dynamic) flow. The specimens were tested sequentially in each of 4 conditions: 1) bilateral full abduction (*Control 1*); 2) transection of the suture on the side without PMMA; 3) bilateral abduction achieved by replacing the suture (*Control 2*); and 4) cutting the suture on the PMMA side. Tracheal pressure and flow and pressure in the flow chamber were recorded using pressure and flow transducers. The strain experienced by each suture during bilateral abduction (*Controls 1* and *2*) was measured. Statistical comparison of the 4 conditions was performed using a mixed effect model with Tukey's *post hoc* test for multiple comparisons. The strain gauge data were analysed by paired comparison of the regression slopes.**

Results: **In the static and dynamic states, tracheal pressure increased and tracheal flow decreased when the suture on the non-cement side was cut ($P<0.05$). There was no significant difference in any outcome measure between PMMA injected into the CAJ and bilaterally abducted specimens (*Controls 1* and *2*) for either condition. The rate of increase in strain with increasing translaryngeal pressure was significantly less on the suture with PMMA placed in the CAJ ($P = 0.03$).**

Conclusions: **These data provide strong evidence that injecting PMMA into the CAJ resists the collapsing effect of physiological airflows and pressures *in vitro* and reduces the force experienced by the laryngoplasty suture during maximal abduction.**

Potential relevance: **Augmentation of prosthetic laryngoplasty with this technique may reduce arytenoid abduction loss in the early post operative period.**

Introduction

The current gold standard for treating recurrent laryngeal neuropathy (RLN) in horses is a prosthetic laryngoplasty, with or without vocal cordectomy or ventriculectomy (Hawkins *et al.* 1997; Kidd and Slone 2002; Dixon *et al.* 2003; Kraus *et al.* 2003). The frequent and significant loss of arytenoid cartilage abduction seen in the immediate post surgical period is one limitation of this technique (Dixon *et al.* 2003; Brown *et al.* 2004). This loss of abduction leads to a reduction in cross-sectional area of the *rima glottidis* and the return of exercise intolerance and abnormal respiratory noise (Schumacher *et al.* 2000; Dixon *et al.* 2003; Brown *et al.* 2004). It may also contribute to the modest 48–68% post operative success rate observed in racehorses (Russell and Slone 1994; Hawkins *et al.* 1997; Strand *et al.* 2000; Davenport *et al.* 2001; Kidd and Slone 2002; Radcliffe *et al.* 2006).

A variety of techniques and materials are used to perform prosthetic laryngoplasty in horses. Although polyester is the most widely used suture material, a variety of others have been used, including steel, mersilene, lycra and nylon (Marks *et al.* 1970; Russell and Slone 1994; Tetens *et al.* 1996; Hawkins *et al.* 1997; Davenport *et al.* 2001; Dixon *et al.* 2001; Kidd and Slone 2002; Scherzer and Hainisch 2005). These sutures have differing amounts of elongation at physiological loads, which may affect cross-sectional area of the *rima glottidis* (Cheetham *et al.* 2006). In order to strengthen the prosthesis and reduce pull through at the cricoid or arytenoid cartilages, surgeons may place a single or double strand of suture (Russell and Slone 1994; Tetens *et al.* 1996; Hawkins *et al.* 1997; Davenport *et al.* 2001; Dixon *et al.* 2001; Kidd and Slone 2002; Scherzer and Hainisch 2005) or different anchoring techniques, including a bone trochar and steel-beaded cable (Schumacher *et al.* 2000; Herde *et al.* 2001; Rossignol *et al.* 2006).

It was recently suggested that curettage of the cricoarytenoid joint (CAJ) might induce fibrosis of the joint and reduce loss of abduction in the post operative period (Parente 2003); however, the present authors have observed loss of abduction in cases that had curettage. One disadvantage of the technique is that loss of abduction often occurs in the early stages post operatively and may precede fibrosis. It is proposed that polymethylmethacrylate (PMMA) may provide immediate joint ankylosis and increased post operative stability. This would offer an advantage over joint curettage. The aim of this study was to test the hypothesis that injection of PMMA into the CAJ resists the forces produced by physiological laryngeal flows and pressures.

