November 5, 2013

National Institutes of Health (NIH)
9000 Rockville Pike
Bethesda, Maryland 20892

Please accept the following R01 application titled, “Magnetic Guidance for Improved Cochlear-Implant Insertion,” in response to PA-13-302. This is a resubmission of R01 DC013168-01.

Please assign this application to the following:
   Institutes/Centers
       National Institute of Deafness and Other Communication Disorders - NIDCD
   Scientific Review Groups
       Bioengineering of Neuroscience, Vision and Low Vision Technologies - BNVT

The reason for this request is that the BNVT study section reviewed the initial submission of this proposal on 10/01/2012, with program contact Roger Miller. This research proposal involves the use of magnetic guidance method to reduce the trauma associated with the surgical insertion of cochlear-implant electrode arrays. The research will be conducted by a multidisciplinary team consisting of experts in the fields of medical robotics, magnetic manipulation, heat transfer, and otolaryngology and cochlear-implant surgery. The PI is an Early Stage Investigator.

All required documentation has been attached to the application. Thank you for your consideration.

Sincerely,

Jake Abbott
### SF 424 (R&R)

#### 1. TYPE OF SUBMISSION*
- ☐ Pre-application
- ☐ Application
- ● Changed/Corrected Application

#### 2. DATE SUBMITTED
- 2013-11-05

#### 5. APPLICANT INFORMATION
- **Legal Name**: University of Utah
- **Street1**: 75 South 2000 East
- **City**: Salt Lake City
- **State**: UT: Utah
- **ZIP / Postal Code**: 84112-8930

#### 8. TYPE OF APPLICATION*
- ☐ New
- ● Resubmission
- ☐ Renewal
- ☐ Continuation
- ☐ Revision

#### 9. NAME OF FEDERAL AGENCY*
- National Institutes of Health

#### 12. PROPOSED PROJECT
- **Start Date**: 07/15/2014
- **Ending Date**: 07/14/2019

#### 13. CONGRESSIONAL DISTRICTS OF APPLICANT
- UT-002

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**APPLICATION FOR FEDERAL ASSISTANCE**

- **Tracking Number**: GRANT11521489
- **Funding Opportunity Number**: PA-13-302
- **Received Date**: 2013-11-05T18:59:56.000-05:00

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**Organizational DUNS**: 009095365

- **Prefix**: First Name: BRENDA
- **First Name**: BRENDAR
- **Middle Name**: Maldonado
- **Last Name**: MALDONADO
- **Suffix**
- **Email**: brenda.maldonado@osp.utah.edu

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**Is this application being submitted to other agencies?**
- ☐ Yes
- ● No
- What other Agencies?

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**OMB Number**: 4040-0001
**Expiration Date**: 06/30/2016

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**CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER**

**PROPOSED PROJECT**

**DESCRIPTIVE TITLE OF APPLICANT’S PROJECT**

Magnetic Guidance for Improved Cochlear-Implant Insertion

---

**PERSON TO BE CONTACTED ON MATTERS INVOLVING THIS APPLICATION**

**Prefix**: BRENDA
**Position/Title**: Contracts Administrator
**Street1**: 1471 EAST FEDERAL WAY
**City**: SALT LAKE CITY
**State**: UT: Utah
**ZIP / Postal Code**: 84112-8930

**Phone Number**: 801-581-8019
**Fax Number**: 801-581-3007
**Email**: brenda.maldonado@osp.utah.edu
SF 424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION
Prefix: Dr.  First Name*: JAKE  Middle Name: J  Last Name*: ABBOTT  Suffix: 
Position/Title: Assistant Professor
Organization Name*: University of Utah
Department: MECHANICAL ENGINEERING
Division: COLLEGE OF ENGINEERING
Street1*: 50 CENTRAL CAMPUS DR RM 2110
Street2: 
City*: SALT LAKE CITY
County: SALT LAKE
State*: UT: Utah
Province: 
Country*: USA: UNITED STATES
ZIP / Postal Code*: 84112-9208
Phone Number*: 801/585-6672  Fax Number: 801-585-9826  Email*: jake.abbott@utah.edu

15. ESTIMATED PROJECT FUNDING
a. Total Federal Funds Requested* $1,842,850.00 
b. Total Non-Federal Funds* $0.00 
c. Total Federal & Non-Federal Funds* $1,842,850.00 
d. Estimated Program Income* $0.00

16. IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?*
a. YES ○ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:
   DATE: 
   b. NO ● PROGRAM IS NOT COVERED BY E.O. 12372; OR ○ PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)
* I agree*

* The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.

