In vitro analysis and cadaver feasibility study of a peritoneal dialysis catheter tungsten weighted anchor

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Abstract

Objective: Peritoneal dialysis (PD) catheters function best when residing within the retrovesical space of the peritoneal cavity, but they frequently migrate and fail. A novel variable length and conforming PD catheter weighted anchor to prevent migration has been evaluated.

Methods: Test devices were placed in normal saline for 21 months. The effluent was periodically measured for heavy metals, including tungsten. The water-tight property of the device was also tested separately. Four cadavers were subjected to three-dimensional imaging and maneuvering to evaluate percutaneous insertion, function, stability within the retrovesical space, and percutaneous retrievability in 10 test devices.

Results: Liquid leakage was low, with a mean absorbance of the test device effluent saline of 0.015. Mean methylene blue absorbance of the test device was significantly lower than the positive control (p value = 0.01). Leakage of tungsten from devices made with medical grade Silastic tubing was also low, with a mean of 0.362 μg/L in the effluent saline, compared to a background concentration of 0.166 μg/L. Each test device was successfully inserted into the retrovesical space and retrieved percutaneously and remained completely intact following placement and insertion. No test device migrated as shown on axial cone beam CT imaging. Mean flow times and volumes were satisfactory at 3 minutes and 0.92L, respectively, for all test devices. For all catheters, the mean flow rate was 312 cc/min. No significant difference was found between the pre-roll and post-roll mean flow rates of the test devices (p value = 0.35).

Conclusion: This PD catheter weighted anchor showed stability, with minimal leakage of tungsten. All test devices were successfully inserted and retrieved percutaneously, with no damage or migration, and mean flow rates were satisfactory. Further investigation is warranted.

Keywords: Peritoneal dialysis catheter; Cadaver study; Tungsten; Catheter migration; Weighted anchor

Introduction

Peritoneal dialysis (PD) is a low cost, and often physiologically beneficial, option for many patients with end stage renal disease (ESRD). However, its utilization has decreased in the United States, as 9.7% of prevalent ESRD patients were being treated with PD in 2014, whereas only 7.1% were utilizing PD in 2017 [1,2]. This recent decrease in PD utilization has occurred despite economic incentives. The Centers for Medicare and Medicaid Services ESRD Prospective Payment System was introduced in 2011, which highlights the fact that PD is more cost-effective than in-center hemodialysis [3].

The two most common reasons that PD fails, requiring many patients to transfer to hemodialysis, are infectious and mechanical complications of the PD catheter [4]. Optimal function of the PD catheter is often dependent on its ability to reside within the retrovesical space of the pelvis in men, or cul de sac (pouch of Douglas) in women [5,6]. The retrovesical space is a dependent portion

of the peritoneal cavity in the supine or upright body positions, where fluid tends to accumulate. In addition, the retrovesical space is free of omentum and small bowel, which can impede PD catheter function. Unfortunately, catheter migration out of the retrovesical space of the pelvis is a common cause of PD failure [7]. Catheter migration has been reported to occur as high as 35% [8]. Revision of PD catheter migration is often unsuccessful, usually resulting in PD catheter replacement [9]. PD catheter malfunction is one of the major barriers to increasing the utilization rate of PD.

This study has evaluated multiple variations of a prototype PD catheter device which combines an effective weight effect at the intraperitoneal terminus of the catheter with other features, such as maintaining the same low profile throughout the PD catheter length. The device, when combined with a coiled PD catheter, creates a variable length catheter which conforms to the retrovesical pouch of the peritoneal cavity. This PD catheter weighted anchor can be retrofitted to modify any commercially available existing PD catheter, or it can be fabricated into a new PD catheter design. It can be placed percutaneously, laparoscopically, or with open surgery. It is low profile so that it can be placed through the same 18-French peel away sheath as the currently available standard PD catheters, which allows it to be placed percutaneously, and it will adjust the effective length of a coiled PD catheter by preventing elastic recoil out of the retrovesical space in larger patients.

The evaluation of this prototype PD catheter consisted of two parts. First, the stability of the device to prevent leakage of tungsten and other heavy metals over a 21-month period was measured. Second, the application of three-dimensional radiographic imaging to monitor percutaneous insertion, function, stability within the retrovesical space, and percutaneous removal in cadavers was performed.

Methods

The University of Vermont Research Protections Office determined that this project was exempt from review by the Institutional Review Board.

The University of Vermont and the University of Vermont Medical Center protocols governing the use of cadavers in research were followed in all cases. The consent forms are on record at the University of Vermont and the University of Vermont Medical Center.

Benchtop *in vitro* study

Test devices were created under sanitary conditions by inserting five 4 mm diameter tungsten-carbide ball (ACER Racing, Los Angeles, CA) into the center of 4 cm long sections of Silastic tubing, four with medical grade tubing (Merit Medical, South Jordan, UT) and two with laboratory grade tubing (Tri-anim Health Services, Dublin, OH) (Figure 1). The ends of each column of tungsten-carbide balls were bordered by two 4 mm in diameter stainless steel balls (VXB, Anaheim, CA), which were secured with 0 Prolene sutures to create a water-tight fit.

A single 4 cm long section of medical grade Silastic tubing was filled with 1% methylene blue and sealed at both ends with 4mm in diameter stainless steel balls and 0 Prolene sutures to create a water-tight fit.