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[Paper received for publication 03.12.07; Accepted 26.02.08]

Materials and methods

Ten equine larynges from mature horses (age mean 6.4 years, range 2–15 years, 2 geldings, 7 mares and one colt, 5 Warmbloods, one Thoroughbred, 2 Quarter Horses and 2 mixed breed) were collected and frozen at -10ºC within one hour of death. The specimens were prepared as described by Cheetham *et al.* (2008a). Briefly, the *cricopharyngeus* muscle and oesophagus were left intact, and the larynges wrapped in a nonpermeable material to prevent desiccation during freezing. Before each experiment, the muscle and oesophagus were removed from each specimen and the larynx allowed to reach room temperature. The trachea was sectioned at the third or fourth tracheal ring and the dorsal cricoarytenoid muscle was removed bilaterally. Prosthetic laryngoplasty suture placement was standardised to ensure care was taken to not penetrate the laryngeal mucosa. A single No. 5 Fiberwire suture with a 40 mm taper-cut needle[1] was placed from the caudal aspect of the cricoid cartilage to the muscular process of the arytenoid cartilage. Cartilage penetration with the needle was standardised. The cricoid suture placement started 4 mm lateral to the dorsal midline of the sagittal ridge and exited through the cartilage 4 mm lateral to the sagittal ridge and 10 mm rostral to the caudal edge of the cricoid. The suture was then passed through the centre of the arytenoid cartilage muscular process in a caudodorsal to cranioventral direction at a 30–40º angle to the frontal plane and 8 mm deep to the apex of the muscular process. The suture was preplaced so it passed directly beneath the centre of the insertion of the tendon of the lateral neuromuscular compartment of the dorsal cricoarytenoid muscle onto the muscular process of the arytenoid cartilage.

Polymethylmethacrylate (Technovit)[2] (2 ml) was injected into one randomly selected cricoarytenoid joint (CAJ) in each cadaver. The lateral aspect of the CAJ was opened using a haemostat ventral to the tendon insertion of the lateral neuromuscular compartment of the dorsal cricoarytenoid muscle onto the muscular process (Cheetham *et al.* 2008b). The tendon was not reflected. The rostral surface of the cricoid cartilage and caudal surface of the arytenoid cartilage were curetted using a Miller rasp, and 2 ml of PMMA was mixed to a paste-like consistency and inserted into the joint using a 3 ml syringe without a needle. Both arytenoid cartilages were then abducted to the optimal degree for laryngoplasty (Dixon *et al.* 2003), and each suture tied with 5 throws. Preplacement of the suture prior to injection of PMMA is important as the cement sets quickly and arytenoid abduction should be performed rapidly following injection. A small amount of PMMA was extruded from the CAJ, as the suture was tied and the arytenoid cartilage abducted, and this excess was removed prior to testing.

The specimen was then placed into an *in vitro* cyclic flow model shown recently to produce airflows and pressures comparable to those generated by horses at maximal exercise (Cheetham *et al.* 2008a). Briefly, this comprised a vacuum system (two 16 gallon vacuum cleaners)[3] attached in parallel, with a rheostat used to generated negative pressure and produce an inspiratory flow that could be varied, and a PVC pipe containing a cycling valve that cycled at 2 Hz producing intermittent airflow; 2 Hz was selected as this mimics the respiratory frequency of a horse at maximal exercise (110–120 breaths/min: Ducharme *et al.* 1994; Radcliffe *et al.* 2006). This pipe was connected to the caudal aspect of the trachea by a clamp. The tip of the epiglottis was secured to a wooden board with a 14 gauge needle to prevent retroversion. This system was enclosed in a flow chamber (30 x 15 x 15 cm wooden box with a Plexiglass lid). A brass constrictive inlet valve with a cross-sectional area that could be varied from 340–760 mm^2 was used to generate negative pressure rostral (upstream) of the larynx and mimic the subatmospheric pressure within the pharynx of an exercising horse. Two ultrasound flow meters[4] were placed in the trachea to measure airflow. The ultrasonic transducers were calibrated as described previously (Radcliffe *et al.* 2006). Two Teflon catheters[5] (1.3 mm ID, 1.9 mm OD) in phase from 1–20 Hz were placed so that the ports lay within the trachea and flow chamber and were parallel to the direction of airflow (Nielan *et al.* 1992; Ducharme *et al.* 1994; Radcliffe *et al.* 2006). The catheters were then attached to differential pressure transducers (Celesco LCVR)[6] referenced to atmospheric pressure and calibrated as previously described (Nielan *et al.* 1992; Ducharme *et al.* 1994; Radcliffe *et al.* 2006).

