TITLE: Peripheral Intravenous Catheter Securement With Tissue Adhesive Compared to Conventional Dressing: A Randomized Controlled Trial

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Peripheral Intravenous Catheter Securement with Tissue Adhesive Compared to Conventional Dressing: A Randomized Controlled Trial

Background/Scientific Rationale:

Nearly all hospitalized patients require intravenous (IV) access for treatment. Patients rely on functional vascular access to receive life saving IV therapies. Generally, peripheral IVs have high failure rates with 19-25% of IVs failing prior to completion of therapy and 45-56% of ultrasound-guided peripheral IVs failing prior to completion of therapy. Dislodgment, infiltration/extravasation, and phlebitis are common complications that lead to early failure. [1-5] IV restarts are a common procedure and are unfortunately simply a part of a normal workday for nurses. A failure rate of up to 56% in a technology that is over 75 years old is unacceptable.

If access is lost, patients may experience treatment delays, dissatisfaction from repeat needle-sticks, and health complications if the patient's condition becomes critical. IV failure can result in a number of negative health/quality outcomes including phlebitis and infections and/or skin necrosis from caustic medication infiltration; utilization of invasive procedures such as peripherally inserted central catheters (PICC) and central lines; and wasted medical/nursing time.[6]

Because failure rate is high, it is important to approach insertions methodically to improve survival rates. One area of opportunity is securement of the catheter. Accidental dislodgment is a common cause of early IV failure accounting for up to 50% of catheter failures.[7] Beyond dislodgment, inadequate fixation of the catheter to the patient's skin causes micromotion, leading to vein irritation and entry of skin bacteria into the entry site. This micromotion leads to phlebitis, occlusion, and infection.[8] Standard practice for securement involves placement of a polyurethane dressing with clear tape. A variety of additional devices are available on the market including tissue adhesives, specially designed securement dressings, and sutureless securement devices. The evidence suggests the use of tissue adhesives may decrease peripheral IV failure with a decrease in dislodgments and occlusions compared to the alternatives.[8] Bugden et al. found that skin glue reduced catheter dislodgment by 7% and reduced peripheral IV failure by 10%.[9]

While some evidence supports the use of tissue adhesives for securement, further randomized controlled trials are needed to assess the effectiveness of this intervention. Further, only one prospective, randomized trial evaluated patients in the emergency room setting. Nearly 50% of all hospital admissions start in the emergency department (ED) and 80% of hospitalized patients require IV access. This highlights the importance of understanding the impact of tissue adhesives on peripheral IV survival for patients admitted through the ED. While Bugden found that skin glue reduced IV failures for patients hospitalized from the

ED, patients were only followed for 48 hours. The general consensus is to continue using IVs as long as there is no clinical indication for removal. [10] As the average hospital length of stay in the United States is 4-6 days, it is clear that the 48 hour cutoff is a critical flaw in the analysis and further investigation over a longer time period is urgently needed.

We propose a prospective randomized controlled trial to evaluate peripheral IV failure with ED patients that are hospitalized comparing securement with standard securement plus Adhezion Biomedical SecurePortIV™ to standard securement.

Specific Aim 1: Test the prediction that the experimental securement solution of standard dressing plus Adhezion Biomedical SecurePortIV™ will have a lower probability of failure compared to the control standard of care securement.

For Aim 1, an improved survival of the experimental securement solution will be evaluated by functionality of catheter for intravenous therapy prior to patient discharge. The event is failure of functionality identified during follow-up assessment during hospitalization. Duration of dwell and functional failure of the catheter will be employed to estimate catheter survival.

Specific Aim 2: Determine the difference in cause-specific IV failure rates between the experimental and control groups. Specific etiologies to be evaluated include dislodgment, infection, phlebitis, and occlusion.

Specific Aim 3: Determine the difference in costs associated with the experimental group versus the control group. Cost calculation will include all costs of placement in each group: labor and material.

