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TITLE: Consortia for Improving Medicine with Innovation & Technology

PRINCIPAL INVESTIGATOR: John A. Parrish, M.D.

CONTRACTING ORGANIZATION: General Hospital Corporation
Cambridge, MA 02138

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13. SUPPLEMENTARY NOTES

14. ABSTRACT
The Consortia for Improving Medicine with Innovation & Technology (CIMIT) is a consortium of nonprofit Boston-area institutions based at Massachusetts General Hospital and includes Brigham and Women's Hospital, Massachusetts Institute of Technology, Draper Laboratories, Beth Israel Deaconess Medical Center, Boston Medical Center, Boston University, Boston Children's Hospital, Harvard Medical School, Newton-Wellesley Hospital, Northeastern University and VA Boston Healthcare System. The overall goal of CIMIT is to combine clinical and technological excellence and educational components to generate, develop, and reduce to practice innovative and high-impact concepts to improve military and civilian healthcare.

15. SUBJECT TERMS
Nothing listed

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
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CIMIT Scientific Project Awards Supported by W81XWH-09-2-0001
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Principal Investigator	Award Title	Fiscal Year	Award ID	CIMIT No.	Award Status
Ackerman, Jerome	Vascular Repair by MR Coagulation	2013	Out - 001834	13-1180	Award Closed
Agar, Nathalie	Intraoperative Stereotactic Molecular Imaging of Tumor Boundaries by Mass Spectrometry	2011	Out - 001577	11-216	Award Closed
Armoundas, Antonis	Advanced Pacing Methods for Preventing Life Threatening Arrhythmias	2011	Out - 001602	11-157	Award Closed
Bergethon, Peter	Multi-optode probe for evaluation of diabetic neuropathy	2009	Out - 000657	09-456	Award Closed
Bianchi, Matt	Telemedicine Strategy for Chronic Sleep Disorder Management	2013	Out - 001836	13-1240	Fully Released
Bickmore, Timothy	Optimizing Hospital Workflow and Quality through Patient Engagement	2012	Out - 001696	12-1035	Fully Released
Bizzi, Emilio	A Fully Autonomous Brain-Body Interface for Patients with Neuromuscular Injury or Disease	2011	Out - 001579	11-282	Award Closed
Blesius, Carl	Large Scale Learning Management/Competency Tracking System	2013	Out - 001840	13-2193	Fully Released
Bonato, Paolo	Combining galvanic vestibular stimulation and motor training in traumatic brain injury survivors with neglect	2010	Out - 000668	10-479	Award Closed
Borsook, David	Optical imaging for Rapid Determination of Pain: Field and Surgical Application	2014	Out - 001882	14-1882	Fully Released
Cash, Sydney	Microelectrode recordings and advanced algorithms for seizure prediction	2009	Out - 000691	09-325	Award Closed
Channick, Colleen	Creation of Amino Alcohol-Based Poly(ester amide) Elastomer Bioabsorbable airway Stent	2011	Out - 001580	11-401	Award Closed
Collins, John	Acceleration of Hand Hygiene Process Development and Manufacture	2011	Out - 001681	11-1681	Award Closed
Colson, Yolonda	Expansile nanoparticles for tumor-targeted drug delivery to prevent lymph node metastases in breast cancer	2010	Out - 000703	09-433	Award Closed
Cunningham, Miles	Optimizing Convection Enhanced Delivery of Therapeutics to Treat Intractable Epilepsy	2012	Out - 001716	12-1319	Award Closed
Dai, Tianhong	Antimicrobial Photodynamic Therapy for Prevention and Treatment of Surgical Site Infections	2013	Out - 001838	13-1021	Award Closed

Dai, Tianhong	Ultraviolet C Light for Prophylaxis and Treatment of Multi-drug Resistant Infections Associated with Burns in the Combat Casualty	2013	Out - 001839	13-1033	Award Closed
Del Nido, Pedro	Catheter-based adaptable device for closure of intracardiac defects in children	2011	Out - 001581	11-351	Award Closed
DeMoya, Marc	MGH Surgical Simulation Program	2013	Out - 001841	13-1307	Award Closed
Denis, Gerald	Ultrasound-directed delivery of cancer chemotherapeutic drugs	2009	Out - 000728	09-116	Award Closed
Dixon, Ronald	Healthcare 360: A technology-enabled model for general medical care	2009	Out - 000735	09-182	Award Closed
Duggan, Michael	Surviving Blood Loss Through Pharmacological Resuscitation	2014	Out - 001887	14-1887	Fully Released
Edelman, Elazer	Optimizing Tissue Engineering Therapies for Airway Injury in the Battlefield	2014	Out - 001883	14-1883	Fully Released
Elman, Igor	Novel predictors of pharmaco-therapeutic outcomes using functional reciprocity between heightened stress reactivity and emotional numbing in PTSD	2010	Out - 000749	10-515	Fully Released
Fennessy, Fiona	Computer-assisted tumor blood vessel tortuosity analysis at 3T, as a method of assessing ablative therapy response	2009	Out - 000755	09-359	Award Closed
Fregni, Felipe	Closed loop, detect-and-treat systems for epilepsy	2010	Out - 000765	10-522	Award Closed
Golby, Alexandra	A hybrid optic-electromagnetic surgical tool tip tracking system for neurosurgery	2010	Out - 000771	10-397	Award Closed
Goldman, Julian	PCA Monitoring Safety Interlock to Decrease Adverse Clinical Events	2011	Out - 001583	11-443	Award Closed
Goldman, Julian	Improving continuity of care for veterans by electronically exchanging MGH, VA, and DoD medical record data	2012	Out - 001714	12-1265	Award Closed
Gordon, James	Infrastructure for a National Simulation Proving Grounds: The CIMIT-Boston Simulation Consortium (Parotidectomy Surgical Simulator / Intraosseous Device Placement / Cricothyrotomy Model / Soft Tissue Simulant Rapid Prototyping	2013	Out - 001842	13-2191	Fully Released
Gordon, James	Low-cost, High-performance, Modular Patient Simulation System	2013	Out - 001843	13-2134	Fully Released

Gray, James	Using network analysis to improve the qualities of NICU care teams and their function	2011	Out - 001584	11-346	Award Closed
Guo, Lifei	A Novel Stent-Based, Sutureless Device for Rapid Vascular Anastomosis in Microsurgery	2010	Out - 001132	10-1132	Award Closed
Gupta, Rajiv	Dynamic Imaging and Neuro Intervention Guidance Using Dual Energy CT: Translation into Practice	2014	Out - 001884	14-1884	Fully Released
Guttag, John	A Novel Algorithm to Detect the End of a Seizure and the Post-Seizure Period	2011	Out - 001585	11-484	Award Closed
Hacking, Adam	Non-invasive Fasciotomy to Treat Extremity Compartment Syndrome	2012	Out - 001706	12-1173	Award Closed
Harris, N. Stuart	Novel Neuroimaging in Acute Mountain Sickness	2011	Out - 001586	11-306	Award Closed
Harris, N. Stuart	Early Time Course and Severity of Cerebral Edema and Acute Exposure to High Altitude	2010	Out - 001135	10-1135	Award Closed
Harris, R. Scott	Enhanced inhalation therapy for emphysema	2011	Out - 001587	11-341	Fully Released
Hata, Nobuhiko	Swimming capsule endoscope	2009	Out - 000806	09-368	Award Closed
Hauser, Carl	A Rapid PCR-Based, Point of Care Test To Discriminate Between Sterile and Infective SIRS	2011	Out - 001588	11-217	Award Closed
Hoge, Elizabeth	The Effect of Oxytocin on Fear Memory Consolidation: A Novel Intervention to Prevent PTSD	2011	Out - 001589	11-542	Award Closed
Hooper, David	Rapid Screening of MRSA-colonized Patients in the Ambulatory Setting	2012	Out - 001701	12-1082	Award Closed
Horng, Steven	Developing and validating an integrated intelligent sepsis monitoring system	2012	Out - 001713	12-1262	Award Closed
Howe, Robert	SEAS - CIMIT Medical Devices Graduate Design Course	2011	Out - 001683		Award Closed
Hung, Judy	Polymer injection for treatment of ischemic mitral regurgitation	2009	Out - 000814	09-331	Award Closed
Ingber, Donald	Microfluidic blood cleansing device for sepsis therapy	2010	Out - 000819	09-303	Award Closed
Kang, Dongkyun	Comprehensive microscopy for intraoperative margin assessment	2012	Out - 001693	12-1012	Award Closed
Karlinsky, Joel	Interoperability of Portable X Ray Machines with Ventilators in Monitored Settings	2011	Out - 001591	11-348	Award Closed
Karp, Jeffrey	A Drug Delivery Platform for Near Term Impact on Patient Care	2010	Out - 000837	10-592	Award Closed

Kaushal, Shalesh	Low Energy Laser as a Therapeutic for Dry Age-related Macular Degeneration	2011	Out - 001607	11-397	Award Closed
Kheir, John	Use of topical oxygen mirobubbles to enhance wound healing	2010	Out - 000841	10-453	Award Closed
Kreiman, Gabriel	Memory Alteration through Theta Phase-Locked Electrical Stimulation	2011	Out - 001578	11-109	Award Closed
Kumar, Sandeep	Non-invasive brain stimulation for improving stroke related dysphagia	2012	Out - 001708	12-1187	Award Closed
Lee, Yong-Tae	Improving Recovery after Stroke via Electrical Stimulation of Proprioceptors	2011	Out - 001593	11-397	Award Closed
Lev, Michael	EIS as an "EKG for the Brain": Portable Point-of-Care Detection of Acute Traumatic Hematoma	2012	Out - 001694	12-1031	Award Closed
Lim, Chun	Augmented reality glasses for the treatment of visuospatial neglect	2009	Out - 000870	09-120	Award Closed
Lin, Alexander	Neurochemical and Multimodal Biomarkers for Chronic Traumatic Encephalopathy	2011	Out - 001592	11-127	Award Closed
Little, Patrick	Xenon anesthetic - FY10 Student Project	2010	Out - 001093		Award Closed
Little, Patrick	Harvey Mudd College Student Research Project	2009	Out - 001094		Award Closed
Mavroidis, Constantinos	Smart Orthoses for Home Based Tele-Rehabilitation Systems	2012	Out - 001715	12-1278	Award Closed
Mazumder, Malay	Electrostatic dry powder inhaler for constant dose respiratory drug delivery	2010	Out - 000885	10-512	Award Closed
McLaughlin, Bryan	An implantable, wireless electrode derivation for chronic EEG recording in epilepsy	2010	Out - 000888	10-418	Award Closed
Moss, Frank	Collaborative Virtual Rehabilitation Interface with Home Treatment Integration	2011	Out - 001594	11-358	Award Closed
Newbower, Ronald	Handwashing compliance reminder and documentation	2009	Out - 000904	09-221	Award Closed
O'Donnell, Lauren	Diagnosis of diffuse axonal injury using robust tract-based quantification of diffusion tensor imaging	2011	Out - 001596	11-298	Award Closed
Orr, Scott	Event-related P2 slope as a predictor of response to SSRIs in a veteran population	2011	Out - 001597	11-189	Award Closed
Ottensmeyer, Mark	Improvements and User Testing of Modular Enhancements for Mannequin-based Medical Simulators	2013	Out - 001846	13-2130	Fully Released

Ottensmeyer, Mark	Low cost, modular enhancements for mannequin-based medical simulators	2012	Out - 001703	12-1126	Fully Released
Ottensmeyer, Mark	Eye trauma simulator	2010	Out - 000900	10-331	Award Closed
Pang, Trudy	Development of a Stat EEG Prototype for Rapid Diagnosis of Non-convulsive Status Epilepticus for Community Hospital Settings	2012	Out - 001709	12-1198	Award Closed
Pascual-Leone, Alvaro	Noninvasive, Physiologic Characterization of Cortical Plasticity After Mild Traumatic Brain Injury in Humans	2011	Out - 001598	11-490	Award Closed
Pascual-Leone, Alvaro	Near-infrared photobiostimulation as a means of neuromodulation in stroke	2009	Out - 000921	09-153	Award Closed
Patz, Samuel	Magnetic Resonance Pulmonary Edema Monitor	2013	Out - 001847	13-1156	Fully Released
Pelton, Stephen	Development of safe and effective novel transtympanic membrane strategy for treatment of acute bacterial otitis media	2009	Out - 000923	09-330	Award Closed
Pollock, Nira	Development of a Novel Paper-based Point-of-care Test for Liver Function	2011	Out - 001572	11-141	Award Closed
Poznansky, Mark	A cutaneous laser system for augmenting the immunogenicity of HIV vaccines	2010	Out - 000930	10-394	Award Closed
Raemer, Daniel	Development of a Surgical Hemmorrhage Control Training Simulator	2013	Out - 001849	13-1024	Award Closed
Rattner, David	Natural orifice translumenal endoscopic surgery (NOTES)	2010	Out - 000934	08-442	Award Closed
Rattner, David	Natural orifice translumenal endoscopic surgery (NOTES)	2009	Out - 000938	08-442	Award Closed
Redmond, Robert	Optimal Time and Method of Repair of Peripheral Nerve Injury Involving Nerve Deficit	2013	Out - 001856	13-1856	Award Closed
Redmond, Robert	Preventing Leakage from Colon Anastomosis Sites	2011	Out - 001599	11-184	Award Closed
Redmond, Robert	A photo-activated nanofiber graft material for enhanced tendon repair	2010	Out - 000941	10-193	Award Closed
Reisner, Andrew	Identification of life-threatening conditions in trauma patients by automated processing of vital signs data	2011	Out - 001718	11-1718	Fully Released
Reisner, Andrew	Automated processing of physiologic registry for assessment of injury severity (APPRAISE BMF)	2011	Out - 001668	09-509	Award Closed

Rotenberg, Alexander	A novel application of intranasal Huperzine A in treatment of traumatic brain injury	2011	Out - 001600	11-269	Award Closed
Rotenberg, Alexander	A Novel Metric of HuperzineA Pharmacodynamics Efficacy	2014	Out - 001885	14-1885	Fully Released
Sacco, Dianne	Advanced Ureteroscope Navigation System for Calculi Removal	2011	Out - 001603	11-442	Award Closed
Saukkonen, Jussi	Low-Cost, Low Maintenance Mechanical Ventilator for Developing World or Mass Casualty	2011	Out - 001606	11-169	Award Closed
Saukkonen, Jussi	Development of an interactive, clinical algorithm-driven interoperable smart ventilator	2011	Out - 001604	11-251	Award Closed
Schlaug, Gottfried	TDCS - stroke recovery	2009	Out - 000959	09-392	Award Closed
Shenton, Martha	Improving Imaging of Diffuse Axonal Injury in Traumatic Brain Injury	2011	Out - 001608	11-539	Award Closed
Sheridan, Roberto	Endotracheal tube imaging device	2009	Out - 000965	09-348	Award Closed
Sipahi, Rifat	Building Handheld Devices to Accommodate Essential Tremor	2012	Out - 001711	12-1230	Award Closed
Slocum, Alexander	MIT 2.75 Design Class	2012	Out - 001733		Award Closed
Slocum, Alexander	MIT 2.75 Design Class	2011	Out - 001647		Award Closed
Slocum, Alexander	MIT- CIMIT Precision Medical Devices Graduate Design Course 2.75	2014	Out - 001911		Fully Released
Slocum, Alexander	MIT-CIMIT Precision Medical Devices Graduate Design Course 2.75	2009	Out - 001097		Award Closed
Slocum, Alexander	MIT 2.75 Design Class	2010	Out - 001099		Award Closed
Spector, Jonathan	Resuscitation technology for saving newborn lives	2010	Out - 000978	10-240	Award Closed
Sridhar, Srinivas	Multi-Modal Imaging Nanoplatforms for Image-Guided Therapies	2013	Out - 001857	13-1087	Award Closed
Subramaniam, Balachundhar	Echocardiography guided central oximetry	2011	Out - 001609	11-457	Award Closed
Teng, Yang	Treatment of Spinal Cord Injury Pain with Huperzine A: A Pre-clinical Study	2011	Out - 001614	11-527	Award Closed
Teng, Yang	Carbon monoxide mediated neural protection for treating spinal cord injury	2011	Out - 001613	11-532	Award Closed
Thompson, Christopher	Utilization of a Novel Kinematics System to Improve Quality in Colonoscopy	2011	Out - 001610	11-291	Award Closed
Tokuda, Junichi	Robot-assisted laparoscopic prostatectomy guided by patient-specific models	2011	Out - 001611	11-325	Award Closed
Tolkoff, Josh	Automated Capillary Refill Detector: Hydration Monitor	2011	Out - 001687	11-1687	Award Closed
Toner, Mehmet	A label-free viral detection microchip for point-of-care applications	2010	Out - 000999	09-440	Award Closed

Tullius, Stefan	A system to measure continuous flow and perfusion to ensure successful kidney transplantation	2010	Out - 001008	10-582	Award Closed
Unlu, M. Selim	BU/CIMIT Applied Healthcare Engineering Fellowship 2009 Projects	2009	Out - 001103		Award Closed
Uygun, Korkut	High Efficiency Hepatocyte Isolation System	2012	Out - 001732	12-1732	Fully Released
Vakoc, Benjamin	An image-guided laser therapy catheter for Barrett esophagus	2010	Out - 001019	10-480	Award Closed
Weiner, Debra	Handheld simulation procedure training device	2010	Out - 001041	10-179	Fully Released
Weinstock, Peter	Development of an integrated child circulatory system simulator to enhance patient safety via procedural skills and team training in pediatrics	2010	Out - 001043	10-225	Award Closed
Wilson, Kim	Using Mobile Electronic Protocols to Improve Newborn Survival in Developing Country Settings	2011	Out - 001605	11-233	Award Closed
Winograd, Jonathan	Immediate Restoration of Transected Peripheral Nerves with Polyethylene Glycol and Methylene Blue (PEG/MG Fusion)	2013	Out - 001850	13-1144	Award Closed
Yarmush, Martin	Development of Immuno -Therapy Laden Scaffolds for the Prevention of Post-Burn and Traumatic Injury Infection to Enhance Wound Healing and Repair	2012	Out - 001695	12-1034	Award Closed
Yoo, Seung-Schik	Direct functional brain mapping using image-guided focused ultrasound	2010	Out - 001064	10-142	Award Closed
Yun, Seok-Hyun	Dynamic cross sectional and functional imaging of vocal folds (4D laryngoscopy)	2010	Out - 001068	10-106	Award Closed
Yun, Seok-Hyun	Novel ocular biomechanical analysis	2009	Out - 001069	09-148	Award Closed

CIMIT PROGRESS AND FINAL REPORT NARRATIVE

Proposal Title:	Telemedicine Strategy for Chronic Sleep Disorder Management
Principal Investigator:	Matt Bianchi
CIMIT Project No.:	13-1240
This is a:	[ ] Progress Report [x] Final Report
Report Period: *	To October 14, 2016
Report Period Ending:	October 14, 2016

** This report format is intended to be a cumulative description of your progress. After your initial report period, you do not need to remove information previously entered unless it is no longer accurate. To add current information, please mark the end of your previous entries, and then describe your latest accomplishments.*

I. Overall Objectives and Approach: A brief description of the proposed work and specific aims.

This project was previously approved for re-purposing, and with the current title being "Sleep disorder system development for predictive analytics".

Aim 1: To optimize algorithms for apnea detection and sleep quality based on respiration patterns.
We have recently shown that apnea detection is feasible using only respiratory movements in a small cohort of 100 patients[1]. To demonstrate that this technique can generalize across diverse patient populations, we propose to use machine learning methods applied to a large database of 3000 patients from the MGH Sleep Lab. We will implement this system via a web-based platform to manage and display respiration data outputs.

Aim 2: To validate lab-based algorithms using respiration data obtained in the field with home-monitoring devices
We have collected home-based data using smart-shirt and smart-belt devices that record respiration over multiple nights, in subjects with and without OSA. Our ongoing studies (funded independently) continue to feed this important database of field data, to determine the extent to which our lab-based optimizations (Aim 1) can generalize to the home setting.

Aim 3: Ongoing development and selection of Respiration Monitoring 'wearables' and associated data extraction.
We will compare alternative devices (Mimo from Rest Devices, BioHarness from Zephyr, Equivital from Respironics, and the Hexoskin smart shirt) regarding key technology aspects. We have purchased these devices from other funds and will focus on algorithm-relevant analysis of our field acquired experiences.

II. Progress on Specific Aims and Summary of Results: Describe the results obtained and milestones achieved. Be sure to address any changes to the innovative potential of the project.

We have completed collection in-lab and at-home data from 50 patients (1 lab, 3 home, each), and are preparing a manuscript (see below).

We used an outside consultant for implementing the architecture of our Sleep Apnea Monitoring (SAM) system, which consists of data import and management, algorithm

implementation, display, and export, which has been completed and an operational web site prototype was finalized (user manual is attached).

Algorithm development has included completed database creation – we reached 10,000 patient exports in September 2016. This includes EDF (raw signals), notation files (.csv), and quality assessments including de-identification, linking, and storage. For algorithm work based on this massive data set, parameter optimization is ongoing but a functional version can be implemented in real time using the SAM system. For example, in under 60 seconds we can run pre-processing, movement detection, and apnea detection, on a full night of respiration data. Further improvements are expected in terms of computational efficiency.

Manuscript preparation: based on analysis of the n=50 subjects (1 lab night, 3 home nights, for each one), we are reporting excellent recording fidelity in the lab, somewhat more variable in the home (ie, with self-application of the monitor). We are reporting 3 categories: feasibility, movement detection, and apnea detection, and lab-vs-home comparisons of each.

III. Issues Encountered and/or Concerns: Include any important modifications to the original plans.

Algorithm performance continues to play out, as apnea detection very sensitive to signal features in the amplitude domain, which can change within a night, as well as across subjects. We have improved "moving window" normalization to address this, and we use change-points to segment data uniquely for each night, instead of applying a one-size fits all routine. We maintain a "QA" step in the algorithm to identify minimal requirements of the signal amplitude and resolution to ensure algorithm performance (ie, identify data quality limits).

For comparison with other devices, we have been waiting for the upgraded Beddit device (just became available and is pending shipment). This is the only device among the 5+ others we considered that would be feasible alternative to the Zephyr we've been using. We have recorded over 200 nights in the sleep lab on a separate IRB, and ran into exporting and data drop out issues that are still being sorted out. A new company recently contacted us (AirGo), and we are looking into it as a zephyr-alternative belt as it may have some key advantages.

IV. Next Steps and Future Plans: Describe upcoming plans to accomplish your aims and milestones as described above and to continue this work towards achieving patient impact.

1) Publish article on the Zephyr home vs lab study (n=50 subjects)
2) Continue parameter optimization for apnea detection (the most challenging step) on the now-massive data set (10,000 PSGs).
3) Continue to develop relationships with device companies like Airgo, Beddit, for future advances
4) Re-Apply for new round of grants. Doris Duke Foundation in November, and NIH R01 next June cycle (2017)

V. Presentations:

Dr Bianchi has presented preliminary algorithm results at the international World Association of Sleep Medicine in South Korea

(Sept30 update: we have made local presentations at MGH events)

Dr Bianchi returned to Seoul to deliver a keynote address to the Korean Sleep Society conference in July 2016, and two other grand rounds lectures (neurology, two hospitals), to present work directly related to device-based home monitoring that included this work.