Eight Erlenmeyer flasks were filled with 500 ml of medical grade normal saline and A) normal saline negative control; B) 0.1ml of 1% methylene blue for a concentration of 0.02% as a positive control; C) Five 4 mm in diameter tungsten-carbide and two 4mm in stainless steel balls as a positive control; D) the methylene blue device; E) one test device; F) one test device; G) two test devices; and H) two test devices. The flasks were stored in the dark at room temperature for 21 months. Two ml effluent saline samples were drawn from each flask, using sterile 10 cc syringes to manually withdraw the fluid and transferring the fluid samples to test tubes, at the following time points: 1 day, 14 days, 3 months, 6 months, 9 months, and 21 months. Samples A, B, and D were tested for methylene blue (668 nm) by ultraviolet visible photometry. Samples A, C, E, F, G, H, I, and J were digested with 0.280 ml of nitric acid (TraceMetal Grade, Thermo Fisher Scientific, Waltham, MA) and then analyzed for tungsten, iron, cobalt, and chromium (6, 9, and 21 month measurements) by inductively coupled plasma mass spectrometry (ICP-MS) by the Meadowlands Environmental Research Institute

A.   B.
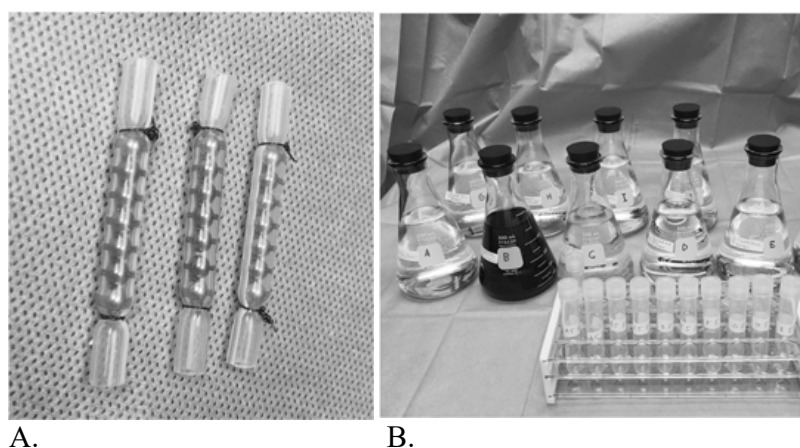
Figure 1: Devices and flasks tested for leak.

(Rutgers University, Newark, NJ).

Cadaver study

Total 10 test devices of varying designs (flexible straight, segmented, and curled), lengths (8 to 16 cm), and weights (10.5 to 20.6 g) were attached to the terminal coiled ends of 8 Merit (Merit Medical, South Jordan, UT) and 2 Swan Neck Missouri Covidien (Covidien LLC, Mansfield, MA) curled PD catheters using 0 Prolene sutures (Figure 2). The devices were created by inserting multiple 4mm diameter tungsten-carbide balls into the center of medical grade Silastic tubing, with a 4 mm in diameter stainless steel ball bordering each end. The ends were tied securely with 0 Prolene sutures. This created a water-tight attribute of each device, which remained intact throughout the study.

Four non-embalmed male cadavers were used within 24 hours from the time of expiration. Percutaneous insertion of all PD catheters and devices were successfully accomplished using the following percutaneous image guided technique. A needle was used with ultrasound guidance to enter the peritoneal cavity through the anterior abdominal wall and rectus muscle. A fluoroscopic and digital acquisition peritoneogram was obtained to ensure an intraperitoneal position and to delineate the retrovesical space. A 0.035-inch diameter guide wire was advanced into the peritoneal space and the needle was removed. Then, a 4-French angled angiographic catheter was used with the guide wire, to enter the retrovesical space. A 0.035-inch guide wire was coiled in the retrovesical space, the 4-French angiographic catheter was removed, and an 18-French peel away sheath (6.5 mm outside diameter) was directed into the retrovesical space. The guide wire was removed and the PD catheter with attached device was pushed through the peel away sheath and into the retrovesical space. Water based sterile lubricant was used to decrease the coefficient of friction as necessary, to ensure that the PD catheter and weighted anchor combination travelled easily through the sheath without kinking or overlap of the tungsten balls. No difficulty was encountered during any of the insertions. The peel away sheath was removed, and the PD catheter was attached to the skin without creating a subcutaneous tunnel.

For each cadaver, one liter of normal saline was attempted to be infused and drained through each PD catheter via gravity. Flow rates and volumes were recorded. Table (Philips Allura table level at -9cm for infusion, +18 cm for drainage, and +6cm for cone beam CT), infusion pole (normal saline bag 6 feet above floor), and drainage bag (bag placed on floor) heights were standardized and consistent for all cadavers and all infusions and drainages. Between infusions and drainages for each PD catheter, each cadaver was manually rolled 360 degrees around the vertical axis to provoke migration. Peritoneograms in multiple 3-dimentional projections, as well as axial cone beam CT scanning (XperCT, Philips Medical Systems, The Netherlands) were obtained before and after each roll to detect migration. Images were recorded and archived.

Finally, each PD catheter and device were removed percutaneously. Each catheter and device were examined for tears and ruptures, and any breach in integrity was noted.

Statistical analysis for benchtop *in vitro* and cadaver studies

Comparisons of tungsten concentrations between the normal saline negative controls and the devices made of medical grade silastic tubing, as well as between the medical device made with laboratory grade silastic tubing and the devices made with medical grade silastic tubing, were performed with repeated measures mixed model analyses of variance. All effluent metal data was log transformed for normality. Comparison of the positive methylene blue control to the saline effluent of the methylene blue device was done using the Wilcoxon rank sum test. Cadaver study catheter flow rate comparisons were done using repeated measures mixed model analyses of variance. P values < 0.05 were considered to be statistically significant. All statistical analyses were performed using SAS version 9.4 statistical analysis software (SAS Institute, Inc., Cary, NC).

Results

Benchtop *in vitro* study

Heavy metal and methylene blue assay measurements are shown in Table 1.