Prior to testing any larynges, the inlet value was adjusted to give the most negative pressure possible within the flow chamber. In order to control for variations in laryngeal cross-sectional area, the cycling valve was maximally opened and flow generated by the vacuum system adjusted to give a target pressure within the trachea of -33 mmHg prior to testing each larynx (Ducharme *et al.* 1994). Static flow was then applied for 30 s. Pressure in the chamber ($P_{chamber}$) and tracheal flow (Q) and pressure ($P_{tracheal}$) were recorded at 500 Hz using custom software (Matlab)[7].

Each specimen was tested sequentially under 4 conditions: 1) both arytenoid cartilages were optimally abducted as described above (*Control 1*); 2) both strands of the suture on the side without PMMA injected into the CAJ were cut (*CutSx*); 3) this suture was replaced and retied to achieve the same optimal degree of abduction (*Control 2*); and 4) both strands of the suture on the PMMA-injected side were cut (*PMMA*). This sequence was chosen so the effect of PMMA alone could be evaluated. For each condition, static flow was maintained for 30 s the cycling valve was then activated and data recorded for an additional 30 s. Individual cycles were identified from the data. Due to slight variability in cycle length and to allow calculation of an average cycle, data were interpolated to average cycle length using Matlab[7]. Mean and standard deviations of peak values for each outcome measure, condition, and larynx were determined under both static and cycling conditions. Impedance was calculated by dividing translaryngeal pressure by tracheal flow ($[P_{tracheal}-P_{chamber}]/Q$).

E-shaped buckle transducers were fitted to each suture (PMMA side and non-PMMA side) in order to measure suture strain experienced during cyclic loading the presence and absence of PMMA. The design and validation of these transducers has been described elsewhere (T.H. Witte *et al.*, unpublished data). Briefly, a single element foil strain gauge with pre-attached 3-lead wires[8] was bonded to the central arm using cyano-acrylate adhesive[9]. The entire transducer was then coated with xylene-cured polyurethane[10]. The transducer was applied to the suture such that the suture passed over the outer strands and under the central arm of the E. Strain gauge resistance change therefore occurred as a result of deformation of the central beam of the buckle in response to tension on the suture. The buckle transducers were attached to the dorsal strand of each suture. Strain gauge data were collected via a 12-bit AD card[11] and recorded at 500 Hz using Matlab[7]. The transducers were re-zeroed prior to testing of each condition.

A mixed-effect model (with specimen as a random effect and experimental condition as the fixed effect) was fitted to the data for each outcome measure ($P_{chamber}$, $P_{tracheal}$, Q, impedance) in both the static and cycling testing states. The rationale for using a mixed model analysis of the data was to control for potential clustering of observations by specimen that could be due to factors other than experimental ones. A Tukey's *post hoc* test was used to make multiple comparisons between the 4 conditions to test whether PMMA injection into the CAJ resists the forces produced by physiological laryngeal flows and pressures. The strain gauge data were analysed for the 2 conditions with bilateral abduction (*Controls 1* and *2*). Individual slopes of the relationship between the absolute value of translaryngeal pressure and force were determined using regression. The slopes for the sutures with and without PMMA in the CAJ were compared using a paired *t* test. The absolute value of translaryngeal pressure (TLP) was used to facilitate interpretation. Statistical analysis was performed using S-plus[12] and JMP[13]. Significance was set at P<0.05.

Results

The *in vitro* testing system performed well in all tests and all 4 conditions were tested for each larynx (n = 10). In both static and cycling states, all specimens experienced complete collapse of the arytenoid cartilage to grade C (Hammer *et al.* 1998) when tested after cutting the suture on the non-cement side (*CutSx*). We also observed simultaneous collapse of the contralateral vocal cord. Mild loss of abduction was occasionally observed on the side with PMMA following transection of the suture. Although this was not quantified, it appeared this loss did not produce significant changes in tracheal flow or pressure.