VI. Publications: Please mark updates and new entries with an asterisk*. If it is easier to provide the Pubmed link, please feel free to include it rather than the citation.

None to date

VII. Enabled Funding: Funding received for the continuation or expansion of this research. Please include the Award PI, Title, Sponsor, Award ID, Total Budget for Project Period.

None to date
AHRQ R01 was submitted in Feb 2016, but was not scored.
MGH – ECOR funding application: denied
NIH – administrative supplement collaboration with Pain-group using the Zephyr device for apnea detection and sleep quality - denied

VIII. Patent Disclosures and Filings: Please include the Stage, Inventors, Title, Assignee, Status, Application/Patent Number and Date Filed. Please mark updates and new entries with an asterisk *.

None to date

IX. Technology Readiness Level: Assess the stage of development that best describes your solution at this current time.

6 Please enter a value between 2 and 10 see Technology Readiness Levels, below)**

If you feel it would be helpful to elaborate on your assessment of the readiness level, please use the space below for comments.

We have tested wearables in human subjects against the gold standard PSG (in-lab), and feasibility of recordings at home as well (items 4 and 6). We have shown that the portable Zephyr belts, and application of basic algorithms to belt data, is equivalent to the gold standard belts used in clinical PSG. We have tested the Beddit device as well but signal quality was sub-optimal. We have a functional SAM system online, including implementation of algorithms (from MATLAB, via the online portal), and data visualization. We are actively engaging beddit re: updated device, and a new company, AirGo, with a novel belt that may have advantages relative to Zephyr.

CIMIT PROGRESS AND FINAL REPORT NARRATIVE

Proposal Title:	**Optical Imaging for Rapid Determination of Pain: Field and Surgical Application**
Principal Investigator:	David Borsook
CIMIT Project No.:	**14-1882**
This is a:	[ ] Progress Report [x] Final Report
Report Period: *	Thru March 31 2016
Report Period Ending:	Sept 2016 (MGH CIMIT Grant ends)

** This report format is intended to be a cumulative description of your progress. After your initial report period, you do not need to remove information previously entered unless it is no longer accurate. To add current information, please mark the end of your previous entries, and then describe your latest accomplishments.*

I. Overall Objectives and Approach: A brief description of the proposed work and specific aims.

To develop a portable system (in field) to measure evoked and ongoing pain.

II. Progress on Specific Aims and Summary of Results: Describe the results obtained and milestones achieved. Be sure to address any changes to the innovative potential of the project.

We have developed approaches to measure both of these- for evoked we now have data for a specific signal in healthy subjects (initially supported by CIMIT), sedated subjects and anesthetized subjects. The latter two were supported by funds from a Foundation New York.

III. Issues Encountered and/or Concerns: Include any important modifications to the original plans.x

Funding was receved late. We have a plan to provide a prototype by July 1.

IV. Next Steps and Future Plans: Describe upcoming plans to accomplish your aims and milestones as described above and to continue this work towards achieving patient impact.

We have developed a portable prototype. We have used related work to develop this given the timeline we now have.

V. Presentations:

As noted, no funding was available until late March. No presentations have been provided.

VI. Publications: Please mark updates and new entries with an asterisk*. If it is easier to provide the Pubmed link, please feel free to include it rather than the citation.

None. No publications from this so far.

VII. Enabled Funding: Funding received for the continuation or expansion of this research. Please include the Award PI, Title, Sponsor, Award ID, Total Budget for Project Period.

Integrated data from other work, initially sponsored by CIMIT in 1999/2000.

VIII. Patent Disclosures and Filings: Please include the Stage, Inventors, Title, Assignee, Status, Application/Patent Number and Date Filed. Please mark updates and new entries with an asterisk *.

Patent will be filed on the new technology.

IX. Technology Readiness Level: Assess the stage of development that best describes your solution at this current time. After July, prototype will be ready for deployment and evalution for futher improvement. Will need to enable this with software development

X.

7	Please enter a value between 2 and 10 see Technology Readiness Levels, below)**

If you feel it would be helpful to elaborate on your assessment of the readiness level, please use the space below for comments.

From related work we have a specific pain signal for evoked and ongoing pain/nociception; a prototype has been developed. The only missing link is software development for real time processing. We have developed metrics for both evoked pain (e.g., surgical incision) or ongoing pain (e.g., from prior tissue damage during surgery). .

CIMIT PROGRESS AND FINAL REPORT NARRATIVE

Proposal Title:	**Optimizing Tissue Engineering Therapies for Airway Injury in the Battlefield**
Principal Investigator:	**Elazer R. Edelman, M.D., Ph.D**
CIMIT Project No.:	**14-1883**
This is a:	[ ] Progress Report [x] Final Report
Report Period: *	Funding start date
Report Period Ending:	August 2016

** This report format is intended to be a cumulative description of your progress. After your initial report period, you do not need to remove information previously entered unless it is no longer accurate. To add current information, please mark the end of your previous entries, and then describe your latest accomplishments.*

I. Overall Objectives and Approach: A brief description of the proposed work and specific aims.

Airway inhalation injury is a major and poorly treated health risk producing local tracheal damage, and severe lung damage, and indeed respiratory failure is the most common cause of death in burn centers. Additionally, exposure of civilians and firefighters to fire and smoke is complemented by the potential damage of chemical toxins in the workplace and even the battlefield. Despite this crucial yet unmet medical need, treatment modalities for this injury pattern remain disappointing and in fact the major approaches are largely supportive in nature.

In the current study we are working towards harnessing both tissue engineering and cell transplantation technologies to provide biological substitutes to return normal health and function to diseased tissues, and offer new arenas to explore and exploit tissue repair. By embedding bronchial epithelial (EP) and endothelial cells (EC) within porous matrices, we have engineered stable cell constructs with a matrix micro-environment allowing for healthy cell phenotype and signaling preservation. We have previously shown that the quiescent phenotype achieved by matrix-embedded cells immediately controls local inflammation, proliferation, thrombosis and remodeling with no demonstrable immune response. Thus here we aim to use this and similar expanded approaches to accelerate our understanding and treatment approaches to airway inhalation injury in civilian and military populations. We have devised a two-pronged overlapping set of timelines to reach these goals. Specific aims include:

1. ***Maximize device efficacy by optimizing material, cells and methods of delivery***- Preliminary results have shown how different material properties affect the repair capabilities of matrix-embedded (ME) cells. Noninvasive (injectable and expandable gel formulations of ME cells) and minimally invasive (cells embedded in implantable porous gelatin matrices) delivery methods for ME cells to injured regions will be optimized and tested in our large animal injury models to determine the ideal procedures for applying the repair abilities of ME cells to wounded patients. The development of multi-modal delivery methods of ME cells will allow for the rapid and efficient deployment of treatment for inhalation injury.

2. ***Examine how EP and EC together affect the mode of airway repair, and the***

***extent of tissue injury*, *downstream, adjacent and at a distance from the site of injury*.** The biosecretory, immunological and functional properties of injured cells and tissues and repair responses elicited by ME cells will be characterized both in our *in* vivo airway injury model as well as in a series of specially designed *in vitro* assays to mimic native tissue repair and regenerative responses.

Ultimately then our goal is to drive our work as rapidly as possible into the clinic through the rigor of large animal testing, modification of formulations based on these experiments and then design of clinical trials.

II. Progress on Specific Aims and Summary of Results: Describe the results obtained and milestones achieved. Be sure to address any changes to the innovative potential of the project.

1. Optimizing ME cellularized devices.

Implantable porous gelatin matrix formulations

Large animal pilot studies using an airway brush injury model in domestic swine (n = 4) have been completed for implantable ME-EP/EC formulations. The goals of these studies were to evaluate and make adjustments as necessary to device deployment approaches, as well as to evaluate initial device efficacy in a model in which injury extent mimics that seen in burn or inhalation injury patients. Successful and reproducible implantation of cellularized devices into the soft tissue surrounding areas of brush-injured trachea was achieved. Preliminary findings from histology collected at days 7- and 14-post-injury and implantation revealed complete restoration of bronchial epithelium and architecture, and functional airway recovery after controlled tracheal injury in pigs implanted with ME-EP/EC but not acellular matrices alone. Additionally, segments of injured trachea treated with cellularized gelfoam appeared to have less inflammation, fibrosis and ulceration with overall better epithelial regeneration and increased numbers of goblet cells (possibly indicating faster healing) when compared to the segments of injured trachea which were either untreated, or treated with gelfoam alone.

Remaining major milestones for this tier include quantification of improved healing properties associated with cellularized device treatment, as well as to determine active dose levels of ME-cells.

Injectable expandable gel formulations

Currently we have devised a functional method for embedding ME-EP/EC using expandable gelatin particles consisting of similar formulations as the matrices discussed above (unpublished data). Preliminary biosecretory characterization of this prototype is complete and suggests a functional a quiescent cellular phenotype is maintained, similar to that observed from cellularized matrices. Further characterization of the cellular repair capabilities, viability, biosecretion and immunological response using varying cell ratios in an *in vitro* model of tracheal injury are next to be completed. These assays are already established in our lab and will allow for rapid translation of this technology into large animal pilot studies.

2. Examining the molecular mechanisms of airway repair via ME-EP/EC

We have been using a series of *in vitro* studies to probe molecular mechanisms of matrix-embedded cell mediated airway repair and regeneration. In wound healing assays a confluent layer of epithelial cells is established to model intact airways, a scratch wound is induced and wound repair is observed in the presence of conditioned media (CM) from

varying matrix-embedded cultures. CM from ME-EP alone has shown to promote most rapid cellular wound closure and proliferation over ME-EC or ME-EP/EC conditioned media. Additionally, ME-EP CM also promotes enhanced cell proliferation at wound edges as observed with Ki-67 staining. E-cadherin expression is a cell-surface marker for preserved epithelial barrier function and subsequently health. We have observed that combined CM from EC and EP cultured separately enhanced EP E-cadherin expression.

Results Summary:
For implantable cellularized matrix formulations we have completed pilot large animal studies in swine (n = 8) and have optimized device implantation in soft tissue near controlled tracheal injuries. Preliminary studies show that ME-EC/EP are able to fully recapitulate tracheal epithelial linings after injury, and also enhance airway repair overall. We are currently quantifying physiologic findings, and also preparing additional trials to further evaluate and optimize cell dosage. Currently an alternate injury model using inhalation of wood smoke is also being developed to assess the efficacy of our device in additional mechanisms of acute airway injury.

A method for generating injectable expandable gelatin formulations have been established and preliminary biochemical analyses suggest a functional cellularized phenotype is preserved. Further *in vitro* analyses are currently being performed and we are preparing to move this device into pilot large animal testing soon.

I*n vitro* studies probing the molecular mechanism of ME-EC/EP tracheal repair and regeneration suggest the complete reparative capabilities of these devices arise from a synergistic yet differential set of contributions from EC and EP embedded cells. It appears that EP may be responsible for restoring the physical epithelial barrier while both EP and EC may contribute to maintaining damaged epithelial function and health. Ongoing studies further investigate potential synergistic reparative roles.

III. Issues Encountered and/or Concerns: Include any important modifications to the original plans.

Our work has primary goals – creation of formulations that can be used clinically, in the field and in the hospital, and further delineation of the basic biology at hand. The former will ensure clinical impact and the latter optimization of formulation. We are close on both tracks and are attempting to continue our work on the science while propelling clinical formulation development forward.

Work these past months have revealed so very much about potential device handling in light of basic biology at play. We are excited to report that this promising work is ongoing.

IV. Next Steps and Future Plans: Describe upcoming plans to accomplish your aims and milestones as described above and to continue this work towards achieving patient impact.

Remaining work is therefore directed at quantifying physiologic findings relating to airway health, and also to creating those formulations most likely to see clinical impact such as injectable formulations. We will expand our large animal testing, continue formulation development in light of large animal findings and begin design of clinical trials.

Optimizing expandable gel formulations
In addition to our current cellularized gelatin particles consisting of similar formulations as the porous matrices, we will also begin optimization of injectable formulations using Pluronic

gel copolymers. Pluronic gels are water soluble, exhibit low toxicity and some, such as Pluronic F127, have been approved for clinical use. Aqueous solutions of Pluronic F127 that are moderately concentrated (15-30%, w/w) at room temperature exhibit thermal gelation at physiological temperatures, and in fact this particular gel formuation has been demonstrated to be effective for perivascular delivery of cellular metabolites in arterial injury models using a similar device deployment strategy proposed here. Indeed, Pluronic F127 can support tracheal epithelial generation in a composite cell-polymer for tracheal constructs. This formulation will offer another alternative for injectable therapies and we anticipate this development will be possible with minimal difficulties given our extensive experience working with both ME cells as well as an array of polymers for medical devices.

Development of proper product placement and effective peribronchial/peritracheal injection administration of both injectable formulations will be conducted in harvested and preserved swine neck samples collected from healthy animals. Necessary outcomes from this milestone include defining the characteristics of the EC/EP within the Pluronic gel as well as confirming the ability of these cells to maintain healthy biosecretory function suggestive of their ability to promote airway repair *in vitro* just as their matrix- and gelatin particle-embedded counter parts. Importantly, should characteriztion suggest one injectable formulation to retain enhanced biosecretory function over the other, we will choose to move this product along into the next phase of testing.

Assuming all outcomes described above are met, we plan to move injectable formulations directly into large animal pilot trials to validate the established mode of administration, duration of maximal therapeutic effect as well as confirm and compare clincial efficacy and safety for injectable formulations using proven methods and techniques already achieved with cellularized gelatin matrices. Achievement of this milestone will allow for preparation for expanded large animal testing.

V. Presentations:

Duggan, N. *"Matrix-embedded endothelial cells promote tissue repair and regeneration in acute airway injury."* Sarnoff Cardiovascular Research Foundation Annual Meeting (2016).

VI. Publications: Please mark updates and new entries with an asterisk*. If it is easier to provide the Pubmed link, please feel free to include it rather than the citation.

N/A

VII. Enabled Funding: Funding received for the continuation or expansion of this research. Please include the Award PI, Title, Sponsor, Award ID, Total Budget for Project Period.

Elazer R. Edelman, M.D., Ph. D., MIT, Boston Biomedical Innovation Center DRIVE Grant, $200,000 direct costs.

VIII. Patent Disclosures and Filings: Please include the Stage, Inventors, Title, Assignee, Status, Application/Patent Number and Date Filed. Please mark updates and new entries with an asterisk *.

N/A

IX. Technology Readiness Level: Assess the stage of development that best describes your solution at this current time.

6 Please enter a value between 2 and 10 see Technology Readiness Levels,

☐ below)**

If you feel it would be helpful to elaborate on your assessment of the readiness level, please use the space below for comments.

CIMIT®
Consortia for Improving Medicine with Innovation & Technology

CIMIT PROGRESS AND FINAL REPORT NARRATIVE

Proposal Title:	Dynamic Imaging and Neuro Intervention Guidance Using Dual Energy CT: Translation into Practice
Principal Investigator:	Rajiv Gupta
CIMIT Project No.:	14-1884
This is a:	[ ] Progress Report [X] Final Report
Report Period: *	September 30, 2014 to June 15, 2016
Report Period Ending:	June 15, 2016

** This report format is intended to be a cumulative description of your progress. After your initial report period, you do not need to remove information previously entered unless it is no longer accurate. To add current information, please mark the end of your previous entries, and then describe your latest accomplishments.*

I. Overall Objectives and Approach: A brief description of the proposed work and specific aims.

The objective of our study is to improve the outcome of patients with Intracranial hemorrhage (ICH). ICH, which may be in brain parenchyma or meningeal spaces, is commonly encountered in combat care due to head trauma. While many cases of ICH can be managed conservatively, a significant proportion of cases of ICH can progress rapidly in size and become life threatening. Hematoma expansion in patients ICH is strongly associated with increased morbidity and mortality. Since this is the only modifiable predictor of outcome, it is an appealing therapeutic target. Therapies preventing expansion of bleeding can provide a key opportunity to decrease final bleeding volume and improve patient outcome. A method that can differentiate stable ICH from those that are likely to progress over time is very desirable for patient triage.

The presence of active leakage of iodinated contrast from the vessels, known as the “spot sign”, has been shown to be an indicator of ongoing bleeding and, as such, an accurate and powerful predictor of hematoma expansion, mortality, and poor outcome. Using the spot sign and contrast leakage to identify patients whose hematoma is expected to grow is the effective way of triaging patients into therapeutic interventions and improving the overall outcome. Therefore, the key specific aim of this study is to develop a new methodology using Dual Energy CT (DECT) to predict ICH that is likely to increase in size. This will be accomplished by assessing if there is early extravasation of administered intravenous iodinated contrast agent, a surrogate marker for active intracranial bleeding. Dual Energy CT will be used to detect active contrast extravasation into the intra-cerebral hematoma and the data will be analyzed to see how well this metric predicts hematoma expansion in patients with intra-cerebral hemorrhage.

II. Progress on Specific Aims and Summary of Results: Describe the results obtained and milestones achieved. Be sure to address any changes to the innovative potential of the project.

We completed the review by Partners Institutional Review Board and obtained the IRB permission to conduct this study in the 3rd quarter of 2014. We also completed the review by DoD HRPO and received the permission to start enrolling the patient. The fund number for this project was established on Aug 15, 2014. The installation of the Dual Energy CT scanner in the

MGH Emergency Department was completed on Sept 15th, 2014. After the scanner completed the initial calibration studies, we started screening patients for possible enrollment in this study in the emergency department of Massachusetts General Hospital at the end of 2014.

To this date, over 30 patients with intra-parenchymal hemorrhage have undergone DECT angiography of the head in the emergency department. Of these, 16 patients met the inclusion criteria and had follow up head CT. The amount of iodine in the hematoma and the volume of the hematoma have been measured in these 16 cases.

The preliminary results showed that DECT material decomposition can accurately differentiate between calcification and hemorrhage in patients presenting for emergency head imaging, and can help correctly classify the lesions that may be misinterpreted by single energy image alone. In addition, DECT enabled iodine measurement within an intra parenchymal hematoma. We have presented the results these cases as a scientific poster at Military Health System Research Symposium (MHSRS) annual meeting 2015 and also at MHSRS 2016.

Here are few cases showing relation of iodine concentration on DECT delayed exam and hematoma expansion on subsequent CT exam.

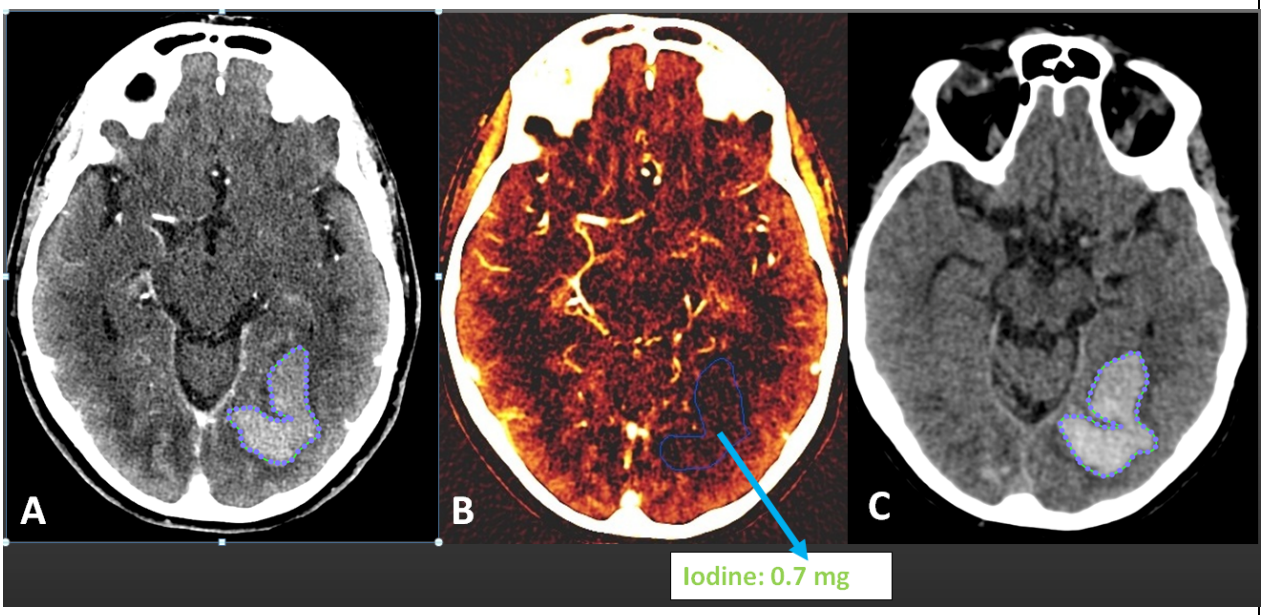


Figure 1: Minimum iodine concentration (0.7 mg) on delayed DECT images (B) and no hematoma expansion on subsequent CT exam (C)

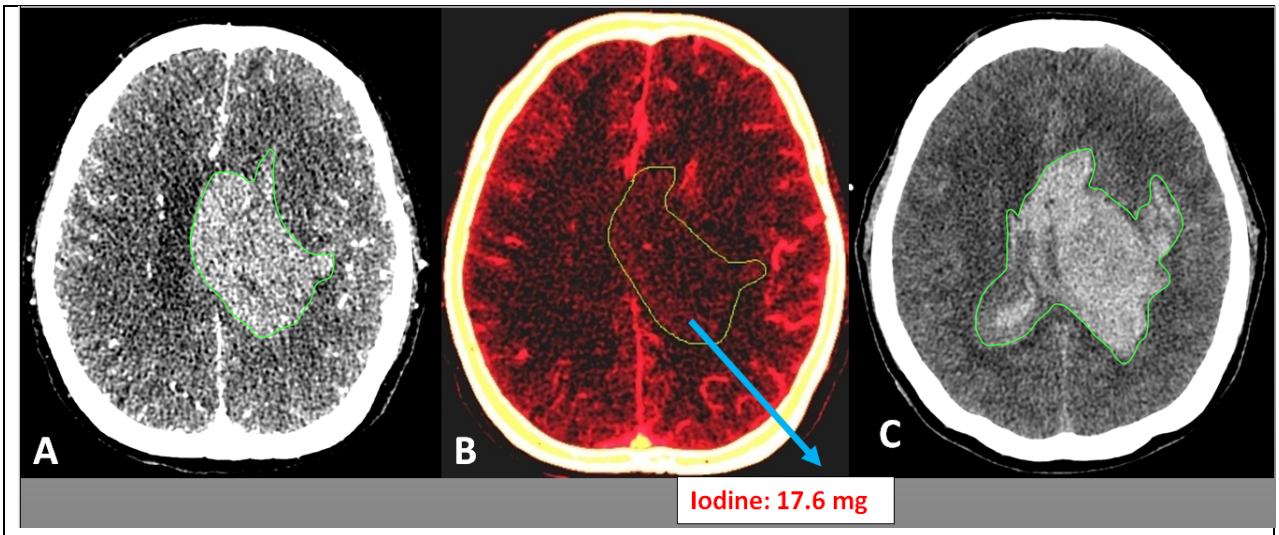


Figure 2: Higher iodine concentration (17.6 mg) on delayed DECT images (B) and hematoma expansion on subsequent CT exam (C)

In addition, we have developed an automated algorithm to automatically identify the hematoma region of interest (ROI) on DECT virtual non-contrast image series, to replicate the similar region of interest (ROI) to DECT Iodine overlay image series, to statistically identify spot signs, and to assess relative iodine concentration in the hematoma and in spot signs to determine extravasations of intra-cerebral hematoma. A case depicting these steps is shown below.