A.   B.   C.   D.
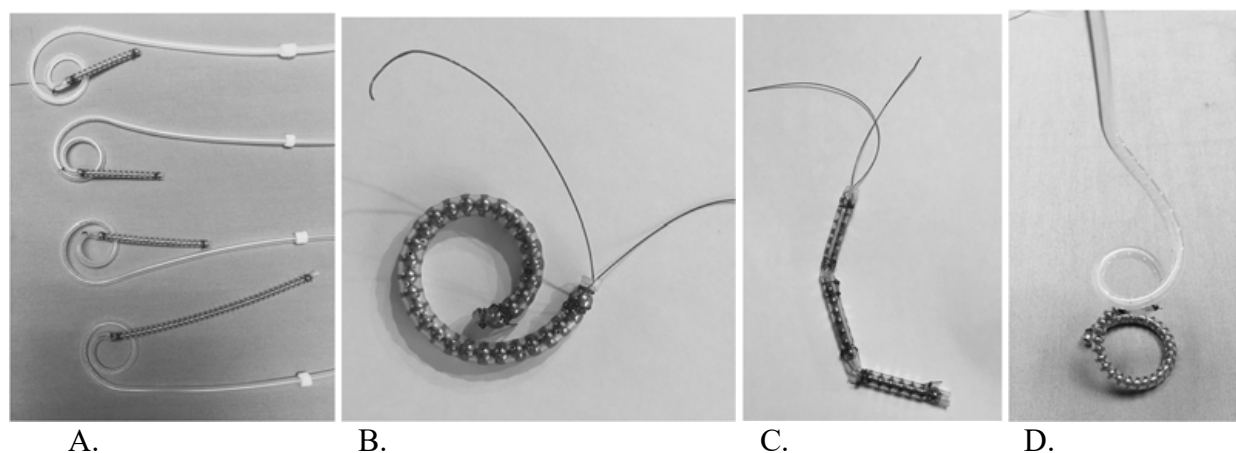
Figure 2: Spectrum of devices tested in cadavers.

	1 day	14 days	3 months	6 months	9 months	21 months	P-values
A MB	0.000 A	0.000 A	0.000 A	0.000 A	0.000 A	0.000 A	
A W	0.10 µg/L	NA	0.03 µg/L	NA	NA	0.529 µg/L	
A Fe	596 µg/L	NA	1088 µg/L	NA	NA	23.0 µg/L	
A Co	0.12 µg/L	NA	0.10 µg/L	NA	NA	0.028 µg/L	
A Cr	NA	NA	NA	NA	NA	0.075 µg/L	
B MB 0.02% concentration	0.630 A	0.651 A	NA	0.588 A	0.583 A	0.147 A	
C W	12.3 µg/L	118 µg/L	299 µg/L	517 µg/L	563 µg/L	610 µg/L	
C Fe	173 µg/L	1525 µg/L	220 µg/L	533 µg/L	1747 µg/L	398 µg/L	
C Co	275 µg/L	2889 µg/L	2873 µg/L	12295 µg/L	13696 µg/L	12548 µg/L	
C Cr	NA	NA	NA	58.3 µg/L	66.2 µg/L	33.4 µg/L	
D MB	0.000 A	0.037 A	0.005 A	0.006 A	0.004 A	0.038 A	0.01 v. B MB
E W	0.07 µg/L	0.15 µg/L	0.49 µg/L	0.101 µg/L	0.520 µg/L	2.24 µg/L	
E Fe	363 µg/L	98.6 µg/L	2189 µg/L	520 µg/L	240 µg/L	330 µg/L	
E Co	0.07 µg/L	0.10 µg/L	0.28 µg/L	0.087 µg/L	0.759 µg/L	0.125 µg/L	
E Cr	NA	NA	NA	0.091 µg/L	0.769 µg/L	0.503 µg/L	
F W	0.03 µg/L	0.06 µg/L	0.16 µg/L	0.078 µg/L	0.236 µg/L	1.11 µg/L	
F Fe	118 µg/L	1926 µg/L	17.9 µg/L	326 µg/L	94.5 µg/L	1500 µg/L	
F Co	0.04 µg/L	0.18 µg/L	0.14 µg/L	0.071 µg/L	0.092 µg/L	0.228 µg/L	
F Cr	NA	NA	NA	0.684 µg/L	0.154 µg/L	4.86 µg/L	
G W	0.06 µg/L	0.09 µg/L	0.15 µg/L	0.124 µg/L	0.161 µg/L	0.68 µg/L	
G Fe	2284 µg/L	2236 µg/L	1055 µg/L	1621 µg/L	694 µg/L	616 µg/L	
G Co	0.19 µg/L	0.18 µg/L	0.14 µg/L	0.255 µg/L	0.168 µg/L	0.090 µg/L	
G Cr	NA	NA	NA	1.83 µg/L	4.66 µg/L	0.549 µg/L	
H W	0.14 µg/L	0.35 µg/L	1.04 µg/L	1.15 µg/L	1.31 µg/L	2.55 µg/L	0.10 v. All W (E, F, G)
H Fe	481 µg/L	351 µg/L	1163 µg/L	114 µg/L	3081 µg/L	255 µg/L	

H Co	0.15 µg/L	0.21 µg/L	0.67 µg/L	0.422 µg/L	0.842 µg/L	0.341 µg/L	
H Cr	NA	NA	NA	0.061 µg/L	28.7 µg/L	0.426 µg/L	
I W	NA	NA	NA	0.028 µg/L	0.056 µg/L	0.322 µg/L	
I Fe	NA	NA	NA	204 µg/L	201 µg/L	1820 µg/L	
I Co	NA	NA	NA	0.039 µg/L	0.048 µg/L	0.360 µg/L	
I Cr	NA	NA	NA	1.849 µg/L	0.631 µg/L	1.74 µg/L	
J W	NA	NA	NA	0.015 µg/L	0.094 µg/L	0.318 µg/L	
J Fe	NA	NA	NA	97.3 µg/L	160 µg/L	17.2 µg/L	
J Co	NA	NA	NA	0.046 µg/L	0.873 µg/L	0.061 µg/L	
J Cr	NA	NA	NA	0.010 µg/L	0.099 µg/L	0.067 µg/L	
All W (E, F, G)							0.16 v. A W

A: normal saline negative control, B: methylene blue positive control, C: bare tungsten-carbide and stainless steel balls positive control, D: methylene blue device, E: one test device, F: one test device, G: two test devices, H: two test devices with laboratory grade silicone tubing, I: normal saline negative control, J: normal saline negative control, MB: methylene blue, W: tungsten, Fe: iron, Co: cobalt, Cr: chromium, NA: no measurements obtained, All W (E, F, G): all tungsten devices with medical grade tubing.

Table 1: Saline bath assays for heavy metal and methylene blue.