Study Design:

We propose a prospective, single-site, parallel, two-arm randomized investigation of catheter survival when securement strategies are evaluated. Specifically, conventional securement with polyurethane dressing and tape will be compared with experimental securement with tissue adhesive, polyurethane dressing and tape. The primary objective of this study is to demonstrate that there is better survival of the catheter securement with the tissue adhesive. Exploratory secondary and adjusted multivariable analyses will also be conducted.

Pre-Enrollment Staff Training:

The proper application of the tissue adhesive requires some education and training of staff. Research staff performing patient enrollments will be trained to place the tissue adhesive by the Adhezion clinical/education team. A possible training may include a short didactic and hands-on session and application of the solution on

healthy volunteers/patients. Enrollment will begin once staff are deemed proficient in the procedure.

Study Population and Eligibility:

Inclusion Criteria:

A convenience sample of patients with expected greater than 48 hours admission likelihood will be eligible for enrollment.

1. All adult patients greater or equal to 18 years of age
2. Admission from the ED to a progressive floor expected for over 48 hours OR 2a: Admission from ED to any floor type with express approval from the Principal Investigator
3. IV placement in the antecubital fossa, forearm, wrist or hand
4. IV placement in the Emergency Department
5. Enrollment within 8 hours of IV insertion
6. 18 or 20 gauge 1.16 inch IV catheter

Exclusion Criteria:

1. Patients with ultrasound-guided IV insertions
2. Alternate site of cannulation
3. Voluntary withdrawal
4. Patients with a non-standard polyurethane dressing
5. Known allergy to cyanoacrylate or formaldehyde

The survival analysis will only be performed on patients that have an IV dwell time greater than 48 hours. Over 85% of patients admitted to a progressive floor have length of stay greater than 48 hours. The sample size calculation reflects an assumed 10 - 15% exclusion rate.

Study Procedure:

Initial Assessment:

Patients admitted from the ED to a progressive floor are eligible participants. Research staff will approach a convenience sample of patients admitted to the progressive floors based on screening of the electronic medical record. These patients are admitted to a progressive floor but approached by research staff when physically in the emergency department waiting for a room assignment. The principal investigator may also choose to include additional patients admitted to non-progressive inpatient units. The principal investigator will inform the research staff when such cases arise. Similar to other study subjects, these patients will be approached in the Emergency Department. If the patient agrees to participate in the

trial, the study subject will be consented by the research staff. Research staff will confirm functionality of the existing IV previously placed by ED staff. The assessment will include observing for blood return into the tubing upon aspiration and/or unobstructed flush with a minimum of 1-2 ml of normal saline. Staff will also observe the site for any signs of redness or tenderness.
A tourniquet may be applied as needed. If the patient is actively receiving an infusion, the drip will briefly be halted to evaluate for functionality. Functionality will be assessed with the existing dressing in place. If the catheter is functional and free of any signs of complications, study subjects will be randomized by a computer generated 1:1 envelope system to either the control group: polyurethane dressing + clear tape or the experimental group: polyurethane dressing + clear tape + tissue adhesive. If the IV is not functional, a new catheter will be inserted in a new location, documented, and patient continues in the study. For the control group, the polyurethane dressing will be gently removed. Dressing will be removed carefully to minimize any potential dislodgments or skin injury. The site will be evaluated for oozing or blood and as needed cleaned with sterile gauze. Once the site is completely dry, a new polyurethane dressing will be applied and reinforced with tape in a standard fashion. See Appendix A for pictures depicting standard dressing application with tape. Once securement is complete, functionality will be reassessed per protocol above. For the experimental group, the existing securement will be gently removed. The site will be evaluated for oozing or blood and as needed cleaned with sterile gauze. Once the site is completely dry, the tissue adhesive will be applied per directions in Appendix B. A new standard polyurethane dressing will be applied and tape will be applied per the standard approach. Once securement is complete, functionality will be reassessed per protocol above. The time of the new dressing application will be noted as time zero. Catheter dwell time will begin at this point.

Additional data variables collected at the initial assessment include: demographics such as age, sex, INR>1.5, platelets < 50, insertion site details, hours from insertion to recruitment, inserter credentials.