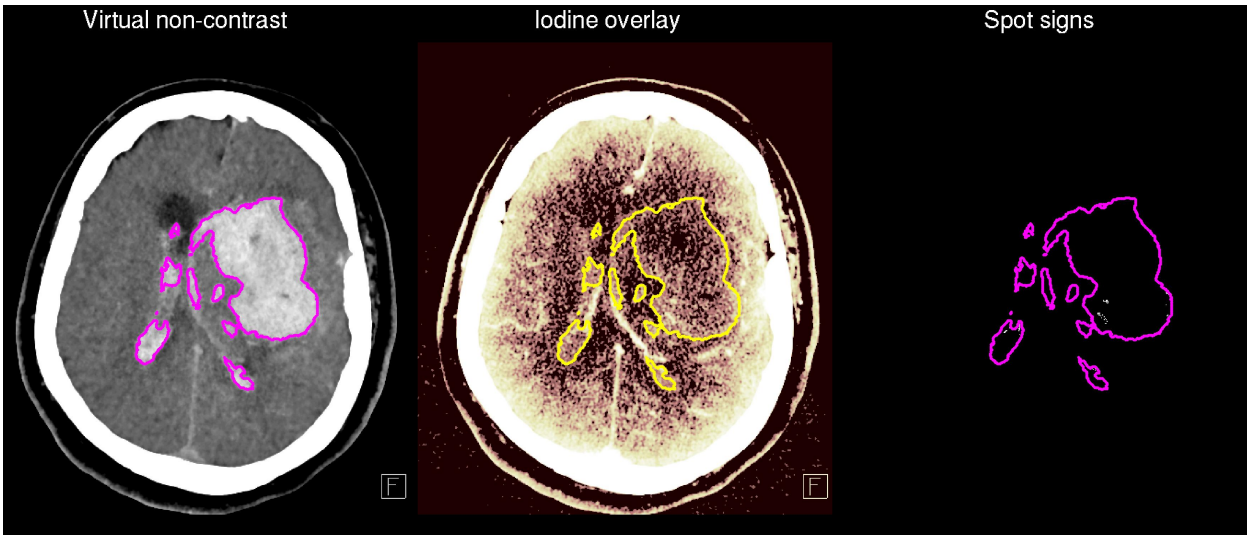


Figure 3: A case (#8 on Table 1) showing the automated classification and characterization of spot-signs. In this case, automatically identified hematoma volume was 97 cm3, and the total volume of spot signs was 148 mm3 (i.e., <0.15% of the total hematoma). Follow-up head CT showed expansion of hematoma. Spot signs were identified statistically, based on the intensities of pixels on the iodine overlay image compared to those of overall hematoma ROI.

We have scanned and analyzed 16 patients with this approach. The results of these scans is shown in Table 1.

Case #	Hematoma Volume (mm^3)	Spot Sign Volume (mm^3)	Ratio	Relative Hematoma Iodine	Relative Spot-Sign Iodine	Score	Expanded
1	73574.4	178.3	0.242%	12	101	1498.9	y
2	14962.0	2.0	0.014%	46	164	7.2	n
3	14645.3	38.7	0.264%	70	213	118.4	y
4	184.6	0.0	0.000%	182	0	0.0	n
5	2247.6	4.8	0.213%	38	124	15.8	n
6	10535.5	0.0	0.000%	67	0	0.0	n
7	53632.5	26.6	0.050%	76	251	87.6	y
8	96993.3	148.4	0.153%	87	231	395.3	y
9	28543.1	0.0	0.000%	83	0	0.0	n
10	59236.1	5.2	0.009%	102	209	10.6	n
11	11504.6	5.4	0.047%	63	133	11.4	n
12	8499.4	4.1	0.048%	137	218	6.5	n
13	41042.4	47.4	0.115%	80	175	103.3	n
14	73559.2	96.8	0.132%	90	191	204.5	n
15	9244.7	30.3	0.327%	38	162	128.0	n
16	289.8	0.0	0.000%	9	0	0.0	n

Table 1. Hematoma and spot-sign volumes and relative iodine contents (expressed as pixel intensities) in each of the 16 cases assessed by our algorithm. The "score" is the spot sign volume weighted by spot sign iodine content relative to hematoma iodine content, and cases with a score > 50 are classified as expanders. Rows highlighted in green and red indicate, respectively, the true positive and false positive cases, and rows without highlight denote true negatives (there are no false negatives). Last column ("Expanded") denotes whether the follow-up CT scan showed hematoma expansion.

Follow-up CT scans showed hematoma expansion in 4 of the 16 patients. Hematoma volume was significantly higher in expanders (60±17 vs 23±13 cm^3; t-test, p=0.03). Our automated algorithm correctly identified all 4/4 patients with and 9/12 without hematoma expansion (i.e., 100% sensitivity and 75% specificity). While false positive "spot signs" were identified in 3 of the patients without hematoma expansion, the volume of these false positive signs were substantially smaller compared to those with expansion (2±3 vs 96±43 mm^3; p<0.01), and their relative iodine content was markedly lower (non-expanders vs expanders iodine content 62±17 vs 78±24 [arbitrary units] in the hematoma and 143±25 vs 48±44 in the spot sign; p=0.06), suggesting that the specificity of our algorithm can be substantially improved when the noise is better accounted for in a larger cohort of patients. We have submitted the results these cases as a scientific poster at Military Health System Research Symposium (MHSRS) annual meeting 2016

III. Issues Encountered and/or Concerns: Include any important modifications to the original plans.

The last changes to the protocol were submitted to the IRB on 04/23/2014 and were approved on 04/29/2014 (Amendment #8). These changes include the following items.

1. As requested by DoD HRPO, a United States Department of Defense (DOD) was added as the new study sponsor/funding agency for this study.
2. Since the original submission of this IRB protocol, the default departmental imaging protocol for detection and management of intracranial hemorrhage has changed. The amendment #8 reflected this change. Specifically, the additional scan requested for research purposes is now a part of the baseline default protocol. Therefore,

participation in this study does not expose the patient to any more radiation than the baseline default imaging.

3. A new Dual Energy CT scanner is currently being installed in the Emergency Department (ED). Therefore, all imaging will be done in the ED and patient transport to Blake building, as envisioned in the prior submission of the protocol, is no longer required. The IRB protocol was modified to reflect this change.

The IRB approved consent form was modified to reflect the fact that representatives of the DOD are authorized to review research records and that representatives of the DOD are listed as one of the parties to whom private health information may be disclosed.

The original IRB protocol, required us to prospectively obtain patient's or surrogate's permission to use and analyze the data. We found this to be difficult in the clinical environment surrounding acute intracranial hemorrhage in the Emergency Department. Many times the patient is not in a physical condition to understand the requirements of the study and give informed consent. At the same time, a surrogate is not available to given informed consent for enrollment at the time of the scan.

It should be noted that this study does not require any change in the default clinical scan protocol, or any other alteration in the clinical care of patient. The patients are ordered for a dual energy scan based on the clinical necessity. The appropriate dual energy CT is performed on the patient irrespective of whether he or she is enrolled in the current study. The patients are worked up as usual and images are processed as per the clinical protocol. Therefore, each patient is managed according to the default departmental protocol for detection and management of intracranial hemorrhage and the study in no way alters the course of the patient care. The risk category of the study is Minimal Risk.

Given that the data is analyzable retrospectively, we have requested the IRB to allow us to enroll these patients retrospectively as a part of a retrospective study that analyzes the data that has already been acquired. A new retrospective protocol linked to the original one with waiver of the consent form has been submitted to the IRB. We will submit this modification to HRPO in the coming weeks once Partners IRB has approved this amendment. We expect the patient enrollment to be considerably accelerated by this amendment.

IV. Next Steps and Future Plans: Describe upcoming plans to accomplish your aims and milestones as described above and to continue this work towards achieving patient impact.

The main objective of this study, namely, the ability to accurately predict which patients will undergo hematoma expansion, is the "Holy Grail" of intra-cerebral hemorrhage imaging. So far, we have performed DECT exams in 16 patients and the results have been as hypothesized initially at the beginning of the study.

We had hoped that DECT will better demonstrate early extravasation of iodine contrast, and this surrogate marker will be a more accurate predictor of hematoma expansion in ICH. Our results to date support this hypothesis and preliminary results show that DECT of the head can detect early extravasation of iodine contrast. Our automated detection algorithm for spot signs as a surrogate marker can provide an accurate predictor of hematoma expansion in ICH. Future refinement and validation with a larger cohort of patients are needed.

Based on the strength of our results, we have made dual energy delayed CT of the head at 90 seconds as a default protocol for ICH assessment in our hospital. This change, which will allow us to assess DECT protocol for much larger number patients than funded under the current protocol, completes our initial validation of the hypothesis that DECT can predict

hematoma expansion.

Phase II of this project will target performing this study on a single energy scanner, the type that is likely to be available in the field. We will also try to further propagate the DECT methodology to military facilities where a dual energy scanner is available.

V. Posters and Presentations:

1. Daftaribesheli L, Hu R, Young J, Padole A, Wu M, Pomerantz S, Romero J, Lev M, Gupta R. The Efficacy of Dual Energy CT in Characterizing Intracranial Hemorrhage in the Setting of Acute Head Trauma. Military Health System Research Symposium (MHSRS) 2015.
2. Daftaribesheli L, Ahmadi E, Khalilzadeh O, Gupta R. Application of the dual energy CT scan for differentiation of parathyroid gland from thyroid gland based on enhancement characteristics. Oral presentation in Radiology Society of North America (RSNA), Chicago, December 1-6, 2014.
3. Daftaribesheli L, Mayich MS, Ginat DT, Gupta R. Clinical applications of dual energy CT in head and neck imaging. Poster presentation in Radiology Society of North America (RSNA), Chicago, December 1-6, 2014.
4. Dynamic Imaging and Neurointervention Guidance Using Dual Energy CT: Translation to Practice. Tan CO, Hu R, Padole A, Daftari Besheli L, Lev MH, Forghani R, Young J, Romero J, Gupta R. Military Health System Research Symposium (MHSRS) 2015.
5. Temporal Evolution of Vasospasm and Clinical Outcome after Intra-arterial Vasodilator Therapy in Patients with Aneurysmal Subarachnoid Hemorrhage. Daftari Besheli L, Tan CO, Bell DL, Hirsch JA, Gupta R. Military Health System Research Symposium (MHSRS) 2015.

VI. Publications: Please mark updates and new entries with an asterisk*. If it is easier to provide the Pubmed link, please feel free to include it rather than the citation.

1. Ginat DT, Mayich M, Daftari Besheli L, Gupta R. Clinical applications of dual energy CT in head and neck imaging. Accepted for publication in Head & Neck, 2014
2. Dinkel J, Catherine PM, Khalilzadeh O, Goenka AH, Yoo A, Hirsch J, Gupta R. Technical limitations of Dual Energy CT in neuroradiology: 30 months institutional experience and review of literature. Journal of neurointerventional surgery.
3. Aran S, Besheli LD, Karcaaltincaba M, Gupta R, Flores EJ, Abujudeh HH. Applications of Dual-Energy CT in Emergency Radiology. AJR Am J Roentgenol. 2014 Apr;202(4):W314-24.
4. Won SY, Schlunk F, Dinkel J, Karatas H, Leung W, Hayakawa K, Lauer A, Steinmetz H, Lo EH, Foerch C, Gupta R. Imaging of Contrast Medium Extravasation in Anticoagulation-Associated Intracerebral Hemorrhage With Dual-Energy Computed Tomography. Stroke. 2013 Aug 6.

VII. Enabled Funding: Funding received for the continuation or expansion of this research. Please include the Award PI, Title, Sponsor, Award ID, Total Budget for Project Period.

A static CT concept proposal submitted as a part of the CIMIT DoD Joint War Fighter Proposal.

VIII. Patent Disclosures and Filings: Please include the Stage, Inventors, Title, Assignee, Status, Application/Patent Number and Date Filed. Please mark updates and new entries with an asterisk *.

IX. Technology Readiness Level: Assess the stage of development that best describes your solution at this current time.

4 Please enter a value between 2 and 10

If you feel it would be helpful to elaborate on your assessment of the readiness level, please use the space below for comments.

The proof of concept has been demonstrated previously by our research. This project, if successful, will bring this concept from TRL 3 to TRL 4.

CIMIT PROGRESS AND FINAL REPORT NARRATIVE

Proposal Title:	Enhanced Inhalation Therapy for Emphysema
Principal Investigator:	Robert Scott Harris
CIMIT Project No.:	11-341
This is a:	[ ] Progress Report [x] Final Report
Report Period: *	April 1, 2016 to September 30, 2016
Report Period Ending:	September 30, 2016

** This report format is intended to be a cumulative description of your progress. After your initial report period, you do not need to remove information previously entered unless it is no longer accurate. To add current information, please mark the end of your previous entries, and then describe your latest accomplishments.*

I. Overall Objectives and Approach: A brief description of the proposed work and specific aims.

Project Overview: It was proposed to design and build a small proof-of-concept device to enhance the delivery of aerosol drugs to the emphysematous lung. The device sends pressure pulses deep into the lung as the user exhales through it. In this CIMIT project the device will be evaluated in a limited number of studies assessing its effect for reducing hyperinflation, and its capacity to enhance ventilation distribution in emphysematous patients.

Specific Goals: 1) To design and build a novel, small proof-of-concept RPP delivery device **2)** to use that device in a limited number of studies to evaluate its efficacy for reducing global and regional hyperinflation, and enhancing ventilation distribution.

II. Progress on Specific Aims and Summary of Results: Describe the results obtained and milestones achieved. Be sure to address any changes to the innovative potential of the project.

We worked extensively with the RPP device to ensure that the generated pressure waveforms are similar to those used in the Columbia study 30 years ago. We also modified the device to make sure that reliable measures of inspiratory capacity will be obtained. At present the device is ready for the first proof of concept study. We have conducted a number of mock studies and tested the device on ourselves with satisfactory results. Since the last report, we had begun to identify possible subjects to enroll, but we had to delay recruitment due to the main investigator responsible for recruitment and conduct of the study being out on medical leave. That investigator has now returned and we have conducted more tests on with the device and readied an area in the laboratory to accept volunteers for study. We have contacted and enrolled our first hyperinflated COPD subject, who we plan to study in the next few weeks. We plan on finishing the pilot studies by the end of the calendar year. This pilot study will then serve as preliminary data for a larger grant application to the National Institutes of Health where we will enroll a larger cohort of COPD subjects and measure lung function, imaging and quality of life outcomes both with and without the device.

III. Issues Encountered and/or Concerns: Include any important modifications to the original plans.

The main issues we have encountered involved reproducing the particular waveform of the pulses, which we wanted to be sharp and faithful to the original RPP device built over 30 years ago. That device was large, heavy and unsuitable for clinical use. Producing the same waveform proved difficult with a small, compact device, but we have now achieved that goal.

IV. Next Steps and Future Plans: Describe upcoming plans to accomplish your aims and milestones as described above and to continue this work towards achieving patient impact.

Originally, we thought we would proceed with the measurements in the 10 subjects, but if we find dramatic improvements in inspiratory capacity with a smaller number, we would use this data to apply for NIH funding to study a larger cohort. The original data collected over 30 years ago suggests that the change in inspiratory capacity could be large, so if we can reproduce that result in a small group of subjects, there would be no need to study the full 10 subject cohort.

V. Presentations:

None so far, but we hope to study the first subject before the American Thoracic Society abstract deadline in November. There is also a chance to submit "late-breaking" abstracts before the Annual Meeting in May, 2017.

VI. Publications: Please mark updates and new entries with an asterisk*. If it is easier to provide the Pubmed link, please feel free to include it rather than the citation.

VII. Enabled Funding: Funding received for the continuation or expansion of this research. Please include the Award PI, Title, Sponsor, Award ID, Total Budget for Project Period.

VIII. Patent Disclosures and Filings: Please include the Stage, Inventors, Title, Assignee, Status, Application/Patent Number and Date Filed. Please mark updates and new entries with an asterisk *.

The device was Disclosed to the Partners TLO in November 2012. The disclosure is titled "Reverse Pressure Pulse Generator" and is listed as MGH File No. 21949 (Q&B 00584). The inventors listed on the disclosure are Elliot Greenblatt Jose Venegas, and Scott Harris.

The TLO has filed a provisional patent for the device.

IX. Technology Readiness Level: Assess the stage of development that best describes your solution at this current time.

7 Please enter a value between 2 and 10

X. Technology Readiness Level: Assess the stage of development that best describes your solution at this current time.

7 Please enter a value between 2 and 10 (see Technology Readiness Levels, below)**

If you feel it would be helpful to elaborate on your assessment of the readiness level, please use the space below for comments.

The device is ready to be used on human subjects in our laboratory. We may run into small technical issues and the external form will need to be refined and simplified if and when it is ready to be disseminated to other sites for clinical testing.

CIMIT PROGRESS AND FINAL REPORT NARRATIVE

Proposal Title:	Handheld Simulation Procedure Training Device: An In-a-Box Solution, An Out-of-the-Box Approach, A Health Care Paradigm Shift
Principal Investigator:	Debra Weiner, MD, PhD
CIMIT Project No.:	10-179
This is a:	[ ] Progress Report [X] Final Report
Report Period: *	Mar 31, 2016
Report Period Ending:	September 30, 2016

** This report format is intended to be a cumulative description of your progress. After your initial report period, you do not need to remove information previously entered unless it is no longer accurate. To add current information, please mark the end of your previous entries, and then describe your latest accomplishments. .* ***PLEASE NOTE: EACH PARAGRAPH WITH NEW CONTENT IS PROCEEDED BY ****

I. Overall Objectives and Approach: A brief description of the proposed work and specific aims.

GOAL

To create a handheld simulation procedure training device that will enable any health care provider to learn, practice and ultimately perform medical procedures on demand, in real-time, at point-of-care in any environment.

BACKGROUND

Procedure competency is essential for high-quality patient care and safety. The traditional patient based “see one, do one, teach one” approach to procedure training compromises patient care and endangers patient safety. It also may not provide the optimal learning experience due to timing of the opportunity, limited knowledge and expertise of the teacher, and a dynamic that lacks key elements of effective adult learning.

Simulation is exceedingly valuable for medical training including procedure training. Simulation provides a life-like experience for trainees and clinicians to acquire and maintain procedure skills. To date, simulation training has been limited to specialized, high-tech centers. Expensive equipment and human resource costs and inadequate availability of facility space, limit the location and number of simulation sites making simulation training unavailable to the vast majority of health care providers. Given these limitations, simulation training is most often prioritized to care of the critically ill or injured patient for whom expertise is the most critical and experience is often the most limited, or to major procedures. Integration of simulation into training, particularly for minimally invasive procedures, has therefore, been a challenge.

A low-cost, handheld simulation system for the training of minimally-invasive procedures anywhere, anytime, including both real-time at point-of-care and

discretionary time, would bring this effective form of training to a broader scope of providers. It has the potential to create a paradigm shift in accessibility to high-tech, high fidelity non-patient based procedure training, and could ultimately expand and enhance the access, quality and safety of health care across all populations.

SPECIFIC AIMS

1. **Build and couple a haptic block with an iPhone** that integrates a tactile user interface with visual and auditory representations of procedures to create a dynamic and interactive training system.
2. **Develop and deploy a proof-of-concept procedure training module** for intravenous (IV) catheter placement.
3. **Conduct a validation study** to determine the effectiveness of the system for training.

II. Progress on Specific Aims and Summary of Results: Describe the results obtained and milestones achieved. Be sure to address any changes to the innovative potential of the project.

PROGRESS

Aim 1. Development of a handheld procedural training device

The design of the hardware as described in the previous report has remained stable. In October, 2011, an updated gel block with vessel was fabricated, and a series of additional blocks were made for demo purposes including for a platform presentation by Dr. Weiner at the International Pediatric Simulation Symposia and Workshops (IPSSW2011), Toulouse, France, October 28, 2012.

The gel block/needle combination previously reported relied on a graphical display to show flash-back, demonstrating that the cannula had reached the lumen of the desired vessel successfully. This requires that the user is looking not at the training device (proxy for the patient's arm), but at the tablet screen instead. Discussions within the team lead to the determination that we should include a co-located method for presenting this information. Since the gel blocks will not support the inclusion of a pressurized reservoir of fake blood, we developed the concept of including an illuminated cue built into the needle itself in the form of red LEDs installed where the first few drops of blood would appear. Using analog control of LED brightness could represent flow rate – turning on the LEDs could represent entry into the lumen and continued flow, while dimming the light could represent penetrating too deeply. The exact format of the use of lighting cues will be determined following completion of this new feature.

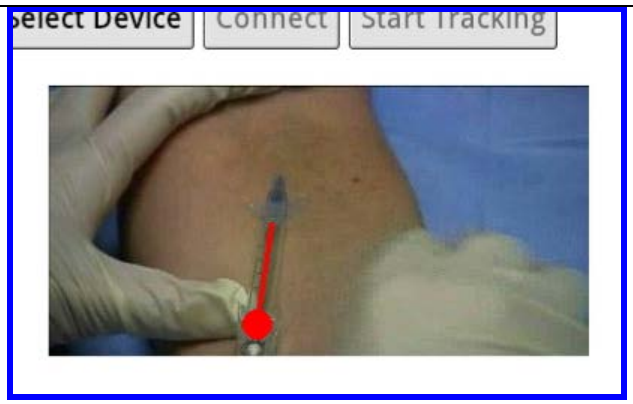
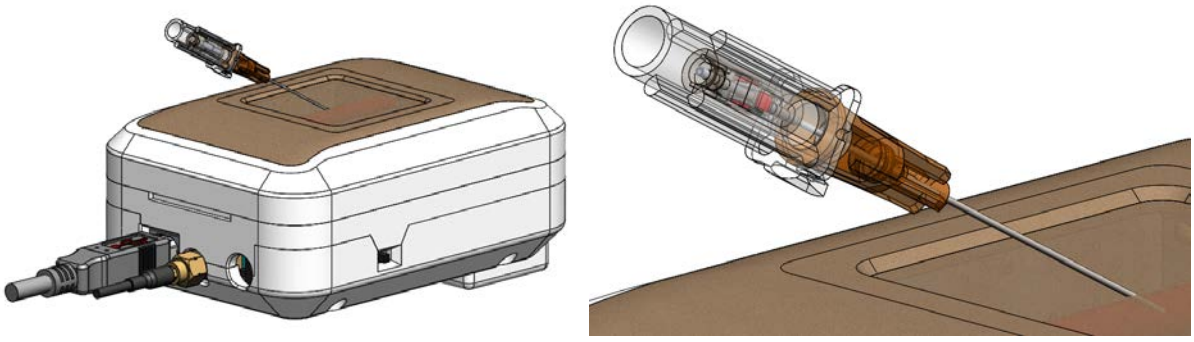


Figure. Existing graphical indicator of flashback, overlaid on static image of arm shown to user as part of tablet-based content during cannulation test

Following these discussions, designs to provide this feature were developed, both at the needle end and in the modifications of the "haptic block" circuitry.