Over the 21-month evaluation period, mean methylene blue absorbance of the saline negative control measurement, 0.02% methylene blue positive control, and water-tight methylene blue test device using medical grade silastic tubing were 0.000, 0.520, and 0.015, respectively. Mean methylene blue absorbance of the test device was significantly lower than the positive control (p value = 0.01). This confirmed that liquid methylene blue leakage from the test device was low. Leakage of tungsten from the test devices using medical grade silastic tubing over 21 months was also low, although the difference of the mean tungsten concentration leakage amount between the saline negative control and the tungsten devices made with medical grade silicone did not reach statistical significance (p value = 0.16). Concentration of free-floating tungsten in saline baths with bare tungsten-carbide balls (positive control) increased with time, as expected, from a low of 12.3 µg/L to a high of 610 µg/L, with a mean of 353 g/L. In test devices with medical grade silastic tubing, the leakage of tungsten increased with time, from a low of 0.03 µg/L to a high of 2.24 g/L, with a mean of 0.362 µg/L. However, the leakage of tungsten from the test devices made with laboratory grade silastic tubing was higher, ranging from a low of 0.14µg/L to a high of 2.55 g/L, with a mean of 1.09 µg/L. The ambient concentration of tungsten in normal saline ranged from a low of 0.10 µg/L to a high of 0.529 µg/L, with a mean of 0.166 g/L. However, the difference of the mean tungsten concentration leakage amount between devices made with laboratory grade Silastic tubing and medical grade Silastic tubing did not reach statistical significance (p value = 0.10). The percent increase in concentration of tungsten leaked from the test devices compared to the ambient concentration in medical grade normal saline was 218% for medical grade silastic tubing versus 657% for laboratory grade silastic tubing. The concentrations of the constituent heavy metal components of stainless steel (iron, cobalt, and chromium) within the saline baths of the test devices, also tended to increase with time.

Cadaver study

Each test device was easily and successfully inserted into the retrovesical space using percutaneous image guided technique with an 18-French peel away sheath. In addition, each test device was successfully retrieved intact using percutaneous technique. No tear, rupture, or breach in integrity was visualized on any of the test devices, post retrieval. No test device migrated, as depicted on biplane radiographic imaging, peritoneography, and axial cone beam CT scanning, despite filling the peritoneum with saline and provocative maneuvering (360-degree rolls of the cadavers for each test device) (Figures 3-6).

Saline flow rates for each test device and cadaver are shown in Table 2. All in-flow and out-flow rates (total volume within 10 min) and volumes (greater than 0.7 L in or out) were acceptable, except for a low volume of 0.2 L drained out of the Merit catheter with no device after the roll in cadaver 1, low volume of 0.6L out of the Covidien catheter with an 8 cm straight device prior to the roll in cadaver 2, and a low volume of 0.5 L out of the Merit catheter with an 8 cm straight device prior to the roll in cadaver 3. For test devices, all volumes were infused or drained within a mean time of 3 minutes and the mean volume was 0.9 L. For all catheters, the mean flow rate was 312 cc/min, which is well above the threshold rate of 100 cc/min (Figure 7).

	Flow Rate In	Flow Rate Out	Post Roll Flow Rate In	Post Roll Flow Rate Out	Mean Flow Rate	P-values
Cadaver 1						
A	1L/4 min = 250	0.8L/6 min = 133	1L/3 min = 333	0.2L/3 min = 67	196	
B	1L/3 min = 333	0.9L/8 min = 112	1L/3 min = 333	0.8 /2 min = 400	294	
C	1L/3 min = 333	0.9L/3 min = 300	1L 3 min = 333	1L/3 min = 333	325	
Cadaver 2						
D	1L/3 min = 333	1L/3 min = 333	1L/3 min = 333	0.9L/3 min = 300	325	
E	1L/3 min = 333	0.6L/3 min = 200	1L/4 min = 250	0.8L/4 min = 200	246	
F	1L/4 min = 250	0.7L/1 min = 700	1L/3 min = 333	0.8L/4 min = 200	371	
Cadaver 3						
G	1L/2 min = 500	0.5L/2 min = 250	1L/2 min = 500	0.8L/3 min = 267	379	
H	1L/3 min = 333	1L 2 min = 500	1L/3 min = 333	0.9L/3 min = 300	366	
I	0.8L/4 min = 200	0.7L/4 min = 175	1L/4 min = 250	0.8L/5 min = 160	196	
J	0.7L/2 min = 350	0.8L/2 min = 400	0.8L/3 min = 267	0.8L/3 min = 267	321	
Cadaver 4						
K	1L/2 min = 500	0.8L/3 min = 267	1L/3 min = 333	0.9L/3 min = 300	350	
L	1L/2 min = 500	1L/3 min = 333	1L/3 min = 333	1L/3 min = 333	375	
Pre v. Post Roll Mean In and Out						0.35
Pre v. Post Roll Mean In						0.41
Pre v. Post Roll Mean Out						0.53
Catheters With v. Without Devices Mean In and Out						0.23