18. SFLLL or OTHER EXPLANATORY DOCUMENTATION
File Name: 

19. AUTHORIZED REPRESENTATIVE
Prefix:  First Name*: Brent  Middle Name:  Last Name*: Brown  Suffix: 
Position/Title*: Director
Organization Name*: University of Utah
Department: OFFICE OF SPONSORED PROJECTS
Division: VP FOR RESEARCH
Street1*: 75 South 2000 East
Street2: 
City*: Salt Lake City
County: Salt Lake
State*: UT: Utah
Province: 
Country*: USA: UNITED STATES
ZIP / Postal Code*: 84112-8930
Phone Number*: 801-581-6903  Fax Number: 801-585-5749  Email*: ospawards@osp.utah.edu

Signature of Authorized Representative* 
Brent Brown  Date Signed* 11/05/2013

20. PRE-APPLICATION
File Name: 

21. COVER LETTER ATTACHMENT
File Name: CoverLetter_Nov2013__2_1009467248.pdf
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### Project/Performance Site Location(s)

#### Project/Performance Site Primary Location

- **Organization Name:** UNIVERSITY OF UTAH
- **Duns Number:** 009095365
- **Street1:** 50 CENTRAL CAMPUS DR RM 137 KENN
- **City:** SALT LAKE CITY
- **County:** SALT LAKE
- **State:** UT: Utah
- **Province:** USA: UNITED STATES
- **Zip / Postal Code:** 84112-9208
- **Congressional District:** UT-002

#### Project/Performance Site Location 1

- **Organization Name:** University of Utah
- **DUNS Number:** 009095365
- **Street1:** 100 North Mario Capecchi Drive
- **City:** Salt Lake City
- **County:** Salt Lake
- **State:** UT: Utah
- **Province:** USA: UNITED STATES
- **Zip / Postal Code:** 84113-1103
- **Congressional District:** UT-002

#### Project/Performance Site Location 2

- **Organization Name:** The Vanderbilt University
- **DUNS Number:** 004413456
- **Street1:** 1400 18th Avenue South
- **City:** Nashville
- **County:**
- **State:** TN: Tennessee
- **Province:**
- **Country:** USA: UNITED STATES
- **Zip / Postal Code:** 37212-2809
- **Congressional District:** TN-005
Project/Performance Site Location 3

I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: Oregon Health & Science University
DUNS Number: 096997515
Street1*: 3181 SW Sam Jackson Park Road
Street2: City*: Portland
County:
State*: OR: Oregon
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: 97239-3098
Project/Performance Site Congressional District*: OR-001

Additional Location(s)
## RESEARCH & RELATED Other Project Information

1. **Are Human Subjects Involved?**  
   - **Yes**  
   - **No**  
   1.a. If YES to Human Subjects  
      Is the Project Exempt from Federal regulations?  
      - **Yes**  
      - **No**  
      If YES, check appropriate exemption number:  
      - 1  
      - 2  
      - 3  
      - 4  
      - 5  
      - 6  
      If NO, is the IRB review Pending?  
      - **Yes**  
      - **No**  
      IRB Approval Date:  
      Human Subject Assurance Number

2. **Are Vertebrate Animals Used?**  
   - **Yes**  
   - **No**  
   2.a. If YES to Vertebrate Animals  
      Is the IACUC review Pending?  
      - **Yes**  
      - **No**  
      IACUC Approval Date:  
      Animal Welfare Assurance Number  
      A3031-01

3. **Is proprietary/privileged information included in the application?**  
   - **Yes**  
   - **No**  

4.a. **Does this project have an actual or potential impact - positive or negative - on the environment?**  
   - **Yes**  
   - **No**  

4.b. If yes, please explain:  

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed?  

4.d. If yes, please explain:  

5. **Is the research performance site designated, or eligible to be designated, as a historic place?**  
   - **Yes**  
   - **No**  

5.a. If yes, please explain:

6. **Does this project involve activities outside the United States or partnership with international collaborators?**  
   - **Yes**  
   - **No**  

6.a. If yes, identify countries:  

6.b. Optional Explanation:

### Document References

7. **Project Summary/Abstract**  
   - Filename: ProjectSummary_Nov20131009467240.pdf

8. **Project Narrative**  
   - Filename: ProjectNarrative_Nov20131009467243.pdf

9. **Bibliography & References Cited**  
   - Filename: Bibliography_Nov20131009467244.pdf

10. **Facilities & Other Resources**  
    - Filename: Facilities_Nov20131009467245.pdf