Surface mount technology (SMT) LEDs are small enough to fit within the barrel of the cannulas that we are using for this system, so a carrier was designed to provide mechanical support and electrical insulation between the lights and the existing central conductor that is used to detect needle position within the gel block. In parallel, an assembly/soldering jig was created to hold the various components in place, since the LEDs are 2x1.25x0.8mm in size, and at present, manual assembly is required. The Simulation Group fabrication facilities include an Objet Eden 260V rapid prototyping system, which supports creation of parts of such tiny dimensions.

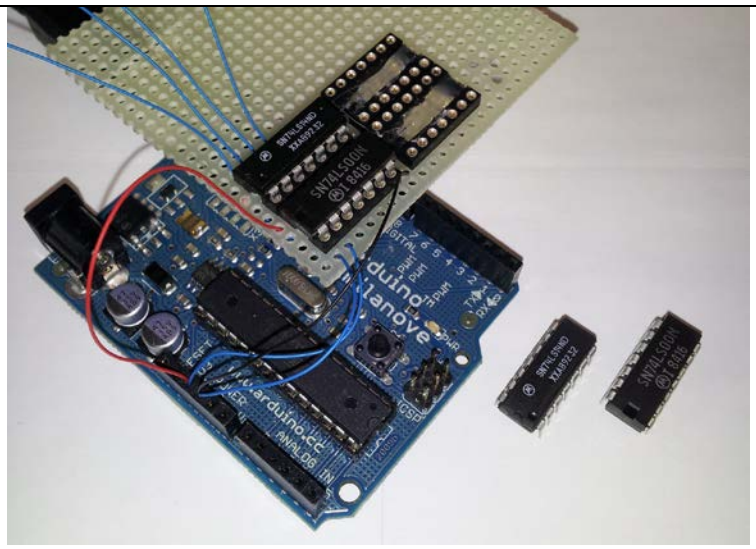


Current Haptic Block, with detail of cannula, showing LED holder mounted inside the needle

New flashback components and first test of assembled LED array

At present, the LED holder needs to be revised once more – manual soldering of components results in excess solder remaining on the LED assembly, for which sufficient clearance was not included in the most recent version of the holder.

To support the use of the flashback indicator, the circuitry that drives the haptic block position detection needed to be modified. The system uses an Arduino microcontroller, which includes 14 digital I/O pins. Two are used for the wireless serial communication with the tablet, using Bluetooth. The other twelve pins were dedicated to driving the voltage gradient circuitry, four pins for each of the three axes, x, y and z, with none remaining for other purposes. To free up one of the digital pins to provide a PWM drive signal to the LEDs, we observed that each axis has only three distinct states: turned off, turned on and driving sensing current in one direction, turned on and driving sensing current in the reverse direction. Three states require only two bits to define them (on/off, direction +/-) so it should be possible to control the block with half as many digital I/O pins. Using standard logic blocks (NAND, inverter), we designed a circuit that would accomplish current operation with this reduced number of control pins. Initial experiments using surface mount differential NAND/AND multifunction chips were performed, with the expectation that the differential output pins (either high/low, or low/high) would be suitable for driving the haptic block voltage gradient circuits, using a minimal number of additional chips. Unfortunately, these tests were unsuccessful due to a misunderstanding of the differential chip function, in which only small voltage differences between the output pins are generated (one higher than the other, or vice versa), insufficient for this purpose (not shown clearly on the spec sheet). Following this test, we returned to standard, single function logic chips and have set up and tested the circuit for the z-axis segment of the haptic block, with success. In the next period, we will complete the wire-wrap prototype version shown below, confirm full function, then consider whether this is compact enough to use within the existing device, or create a smaller version.



Test circuit for reduction from 12 digital pins used for haptic block voltage gradient control to 6 digital pins, leaving remaining pins for flashback LED assembly control.

In addition to circuitry changes, we have made progress towards completing the set of desired gel blocks to support both straight vein access and bifurcated vein access. The first element was completion of a concept test for adding a vessel wall to the previously developed gel blocks, the second element was a new set of molds for the bifurcated vessel.

In earlier progress reports, we described that the gel blocks in use are gelatin-based, with the addition of saline solution to provide controlled conductivity, food-grade corn syrup to increase friction during cannula insertion, and shredded fiber to prevent gel fracture and provide some tissue-simulating texture. A skin layer of gel-impregnated paper towel caps the block, with a mandrel holding a space for a vessel, to be back-filled in a second molding step with a lower concentration gel to provide a difference in sensation of needle insertion between passage through tissue and entry into the vessel. The new molds support a mandrel wrapped helically with a strip of the gel-impregnated paper, creating not only the vessel cavity, but a puncturable vessel wall, which was demonstrated for Dr. Weiner in March and found to be an acceptable first iteration. This was first done for the straight-vessel version. Following this, a bifurcated vessel mold was designed and fabricated, with a multi-part mandrel to allow easy removal for subsequent back-filling of the softer gel for the vessel contents.

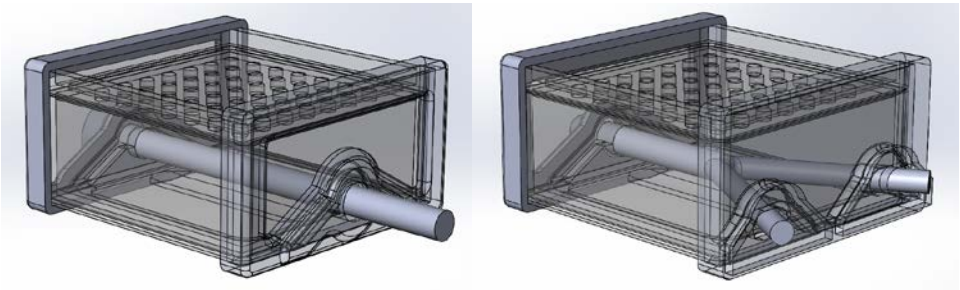


Figure. Mold designs and fabricated molds, with straight-vessel mold filled with gel.

A redo of the sensed voltage to x/y/z position mapping with the current gel recipe is underway, and evaluation of the effects of the presence of the vessels will be conducted in the next period.

* beginning of new Specific Aim 1 material for period to Sept. 30, 2013

Progress on Specific Aim 1:
In the previous report, we described a new feature that had been added to the system: an LED indicator for flashback, which illuminates when the vessel lumen would be determined to have been penetrated. A complicating factor to implementing this was the limited number of digital I/O pins on the Arduino platform, which was addressed through the creation of a digital logic circuit, which was found to be unsuccessful due to a misunderstanding of the function of the chips selected. With better understanding, a new circuit board design was initiated. A conversation with Mr. Ryan Bardsley regarding the details of Arduino function revealed that the analog input pins are actually general purpose I/O pins, and can be reassigned as digital output pins. Further, software libraries are available to cause them to behave as analog output lines (strictly: PWM output), with a lower frequency than the dedicated PWM lines, but sufficient to appear to be a continuous signal to the human eye. The logic solution proposed earlier was bypassed, and the flashback LEDs are now controlled directly by the repurposed analog input (now PWM output) lines.

In addition, the original arrangement of LEDs was modified to produce an easier-to-assemble, more compact configuration that fits better within the barrel of the IV cannula. An additional connector, using a stereo audio plug and jack combination, was installed to provide for a removable connection to the LEDs.

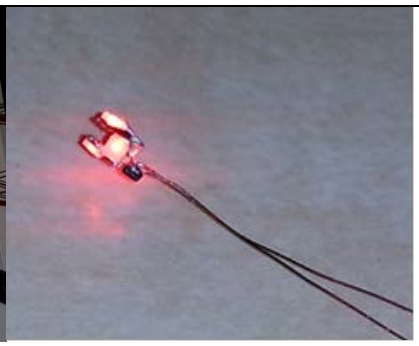
Additional recipes for the gel blocks were tested during this period. Earlier in this project, we tested the use of oil of wintergreen as an antimicrobial agent, with limited/unclear results. Further searching during this period uncovered two approaches, related to the production of gelatin mounting for microscope slides: in this case the gelatin is mixed with glycerin, which was hoped would resolve the evaporation of water problem (gel block shrinkage during extended use), and addition of Listerine mouthwash, as an antimicrobial. Glycerin-based blocks did indeed gel, however were found to be non-conductive, so not suitable for this application. Listerine, added at approximately 4% by liquid weight, was found to dramatically reduce/retard the growth of mold and bacteria in the few blocks that were tested. Refrigerated shelf-life of

prepared blocks was at least weeks, if not longer.

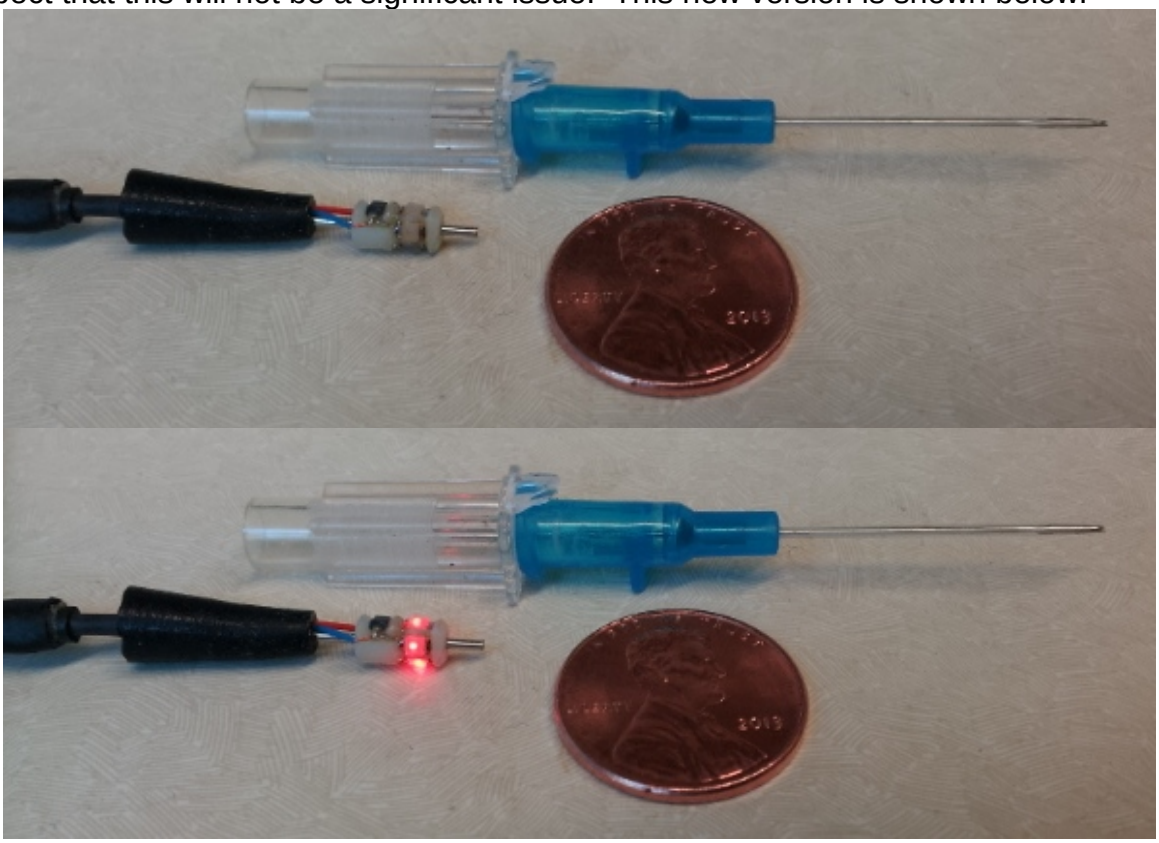
With the new blocks, recalibration was necessary. Certain software glitches in the calibration software had been causing incomplete data set collection when data acquisition time-outs occurred. Adding an error-trapping routine to the Matlab code, which reissued the request for data following a time-out resolved this problem. These events are rare enough that multiple reissues are not necessary.

In terms of developing the application, progress was made in developing efficient methods for mapping the voltages measured by the Arduino to geometric locations within the gel block. Earlier approaches attempted to find algebraic descriptions that mapped between x/y/z position and Vx/Vy/Vz measurements, however these were not particularly accurate, though as previously reported, were relatively fast in terms of calculation speed. During the current period, we found an approach typically used in finite element analysis approaches, namely tetrahedral mesh "walking". This method assumes an arbitrary test point within the Vx/Vy/Vz mesh of measurements, and by stepping through tetrahedral elements in the direction that approaches the Vx/Vy/Vz measurement from the Arduino, the true tetrahedron occupied by the needle tip can be determined, and the dimensionless position within that tet. Using the dimensionless result and the x/y/z coordinates of the corresponding geometric space tetrahedron, the needle tip location can be found. This algorithm was implemented in a Matlab script to create the voltage- and position-space arrays of tetrahedral (and arrays of adjacent elements) and test the algorithm. This worked quite fast in Matlab, which is optimized for matrix and vector calculation. The Matlab script was ported to the AppInventor code, which is far less efficient – in fact the calculation in this form took approximately 3 seconds per measurement – highly unacceptable. To resolve this issue, another approach was found, in which complex calculations are exported from the AppInventor app, to be processed by Javascript in the process of generating a web page with no content except its own title. The numerical result is posted in the web page title, which in turn is accessible to the AppInventor code which called the web page. Speed of calculation has been tested at 10s of milliseconds or better, which will be more than acceptable. We are now in the process of integrating this approach into the existing application, so that the sensor measurements are properly exported with the call to Javascript, and the result properly processed so that entry into tissue, entry into the vessel lumen and successful removal of the stylet can be determined.

Summary of Results for Aim 1:
During the previous period, we presented a new feature to the device, a tiny assembly of red LEDs that fit within the barrel of the IV cannula, and would be turned on when flashback or other bleeding would occur during the course of a training scenario. The figure below shows the first version of this assembly, with two opposing pairs of LEDs, one slightly ahead of the other. This version was found to be very difficult to assemble and subject to short-circuiting against the core of the stylet, as it is installed on the inside of a holder that surrounds the stylet core.

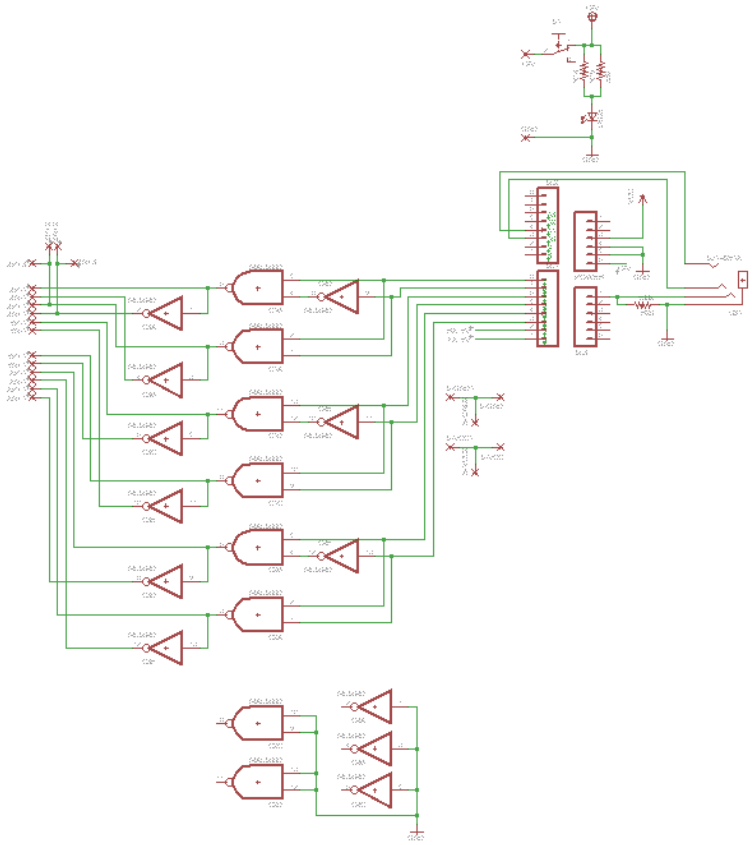


An improved version was developed during this period, in which the holder fully insulates the LEDs for the stylet, and also aligns the LEDs to form a single ring around the holder. While the LEDs are not diffused as well as with the earlier version, we expect that this will not be a significant issue. This new version is shown below.

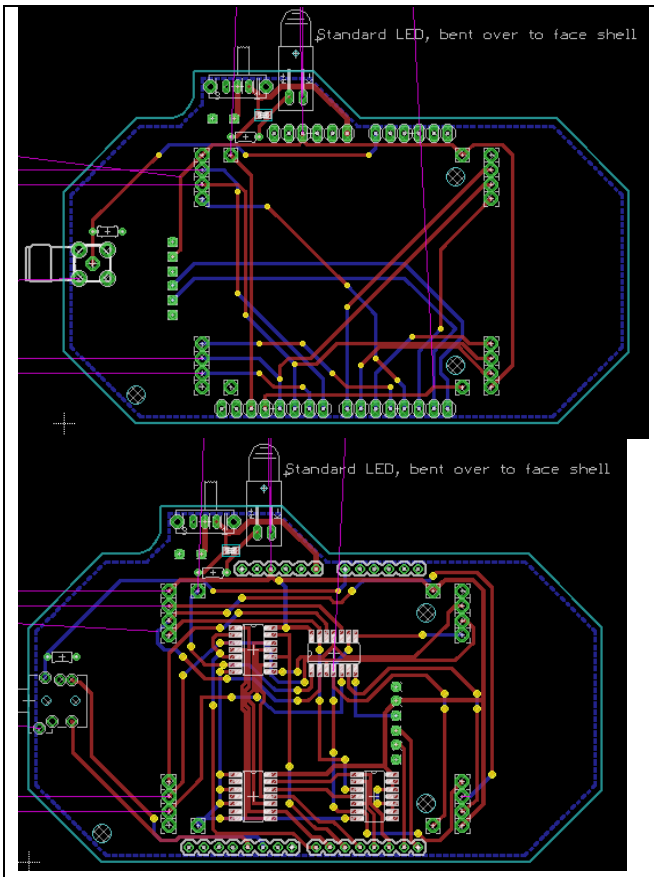


As described in the previous report, all of the available digital IO lines on the Arduino were already in use to control the haptic block circuit and to communicate over the Bluetooth module. Early during this reporting period, we investigated the use of a digital-logic based solution, which takes advantage of the symmetry of the control signals of the haptic block; pairs of signal lines in each of the x/y/z directions always have opposite outputs (one is high, the other is low, and when one switches, so does the other). As a result, only have as many digital lines are necessary to control the block circuitry, provided that for each digital line, another chip outputs both the digital signal and also its inverse. Using standard logic gates and a truth table relating a new

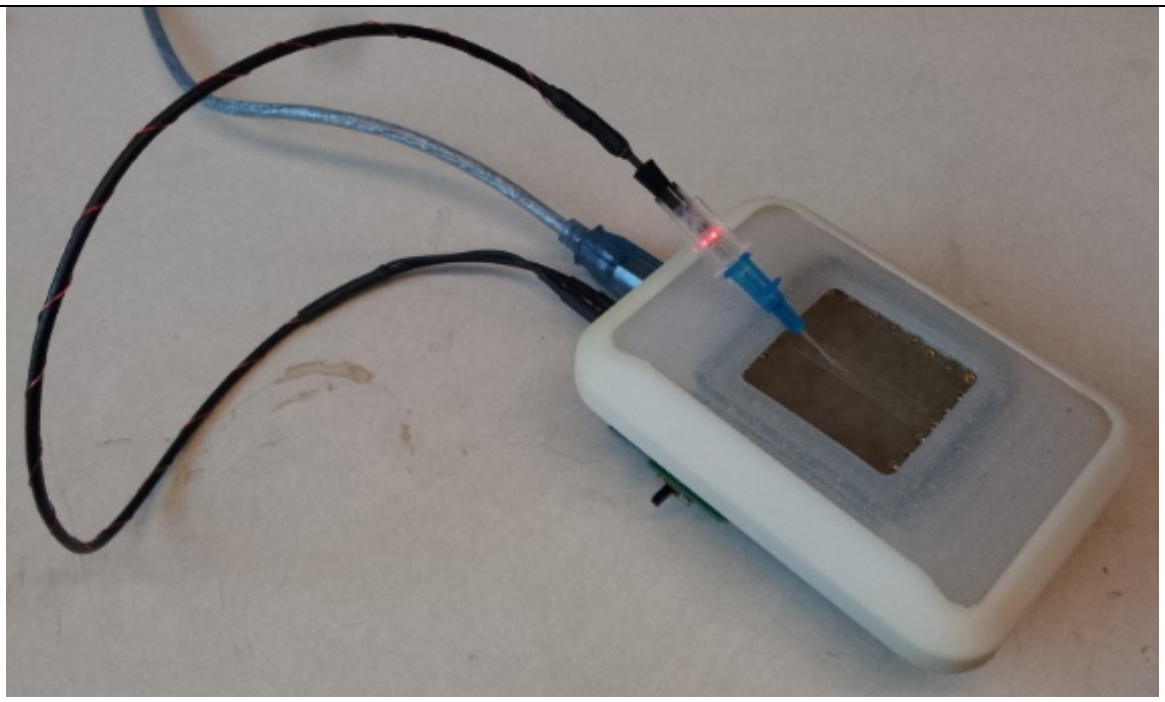
set of control signals (using half of the digital lines) to the haptic block circuit, the following circuit was designed and implemented. Now 6 I/O lines control 12 haptic block control lines, leaving more than enough lines to control even multiple colored LEDs (beyond the single one implemented).



An initial test (reported previously), using SOIC chips (the only form factor available for a compact version of the circuit which combines multiple gates into single chips, was found not to be functional – the chip outputs were only slightly different from each other, rather than the expected large difference between the output and its inverse. It is believed that the chip outputs are normally channeled to a comparator, which requires only small positive or negative differences to drive its output.
A subsequent test, using individual logic gates was found to be functional, and a new circuit board using SOIC versions of the individual gates was designed (below, left – original PCB for haptic block; below, right – revised version with logic chips).



At about the same time, a conversation with Mr. Bardsley lead to the discovery that a software library exists that allows any digital output pin on the Arduino to be used as a PWM output, even if it is not designed as such. The PWM signal generated has a lower frequency than the purpose-built line, however is still faster than the human vision fusion rate. In addition, the Arduino's analog input pins are actually general purpose I/O lines, which are only set as analog inputs by default. The code was rewritten to make use of one of the analog input lines as a PWM output, and as a result, we returned to the original design of the board, adding only additional connections to link those pins to the LEDs. To provide for easy disconnection of the sensing cable, a 2.5mm stereo jack was installed on the PCB, with a matching connector attached to the sensing cable. This new assembly is shown below.



As described above, new compositions of the gel used to create the blocks were tested during this period. It was previously observed that for extended testing periods (e.g. those involved during the calibration sequence), the water-based gelatin mixture tended to lose water via evaporation and separate from contact with the haptic block circuitry. In seeking alternate materials, recipes involving glycerin were found, such as one used to prepare microscope slides [http://www.microscopy-uk.org.uk/mag/artaug03/wdpart4.html].