All volumes are rounded to nearest 0.1L, all times are rounded to nearest minute, and all rates are in cc/min. A Merit, No device; B Merit 16cm, 20.13g, straight; C Merit 8 cm, 10.5g, straight; D Merit 8 cm, 10.6g, straight; E Covidien 8 cm, 10.83 g, straight; F Merit 16 cm, 20.64 g, straight; G Merit 8 cm, 10.1g, straight; H Merit 8 cm, 10.0 g, straight; I Covidien 8 cm, 10.8 g, straight; J Merit No device; K Merit 12 cm, 17.1g, coiled; L Merit 9 cm, 11.5 g, segmented.
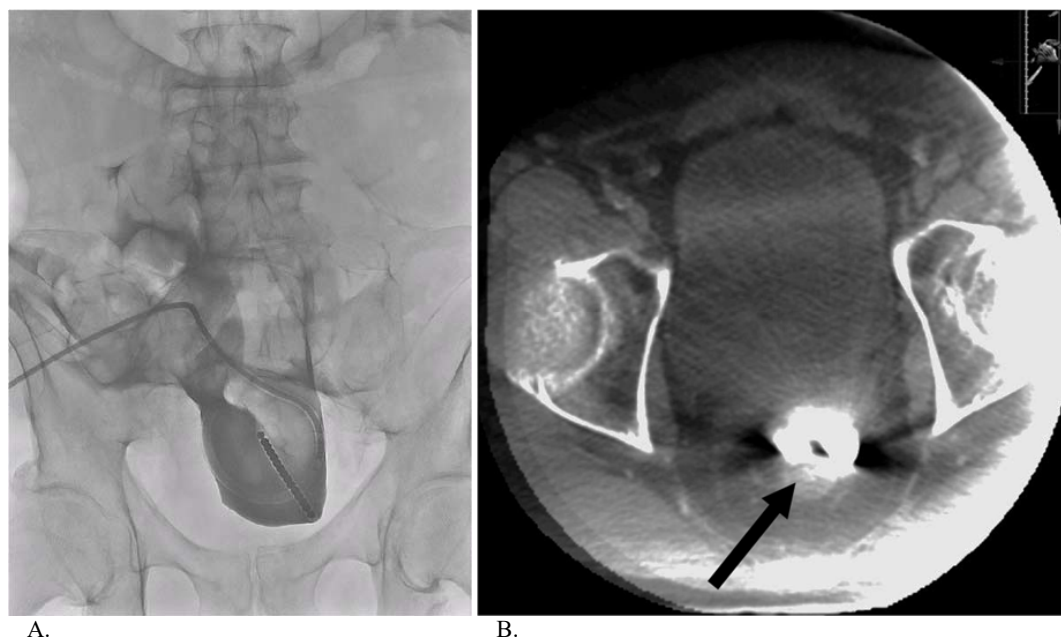
Table 2: Saline infusion and drainage flow rates for each test device and cadaver.

A.
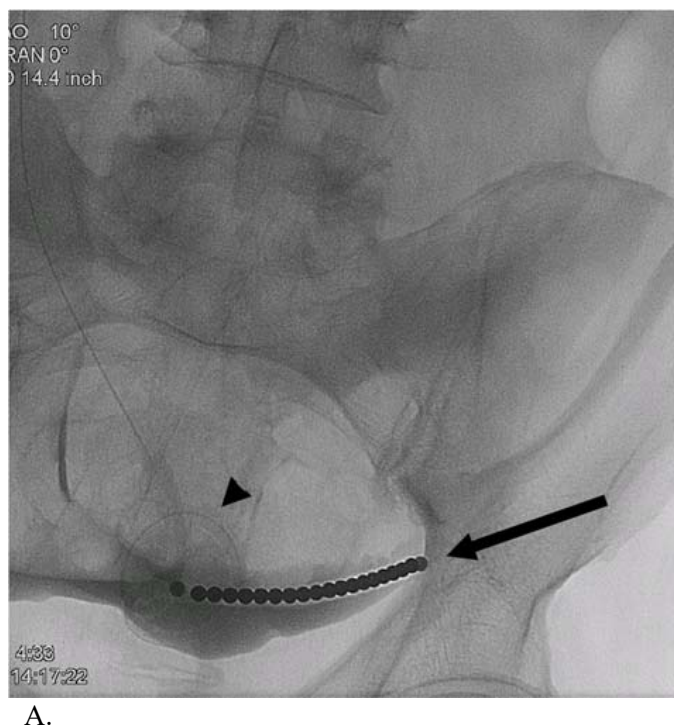
Figure 3: Imaging of device placed in cadaver 1.

A: A-P radiograph of 8 cm straight device (arrow) and attached coil of PD cath (arrowhead) within retrovesical space post roll.