Follow-up Assessment:

After initial assessment, the catheter will be assessed by the research team every 24 +/- 5 hours as long as the patient is hospitalized up to 7 days or 168 hours. At each follow up interval the researcher notes the date/time of evaluation and assesses for any signs and symptoms of complications and functionality of the device. A catheter is functional if the IV flushes without resistance. Catheters will be assessed daily for signs and symptoms of complications.[11] See Appendix C for details regarding the assessment for complications. Any signs or symptoms of complications or lack of functionality will be reported to the patient's primary care team so that management of the IV catheter can be addressed. If the catheter and adhesive are removed early due to catheter failure or complication, or for patient discharge prior to 7 days a medical adhesive remover may be used.

If the catheter was identified to have any signs or symptoms of complications during follow-up assessment the date and time of observation of the complication will be documented in the data collection tool and the primary team will be notified of the complication. If the catheter was removed prior to the follow-up assessment then the IV removal time and the reason for removal will be obtained through chart review. For all catheters removed due to a complication, re-insertion attempt data will be tracked through the medical record in the nursing section for venous lines and need for reinsertion of the IV or escalation to a midline, PICC, or CVC will be noted. If the patient is discharged prior to the time of follow-up assessment then the time of discharge will be documented and the IV will be presumed functional until time of discharge unless otherwise noted in the chart.

The medication administration record will be queried for all medications given through each catheter with specific attention to antibiotics and anticoagulants. Vesicants/irritants that are generally given via central line or considered caustic to the vessel will be noted in both groups. Number of doses will be recorded. See Appendix D for full list of non-neoplastic vesicants.

Additional data gathered by research staff on follow-up evaluation includes: dwell time in days/hours, hospital length of stay, and number of peripheral IVs for duration of stay.

Appendix E represents the data collection documentation tool for all catheter follow-ups.

Statistical Rationale and Analysis Plan:

Sample Size and Power Analysis

For this randomly allocated two-groups experiment, the primary outcome is catheter survival associated with securement devices. Sample size calculation is based on primary outcome: composite or all cause premature removal due to complication of the IV catheter. Based on existing literature, the maximum mean failure rate across major investigations is 25% which functions as the estimated failure rate of the standard of care group. Assuming a minimum difference of 10% needed for prompting a change in practice and based on existing literature, the experimental group (standard of care plus tissue adhesive) is hypothesized to have a composite failure rate of 15%. 154 subjects per group for a total sample size of 308 subjects is the minimum recommendation assuming a 10% dropout rate. To account for a larger dropout percentage, 350 patients or 175 subjects per group is the final sample size to provide 80% power to detect a significant effect.

Statistical Analysis

Characteristics of enrolled patients will be summarized using means [standard deviations] and medians [interquartile ranges] for continuous variables, and frequencies (percentages) for categorical variables. Exploratory data analyses including histograms, Pareto charts, scatter plots, and box plots will be further used to show the distribution. Appropriate transformations and estimation procedures will be performed as necessary. To test the effect of securement strategies on each of aims, we will further use Cox proportional hazard regression models for time-to-event outcomes and logistic regression models for binary outcomes. P-values of less than 0.05 will be considered statistically significant. Analysis will be conducted using SAS 9.4.

Data Collection/Management Plan:

Data will be collected as subjects are enrolled and information will be stored in a password protected excel file until ready for statistical analysis.

Publication and Presentation Plan:

The publication plan is to submit a manuscript to a high impact medical journal. This publication has the potential to significantly change securement practice and enhance quality for patients. The study results will also be presented at least one national meeting and potentially additional vascular access conferences.

Potential Impact:

Optimization of peripheral vascular care is a critical strategy to improve patient outcomes and reduce health care costs. Enhanced dwell times will lead to improved patient/staff satisfaction, decreased interruptions in care with shorter hospital length of stay, and decrease in complications such as thrombosis, bleeding, and infection. At the Royal Oak campus, over 450,000 IV catheters are purchased annually. Across the health system, this number exceeds 2 million catheters per year. In a study by Rickard et al in 2012, a patient required an average of 1.7 IV catheters per admission.[10] With a cost of approximately $35 per catheter for straightforward insertions, even a slight improvement in dwell time has the potential to save our health system millions of dollars.