Initial tests to investigate whether gelatin dissolves in glycerin confirmed that it does, and further, that the molded glycerin-gelatin do form gel blocks. However, on testing the block for electrical conductivity, essential for the proper functioning of the sensing circuit, the block was found to be an insulator.

A subsequent test replaced the corn syrup of the earlier recipe with glycerin, which also gelled, and was also electrically conductive. Further, as recommended from the microscope slide technique for preventing the growth of bacteria and mold, Listerine was added at a concentration of approximately 4%. It was found that not only did the Listerine prevent microbial growth during refrigerated storage, but it also inhibited growth when the block was stored at room temperature for weeks. This additive will continue to be part of the preparation of gels going forward.

Lastly during this reporting period, we have revisited the mathematical approach to converting from voltage measurements made by the Arduino to the corresponding x/y/z positions based on the calibration data. The x/y/z positions used to collect voltage measurements form a regular grid, which can be subdivided into an array of tetrahedral elements, 6 for each cube defined by position grid points. As the voltage measurements follow a distorted version of the same grid, equivalent tetrahedra from the distorted electrical grid can be generated. The tets in each array can be assigned the same numerical index, such that a supporting array that lists the adjacent elements for each tet is identical for both.

To find the tetrahedron which contains the combination of voltage readings measured by the needle, one starts from any arbitrary tetrahedron. The position of the needle tip is compared with each face of the arbitrary tetrahedron, to determine wither the tip position is on the “in” side or the “out” side. If the needle tip is on the outside, the tet that occupies the adjacent space, on the opposite side of the face is selected as the new arbitrary tetrahedron. The comparison of needle tip to tetrahedron faces is repeated, and new, closer tetrahedral are “walked through”, until the needle tip point is on the “in” side of all four faces of a tetrahedron. At this point, dimensionless barycentric coordinates of the needle tip, relative to the faces in electrical coordinates, are calculated. Turning to the corresponding x/y/z tetrahedron, the true geometric position of the needle tip is calculated by applying the barycentric coordinates to the x/y/z faces.

This sequence, including generation of the voltage, x/y/z and adjacency arrays was implemented in Matlab. The following plot shows the path, through the electrical grid, from a low initial point, step by step to the final tetrahedron, a typical point that might be generated by needle insertion into the gel. Barycentric coordinates are calculated, then applied to the orthogonally arranged x/y/z corners of the geometric tetrahedron. Starting with one corner of the tet, the barycentric coordinates are converted to dimensionalized steps in the x, y, and z directions to reach the position of the needle tip in Cartesian space.

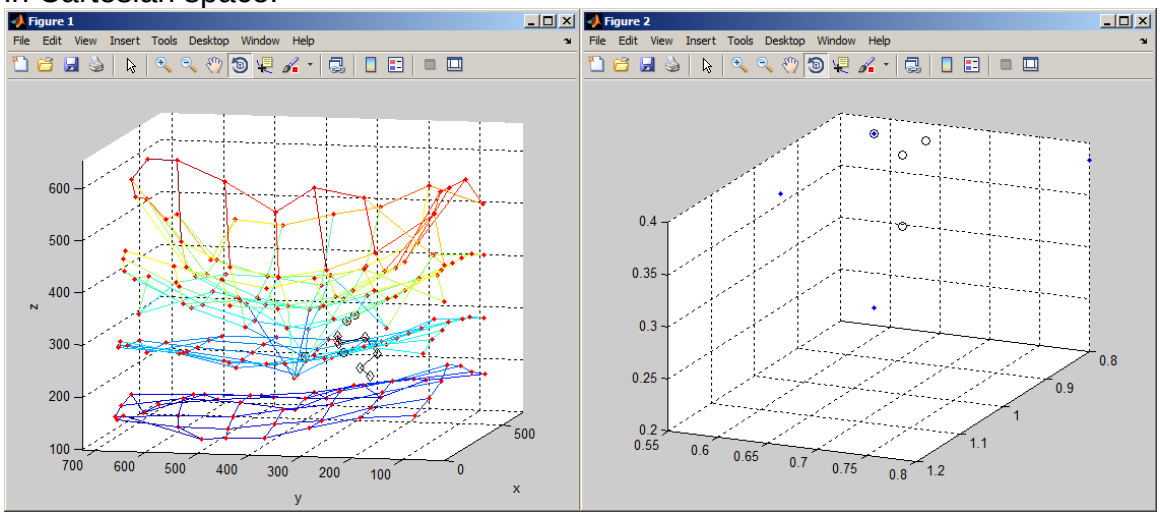


Figure. Left: distorted array of Vx, Vy, Vz electrical coordinates, generated from regularly arrayed points used during calibration. Right: blue points are the corners of the tetrahedron determined by the walking algorithm. Starting from the back, upper corner of the tet, scaled steps based on the barycentric coordinates are taken to the right, towards the viewer, then down to reach the calculated needle tip position.

This algorithm was subsequently ported to the AppInventor application, however it was found that the mathematical calculation speed of the language is very slow. The same calculation that would take under 0.1 seconds using Matlab, would take over 3 seconds, and was dependent on the number of tetrahedral to be walked through to find the solution. While this is long, a naïve search of all tetrahedral in order is typically

significantly longer, on average, than this walking approach.
Given the limitations of AppInventor, another solution was sought to accelerate the calculations. One has been found, through the use of one of the AppInventor tools: a pared-down web browser object. By taking the Vx, Vy, Vz coordinates measured as arguments as part of a URL address, an external HTML file, with a Javascript implementation of the tetrahedral walking algorithm, can perform the calculation much more quickly than AI can do. The resulting x, y, z coordinates are returned in the form of the title field of the web page generated by the HTML/Javascript file, which can be accessed by the AI app.
A test version of this implementation has been completed, and it confirms that the Javascript calculation takes 10s of milliseconds at most to complete, and so appears to be a suitable solution to the calculation speed problem. At present, modification of the AI app to accommodate the Javascript call and response is in progress, so that the app will properly recognize initial contact with the gel, motions through the gel, entry into the lumen, exit from lumen or gel "tissue", and successful removal of the stylet while the cannula is located within the vessel lumen.

* end of new Specific Aim 1 material for period to Sept. 30, 2013

* beginning of new Specific Aim 1 material for period to Mar. 31. 2014

The work to complete the tet-walking coding continued during this period. To isolate each element of the process, we began by creating a version of the haptic block microcontroller code that sends out a standard set of coordinates, rather than taking real measurements. This allowed for testing of communications and position calculation without requiring the presence of a (perishable) gel block. This allowed us to confirm the basic function of sending a URL and receiving the processed data from the HTML script, and develop error-trapping code to ensure that a complete set of 3 data values are received from the haptic block before attempting the coordinate conversion.

The preset coordinates were expanded to create an artificial complete trajectory, from outside the gel block, through entry and passage into the lumen. This allowed for adaptation of the code to take the new data inputs and integrated them with the logic that detects entry into the tissue, detection of presence in the lumen, and then detection of withdrawal of the stylet while still in the lumen, signaling a successful placement (at least to the level of detail developed during this Phase I work). With this logic implemented, the update rate remains at approximately 5Hz – slower than desired, but fast enough to be useful.

New copies of the gel block were fabricated to test the code while taking real, rather than pre-recorded data. These blocks included vessel structures to test manufacturing techniques so that the vessels do not collapse – early versions with low gelatin concentration experienced (likely) osmotic changes, such that the vessels had the water drawn into the surrounding bulk of the block, generating a depression in the skin surface immediately above the vessel. Using non-fiber embedded gelatin of the same

concentration as the surrounding block is likely to be a functional solution, although this will produce less contrast in haptic sensation that would have been the case with low concentration (very soft) gel in the vessel.

Testing with these new gel blocks identified an error in the haptic block code – one of the digital output pins used to control the electrode arrays was also being used in test mode to turn an LED on and off – the setup configuration leaves the LED on, which had the result of turning on part of the array. This caused current to flow continuously through the gel block, melting the gel. This allowed conductive gel to flow into the electronics, causing additional current to flow, even after solving the software glitch. Baking out the electronics resolved this issue, however in a later overhaul of the design, fully sealing the electrode array from the gel (except at the actual contact of electrodes with the gel) should be one of the primary changes.

The last elements of the data acquisition/processing code that was altered during this period included a change to the transmitted format, with non-numeric character indicating the end of a frame of data. This permits unambiguous parsing of data, which previously occasionally resulted in errors when a partial data set was acquired and the remainder being lumped into the next data set. It also allowed improvement in the code so that only one new point is requested for each point processed, eliminating a previously undetected problem in which the amount of received, unprocessed data could grow without bounds.

In addition, the Tet-Walking code was modified so that paths through the mesh that lead outside of the mesh (because it is not guaranteed to be fully convex), the error is caught. In some cases, the walking algorithm has two or more possible valid paths; in the earlier code, those additional paths were ignored – they are now examined to find out if they are valid, and if so, used. If not, a valid Out-of-Bounds error message is returned to the App, rather than hanging the code, which had been the case. When the App receives this message, it does not attempt to make use of the undefined coordinates and calls for a new data point from the haptic block, with the expectation that further motions of the user will lead to a point that can be properly processed.

* end of new Specific Aim 1 material for period to Mar. 31, 2014

* beginning of new Specific Aim 1 material for period to Sept. 30, 2014

During this period, we prepared additional mold pieces to allow production of the gel blocks in parallel fashion. We now have eight full sets of mold parts, which also serve as storage containers to preserve block shape prior to installation into the system.

We fabricated six new gel blocks in July for BCH staff to examine. Three had the same gelatin concentration in the vessel lumen as in the bulk of the block, while three had double the concentration in the vessel. This was intended to create a more palpable vessel structure and generate a slight bulging of the vessel as water from the bulk would move, by osmosis, into the vessel. The difference was noticeable by naive

reviewers.

In preparation for a demonstration at the 2014 MHSRS conference, during August the electrode array was completely disassembled and reassembled with new (back-up) PCBs. The original system had been damaged through flow of saline-laden gel melting into the circuitry and prior attempts at removal of re-solidified gel. The previously unused back-up boards were installed in a slightly different configuration that will allow easier access of test probes to the circuitry should future diagnosis of problems be needed. The boards and electrode were installed on a new frame made from rapid prototyping plastic; this version did not have the additional, unused perforations of the original bread-board circuitry, which were responsible in part for shrinkage of the gel blocks through evaporation, and allowed melting gelatin (when a short circuity or code problem caused current to flow continuously through a section of the block) to reach and damage the circuit boards.

The new circuitry was used to calibrate a gel block and update the tet-walking code with the new coordinate data.

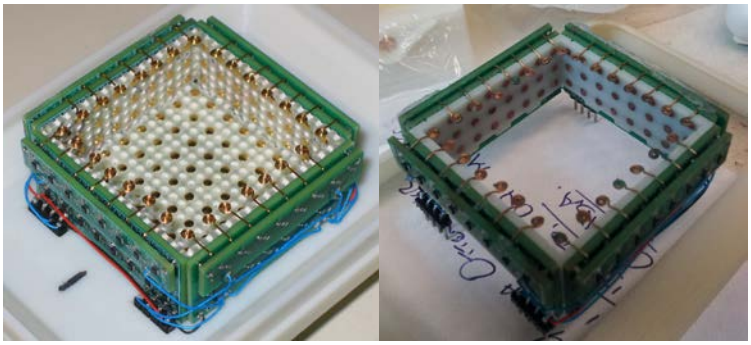


Figure. Old and new electrode arrays. Front right and back left boards are flipped with respect to original design. Electrodes have lost most of their gold plating – new versions to be developed in phase II will seek to resolve degradation of the electrode surfaces, eliminate need for hand-coiled upper z-axis electrode fabrication.

Lastly, during late August and early September, a new gel block which used no water (glycerin, salt, gelatin only) was prepared for evaluation of properties. The water-based blocks suffered shrinkage due to evaporation over the course of an hour or two, causing problems with the needle tracking system as the shrinking gel separated from the electrode arrays. The glycerin-based block was found not only to not shrink, but over the course of days, actually increased in mass by 5g out of an original 40g mass, presumably through the absorption of water from the air. This suggests that there is a “recipe” with some small fraction of added water that will neither shrink nor swell when exposed to air that has moderate humidity (e.g. in air conditioned facilities). Further, after exposure to room air with no protection from microbial contamination for over two weeks, there was no evidence of mold or bacterial growths, even without the inclusion of the Listerine fraction that was previously part of the recipe.

With the same concentration of salt in the glycerin-based gelatin blocks, the resistivity of the material was found to be close to that of the earlier water-based blocks, so no alterations in the circuitry will be needed to accommodate the altered material.

While the use of mostly glycerin in the blocks will increase the cost by approximately $0.80 (~$1.60 total based on cost of 5oz bottles of CVS glycerin), the extended shelf-life and reduction in need to dispose of contaminated blocks should improve the economics of the system.

* end of new Specific Aim 1 material for period to Sept. 30, 2014

* beginning of new Specific Aim 1 material for period to Mar. 31, 2015

Further work on Aim 1 was substantially on hold during this period. We did observe that the lifetime of the glycerin-based block described previously appears to be on the scale of months, without noticeable loss of mass/volume, and without microbial growth, suggesting that shelf life of these components will not be a concern.

* end of new Specific Aim 1 material for period to Mar. 31, 2015

* beginning of new Specific Aim 1 material for period to Sept. 30, 2015

During this period, the original platform that was used to develop the Android app, called App Inventor, was permanently shut down, in favor of a more stable, more extended platform called App Inventor 2. The two systems are not compatible with each other however MIT, which hosts AI2, created a conversion tool to facilitate upgrading old apps into the new environment, with the caveat that it was expected that not all apps would convert without the requirement for some repair/revision. AI1 would remain active after July 15, but only for the purpose of downloading previously developed code.

During June, the last version of the App was saved and converted into AI2. In addition, a complete set of screen shots of the AI1 code was captured, so that all elements of the program could be referred to after the end of AI1 activity. The converted code was mostly functional under AI2 – formatting of text is slightly different and the “bullet” character used in the point-form text content is no longer available, so some editing will be required. The Betadyne application exercise and the graphical/finger tip control of the IV insertion task are still functional. The tourniquet application sequence selection exercise appears to have been improperly converted, due to a change in how random values are generated and handled. Correction of this issue will need to be performed to restore that functionality.

We have requested quotes on hardware to replicate the system to facilitate user testing, so that multiple users can evaluate the system and themselves be evaluated in parallel. Fabricating two more units would cost approximately $1000. We will evaluate whether funds are available for this purpose under the grant or other sources.

Over the 2015 summer period, Mr. Benjamin Lerman, an engineering undergraduate from Northeastern University, worked on a parallel project to create a gelatin extruding 3D printer. As part of his work, we asked him to fabricate some of the gel blocks using the new, glycerol only (no water) recipe for gelatin fabrication. He created a series of new blocks that demonstrated non-evaporation and reasonable behavior as evaluated by nurses at BCH. They found the pop sensation of penetrating skin and vessel was acceptable, as was the sensation of friction as the needle passed through the structures. They requested that the physical "bump" that had previously been included in the mold as a palpable cue to the location of the vessel, be removed and replaced with a flat surface. We 3D printed a new set of mold parts with the flattened surface for future use.

* end of new Specific Aim 1 material for period to Mar. 31, 2015

* beginning of new Specific Aim 1 material for period to Mar 31, 2016

During this period, we completed the update of the software in the App Inventor 2 environment, restoring all of the original functionality. In addition, using newly updated versions of the content that was prepared by Dr. Weiner, we revised the user interface. The text was revised to reflect changes in doctrine that had been made at Children's hospital since the earlier version was completed, and new elements were added to present the full suite of instruments and materials needed. One additional "test" was added, to challenge the user on the proper selection of needle gauge given the example of a neonatal patient who would have a one-time (vs. serial) blood draw. The interface buttons were rearranged to improve the user interaction with the app.

Details of the screens are included under Aim 2

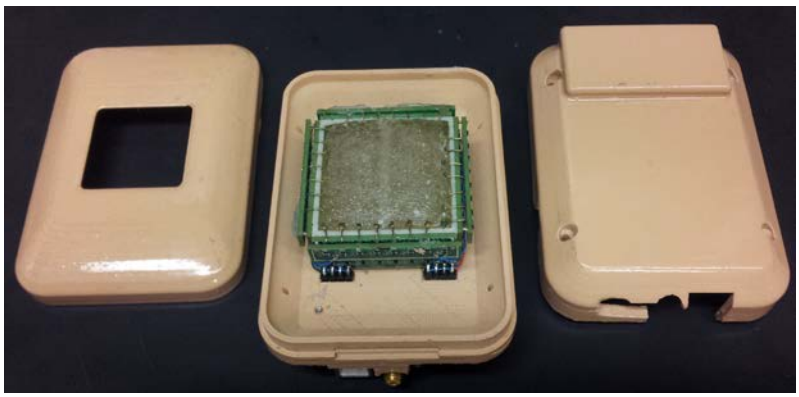
In response to feedback from the earlier users and Dr. Weiner, we replaced the soft silicone surface that surrounds the gel block with a rigid plastic shell for the interface. Due to the presence of the rigid circuit boards surrounding the gel block, the silicone "skin" allows palpation of the rigid structures, which is distracting and unrealistic. The rigid shell that exposes only the region of needle insertion removes this distraction. While a full, soft, tissue-like surface would be desirable, revision of the circuitry and overall design in the next phase of the work will be necessary to accommodate such an interface design.

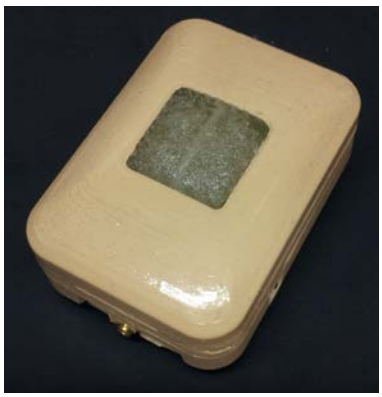
Original upper shell with exposed soft surrounding surface and new rigid shell that focuses attention just on the gel block.

* end of new Specific Aim 1 material for period to Mar. 31, 2016

* beginning of new Specific Aim 1 material for period to Sept. 30, 2016

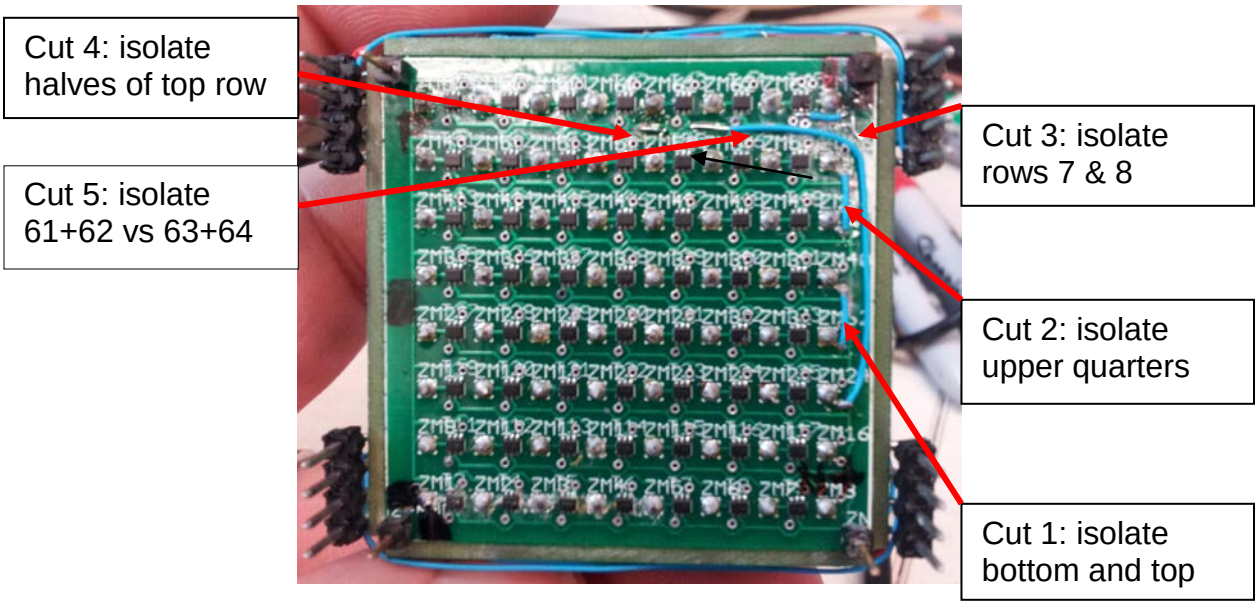
The physical device has been structurally unchanged over this reporting period. New techniques for improving simulator cosmesis that we developed in the course of upgrading another CIMIT-funded simulator (PI Daniel Raemer, "Development of a Surgical Hemorrhage Control Training Simulator", now in its third iteration and being delivered to the University of Auckland (New Zealand) Multidisciplinary Operating Room Simulation project in October 2016) were applied to the shell of the haptic block. Flesh-tone spray paint was applied and a coat of brush-on epoxy was applied to seal and protect the surface.



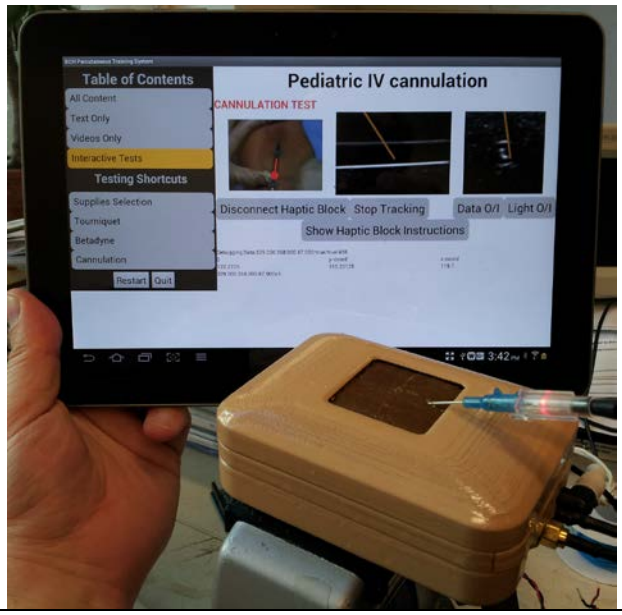


Towards the end of the period, a previously undiscovered problem with the z-axis

circuitry – one of the 64 transistor ICs at the base of the block either had developed (or always had) a short circuit, causing the block to be able to measure z-axis position in one of the two available current directions (upwards or downwards). It was found to be possible to isolate the one non-functioning portion of the circuit by severing traces sequentially to determine which transistor was causing the short, then repairing all but the cuts which connected to the device, bypassing the one element of the 64, leaving the majority of the z-axis system intact. Initial cuts (and repairs in blue wire) shown below.



New gel blocks have been prepared, including food coloring pigments and TiO2 powder to add opacity and skin tinting to the block to provide flesh tones rather than the earlier iterations that used clear gelatin with embedded paper.