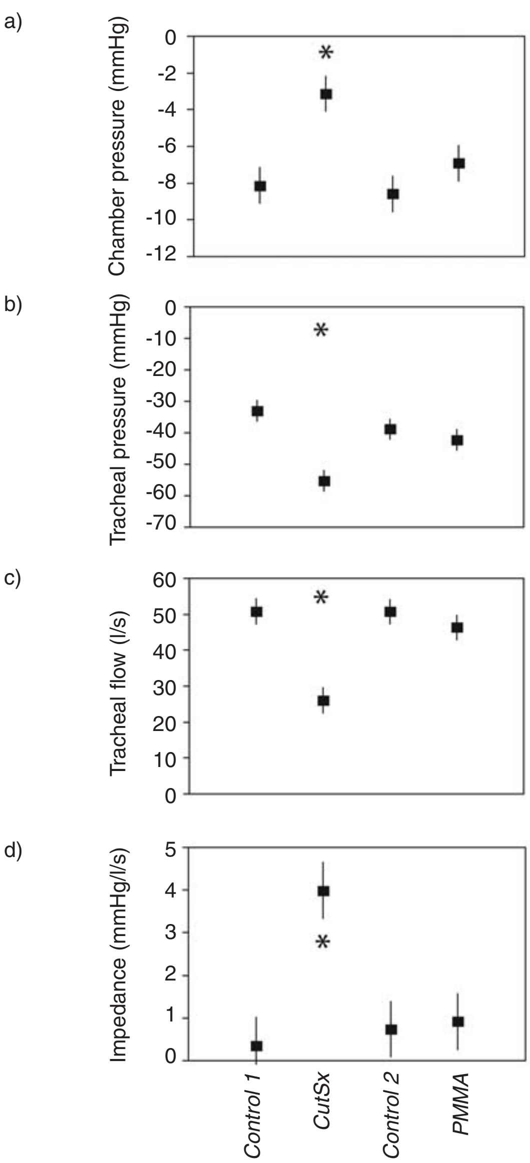

*Fig 1: Static airflow. Least square (adjusted) means for each state (*Control 1, CutSx, Control 2 *and* PMMA*) for pharyngeal pressure (A), tracheal pressure (B), tracheal flow (C) and impedance (D). *Significantly different from other states (P<0.05).*

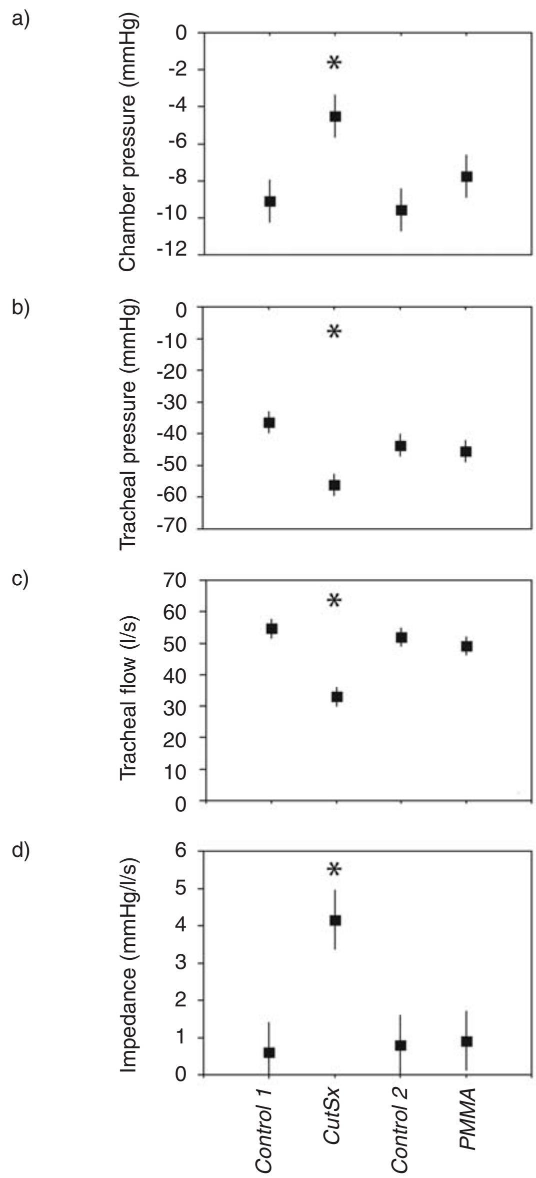

*Fig 2: Dynamic airflow. Least square (adjusted) means for each state (*Control 1, CutSx, Control 2 *and* PMMA*) for pharyngeal pressure (A), tracheal pressure (B), tracheal flow (C) and impedance (D). *Significantly different from other states (P<0.05).*