Principal Investigator:

Amit Bahl, MD is the principal investigator and lead author for this investigation. He is board-certified in Emergency Medicine and subspecializes in Emergency Ultrasound. Further, Dr. Bahl serves as the medical director of the inpatient Vascular Access Team at Beaumont Royal Oak campus. He has authored a number of peer-

reviewed manuscripts with a key focus on ultrasound-guided vascular access. He recently completed three randomized controlled trials assessing catheter dwell time with ultrasound-guided IV insertions.

Site:

Beaumont Health is Michigan's largest health care system and is the most preferred for health care in the tri-county area, according to National Research Corporation survey data. A not-for-profit organization, it was formed in 2014 by Beaumont Health System, Botsford Hospital and Oakwood Healthcare to provide patients with the benefit of greater access to extraordinary, compassionate care, no matter where they live in Southeast Michigan. Beaumont Health has total net revenue of $4.5 billion and consists of eight hospitals with 3,429 beds, 187 outpatient sites, nearly 5,000 physicians, 38,000 employees and 3,500 volunteers. In 2017, Beaumont Health had 175,700 inpatient discharges, 17,800 births and 575,000 emergency visits.

William Beaumont Hospital, Royal Oak (RO) campus is the proposed site for the investigation. It is a 1,100 bed major academic and referral center with Level 1 adult trauma and Level 2 pediatric trauma status. A major teaching facility, Beaumont, Royal Oak has 55 residency and fellowship programs with 454 residents and fellows. Beaumont is the exclusive clinical partner for the Oakland University William Beaumont School of Medicine. The Beaumont Research Institute was established more than 30 year ago at Royal Oak and offers research support services to clinical investigators.

References:

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10. Rickard CM, Webster J, Wallis MC. Routine versus clinically indicated replacement of peripheral intravenous catheters: a randomized controlled equivalence trial. *Lancet*. 2012;380 (9847):1066-1074.
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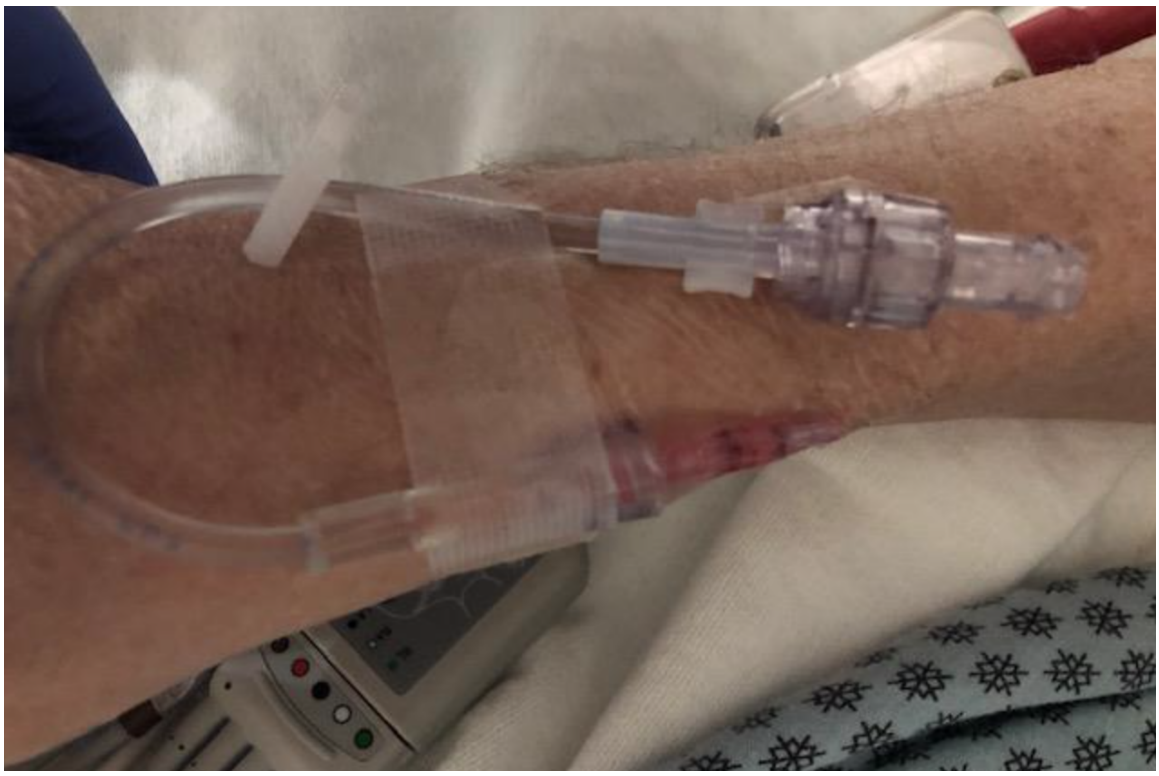
Appendix A: Standard Dressings with Securement