A.   B.
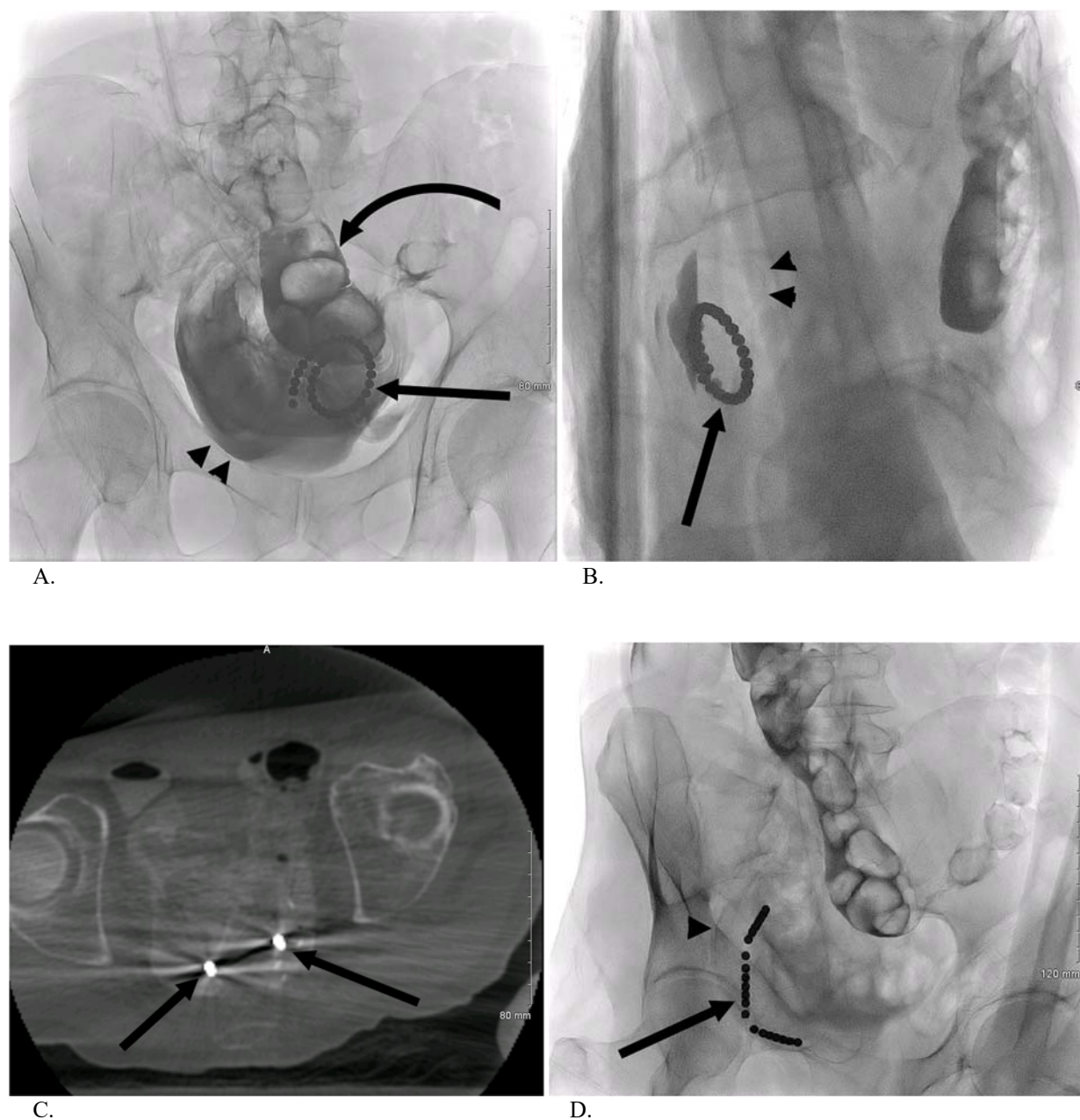
Figure 4: Imaging of device placed in cadaver 2.

A: A-P radiograph of 8 cm device within retrovesical space prior to roll. B: Cone beam axial CT scan showing artifact created by 8 cm device and dense contrast media in retrovesical space (arrow) prior to roll.
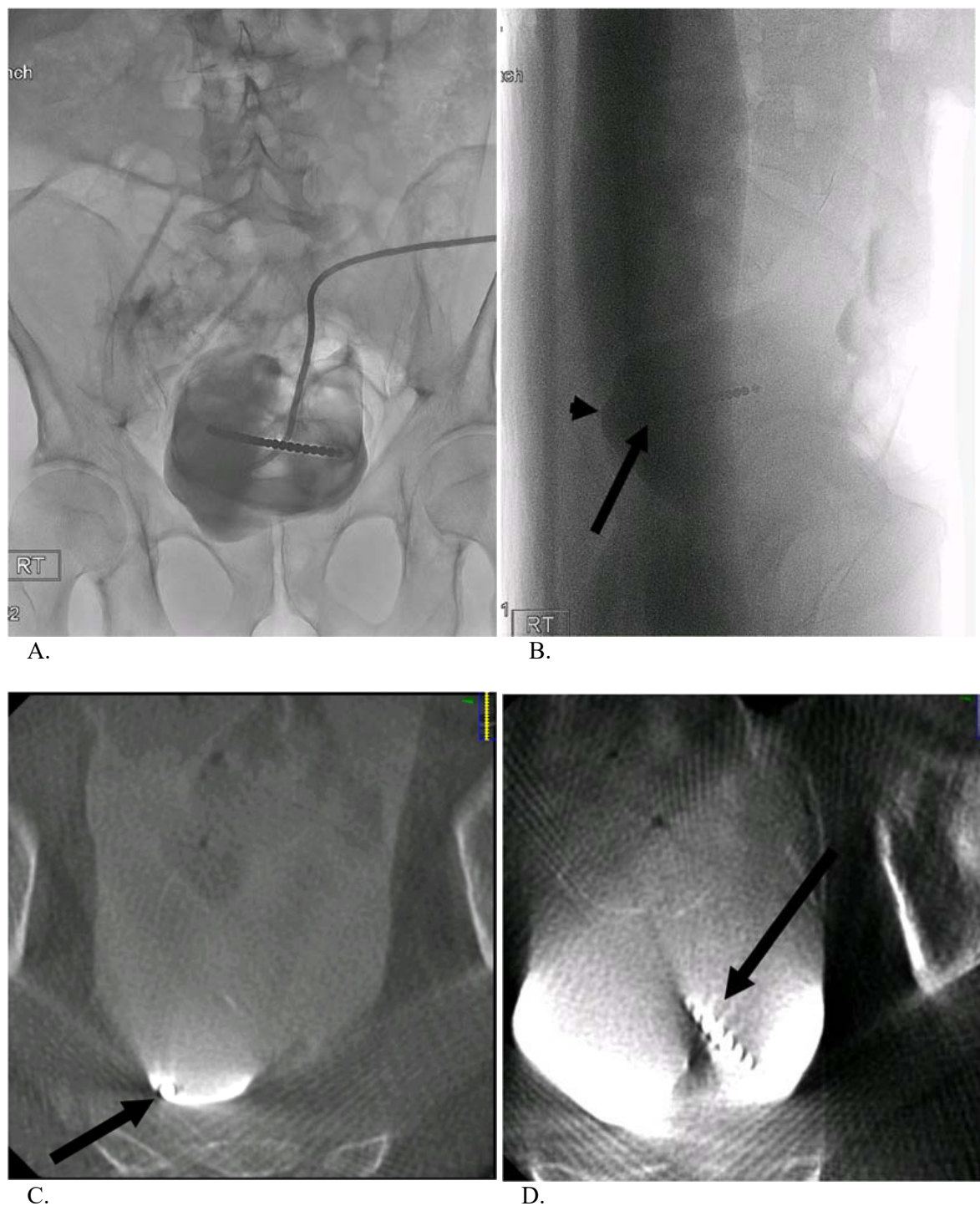
**Figure 5:** Imaging of device placed in cadaver 3.

A: A-P radiograph of 8 cm device in rectovesical space pre roll. B: Lateral radiograph of 8 cm device (arrow) in rectovesical space (arrowhead) post roll. C: Cone beam axial CT showing device (arrow) in rectovesical space pre roll. D: Cone beam axial CT showing device (arrow) in rectovesical space post roll.

Figure 6: Imaging of device placed in cadaver 4.