Static flow

Least square (adjusted) means (± s.e.) for pressure within the flow chamber, tracheal pressure and flow, and impedance for static flow are shown in Figure 1. Pressure within the flow chamber in the *CutSx* condition was significantly lower (less negative) than within the other conditions (P<0.01). Tracheal pressure in the *CutSx* condition was significantly higher (more negative) than the other conditions (P<0.01). Tracheal flow in the *CutSx* condition was significantly lower than within the other conditions (P<0.01). Impedance in the *CutSx* condition was significantly higher than all the other conditions (P<0.01). Multiple pair-wise comparisons revealed no significant differences between the *Control 1*, *Control 2* and *PMMA* conditions in tracheal pressure or flow, pressure in the flow chamber, or impedance.

Dynamic flow (cycling at 2 Hz)

Least square (adjusted) means (± s.e.) for pressure within the flow chamber, tracheal pressure and flow, and impedance for cycling flow are shown in Figure 2. Pressure within the flow chamber in the *CutSx* condition was significantly lower (less negative) than the *Control 1* and *2* conditions (P<0.01). There was no significant difference between the *PMMA*, *Control 1* and *Control 2* conditions. Tracheal pressure in the *CutSx* condition was significantly higher (more negative) than the other conditions (P<0.01). Tracheal flow in the *CutSx* condition was significantly lower than the other conditions (P<0.01). Impedance in the *CutSx* condition was significantly higher than all the other conditions (P<0.01). Multiple pair-wise comparisons revealed no significant differences between the *Control 1*, *Control 2* and *PMMA* conditions in tracheal pressure or flow and pharyngeal pressure or impedance. There was no significant effect of specimen in any model.

Strain gauge data

The force transducers collected data reliably in all tests. The rate of increase in force on the suture with increasing translaryngeal pressure was significantly less on the suture with PMMA placed in the CAJ (P = 0.03). For the suture without PMMA, every 10 mmHg increase in translaryngeal pressure produced a mean ± s.e. increase in force of 0.295 ± 0.171 N. In the suture with cement in the CAJ, every 10 mmHg increase in translaryngeal pressure produced a mean ± s.e. increase in force of 0.233 ± 0.156 N. The difference in the rate of increase in force for the suture with PMMA was 0.0607 N (95% CI, 0.0051–0.116 N).

Discussion

These data strongly suggest that *in vitro* PMMA injected into the CAJ can withstand flows and pressures similar to those generated by a horse at maximal exercise. In both the static and dynamic states, pressure in the flow chamber decreased (less negative), tracheal pressure increased (more negative) and tracheal flow decreased when the suture on the non-cement side was cut. These effects are similar to those in a horse with *grade C* (Rakestraw *et al.* 1991) recurrent laryngeal neuropathy and result from flow restriction at the *rima glottidis* due to a decrease in cross-sectional area (Shappell *et al.* 1988; Tetens *et al.* 1996). The cricoarytenoid joint with PMMA present was able to resist arytenoid collapse at physiological flows and pressures in both static and dynamic conditions.

In both the static and cycling states for all outcome measures, retying the suture on the side without cement (*Control 2*) restored airway mechanics close to the original condition (*Control 1*). There was a small insignificant difference in airway mechanics between the 2 conditions and this may be due to increasing suture cut through at the caudal aspect of the cricoid cartilage when the suture was retied.

The data also show that PMMA injected into the CAJ reduces the force experienced by the laryngoplasty suture *in vitro*. This technique may reduce cut-through of the laryngoplasty suture on the caudal aspect of the cricoid (Goulden and Anderson 1982; Dean *et al.* 1990; Schumacher *et al.* 2000; Stick *et al.* 2001). It should be noted that the sutures were tested only under the range of forces produced by physiological airway flows and pressure and that the effect of swallowing was not evaluated. Swallowing and repeated cycling of the suture in horses with partial paralysis have been proposed as mechanisms for laryngoplasty failure (Davenport *et al.* 2001; Dixon *et al.* 2003; Parente 2003). Force on the suture produced by swallowing has not been determined.