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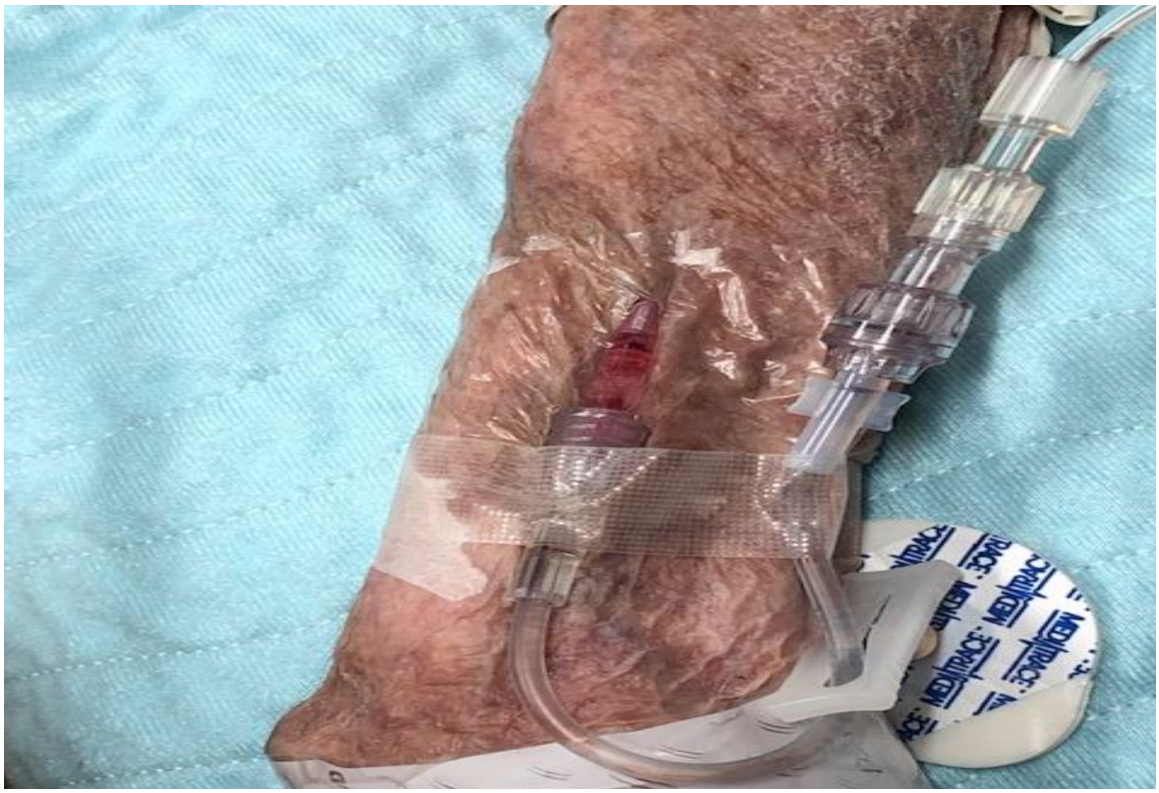
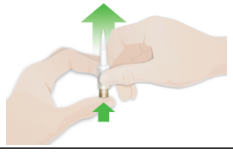
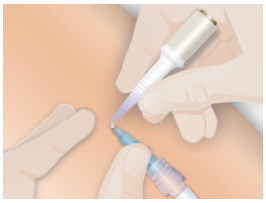
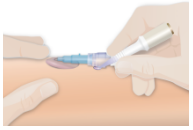
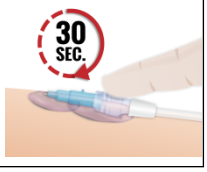