A: A-P radiograph demonstrating rectovesical space (arrowheads), coiled device in rectovesical space (arrow) and contrast media in sigmoid colon (curved arrow) pre roll. B: Lateral radiograph shows coiled device in posterior rectovesical space (arrow) attached to the PD catheter (arrowheads) pre roll. C: Cone beam axial CT shows coiled device (arrows) in rectovesical space post roll. D: Oblique radiograph depicting segmented device (arrow) in posterior rectovesical space (arrowhead) post roll.
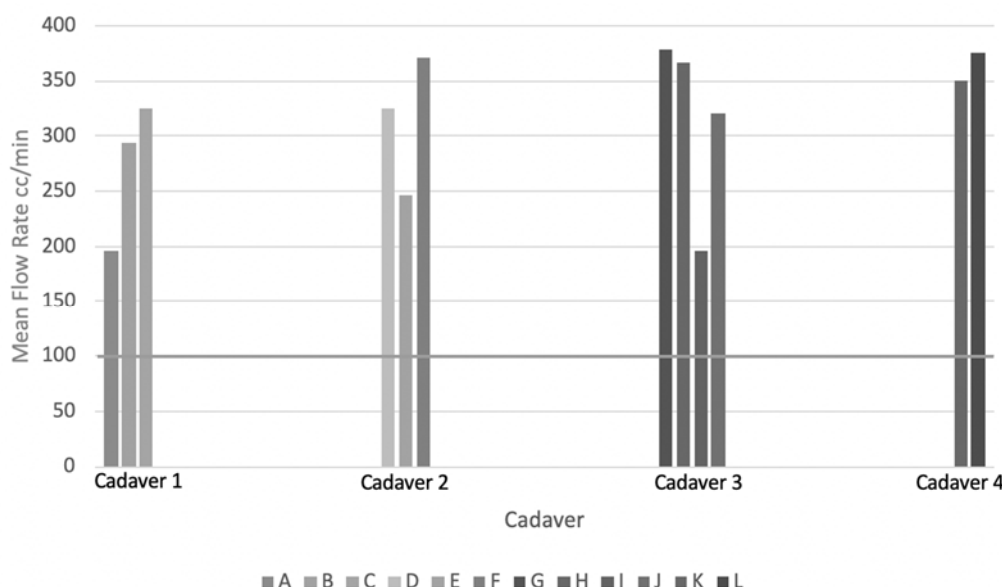
Figure 7: Mean Flow Rates of Each Catheter.

A: Merit No device; B: Merit 16cm, 20.13g, straight; C: Merit 8cm,10.5g, straight; D: Merit 8cm, 10.6g, straight; E: Covidien 8cm, 10.83g, straight; F: Merit 16cm, 20.64g, straight; G: Merit 8cm 10.1g, straight; H: Merit 8cm, 10.0g, straight; I: Covidien 8cm, 10.8g, straight; J: Merit No device; K: Merit 12cm, 17.1g, coiled; L: Merit 9cm, 11.5g, segmented; Threshold flow rate is 100cc/min.

No significant difference was found between the pre-roll and post-roll mean flow rates of the test devices (p value = 0.35), signifying that the provocative maneuvering did not impede flow. Segregating the groups further, no significant difference was identified between the pre-roll and post-roll mean inflow (p value = 0.41) or outflow (p value = 0.53) rates, nor between the mean flow rates of the catheters with or without the devices (p value = 0.23), indicating that device did not inhibit flow compared to catheters without the device located in an optimal position within the retrovesical space of the peritoneal cavity.

Discussion

Previous studies have shown that PD catheter migration out of the retrovesical space is a common cause of PD catheter dysfunction, occurring with a frequency between 12.7 and 35% [6-8]. However, the true rate may be much higher, mainly because it may be under reported. These studies have not utilized the precision of three-dimensional imaging to determine if a PD catheter has migrated. In addition, without the use of imaging that records the position of the PD catheter at placement and three-dimensional imaging at follow up, the baseline position of the PD catheter and the true migration distance at follow up cannot be certain. If a frontal two-dimensional radiograph is used to determine migration distance, all of the PD catheters that migrate in an anterior direction will not be detected. Particularly in obese patients, PD catheters that migrate into the anterior abdominal recess and become dysfunctional due to wrap by omentum and small bowel will appear to be well placed on frontal radiographs.

Di Paolo et al., attempted to ameliorate the problem of PD catheter migration by introducing the "self-locating peritoneal dialysis catheter" (SLPDC) in 1996 [10]. This PD catheter is similar to the straight Tenckhoff catheter in form, but is modified with a 12 g tungsten cylinder incorporated in the tip to keep the catheter tip in the retrovesical space through gravitational forces. Multiple studies have shown improved function, decreased migration, and longer catheter survival with the SLPDC [9-15]. However, drawbacks of the SLPDC include the significantly increased diameter of the terminal tungsten cylinder compared to the nominal diameter of the catheter precluding the ability to place it percutaneously through small sheaths, its inability to vary the length of the effective catheter, and its restricted application to a straight catheter instead of a coiled catheter.

Some reports have made claims that PD catheter migration can be decreased or eliminated by applying various laparoscopic insertions techniques, such as using a three-cuff PD catheter with a low-entry technique, or "advanced laparoscopic" techniques consisting of rectus sheath tunneling and adjunctive procedures [16,17]. Many of these techniques can also be accomplished with the percutaneous method of PD catheter placement. However, it does not appear that these investigations have documented initial PD catheter placement into the retrovesical space or analyzed migration at follow up by using three-dimensional imaging. Therefore, the true PD catheter migration rate remains unknown in these studies.

Like the SLPDC by Di Paolo, this device strives to prevent migration by the inherent anchoring effect of the tungsten, due to gravitational forces into the dependent portion of the pelvis. However, the device evaluated has multiple advantages over the SLPDC, which include its flexible design which conforms to the shape of the retrovesical space, its variable length when associated with a coiled PD catheter, and the applicability to all existing PD

catheters as a modification. Most of all, it is low profile and designed to be placed percutaneously through an 18-French peel-away sheath. Besides the gravitational weight effect, another factor that stabilizes this device in the retrovesical space is its ability to conform to the shape of the retrovesical space and become interpolated due to its flexible properties. By associating this device with a coiled PD catheter, either as an ancillary attachment to a commercially available PD catheter or as an inherent part of a new modified PD catheter, the effective length of the active coil zone of the PD catheter will be increased, ensuring that the infusions and drainages will occur within the most dependent portion of the peritoneal cavity. Currently, proceduralists that place PD catheters rely on a "one size fits all" approach, or a limitation to two different lengths of commercially available coiled PD catheters, while the intraperitoneal distance between the anterior abdominal wall insertion site and the retrovesical space varies significantly among patients. In large patients, commercially available coiled PD catheters are not long enough to stay in place within the retrovesical space. The device tested may rectify this problem by increasing the effective length of the PD catheter and preventing elastic recoil out of the dependent portion of the pelvis.