With each iteration of the blocks, we re-performed the calibration process described earlier, with non-trivial variation between each data set. We are forced to reach the conclusion that variation in preparation results in non-uniformities in the conductivity of the block so that using the 3-axis voltage divider approach may not have the robustness to provide a consistent tracking of needle tip position. In addition, the complexity of the 192-electrode array would be difficult to reduce, so that the cost of the module would be difficult to bring down to a level that would be intermediate between VR-based IV needle systems and unaugmented tissue blocks. In the next phase of the work, already under way, we are investigating the use of the alternate approach, namely measuring current flowing through the needle tip and its distribution between solid electrodes that face the sides of the gel block.

In parallel with the slight modifications of the hardware, the tablet app underwent a final round of modifications to resolve a number of issues that resulted from the transition from App Inventor 1 to 2 (inconsistent handling of JPEG images resulted in the tourniquet test and supplies display pages from malfunctioning – solution, once the problem was identified, was to convert all relevant images to PNG format) and to refine the code in the cannulation test to help in converting it to a useful form for the following phase of the work.

As such, the system is suitable for the remaining user testing exercises, with the recognition that the content will be representative of a polished version, the physical and visual properties of the block are expected to be acceptable, although the tracking accuracy will remain to be improved in the next phase of the work.

* end of new Specific Aim 1 material for period to Sept. 30, 2016

Aim 2. Development of a procedure module to teach IV catheterization

The tablet-based application has remained stable for the most part since the last report. One area of investigation has been an attempt to improve the responsiveness of the cannula insertion test sequence. During cannula insertion, the haptic block measures and transmits the needle tip position to the tablet via Bluetooth radio. The current position is plotted on a background image showing sagittal and transverse ultrasound views of the vessel. A series of graphical lines are drawn over the background image, requiring that for each refresh of the image, the whole image is blanked and redrawn. The process, using the App Inventor environment, has been found to respond fairly slowly, with refresh rates no better than 1-2Hz. This rate is insufficient for reasonable interactivity or detecting with precision when the user has inserted the cannula tip into the vessel, or in the case of errors, when penetration of the far wall of the lumen has occurred. App Inventor supports the use of sprites, which can be independently moved over top of the background image. In principle, a single image of a needle under ultrasound could be moved anywhere over the image without requiring blanking of the background image first. That sprite image would need to be sufficiently large to draw a needle image from one side of the background ultrasound image to the other.

During the process of rewriting this section of the app, it was found that sprites cannot have origin positions beyond the edge of the background image. When only the initial point of the needle should be shown to the user, the remainder of the image would need to extend past the edge of the background image. With the ideal case found to be impossible, another attempt was made, with a series of shorter, overlapping images that essentially "telescope", extending from the image border to the necessary location within the image. While an interesting concept, this was not found to accelerate the frame rate significantly. Investigations in this vein will continue, however a final solution may require rewriting the code completely using alternate programming tools and languages.

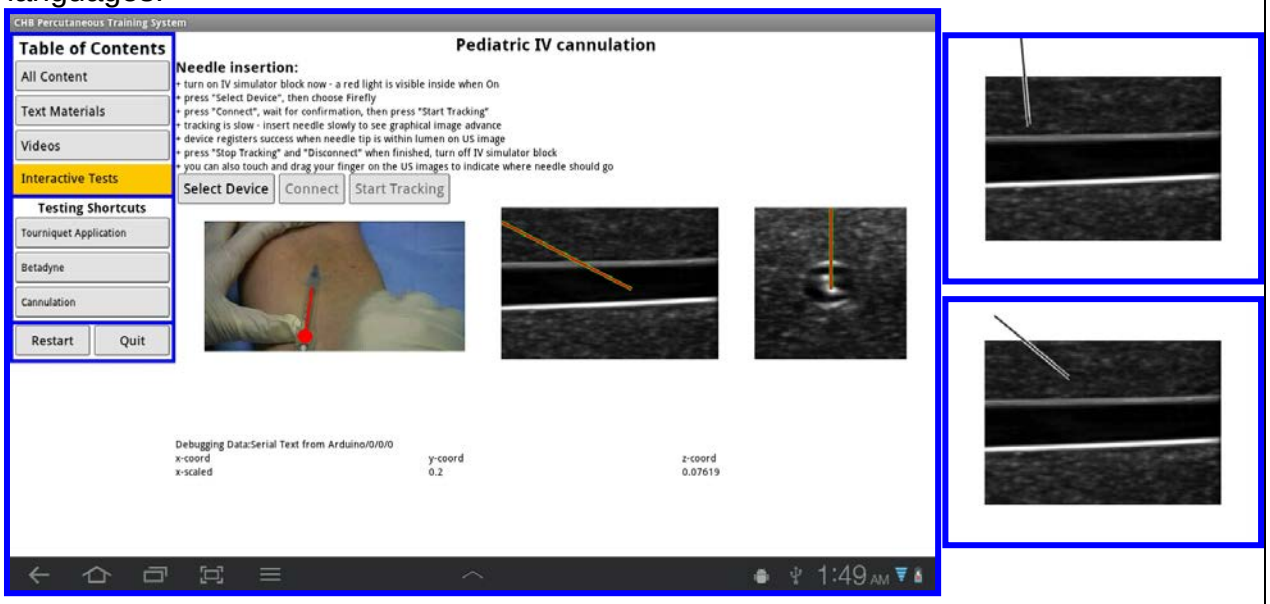


Figure. Screen captures of cannulation screen. Left: Sagittal and transverse vessel images overlaid with line segment drawings of needle, color-coded to indicate successful entry into vessel lumen. Right: Upper and lower images show two image sprites, extending past edge of background image rotated into different orientations and overlapping/telescoping. When shown to users, portions of sprites extending past image boundary are hidden, showing only portion within boundary. Debugging coordinate data also hidden from user.

Finally, the Google App Inventor development environment service was discontinued at the end of 2011. There was a hiatus of a few weeks before the system was reestablished under the control of MIT. There was a further period before which access to this system was approved for use, however we have obtained access as a developer, uploaded the original code and tested the new system to verify that the app continues to function.

Two developments occurred independently of our project in the period after April 1 that have had direct benefits for system development and performance. First, the MIT access to AppInventor has shifted from a test version to a relatively stable and consistent development platform with ongoing improvements. Additionally, the Android OS for the tablet has also been updated. Our recent tests of the ultrasound view frame

rates have increased quite dramatically from 1-2Hz up to nearly 6Hz (5.7Hz). A port of the software to native Android code rather than the AppInventor structure would likely allow much faster frame rates, which would be recommended for future developments (including porting to iOS as well), however at this point, the display appears to be fast enough to be reasonably useful. In addition, the OS upgrades have made the display of application of Betadyne essentially real time and accelerated the playback-scoring/analysis phase. Playback and scoring required an online review and display of the full length vector of recorded application positions, the slowest element of which was replotting the locations to indicate the go (green) / no-go (red) positions.

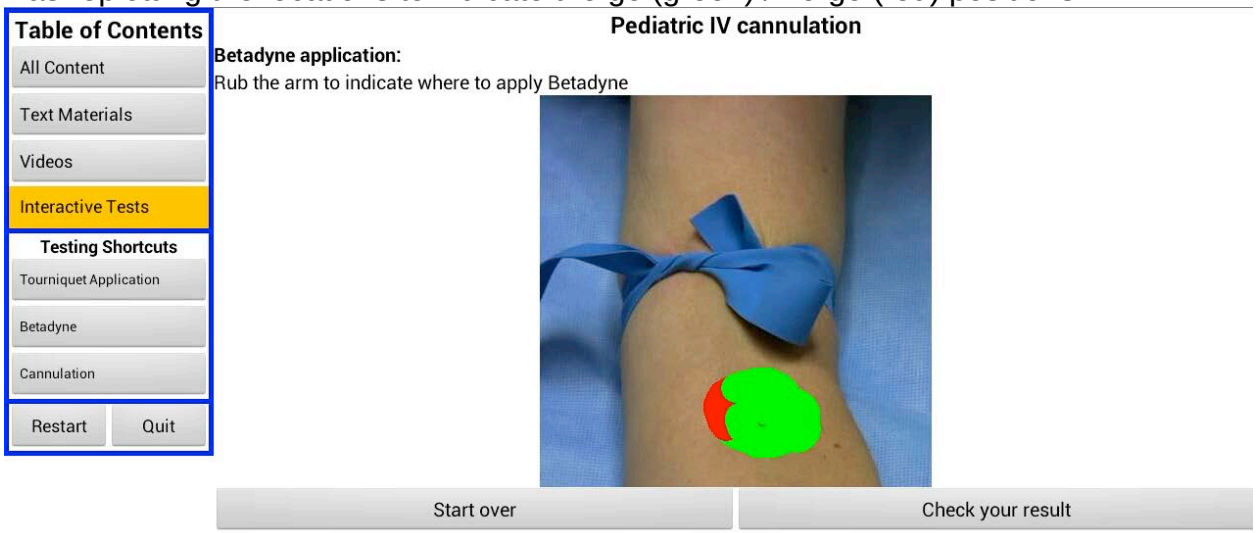
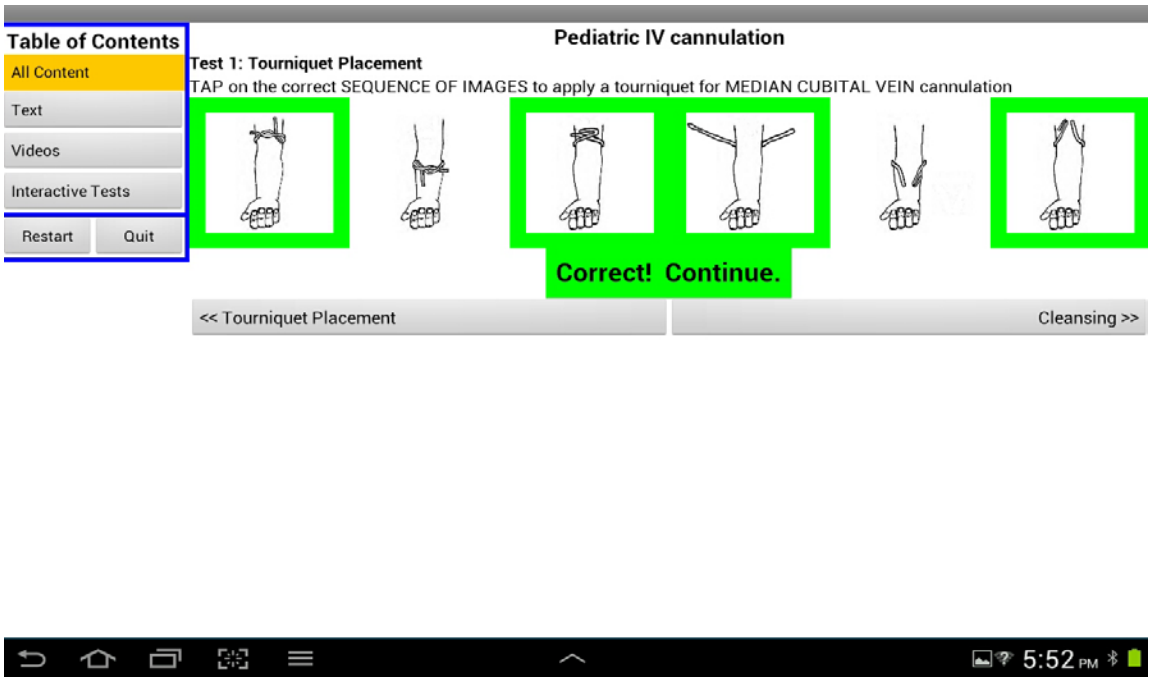


Figure. Screen capture of Betadyne skin cleansing test screen. User rubs their finger over site to be cleansed, green indicates correct application of Betadyne, red incorrect or omitted site of application. Option to repeat the task is provided by selecting 'Start over'. Performance is graded and result is captured to database by selecting 'Check your result'.

* beginning of new Specific Aim 2 material for period to Mar. 31. 2014

Paula Lamagna has reviewed the procedure training documents created by Dr. Weiner and submitted with the last progress report. Documents have been edited. Three versions of the text for IV catheterization have been written: a very complete version that documents all aspects of and related to the procedure, a summarized version that provides only the information required to understand and perform the procedure, and a version that lists the steps of the procedure with minimal detail. The summary version has been loaded onto the tablet. Text of this version has been integrated with the relevant section of video and is seen on screen with the video. Text alone is accessible in sections or in its entirety by selecting from the left side menu. The text is submitted as part of this progress report. Procedure testing has been updated. In addition to improvements to the interactive tests for tourniquet application and skin cleansing already embedded in the module, an additional test for tourniquet application that requires the user to select in appropriate order pictures of steps for performing this task has been added.

Drs. Weiner and Ottensmeyer have received recognition from the International Pediatric Simulation Society (IPSS) for the device and teaching module they have created for this CIMIT grant. Dr. Weiner has been invited by the IPSS procedure subgroup, INSPIRE, to assume leadership of a team to develop an IPSS endorsed PIV training program using the device and training module. The currently 8 person PIV group that she has convened is composed of IPSS simulation experts, several who are leaders of IPSS. Members of this group have reviewed the observer procedure evaluation form, which has been slightly modified based on their recommendations. The procedure evaluation form is submitted as part of this progress report.



* end of new Specific Aim 2 material for period to Mar. 31, 2014

* beginning of new Specific Aim 2 material for period to Sept. 30. 2014

Dr. Weiner has modified the pre and post knowledge test and the use, usability, effectiveness survey. They are being reviewed by Paula Lamagna and the INSPIRE PIV group. Current near final drafts are submitted as part of this progress report.

In response to feedback from Dr. Weiner, the UI of the app was slightly modified to use smaller fonts to eliminate the need to scroll the screen for some of the entries with large amounts of text content. Headings, subheadings and content fonts were all updated.

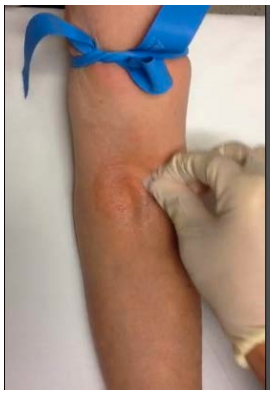
In advance of upcoming user testing, additional requests for changes to the UI and the tests have been made, including revision of the Betadyne/antiseptic application test and addition of a new exercise in the selection of appropriate materials. These will be described in the upcoming work section.

* end of new Specific Aim 2 material for period to Sept. 30, 2014

* beginning of new Specific Aim 2 material for period to Mar. 31. 2015

Pictures showing supplies for IV placement have been generated, with tests requiring user to select the correct cleansing agent, skin anesthetic and IV catheter size. New content is being integrated into the app. Content for changes to the skin cleansing test (previously referred to as Betadyne/antiseptic application test) that reflects change in preferred skin cleansing agent from Betadyne to alcohol or chlorhexidine gluconate and isopropyl alcohol, and change in preferred motion for chlorhexidine gluconate from circular to scrub for has been created. Users will select video showing appropriate technique for their site. Learning module text has been modified to reflect the changes.

Screenshots of Skin Cleansing Technique Videos



Circular

Scrub

Pre and post knowledge tests and the use, usability, effectiveness surveys have been reviewed by Paula Lamagna and by the IPSSW INSPIRE PIV group experts and modified based on recommendations.

* end of new Specific Aim 2 material for period to Mar. 31, 2015

* beginning of new Specific Aim 2 material for period to Sept. 30, 2015

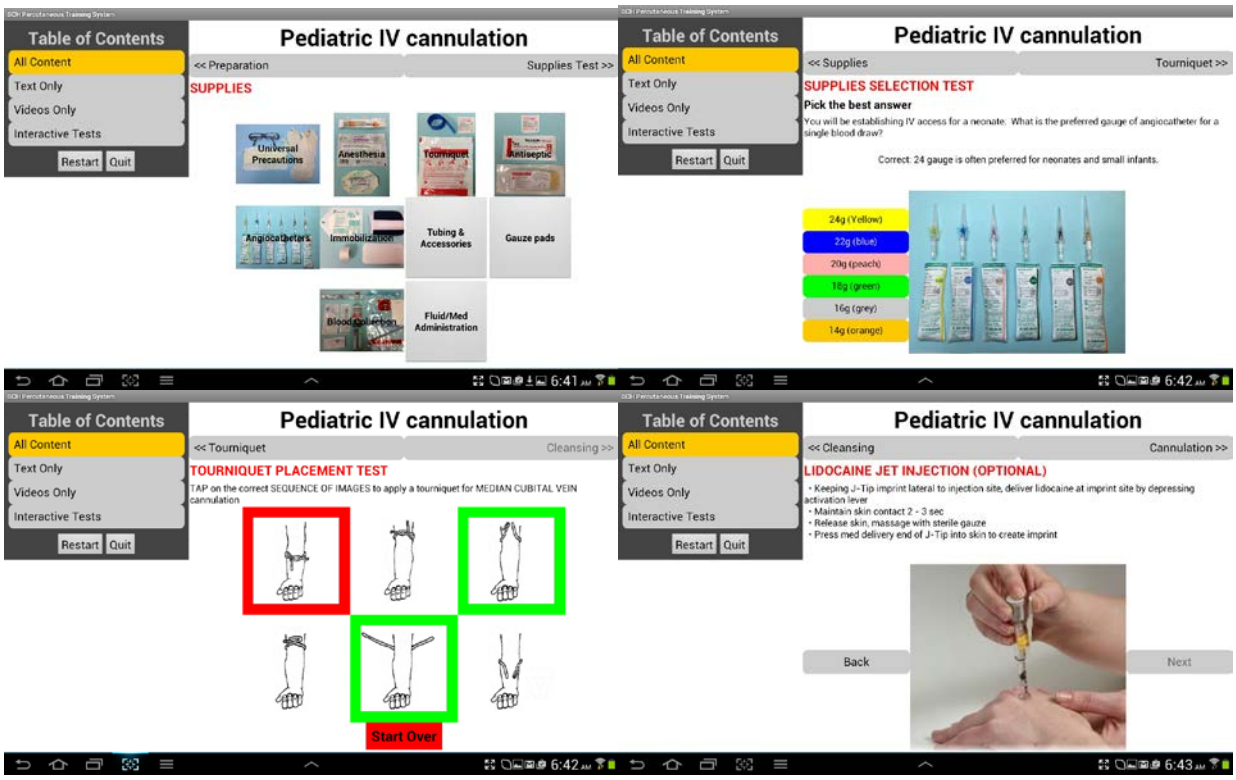
Schematics of tourniquet placement have been replaced by images of the steps of the procedure performed on the same person in whom IV was placed. Voice over script for the teaching module has been modified to reflect additions and changes to text, pictures, videos and tests detailed in the last report.

* end of new Specific Aim 2 material for period to Sept. 30, 2015

* beginning of new Specific Aim 2 material for period to Mar. 31, 2016

Module content has been updated to include pictures of administration of local anesthetic in the form of 1% lidocaine administered by J-Tip™ which is becoming widely used.

As described under the software alterations under Aim 1, updates to the app include new elements of content including anesthetic administration. Examples of the new screens of the app are shown below.



* end of new Specific Aim 2 material for period to Mar. 31, 2016

* beginning of new Specific Aim 2 material for period to Sept. 30, 2016

A number of software bugs in the prototype were identified and resolved during this period. Many of the original images used in the new content were jpeg format. As mentioned above, App Inventor 2 experienced difficulties when changing an image from one jpeg to another (an issue that we did not find identified in the online documentation). This caused the tourniquet test to experience problems in randomizing the images presented – switching the sequence and calling the image files caused error message to appear and blank frames would be displayed. Similarly, for the larger images and details on the supplies, calling for a new image to be displayed would result in no change on the screen. With experimentation, it was found that

switching to other image formats and back to JPEG allowed for the display of the desired image, however this would be a non-optimal solution. Switching between PNG format images was found to work correctly, so all of the images that had to be dynamically changed were converted to PNG format.

This will not be an issue in the next phase of the work, as it will not be developed using App Inventor.

In anticipation of the availability of the new platform, layouts for the new user interface were developed. Teaching module has been updated to leverage enhanced functionality. Users will now be able to select site for IV placement (arm, hand, foot, scalp), media (all, text, text + pictures, videos, tips, tests) and content (indications, contraindications, anatomy, supplies, procedure, troubleshooting, complications). Users will have several options for navigating through the site to customize their experience and maximize the effectiveness and efficiency of their learning. Text and tips documents, each minimally updated from previous to reflect current practice, are included in appendix of this report. For testing purposes, users will select arm as site for IV placement and will be required to view all content. Representative screen shots are below.

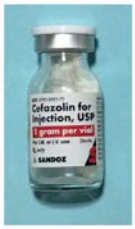
Content
- Indications
- Contraindications
- Anatomy
- Supplies
- Procedure
  - Preparation, Safety
  - Position, Identify Vein
  - Tourniquet
  - Skin Cleansing
  - Lidocaine J-Tip
  - Angiocath Placement
  - Blood Drawing, Flushing
  - Secure IV
  - Clean up
  - Document
- Troubleshooting
- Complications

INDICATIONS

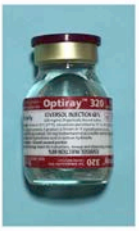
To obtain blood

To administer

Fluids



Medications



Contrast

Blood Products

CONTRAINDICATIONS

Absolute*
- Cellulitis, abscess
- Fracture, soft tissue injury
- Phlebitis, thrombosis

Relative*
- Burn
- Poor perfusion
- Edema
- Bleeding diathesis

*No contraindication if only life saving peripheral IV option

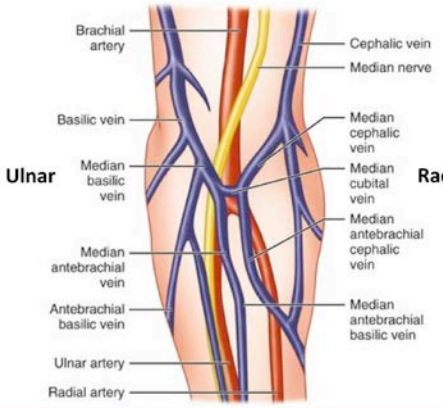
Content
- Indications
- Contraindications
- Anatomy*
- Supplies
- Procedure
  - Preparation, Safety
  - Position, Identify Vein
  - Tourniquet
  - Skin Cleansing
  - Lidocaine J-Tip
  - IV Placement
  - Blood Drawing, Flushing
  - Secure IV
  - Clean up
  - Document
- Troubleshooting
- Complications

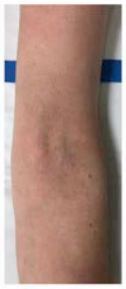
*Anatomy other sites

ANATOMY

Veins -thin-walled, distensible, compressible soft, spongy.
Arteries thicker walled than veins, less distensible, less compressible, pulsatile
Tendons firmer, flatter than veins and arteries, are not compressible or distensible

Antecubital Veins, Arteries, Nerve





*end of new Specific Aim 2 material for period to Sept. 30, 2016

Aim 3. Evaluate, validate the device for procedure training

The device and the module will be trialed by clinicians with varying degrees of experience from trainee to expert, who will be interviewed regarding performance

metrics and accuracy of the device, fidelity of the tactile experience compared to performing the procedure on a patient, accuracy in translating user driven elements into visual representation, and device driven instruction and feedback to the user. Development of pre and post device training knowledge tests is in progress. Skills assessment to compare procedure performance using standard IV arm mannequin and the handheld simulation device is in development. Based on conventions used in simulation training, tasks will be scored as not performed or performed incorrectly; performed correctly with minor deficiencies or errors; or performed correctly. Documentation to assess IV catheterization in patients before and after training with the device is being created. Forms to evaluate device use and usability are also being developed and will capture user demographics; experience with simulation, mobile devices and video games; assessment of the platform, content and effectiveness of the device as a teaching modality, as well as the mobile practice environment it provides. Once the device prototype has been trialed and modified based on feedback, the pilot validation study, which will test use, usability and impact of the device on procedure competency will be performed. Twenty residents in the CHB ED will be enrolled in the validation study. Outline of content of evaluation, validation tools was included in this report as an Appendix for the last report.