Appendix B: Tissue Adhesive Application Instructions

Point the tip towards the ceiling and away from the patient. Press the bottom of the applicator upward.	
Invert the applicator and gently squeeze the ridges to initiate adhesive flow. Place 1-2 drops of adhesive at the catheter-skin junction. ***Allow each drop of glue to "set-up" for a few seconds before adding the next drop.*** ***Make sure the tissue adhesive is surrounding the entire circumference of the catheter.***	
Place an additional 1-2 drops of adhesive under the catheter hub/extension set connection. Apply gentle pressure for 30 seconds to ensure securement between the catheter and the skin surface.	 

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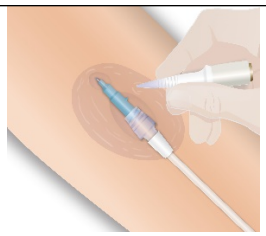
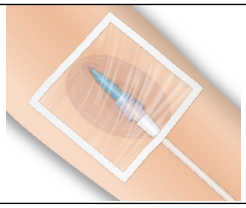
As desired, the remaining adhesive can be spread out beyond the area of the catheter to increase dressing adherence.	
After application of SecurePortIV, a transparent film dressing should be applied per facility protocol.	

Appendix C: Signs and Symptoms of Catheter-Related Complications

1. Any level of pain and/or tenderness with or without palpation
2. Changes in color (erythema or blanching)
3. Changes in skin temperature (hot or cold)
4. Edema
5. Induration
6. Leakage of fluid or purulent drainage from the puncture site
7. Other dysfunction (e.g. resistance with flushing, lack of blood return

Appendix D: List of Vesicants/Irritants

RED LIST Well-recognized vesicants with multiple citations and reports of tissue damage upon extravasation	YELLOW LIST Vesicants associated with fewer published reports of extravasation; published drug information and infusate characteristics indicate caution and potential for tissue damage
Calcium chloride	**Acyclovir**
Calcium gluconate	**Amiodarone**
Contrast media - nonionic	**Arginine**
Dextrose concentration ≥ 12.5%	**Dextrose concentration ≥ 10% to 12.5%**
Dobutamine	**Mannitol ≥ 20%**
Dopamine	**Nafcillin**
Epinephrine	**Pentamidine**
Norepinephrine	**Pentobarbital sodium**
Parenteral nutrition solutions exceeding 900 mOsm/L	**Phenobarbital sodium**
Phenylephrine	**Potassium ≥ 60 mEq/L**
Phenytoin	**Vancomycin hydrochloride**
Promethazine	
Sodium bicarbonate	
Sodium chloride ≥ 3%	
Vasopressin	

Appendix E: Follow Up:

Day	Functional 1: draw 2: flush 3: infusing 4: failed	Removal Time	Reason for Removal	Signs/Symptoms of Complications	Rescue Device 1.PIV 2. USPIV 3. CVC 4. PICC 5. Midline 6. IO	Discharge <48hrs from insertion (if yes, remove patient from study)	Research staff initials
1							
2							
3							
4							
5							
6							
7							
8							
9							
10							

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Reasons for Removal: (1) completion of therapy (2) infiltration (3) phlebitis (4) dislodgement (5) oozing fluid/blood (6) purulent drainage (7) occlusion (8) removed by patient (9) site changed (10) other

Day	Medications transfused via catheter
1	
2	
3	
4	
5	
6	
7	
8	
9	
10	

Signature/Date (completer of post data):

_____