One of the problems with the SLPDC is the large diameter of the tungsten terminus. This precludes percutaneous insertion and causes the entrance channel into the peritoneal space to be quite patulous, which increases the rate of dialysate leakage [18]. Other authors have reported additional complications with the SLPDC, including difficulty in removing it and pain [19,20]. In contrast, the device evaluated is low profile and will not increase the size of the insertion channel into the peritoneal space when placed percutaneously. In addition, it can also be placed laparoscopically and surgically.

Cadavers were chosen to test the device with respect to feasibility of percutaneous insertion and retrieval, ability to stabilize within the retrovesical space following a provocative saline infusion into the peritoneal space and a 360-degree roll, and saline infusion and drainage rates of devices attached to two commercially available PD catheters. All test results were generally favorable, as all devices were successfully inserted through an 18-French peel-away sheath and retrieved. The device and PD catheter combinations always remained in place within the retrovesical space. They also exhibited acceptable infusion and drainage rates, which is a rate greater than 1L in within 10 minutes (100 cc/min) and 1L out within 12 minutes (83 cc/min), in 10 different device and PD catheter combinations and 42 out of 44 infusions or drainages. Human cadavers are the best *in vitro* model for testing this device, as they simulate the supine position of most patients undergoing PD. Four legged live animals are not ideal as a long-term test model, since they generally ambulate and sleep in the prone position. This weighted device would tend to gravitate into a dependent position in most animals, which would place the PD catheter between bowel loops and omentum. Silastic tubing is already known to be biocompatible in humans, so a toxicology analysis in live animals would seem to be superfluous. Despite the inherent rigor mortis and unprepared bowel of the non-embalmed cadavers, acceptable flow rates were still observed.

This study shows that there was a minimal amount of tungsten that leaked out of the test devices made with medical grade silastic tubing. These test devices relied on a water-tight seal created with stainless steel balls and Prolene sutures. A potential liability of the integrity of the device resides with the hand tied Prolene sutures,

which could break or become untied. This risk could be eliminated, and the minimal tungsten leak could be further reduced by incorporating the device into a PD catheter, so that the tungsten balls are completed encased by silicone during the fabrication process. In addition, some of the small amount of tungsten that might potentially leak out of this device in clinical use will be drained out of the peritoneal space during dialysate exchanges, *in vivo*. Normal saline was used in this *in vitro* experiment to simulate peritoneal fluid without dialysate. We believe the large volumes of dialysate exchanges will diminish any effect of leaked tungsten in the clinical environment. It is true that our *in vitro* environment, which was cooler than normal body temperature and relatively quiescent compared to dialysate exchanges, did not exactly simulate the *in vivo* environment. However, we believe that our study was good first step to detect any significant tungsten leak. Tungsten is ubiquitous in the environment and historically has not been associated with toxic effects in humans. In the general population, tungsten blood and urine levels have been measured between 1 to 6 µg/L and 0.085 µg/L, respectively [21]. These "normal" blood levels of tungsten are generally much higher than the concentration of tungsten in the saline baths resulting from the minimal leak observed with test devices up to nine months, and similar to the concentrations in the saline baths observed at 21 months. U.S. Environmental Protection Agency does not require measurement of tungsten in surface water or groundwater, but tungsten levels have been measured up to 337 µg/L in well water [21]. No carcinogenic effect of tungsten in humans has been found [22]. However, some authors have suggested that medical devices use alternative materials other than tungsten [23]. Low-dose tungsten contamination, as found in environmentally polluted drinking water, may affect the biology of stem/precursor thyroid cells and of their progeny, including characteristics of preneoplastic transformation [24].

Furthermore, not only could this device be fabricated with a one-piece design, completely encasing and isolating the tungsten balls within the tubing, the device could also be constructed using only medical grade stainless steel balls. Stainless steel is a safe and biocompatible material with a proven track record in medical devices. Stainless steel is lighter than tungsten, and therefore, more stainless-steel balls would be required to obtain the same weight.

Limitations of this study are primarily related to the limited resources available in conducting the evaluation. Regarding the measurement of tungsten leak, variable time points were used for metal analysis up to 21 months, depending on funds available to perform the analyses. Normal saline was used to simulate intraperitoneal extracellular fluid for the *in vitro* tests, which may not provide a similar inflammatory environment found in peritoneal fluid or hypertonic environment found in dialysate. Likewise, only 10 different device and catheter combinations were evaluated in four cadavers, as procedure room time, available test cadavers, and ancillary staff were restricted due to funding limitations. Ideally, a larger number of cadavers to include female cadavers, using a greater number of device and catheter combinations, with a randomized and controlled evaluation among commercially available PD catheter and device combinations could yield more meaningful results.

Conclusions

In summary, this novel and innovative device has the potential of improving function and durability of existing PD catheters

as a modification or it can be fabricated into a new PD catheter design. This device works by anchoring the PD catheter into the retrovesical space through gravitational forces and interpolation, while increasing its effective length. The device conforms to the shape of the retrovesical space and it stretches the coil of the PD catheter so that its length is customized to each patient. This study has shown that this device is amenable to percutaneous insertion and retrieval and retains acceptable stability and flow rates in cadavers. Tungsten leak from this device is minimal and appears lower than the "normal" tungsten blood levels in humans. This device has the potential to benefit ESRD patients on PD. Further investigation in humans with a fabricated one-piece prototype is warranted.

Competing Interests

CSM declares a patent application (patent pending) on the device of interest described in this manuscript. No other author reports a conflict of interest.

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Author Contributions

CSM designed the study, collected and analyzed data, and wrote the manuscript. GPJ assisted in data collection and reviewed the manuscript. MJD performed the statistical analysis, assisted in writing the manuscript, and reviewed the manuscript. ARB assisted in the design of the study, data analysis, and reviewed the manuscript.

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