Polymethylmethacrylate is an acrylic cement widely used in orthopaedic surgery; it polymerises *in situ* to achieve mechanical interlock with surrounding tissue. This mechanism of action lead to the decision to curette the CAJ surface and then fix the joint with PMMA injection. In addition, by physically occupying the cricoarytenoid joint, it may prevent the muscular process from gliding rostrally or ventrally over the cricoid cartilage. The human cricoarytenoid joint has been shown to have both gliding and rotational components (Kasperbauer 1998; Hunter and Titze 2000), although the precise movement of the equine cricoarytenoid joint has not been described. One disadvantage of PMMA used clinically is that it promotes bacterial adherence (Kendall *et al.* 1996), and antibiotics might be incorporated into PMMA in studies evaluating its clinical efficacy for CAJ stabilisation. It is also possible that intraoperative haemorrhage in the cricoarytenoid joint may interfere with the ability of PMMA to key into the curetted cartilage surface. The contralateral vocal fold collapse seen in these specimens when the suture on the non-cement side was cut is similar to that identified in clinical cases of RLN (Lane *et al.* 2006) and may reflect a local increase in negative pressure on the medial surface of the vocal cord.

We propose that this technique could be readily applied *in vivo*. The surgical approach to the cricoarytenoid joint is straightforward and surgeons may curette the joint to induce fibrosis and reduce the loss of abduction seen post operatively (Parente 2003). One limitation of this technique is that adhesions across the joint take several weeks to mature and a large loss of abduction can be seen in the first 7 days after surgery (Dixon *et al.* 2003). Injecting PMMA into the CAJ could fix the joint in place at the time of surgery. The rapid curing of the PMMA means that the laryngoplasty suture should be pretied before the bone cement is injected into the joint and the arytenoid abducted. In addition, curing of PMMA is exothermic and the subjacent laryngeal mucosa should be careful examined for thermal injury in clinical studies. It is also possible that cricoid and arytenoid cartilage remodelling may allow the joint to deform, even in the presence of PMMA, and so allow abduction loss over a longer period.

In these experiments, PMMA was tested alone rather than in conjunction with a laryngoplasty suture. In a clinical setting, the technique should be used in conjunction with traditional laryngoplasty suture(s). Use of PMMA *in vivo* would require a sterile product appropriate for surgical implantation. Technovit was used in this study for economic reasons. Further work is required to evaluate any interaction between the laryngoplasty suture and PMMA *in vivo* and test the clinical application of this technique.

In conclusion, PMMA injected into the CAJ was able to withstand physiological airway mechanics and reduced the force on the laryngoplasty suture in this *in vitro* model.

Manufacturers' addresses

[1]Ethicon Inc., Piscataway, New Jersey, USA.
[2]Jorgensen Laboratories, Loveland, Colorado, USA.
[3]Genie Jet Vac, Alliance, Ohio, USA.
[4]BRDL Flowmetrics, Birmingham, UK.
[5]Cole-Palmer International, Chicago, Illinois, USA.
[6]Celesco Products, Canoga Park, California, USA.
[7]The Mathworks, Natick, Massachusetts, USA.
[8]Tokyo Sokki Kenkyujo, Tokyo, Japan.
[9]Omega, Stamford, Connecticut, USA.
[10]Micro-Measurements, Shelton, Connecticut, USA.
[11]National Instruments, Austin, Texas, USA.
[12]Insightful Corporation, Seattle, Washington, USA.
[13]SAS Institute, Cary, North Carolina, USA.

Acknowledgements

This work was partially funded by the Harry M. Zweig Memorial Fund. The authors would like to thank Anne Littlejohn for her review of this paper.

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Author contributions The initiation, conception and planning of this study were by J.C., T.H.W., J.J.R. and N.G.D. Its execution was by J.C., T.H.W., J.J.R. and L.V.S., with statistics by J.C., T.H.W. and H.O.M. The paper was written by J.C., T.H.W., J.J.R., H.O.M. and N.G.D.