*This report contains 3 new documents created by Dr. Weiner: 1. 'Intravenous Catheter Placement' that provides full details of the procedure including Pre-procedure: Indications, Contraindications, Supplies, Anatomy; Procedure: Patient/Family Preparation, Set-up, Patient/Caregiver/Provider Positions, Comfort/Distraction Measures, IV Placement, Troubleshooting; Post-procedure Care; Complications; 2. 'IV Catheterization Supply List' that provides a summary of supplies needed and 3. 'IV Catheterization Procedure Summary' that concisely provides steps of IV placement. Dr. Weiner is in the process of finalizing written pre and post IV catheterization tests.

*Dr. Weiner has met with the Boston Children's Hospital IV Team Educator Paula Lamagna, RN who enthusiastically supports the project. She has provided Dr. Weiner with a copy of the written IV catheterization procedure test that she created and uses for teaching. Dr. Weiner and Paula Lamagna are discussing the possibility of her participating in trainee testing of the device.

* beginning of new Specific Aim 3 for period to Sept. 30, 2013

Once this modified device prototype has been trialed and optimized based on feedback, the pilot validation study, which will test impact of the device on procedure competency as well as use and usability will be performed. Testing will be as previously described. Skills assessment to compare procedure performance using standard IV arm mannequin will be based on conventions used in simulation training, for which observers score participant performance of each task required for IV placement as not performed or performed incorrectly; performed correctly with minor deficiencies or errors; or performed correctly. Device use and usability will be assessed by survey and interview that will capture participant demographics; experience with simulation, mobile devices and video games; assessment of the platform, content and effectiveness of the

device as a teaching modality, as well as the mobile practice environment it provides.

The original plan to enroll 20 residents in the CHB ED for the validation study is being modified to include enrollment of pediatric residents on other rotations that provide opportunity for IV placement. Dr. Weiner is now collaborating with Boston Children's Hospital IV Team Educator Paula Lamagna, RN and Pediatric Chief Resident Catherine Distler, MD who are currently training and evaluating IV placement using an arm mannequin. Draft performance evaluation form, pre and post-procedure training tests and device use, usability evaluation forms that include content from the outline submitted with a prior progress report are in development, and will include suggestions by Paula. Lamagna and Dr. Distler based on their experience and forms they are using. Paula Lamagna and Dr. Distler are also reviewing the procedure training documents created by Dr. Weiner and submitted with the last progress report: 1. 'Intravenous Catheter Placement' that provides full details of the procedure including Pre-procedure: Indications, Contraindications, Supplies, Anatomy; Procedure: Patient/Family Preparation, Set-up, Patient/Caregiver/Provider Positions, Comfort/Distraction Measures, IV Placement, Troubleshooting; Post-procedure Care; Complications; 2. 'IV Catheterization Supply List' that provides a summary of supplies needed and 3. 'IV Catheterization Procedure Summary' that concisely provides steps of IV placement. The IRB will be amended with submission of the upcoming continuing renewal due 12/10/13.

* end of new Specific Aim 3 material for period to Sept. 30, 2013

* beginning of new Specific Aim 3 material for period to Mar. 31. 2014

Dr. Weiner has presented her proposed study to her IPSS PIV group and as well to the instructor and colleagues of simulation research course offered by the Boston Children's Hospital Simulation Center that she is taking and of which she has completed 2 of the 6 half day sessions. She has received very favorable feedback from both groups regarding study designs, outcome measures, methods, with a recommendation that half of the participants be randomized to training with the IV arm first and the other half to the handheld training device to control for possible effects that training on the arm first could have on performance using the handheld device. Dr. Weiner is in conversation with her statistician regarding this change and will make this modification if the statistician concurs.

* end of new Specific Aim 3 material for period to Mar. 31, 2014

* beginning of new Specific Aim 3 material for period to Sept. 30, 2014

To expedite testing Dr. Weiner and Paula Lamanga, with assistance from other IV team nurses and current pediatric chief residents Dr. Eric Zwemer and Dr. Jessica Creedon, will test eighteen nurses and twelve residents with limited IV experience who do not yet perform IV as part of their clinical practice but are in roles that include IV placement as within the scope of practice. Within the physician and nurse groups, participants will

randomly be assigned to training on IV arm or handheld training device. Each person will be graded on performance on both the arm and handheld device using standardized check list that has been reviewed and modified based on INSPIRE group recommendations, with Delphi review pending. All participants will complete pre and post test before and after the training modality they learn with first, then after the second modality will have the opportunity to correct any incorrect answers from pre and post tests. Participants will complete the use, usability, effectiveness survey after training on both arm and handheld device. Questions have been added to the survey that will allow comparison of training modalities handheld simulation, arm, patient simulation, patient. We will request that all participants attempt a minimum of 3 IVs in the 3 months after training for the purpose of this study, but recognize that many will not have/take the opportunity to perform that number of Ivs. Attempts and outcome of attempts will be reported.

* end of new Specific Aim 3 material for period to Sept. 30, 2014

* beginning of new Specific Aim 3 material for period to Mar. 31, 2015

Based on further consultation with the Instructor of the Boston Children's Hospital Simulation Center simulation research course that Dr. Weiner completed since the last progress report, with INSPIRE simulation experts and with the statistician for this project, Drs Weiner and Ottensmeyer have strength the study design. Rather than 20 participants each training and being evaluated on both a mannequin arm and the handheld simulation training device in immediate sequence with randomization to which they used first, 42 participants, will be randomized to training with either the mannequin arm or handheld simulation device, 21 participants per group. Duration of participant reporting of patient IV placement/attempts as part of routine clinical practice will be increased from 2-4 weeks to a maximum of 3 month until successful placement of IV in 3 patients. A 3 month knowledge post test has been added. Immediately after taking the 3 month test, participants randomized to the mannequin arm will have the opportunity to trial the handheld simulation training device; and comment on it's use, usability and effectiveness compared to the IV arm; and report whether its use provided information that would have improved their performance on the 3 month test. The number of participants was increased to accommodate unmatched groups with power to detect a 25% difference in knowledge and skills performance between mannequin arm and handheld simulation training device. Each group will have both nurses and pediatric residents. Provider IV placement report forms have been created. Use, usability and effectiveness surveys and consents have been modified for the new study design.

* end of new Specific Aim 3 material for period to Mar. 31, 2015

* beginning of new Specific Aim 3 material for period to Sept. 30, 2015

As mentioned above in the context of fabricating new gel blocks, a small number of nurses evaluated the needle insertion characteristics using then new glycerol-based gelatin and found it to be generally acceptable. Needle puncture forces and friction of

needle passage were both sufficiently realistic. The palpable ridge that was provided over the vessel was requested to be removed as it made location of the vessel too obvious.

A second set of blocks without the ridge was fabricated and evaluated by Dr. Weiner. These blocks varied the gelatin concentration within the vessel lumen from less than that of the surrounding "tissue" to double the concentration, again to enhance the palpability of the vessel. Increased concentration was found to be unrealistic – the vessel should not provide increased resistance as the user presses down harder on it – it should collapse. The lower concentration versions were found to be more realistic, however additional testing will be necessary.

Validation testing has begun. Thus far 10 RNs have enrolled and completed training using the mannequin arm. Dr. Weiner worked with Paula Lamagna to integrate the validation study into the ~3 hour Hospital IV training workshop required for all RNs prior to placing IVs at BCH. Workshops typically have 10-12 participants with enrollment of ~50% at each of 2 workshops. At the beginning of the workshop Dr. Weiner describes the study. Those who volunteered to participate completed a consent form; a survey regarding demographics, relevant previous experience with simulation, mobile devices and video games; and a pre-test. Participants received the standard workshop lecture didactics, and performed IV placement on a mannequin arm. Their performance was assessed by Dr. Weiner and Paula Lamagna using the PIV catheterization evaluation form developed for the study that grades learners on pre-procedure knowledge, pre-procedure preparation and procedure performance. Participants then completed a post-test and a survey to assess content and effectiveness of the training didactics and training device as a teaching modality. They have been asked to track IV performance over the 3 months following training and to complete a 3 month post test.

* end of new Specific Aim 3 material for period to Sept. 30, 2015

* beginning of new Specific Aim 3 material for period to Mar 31, 2016

Education, testing using control IV arm is in progress. Validation testing of handheld device will begin once prototype is rebuilt.

* end of new Specific Aim 3 material for period to Mar. 31, 2016

* beginning of new Specific Aim 3 material for period to Sept. 30, 2016

Rebuilding of the prototype took longer than expected due to demands of other projects. The work is now complete and the final user testing can proceed. Results will be presented in conjunction with the following phase of the work.

Education, testing using control IV arm is complete for RNs and is in progress for MDs. Final validation testing of handheld device can now be completed.

*end of new Specific Aim 3 material for period to Sept. 30, 2016

III. Issues Encountered and/or Concerns: Include any important modifications to the original plans.

Dr. Weiner and Dr. Ottensmeyer continue to pursue this project pro bono, and while demands of other research, clinical and administrative obligations have slowed progress, *both are now able to dedicate more time to this project.

*We have an extension to the funding through 12/10/13. This will permit device completion and conduct user testing as proposed.

* beginning of new issues for period to Mar. 31, 2014

The current completion date is 12/31/14.

* end of new issues for period to Mar. 31, 2014

* beginning of new issues for period to Sept. 30, 2014

User testing was delayed because of another BCH IV training study recruiting the same physician participants this study will recruit. That study has now been completed, which eliminates competition for participants. Physicians who remain novice despite participation in that study, as well as those who did not participate in that study, will be recruited for this study. The study was further delayed by the opportunity for consensus review of procedure check list, pre and post test questionnaire and use, usability, effectiveness by Dr. Weiner's INSPIRE PIV group formed during Q1 2014. NCE has been requested for extension through June 30, 2014.

While the installation of the back-up circuit boards has resolved some of the performance issues that detracted from consistent performance of the system, the electrodes have degraded over the time since original construction. We will make the best use of the system as is until we can revise the design and materials selection in phase II.

* end of new issues for period to Sept. 30, 2014

* beginning of new issues for period to Mar. 31, 2015

The current completion date is 6/30/15. Given increased sample size and increase in duration of IV placement performance monitoring to 3 months, completion date will likely need extension to at least Sept 30, 2015.

* end of new issues for period to Mar. 31, 2015

* beginning of new issues for period to Sept. 30, 2015

Dr. Ottensmeyer's time has been severely constrained due to the requirements of a major CIMIT-associated project (Advanced Modular Manikin), so he has had limited availability to advance the program. He hopes to have more flexibility in the next half-year.

Dr. Weiner's time was unexpectedly limited by the death of her father during the summer. She now has more time.

Cost of developing handheld simulation devices limits the number that can/should be built especially given plans for significant modification as part of continued development for our funded next phase study. This will limit the number of participants who we will be able to simultaneously test using the device, and will likely prolong the testing phase.

We remain intensely committed to the project and are very appreciative of continued support.

* end of new issues for period to Sept. 30, 2015

* beginning of new issues for period to Mar 31, 2016

Dr. Weiner has continued to develop the teaching content that forms the basis of the tablet

As of February Drs. Ottensmeyer and Weiner time have been able to renew their focus on this project and are working towards the final user testing of the prototype. Current completion date is Sept 30, 2016.

Thank you for your continued support.

* end of new issues for period to Mar. 31, 2016

* beginning of new issues for period to Sept, 2016

No new issues to report beyond limited time to devote to the program. Additional reporting of results will be made in conjunction with reporting for 14-1898.
We are committed to completion of the project and appreciate your patience and support.

* end of new issues for period to Mar. Sept, 2016

IV. Next Steps and Future Plans: Describe upcoming plans to accomplish your aims and milestones as described above and to continue this work towards achieving patient impact.

The documents submitted as part of this progress report, along with the existing

video will be reviewed by Paula Lamagna. Dr. Weiner will create a written pre and post procedure training tests and a procedure grading checklist for investigators to evaluate students that will Paula Lamagna will also review. Paula Lamagna and Dr. Weiner will continue to discuss the possibility of her assuming a role in testing the device. If Paula Lamagna is to going to involved in testing, she will complete human subjects training and IRB approval will be obtained to add her to the protocol.

*The new versions of didactic content being assembled by Dr. Weiner will be implemented in the app by Dr. Ottensmeyer. The revisions to the circuitry described above will be completed and implemented for use in testing. Block calibration will be performed and the updated relations between sensor voltages and x/y/z needle tip positions implemented in the App code.

* beginning of next steps and future plans for period to Sept. 30, 2013

As described, the latest algorithm for accurate location of the needle tip within the gel block is being integrated into the app. This is planned for completion as soon as possible, to support testing to be conducted by Dr. Weiner and colleagues at Children's. Once complete, a series of gel blocks with straight vessel segments will be fabricated using the current gel recipe, for use in that testing; additional molds as described in previous reports will be prepared via 3D printing so that blocks can be fabricated in parallel, rather than sequentially.

* end of new next steps and future plans for period to Sept. 30, 2013

* beginning of next steps and future plans for period to Mar. 31. 2014

While the current tracking system is not completely stable, it can be used for testing purposes, and evaluation of the physical characteristics of the vessel-embedded block can be conducted. The plans for testing described previously will be conducted during the next reporting period, towards collection of data and preparation of manuscripts describing the various aspects of the program.

Dr. Weiner plans to work with her simulation research course group and IPSS PIV team to develop a next step multicenter trial of the handheld device and to apply for funding for the trial.

* end of next steps and future plans for period to Mar. 31, 2014

* beginning of next steps and future plans for period to Sept. 30. 2014

Procedure checklist, pre and post knowledge tests, and use, usability and effectiveness survey will be finalized. Dr. Weiner will submit IRB amendments for modifications to checklists, tests, survey and study design, and will submit continuing renewal due 12/4/14. Testing will be initiated.

As mentioned above, the Betadyne/antiseptic application test will be modified, and a new equipment selection exercise will be added to the app.

The current standard operating procedure for cleansing the skin around the IV insertion site is to scrub back and forth instead of in a circular pattern. We will revise the existing test to detect whether the complete area around the puncture site (on a graphical image thereof) has been scrubbed (by rubbing the user's finger over the image in the right area). It may be possible to create a metric to evaluate whether the motion is predominantly aligned in one direction or remains in a mostly circular path, which would permit feedback to the user either to affirm correct technique or remind the user what that technique is should the not use it.

In the current app, a text panel and an image provide information on necessary equipment for IV cannulation. We will be creating a new exercise in which an array of images of needles, gauze, bandages and other relevant equipment is presented and the trainee will need to correctly select all of the essential equipment, not select any irrelevant equipment, and optionally select optional equipment. The code for this exercise will likely be based on the existing code for the tourniquet application sequence test – the sequence will not be important, but tracking which images have and have not been selected will be reused.

* end of new next steps and future plans for period to Sept. 30, 2014

* beginning of new next steps and future plans for period to Mar. 31, 2015

The handheld device learning module is being updated to incorporate the new content and tests for skin cleansing and IV supplies that have been created and are described in Specific Aim 2. Validation testing, using the new study design, tests, questionnaires and reporting forms described in Specific Aim 3, is about to begin.

* end of new next steps and future plans for period to Mar. 31, 2015

* beginning of new next steps and future plans for period to Sept. 30, 2015

Next steps detailed in Specific Aims 1, 2, 3 will be completed to yield a handheld simulation device with training module for validation testing of 21 providers that include RNs and MDs. Testing of 11 MDs using the control arm will be performed.

IRB continuing renewal due 11/23/15 will be submitted.

Although not formally part of this grant, we continue to work with the INSPIRE group on finalizing Delphi review of the PIV procedure checklist for dissemination as an International Pediatric Simulation Society standard for PIV placement.

* end of new next steps and future plans for period to Sept. 30, 2015

* beginning of new next steps and future plans for period to Mar. 31, 2016

With the implementation of the new content, Dr. Weiner will review and make recommendations for final updates to the app, which will be made by Dr. Ottensmeyer. Ottensmeyer will confirm calibration of the haptic block and prepare the series of glycerin-based gelatin blocks that were fabricated in 2015 for user testing. Following that testing, we will complete and submit the final report and continue with the next phase of the work that has already begun.

* end of new next steps and future plans for period to Mar. 31, 2016

* beginning of new next steps and future plans for period to Sept. 30, 2016

Upon completion of the new haptic unit and recreation of the user interface, the device will be testing in 21 MD, RN users as planned. Control group testing will be completed.

IRB continuing renewal due 11/9/16 will be submitted.

Dr. Weiner will present a project update at the International Pediatric Simulation Society (IPSS) INSPIRE meeting at the International Medical for Simulation in Healthcare (IMSH) Conference January 2017, Orlando, FL. The update will include results of the Dephi review and finalization of the IV procedure checklist for IPSS that Dr. Weiner developed as the INSPIRE IV team subgroup leader, based on the work of this grant.

Given tremendous interest and need within our hospital, as well as diverse healthcare settings nationally and internationally, we will seek funding opportunities to use the handheld high fidelity simulation system we have created to improve IV skills for and safety of IV placement with the goal of expediting care, decreasing complications, increase access to care and decrease costs. We have been speaking with AAP and IPSS colleagues, as well as BCH Global Health Program colleagues in the recently restructured and greatly expanded BCH Global Health Program.

The new content presented as this program concludes will serve as the basis for the content used in the 14-1898 program.

* end of new next steps and future plans for period to Sept. 30, 2016

V. Presentations:

A presentation of the system, carefully ensuring that disclosure of the underlying technology was not revealed, was made at the 4th International Pediatric Simulation Symposia and Workshops, Handheld Simulation Procedure Training Device, October, 28, 2011, Toulouse, France (please see publications below).

* beginning of new presentations for period to Mar. 31, 2014

In response to an invitation from the IPSS INSPIRE group, a presentation consisting of slides and video of the training system, was made by Drs. Weiner and Ottensmeyer, at the International Meeting on Simulation in Healthcare. Simulation Training For IV Catheterization. January 24, 2014, San Francisco, CA. The presentation was via Skype since neither investigator could attend. The tracking technology was not described in detail and not functionally demonstrated. The presentation garnered enthusiastic praise for the device and generated interest in the PIV procedure group, which was formally established and had its first group meeting that day, led by Dr. Weiner. Presentation slides and video are available on request.

* end of new presentations for period to Mar. 31, 2014

* beginning of new presentations for period to Sept. 30, 2014

The work was presented at the Military Health Systems Research Symposium, Fort Lauderdale, FL as a poster presentation with 5 minute talk at poster. 8/19/14. A provisional patent was filed prior to the presentation.

* end of new presentations for period to Sept 30, 2014

* beginning of new presentations for period to Mar. 31, 2015

An update on development of the PIV procedure teaching module and performance checklists was given on Dr. Weiner and Ottensmeyer,'s behalf by Dr. Donna Moro-Southerland, who is Dr. Weiner's INSPIRE PIV group co-leader, at the International Meeting on Simulation in Healthcare (IMSH). Simulation Training For IV Catheterization. January 24, 2015, New Orleans, LA.

* end presentation for period to Mar. 31, 2015

* beginning of new presentations for period to Sept. 30, 2015

An update on the project was presented at the International Pediatric Simulation Symposia and Workshops, Vancouver, CA as a talk to the INSPIRE Procedure group on May 3, 2015, and as poster with a 5 min talk at poster on May 6, 2015.

* end of new presentations for period to Sept. 30, 2015

*beginning of new presentations for period to Mar 31, 2016

No new presentations.

* end of new presentations for period to Mar. 31, 2016

*beginning of new presentations for period to Sept. 30, 2016

Based on the work of this grant, Dr. Weiner was invited to be the lead content author for an American Academy of Pediatrics video on peripheral intravenous access. Dr. Weiner has submitted her content and the video is currently in production.

* end of new presentations for period to Sept. 30, 2016

VI. Publications: Please mark updates and new entries with an asterisk*. If it is easier to provide the Pubmed link, please feel free to include it rather than the citation.

Weiner, DL, Ottensmeyer M. Handheld Simulation Procedure Training Device: An In-a-Box Solution, An out-of-the-Box Approach, A Small Form, Big Advance In Simulation Training. Abstract. International Pediatric Simulation Symposia and Workshops. Oct 28, 2011.

Weiner DL, Ottensmeyer M. Handheld Procedure Training: An In-a-Box Solution, An out-of-the-Box Approach, A Healthcare Paradigm Shift. Military Health Systems Research Symposium, Fort Lauderdale, FL. Abstract. Aug 19, 2014.

Weiner DL, Ottensmeyer M. Handheld Procedure Training: An In-a-Box Solution, An out-of-the-Box Approach, A Healthcare Paradigm Shift. International Pediatric Simulation Symposia and Workshops, Vancouver, CA. May 6, 2015.

VII. Enabled Funding: Funding received for the continuation or expansion of this research. Please include the Award PI, Title, Sponsor, Award ID, Total Budget for Project Period.

None. Funding opportunities are being sought and will be pursued for faculty salary support that would expedite the work of this project by decreasing clinical and administrative obligations of PI and by allowing co-PI to elevate the priority this project. Funding would also allow the investigators to continue development beyond the scope of this project to include, not only other procedures for clinicians, but also for patients and family members. Funding will also allow development for other platforms, in particular iPad/iPhone/iPod. Development of this device is increasingly important for improving quality and safety of care delivered by clinicians, as well as to decrease hospital length of stay, improve patient/family understanding of, compliance with, and decrease complications from, procedures they are required to perform at home. More universal ownership of/access to smart phones, tablets, iPhones, iPods, iPads has increased feasibility of handheld device procedure training for home care.

* beginning of new enabled funding for period to Sept. 30, 2013

Based on the experience developed in using gelatin and agar as thermoreversible gel with material properties somewhat akin to living tissue, Dr. Ottensmeyer proposed, for the CIMIT Boston Simulation Consortium 10k competition, the development of a 3D rapid prototyping system that would make use of such materials. The program intends to adapt an existing hobbyist-scale RP machine, through the replacement of the normal plastic filament extruding “print head”, with a temperature controlled gel melter/extruder system. Various materials, including different concentrations of gelatin, agar and carrageenan will be studied to determine their mechanical and thermal properties. The proposal was accepted for funding, and at present, two Harvard SEAS students have chosen elements of the project as their senior thesis topics. They have submitted pre-proposals to their supervisors, and will be meeting with Dr. Ottensmeyer to complete full, extended proposals for early October.

Other funding opportunities are being sought and will be pursued for faculty salary support that would expedite the work of this project by decreasing clinical and administrative obligations of PI and by allowing co-PI to elevate the priority this project. Dr. Weiner and Dr. Ottensmeyer were invited by CIMIT to apply for possible follow-on funding and submitted an application that would allow for 1. development of 1. improved fidelity of the haptic block by using 3D printing to create more realistic anatomy that includes anatomic variants, and further improvement in the speed of visual representation of needle insertion on the portable device, 2 enhancement of the procedure training module to include use of vein finder and ultrasound assisted vascular access, and further development of software that captures use, usability and performance, documents competency, and enables use of iOS platforms in addition to android platform currently in use, and 3.proof-of-concept testing of the enhanced haptic block and Android, iOS platforms by observer evaluation of user performance and user report of use, usability and procedure training effectiveness.

Funding will also be sought to allow the investigators to continue development beyond the scope of IV catheterization based projects to include, not only other procedures for clinicians, but also for patients and family members. Development of this device is increasingly important for improving quality and safety of care delivered by clinicians, as well as to decrease hospital length of stay, improve patient/family understanding of /compliance with, and decrease complications from, procedures they are required to perform at home. More universal ownership of/access to smart phones, tablets, iPhones, iPods, iPads has increased feasibility of handheld device procedure training for home care.

* end of new enabled funding for period to Sept. 30, 2013

* beginning of new enabled funding for period to Mar. 31, 2014

Follow-on funding from DOD’s JWMRP program through CIMIT, as detailed in our

last progress report, was awarded. Start date is Apr. 1, 2014. This will enable complete revision of the circuitry, taking advantage of all lessons learned and more extensive user studies. It will also enable the addition of features including vein-finding, as an add-on to the smartphone/tablet device, porting of the software to other platforms including iOS, and features that capture more data from a scenario, including pre-and post-use survey data.

Dr. Weiner is in the initial phase of developing the text for vein finder and ultrasound assisted vascular access that is part of specific aim 2. The content will be reviewed by local experts in use of these techniques and the INSPIRE PIV Group, Dr. Weiner is consulting with simulation experts at BCH and the INSPIRE PIV Group regarding her proposed study design for proof-of-concept testing proposed as part of specific aim 3.

* end of new enable funding for period to Mar. 31, 2014

* beginning of new enabled funding for period to Sept. 30, 2014

Formal initiation of grant from DOD's JWMRP program through CIMIT initiation has been delayed because protected time for Dr. Weiner to work on the project is contingent on a minimum of 30% funding, which Dr. Weiner now has. With 30% funding her Division Chief will allow her to reduce her clinical time by 20% (not 30%) as of Jan. 1, 2015.

Dr. Ottensmeyer's effort levels are nearly fully obligated to two US Army contracts through February, so he will be unable to participate at the originally budgeted level, however after February, he will increase his effort level. In addition, Dr. Ottensmeyer has hired a new post-doctoral research fellow trained as a mechanical engineer, who will be starting in February. He may be tasked with certain elements of the hardware and software redesign and development of the new features planned for the JWMRP funding.

Dr. Weiner has completed text for ultrasound assisted vascular access that is part of specific aim 2. The content has been reviewed by local experts. It has been incorporated into PIV procedure training checklist for proof-of-concept multicenter testing proposed in the JWMRP grant. The ultrasound content will be reviewed by the INSPIRE PIV Group and Dr. Weiner is working with simulation experts at BCH and the INSPIRE PIV Group on study logistics. An IRB for this study will be submitted in the next 30 days.

* end of new enabled funding for period to Sept. 30, 2014

* beginning of new enabled funding for period to Mar. 31, 2015

Funding for the DOD JWMRP grant began March 19, 2015. The goal of the grant is to improve and enhance form and function of the current handheld simulation

procedure training device. Haptic block fidelity will be improved. Infrared and ultrasound assisted IV placement capability will be developed and supporting learning resources created. Performance steps for US assisted vascular access, reviewed locally during the previous reporting period are currently undergoing Delphi review by the INSPIRE PIV group. Study design for proof-of-concept testing of infrared, ultrasound assist enabled handheld training device for IV placement has been determined in consultation with the BCH Simulation Center research experts, the INSPIRE PIV group, and the statistician for the project. BCH IRB submission for this grant was in the form of an amendment to the IRB for the grant that is the subject of this progress report. The amendment was approved 2/24/15.

* end of new enabled funding for period to Mar. 31, 2015

* beginning of new enabled funding for period to Sept. 30, 2015

No new funding since last report. Due to the lack of availability of the SimGroup team, efforts on the new grant have not yet been initiated beyond early planning meetings.

* end of new enabled funding for period to Sept. 30, 2015

*beginning of new enabled funding for period to Mar 31, 2016

No new enabled funding. The JWMRP funding for the Simulation Group was activated on 2/17/2016 and we will be conducting an accelerated effort to proceed through the follow-on phase of work, ideally to complete it in substantially less than the original year by increasing the effort levels of the personnel involved.

* end of new enabled funding for period to Mar. 31, 2016

*beginning of new enabled funding for period to Sept. 30, 2016

No new enabled funding.

No new enabled funding. The JWMRP funding for the Simulation Group was activated on 2/17/2016 and progress will be reported separately.

* end of new enabled funding for period to Sept. 30, 2016

VIII. Patent Disclosures and Filings: Please include the Stage, Inventors, Title, Assignee, Status, Application/Patent Number and Date Filed. Please mark updates and new entries with an asterisk *.

Discussions regarding copyright and opportunities for patenting, licensing are ongoing with the Innovation Technology Offices at Children's Hospital Boston and Massachusetts General Hospital. A meeting was held at BCH with RVL and TIDO in mid-November, 2011. Discussions will be reinitiated once the prototype has been

tested.

* beginning of new patent disclosures and filing for period to Mar. 31, 2014

Progress on preparation of the invention disclosure was static during this reporting period. We will reinitiate it during the next period, now that a more complete software architecture has been established.

* end of new patent disclosures and filing for period to Mar. 31, 2014

* beginning of new patent disclosures and filing for period to Sept. 30, 2014

A provisional patent was filed by MGH Aug. 18, 2014.
Stage: Provisional
Inventors: Debra Weiner, Mark Ottensmeyer, Ryan Scott Bardsley
Title: Needle Tube Insertion Training Systems and Methods
Status: Pending
Application/Patent Number: 62038591
Date Filed: Aug. 18, 2014

* end of new patent disclosures and filing for period to Sept. 30, 2014

* beginning of new patent disclosures and filing for period to Mar. 31, 2015

Data from upcoming testing will be used to support the provisional patent filed Aug. 18, 2014.

* end of new patent disclosures and filing for period to Mar. 31, 2015

* beginning of new patent disclosures and filing for period to Sept. 30, 2015

The provisional patent filed Aug. 18, 2014 was converted to a PCT patent and filed by MGH Aug. 18, 2015.
Stage: Patent
Inventors: Mark Ottensmeyer, Debra Weiner
Title: System and Methods for a Haptic Medical Simulation Device
Status: Pending
Application/Patent Number: MGH22962, Q&B File 125141.01375
Date Filed: Aug. 18, 2015

* end of new patent disclosures and filing for period to Sept. 30, 2015

*beginning of new patent disclosures for period to Mar 31, 2016

No patent updates, no new patents.

* end of new patent disclosures for period to Mar. 31, 2016

*beginning of new patent disclosures for period to Sept. 30, 2016

No patent updates, no new patents.

* end of new patent disclosures for period to Sept. 30, 2016

IX. Technology Readiness Level: Assess the stage of development that best describes your solution at this current time.

4	Please enter a value between 2 and 10

*Prototype has been tested by PI, RNs to validate simulation of skin, final minor modifications are nearly complete. Plan is to evaluate usability and effectiveness of prototype for IV catheterization for trainees beginning July 2013.

* beginning of new technology readiness level for period to Sept. 30, 2013

TRL will increase to level 4 following completion of implementation of the tetrahedral walking algorithm

* end of new technology readiness material for period to Sept. 30, 2013

* beginning of new technology readiness for period to Mar. 31, 2014

As described in the earlier period, implementation of the Tet-walking algorithm advances brings us to the level of a validated system in the laboratory environment. We will reach level 5 following user testing in the next reporting period. In the program that follows this one, with newly approved funding, we expect to take the system with its current functionality to level 5 or 6, and add new elements that will initially be in earlier TRL levels.

* end of new technology readiness for period to Mar. 31, 2014

* beginning of new technology readiness for period to Sept. 30, 2014

The development work performed was primarily in the form of repairs and minor improvements. As user testing remains pending, the readiness level remains at 4.

* end of new technology readiness for period to Sept. 30, 2014

* beginning of new technology readiness for period to Mar. 31, 2015

The development work performed was primarily in the form of revisions related to Specific Aims 2 and 3. User testing is about to begin. The readiness level remains

at 4.

* end of new technology readiness for period to Mar. 31, 2015

* beginning of new technology readiness for period to Sept. 30, 2015

Control testing using IV mannequin arm is in progress. Device testing is about to begin. The readiness level remains at 4.

* end of new technology readiness for period to Sept. 30, 2015

*beginning of new technology readiness for period to Mar 31, 2016

The readiness level remains at 4, and will rise to 5 following user testing.

* end of new technology readiness for period to Mar. 31, 2016

*beginning of new technology readiness for period to Sept 30, 2016

The readiness level remains at 4, and will rise to 5 following user testing.

* end of new technology readiness for period to Sept. 30, 2016

Intravenous Catheter Placement

IV Catheter Placement Supplies

Local anesthetics

Tip: Topical anesthetics require 20-60 minutes for onset of action. The need for preparation of multiple IV sites may limit use of topical anesthetics. Intradermal lidocaine, has 60-90 sec onset of action

Blood Collection Supplies

Tip: 3mL syringe is appropriate for most patients. Larger syringes increase turbulent flow, increase hemolysis. Consider 1-mL syringe for neonates, small infants. Negative pressure created by larger syringes may collapse vein, impede blood flow.

Tourniquet

Tip: For a hand or foot vein in a neonate, flexing the wrist or extending the ankle and encircling the extremity with your hand, may obviate the need for a tourniquet. For a scalp vein, a rubber band around the head inferior to the vein can be used as a tourniquet

PROCEDURE

Preperation

Explain procedure

Tip: Avoid terms that may cause anxiety in children. Details of what the child will feel can be explained to the child during the procedure.

Consent

Tip: Discuss pain, bruising, infiltration, infection, inflammation

Prepare supplies

Tip: Preparing supplies out of view of the patient may minimize their anxiety.

Tip: If drawing blood, attach empty syringe to extension tubing, and attach injection cap to syringe with normal saline. If only flushing IV, connect syringe with injection cap to extension tubing, fill tubing with saline.

Comforts, distraction

Tip: Stuffed animial, child's own blanket, music, book, television, videos and games on tablet, smartphone,

Positioning, vein identification

Position patient, parents

Tip: Position parent so that the child can see them. Parents who do not want to watch should be positioned out of the line of sight of the procedure, and given the option of leaving the room. If possible parents should not be responsible for immobilizing their child and should never immobilize the intended IV site extremity.

Position assistant, child life

Tip: For arm or hand vein, have assistant immobilize shoulder and elbow. For ankle or foot vein, have assistant immobilize hips and knees. Position child life specialist near head to engage child and block their line of sight.

Vein selection

Tip: Enhance visualization with LED trans illuminator palm of hand, plantar surface of foot to illuminate dorsum, infrared light held several cm above arm, hand, ankle or foot or ultrasound for arm veins.

Tourniquet placement
Tip: Gauze placed under the tied part of the tourniquet can prevent the tourniquet from pinching the skin.

Tip: Untie and retie the tourniquet if it has been on more than a few min to identify a vein and/or after an unsuccessful attempt, before attempting/reattempting IV placement. Prolonged tourniqueting compromises distal blood flow and makes the vein more fragile.

Skin Cleansing
Tip: Pinch wings of applicator to crack ampule, position sponge on skin and press until fluid visible on skin.

Lidocaine Jet injection
Tip: J-Tip manufacturer recommends using end of J-Tip to mark intended IV site, pulling skin so J-Tip mark is adjacent to vein, injecting vein, then releasing skin so anesthetized skin is over vein. (link)

Tip: Inform patient and family that during injection they will hear a pop, then hissing similar to opening a soda can.

Angiocatheter Placement
Traction
Tip: Avoid placing too much traction on the skin. Traction may flatten the vein and make access more challenging, decrease likelihood of flashback when vein is entered, and increase risk of going through the deep wall of the vein.

Inserting Angiocather
Tip: Inserting the angiocatheter too slowly and gently may compress the vein increasing the likelihood of going through the deep wall. Once the angiocatheter is through the skin, short deliberate movements to penetrate the vessel may minimize vein compression.

Remove Needle
Tip: Place gauze under the hub of the needle prior to removing needle to absorb blood that drips from the hub.

Secure IV
Immobilization
Tip: To minimize amount of tape in direct contact with the skin and prevent tape from constricting the vessel, when using an immobilization board, place tape (sticky side to sticky side) or gauze on the part of the tape that faces that child's skin.

IV Catheter Placement Procedure Summary

INDICATIONS

To obtain blood

To administer

- Fluids
- Medications
- Contrast dye
- Blood products

CONTRAINDICATIONS

Absolute Contraindications

- Cellulitis, abscess overlying skin
- Fracture or significant soft tissue injury of the extremity
- Phlebitis, thrombosis of vein

Relative Contraindications

- Burn overlying skin
- Poorly perfused extremity
- Extremity edema
- Bleeding diathesis

ANATOMY (link)

- **Veins** -thin-walled, distensible, compressible soft, spongy
- **Arteries** thicker walled than veins, less distensible, less compressible, pulsatile
- **Tendons** firmer, flatter than veins, arteries, not compressible, distensible

Preferred sites

- Antecubital fossa, forearm-basilic, cephalic, cubital veins
- Hand dorsum-branches basilic, cephalic veins
- Ankle, foot-if nonambulatory, sensation intact-saphenous vein anterior to medial malleolus, branches saphenous dorsum foot
- Scalp-neonate, young infant unable to roll if veins visible-frontal, temporal, and posterior auricular

SUPPLIES (link)

IV Catheter Placement Supplies

- **Nonsterile gloves**, latex-free, consider eyewear, mask *UNIVERSAL PRECAUTIONS*
- **Local anesthetics** Table Tip
  - **Synera®, LMX4®, EMLA®.**
  - **Lidocaine 1% solution,** preferably buffered **+/- J-Tip or** powdered lidocaine in J-Tip (link)
- **Analgesia-if < 6 mo, sucrose 24% (Toot-Sweet, Sweet-Ease)**
- **Tourniquet** Tip
- **Heat pack**
- **Antiseptic-**70% **alcohol**, povidone-iodine (**PDI**®), chlorhexidine gluconate (**CloraPrep®)**
- **Angiocatheters (link)**
  - 22 gauge appropriate for most patients, situations
  - 24 gauge for neonates, small infants
  - 20 gauge for rapid fluid, blood administration, contrast dye, serial blood draws
- **Connector tubing**
- **Sterile injection cap**
- **Normal saline flush**

- **Transparent sterile occlusive dressing (Tegaderm™)**
- **Tape**-silk or paper
- **Gauze pads**, 2 or 4 inch
- **Immobilization board, sleeve,** optional

Blood Collection Supplies
- 1-, **3-, 5-**, 10 mL **syringe(s)** **Tip**
- 1 mL heparinized **blood gas syringe**
- **Specimen tube(s), blood culture bottle(s)**
- **Specimen labels**
- **Specimen bag(s)**
- **Pen**

IV Fluid, Medication Administration Supplies
- **IV administration kit**
- **Delivery pump**

PROCEDURE (link)

Preparation
- Explain procedure. **Tip**
- Obtain consent. **Tip**
- Order local anesthetic, analgesia**.**
- Prepare supplies. **Tip**
- Identify comforts, distractions. **Tip**
- Engage assistant, child life specialist.

Safety
- Hand hygiene.
- ***UNIVERSAL PRECAUTIONS*.**
- Confirm correct patient i.e. perform 'time out'.

Positioning, Vein Identification
- Position patient, parent(s). **Tip**
- Engage, position assistant, child life specialist. **Tip**

Vein Identification (if not previously done)
- Identify IV site by visualization, palpation. To dilate the vein apply tourniquet, warm packs, flick, tap, or rub with alcohol, place extremity in dependent position, have patient make fist to dilate hand, arm vein. (link) **Tip**

Tourniquet Placement (link)
- Slide tourniquet under extremity ≥ 3 cm proximal to intended IV site.
- Loosely wrap tourniquet ends around extremity positioning one end over the other.
- Pull each end taut, use index finger to create a loop in the top end.
- Tuck the loop under the part of the tourniquet encircling arm such that the free end is directed away from the IV site. **Tip**

Skin Cleansing (link)
- **Re-palpate vein if necessary to re-identify**.
- Cleanse area of intended insertion site.
  - **Alcohol**. Start at intended insertion site and proceed outward in a circular motion at least 3-4 cm diameter for 15 sec x 3 or swab 3-4 cm are over vein distal to proximal.
  - **Chlorhexidine-gluconate.** Scrub back and forth at least 3-4 cm for 30 sec. (link)
  - **Povidine-iodine.** Start at intended insertion site and proceed outward in a circular motion at least 3-4

cm diameter x 3. Wipe povidine-iodine off with alcohol.
- Allow the skin to air dry after each application.

Lidocaine J-Tip Injection (optional) (http://jtip.com/product_overview.html)

- Remove J-Tip orange cap and barrel safety.
- Select site of IV catheter injection. **Tip**
- Hold J-Tip 90° against the skin, depress activation lever, maintain skin contact 2-3 sec.
- Massage skin with sterile gauze.
- Use mark from injection as site of angiocatheter insertion. **Tip**

Angiocatheter Placement (link)
- **Remove** angiocatheter **protective sheath, inspect.**
- **Position needle** bevel up.
- **Position** hand over angiocatheter with **thumb, middle finger of dominant hand on either side of barrel** just proximal to hub.
- **Position index finger on push plate** at base of hub.
- **Apply** gentle **traction** to skin distal to insertion site. **Tip**
- **Insert angiocatheter** into skin **over or 0.5 to 1 cm distal to** the **vein** in a rapid smooth motion, entering at a **10- to 45° angle**, depending on perceived depth of vein. **Tip**
- Slowly **advance** angiocatheter to **penetrate** only the **near wall of the vein**.
- As soon as a **flashback** of blood is seen, **lessen the angle** of the angiocatheter so it is nearly parallel to the skin.
- **Advance** at most 1 to 3 mm.
- Hold the barrel of the angiocatheter, use index finger to **advance the catheter**, inserting to hub or w/in a few mm, **independent of the needle.**
- •**Occlude vessel** proximal to catheter.
- **Remove needle** while occluding vessel proximal to catheter. **Tip**
- **Activate** needle **safety mechanism** if not automatic.
- Apply clear occlusive dressing e.g. Tegaderm™ leaving hub accessible.
- If drawing blood, attach extension tubing to hub ± syringe.(see Blood Drawing, Flushing) If not drawing blood, apply injection cap to syringe with normal saline, attach to tubing, fill tubing with normal saline, then attach extension tubing to hub. (see Flushing)

Blood Drawing, Flushing (link)
- **Blood drawing + flushing**
  - Attach empty 1, 3 or 5 mL syringe to extension tubing if not already done.
  - Pull plunger back slowly to collect blood. **Tip**
  - Change syringes as needed to obtain required amount.
  - Loosen tourniquet.
  - Clamp tubing.
  - Remove syringe.
  - Attach injection cap to 10 mL syringe with normal saline
  - Attach syringe with injection cap to tubing
  - Unclamp tubing, infuse saline slowly, access flow, discomfort, edema.
  - Apply needleless transfer device to syringe(s) with blood**,** transfer blood to culture bottle then specimen tube(s), label.
  - Sign, date label(s).

- **Flushing only**
  - Unclamp tubing, infuse saline slowly, assess flow, discomfort, edema**.**
  - If good position verified, clamp tubing, remove syringe, apply injection cap if not previously applied.

Secure IV (link)
- Coil and tape tubing over occlusive dressing (Tegaderm™) leaving tubing end accessible.
- Apply immobilization board, sleeve or other protection. **Tip**

Clean up

- **Discard sharps** in designated container.

Documentation

- Document IV site, procedure details in medical record.

TROUBLESHOOTING

No flashback

Reposition angiocatheter by withdrawing so just the tip remains intradermal, re-advance using a systematic approach that readjusts depth and/or slight change in direction of the needle.

Flashback, no continued blood flow

If initial return of blood ceases, it is possible that the angiocatheter is no longer in the vessel. If it appears that the needle has gone through the vein, suggested by ballooning of the vessel and or ecchymosis, remove the needle, apply gauze, pressure, bandage.

Catheter not advancing

If catheter cannot be advanced once needle removed, it may be against the vessel wall or a valve. Withdraw catheter until blood flow improves, redirect at slightly different angle and/or flush by removing tourniquet and slowly infusing normal saline.

Artery cannulation

If an artery has been entered inadvertently, collect blood if needed, remove catheter, apply gauze, pressure, bandage.

Inadequate blood flow for sample collection

Remove tourniquet, have assistant repetitively squeeze the extremity proximal to the IV site.
Adjust catheter angle by slightly lifting up the hub.
Withdraw catheter 1-2 mm.
Change to a smaller syringe.
Remove syringe, allow blood to drip from tubing into uncapped specimen tubes. Exception blood culture.

Fluid not infusing or infusing with resistance

Check site for signs of infiltration ecchymosis, edema, tenderness, if infiltrate, remove IV
If no evidence infusion, adjust angle of catheter, reattempt, if unsuccessful, remove IV

INFUSION, OBTAINING BLOOD FROM EXISTING IV

Infusion of fluids, medications, blood products, contrast dyes

- Control the rate of infusion with the flow regulator on tubing of IV kit.
- Adjust the angle of the catheter if flow is slow.
- Check the IV site hourly. Warmth, tenderness erythema, cord

Obtaining blood from an existing IV

- If infusing, clamp tubing for > 1 minute.
- Clean IV cap with alcohol.
- Unclamp tubing.
- Use syringe to remove ideally 5 mL of blood to discard, use new syringe to draw specimen. Exception blood culture cannot be drawn off line.

If not using IV for infusing, flush line with 5 mL normal saline, clamp tubing. If infusing, resume.

COMPLICATIONS

- Pain
- Vasovagal syncope
- Nerve, tendon damage
- Hematoma
- Infiltration
- Infection
- Phlebitis, thrombosis, embolism

Table. Local Anesthetics, Analgesia

Anesthetics				
Agent	**Ingredient(s)**	**Time to Onset**	**Duration**	**Comments**
EMLA-cream		45-60 min	4 hr	
LMX-4-cream	Liposomal Lidocaine 4%	20-30 min	1 hr	
Synera-Patch	Lidocaine 70 mg Tetracaine 70 mg	20-30 min	3 hr	Apply immediately after opening, can not be on in MRI
Lidocaine-injectable	Lidocaine 1% buffered	60-90 sec	N/A	Popping, hissing with J-Tip
Analgesia				
Toot-Sweet, Sweet-Ease oral solution	Sucrose 24%	Few min	N/A	Age < 6 mo, pacifier or buccal mucosa

Adapted from Pesaturo, KA, Matthews, M. Topical Anesthesia Use in Children. US Pharm. 2009;34(3):HS-4-HS-7.