11. **Equipment**
Project Summary

Approximately 25 million Americans suffer from sensorineural hearing loss, which is a condition where the cochlea is unable to convert sound into nerve impulses to the brain. A cochlear implant (CI) is an array of electrodes that is surgically inserted into the cochlea to electrically stimulate the nerves responsible for hearing. As the CI is inserted into the scala tympani, delicate intracochlear structures are often damaged, which can result in decreased implant effectiveness and loss of residual hearing, especially when the implant deviates into the adjacent scala vestibuli chamber via rupture of the basilar membrane, which occurs in approximately 33% of insertions. The goal of reducing surgical trauma is especially compelling given that electric acoustic stimulation, which is a relatively new treatment directed at individuals with a considerable amount of residual hearing in the low-frequency range, is receiving greater interest, but requires atraumatic insertions to preserve the patient’s residual hearing. The goal of this project is to demonstrate that magnetic guidance of CIs will reduce trauma relative to manual insertion. Magnetic guidance will be accomplished with an inexpensive clinical system, based on proven robotic and magnetic technologies developed by the investigators. In the proposed work, the investigators will pursue three specific aims: (1) They will test the conjecture that magnetic guidance will reduce insertion forces and forces against the basilar membrane compared to manual insertions, using a CI with a magnet embedded in the distal tip. Tasks include developing cochlear phantoms for experimentation, determining optimal placement of the magnetic manipulator relative to the patient, segmenting the patient’s scala tympani and registering it with respect to the magnetic manipulator and insertion device, developing magnetic-guidance algorithms for free-fitting and precurved CIs for both cochleostomy and round-window insertions, developing real-time force control to be combined with magnetic guidance for improved safety and robustness, and determining if high-frequency vibration of the CI provides additional benefits. (2) They will test the conjecture that the magnet can be safely removed after CI insertion, such that the patient would not be precluded from future MRI scans. Tasks include developing a method for magnet attachment/detachment to the CI, ensuring that the cochlea is not harmed due to heating during the detachment process, and developing a method to safely remove the magnet after detachment from the CI. (3) They will verify the methods developed in the first two aims in human cadaver temporal bones combined with micro CT scans, and in live guinea pigs combined with auditory brainstem response hearing tests and histology. This project is directly relevant to the mission of the NIDCD “to create devices which substitute for lost and impaired sensory and communication function.” More specifically, in the 2012–2016 NIDCD Strategic Plan, in the Priority Area of Hearing and Balance Research, Priority Area 3 includes improved interventions for hearing loss, including cochlear implants.
Project Narrative

Approximately 25 million Americans suffer from sensorineural hearing loss, which is a condition in which the cochlea is unable to convert sound into nerve impulses to the brain. A cochlear implant can be surgically inserted into the cochlea to electrically stimulate the nerves responsible for hearing, but trauma resulting from the surgical insertion can result in decreased implant effectiveness and loss of residual hearing. The goal of this project is to demonstrate that magnetic guidance of cochlear implants during surgical insertion will reduce trauma compared to traditional manual insertion.
Facilities & Other Resources

University of Utah

Dr. Abbott’s (PI) research lab
This space provides resources for design, programming, and evaluation of mechatronic systems and sensors. This space (over 1000 sq. ft.) is filled with computer workstations as well as typical tools and test equipment, such as oscilloscopes and an electronics prototyping station for basic assembly and debugging of electro-mechanical systems. Eight PC computers running Windows and Ubuntu Linux are available for design and analysis of mechatronic and robotic devices and dissemination of results. Standard desk space and office furniture is also available. The PI has an optical breadboard, four linear micromanipulation stages, one rotation stage, and additional components from Thorlabs that are useful for fast prototyping and experimentation. The PI has a number of CCD cameras for image capture. The PI also has a Kleindiek MM3A-LS micromanipulator, a custom-made 6-DOF micromanipulator made from SmarAct stages, and several 5- and 6-DOF human-input devices. The PI has a Motoman robotic manipulator for the positioning of large magnets. The PI has a set of three-axis Helmholtz coils for conducting uniform-magnetic-field experiments, as well as amplifiers to power them. The PI also has a number of novel magnetic manipulation systems that are unique to his lab.

Department of Mechanical Engineering Student Machine Shop
This shop provides standard milling machines, lathes, metal brakes, and hand tools for student use, which includes all necessary tooling for operating this equipment. A three-axis CNC mill is also available and the shop is staffed by a full-time staff member to support the students.

Department of Mechanical Engineering Pro Shop
The Pro Shop supplements student needs when the resources of the Student Machine Shop are insufficient. This shop features HAAS CNC mills and lathes as well a full range of precision tooling and fasteners. This lab is also staffed by a full-time staff member that supports students. If resources of this lab are insufficient, students are referred to the Advanced Manufacturing Lab or the Utah Micro Fabrication Lab.

Dr. Park’s (Senior Personnel) research lab
The Department of Surgery research facilities main lab houses an array of equipment and instrumentation sufficient to successfully complete the experiments outlined in the proposed research. The equipment available in these labs directly applicable to the research proposed in this project includes:

- -20°C and -80°C freezers
- TDT hard/software based ABR and OAE setup is hooked up to an 8’X8’X8 IAC sound proof recording chamber
- fume hoods
- laminar flow tissue culture hoods
- incubators
- inverted microscopes
- thermal cyclers including a Roche LightCycler real-time thermal cycler
- Genetix QArrayMini microarray analyzer with a capacity for 54 slides and 5 source plates
- Molecular Devices kinetic microplate reader with dedicated data capture computer with internet access
- Biotek Fluorescent plate reader with dedicated data capture computer with internet access
- spectrophotometers
- centrifuges (microfuges, refrigerated microfuge, table top preparative centrifuge suitable for serum preparation, and RC5B preparative centrifuges)
- gel electrophoresis apparatus and power supplies
- Kodak ImageMaker 2000R gel/photo documentation system
- vortexers
- waterbaths
- heating blocks
- balances
- water filtration unit

In addition, Dr. Park’s group has access to adjacent support rooms in the research facilities. Examples of equipment available in these facilities include:
- Genetix QArrayMini piezo microarray spotter
- walk-in 4°C cold room
- autoclave/dishwasher room with separate sterile storage area
- equipment room with -20°C and -80°C freezers
- RC-5B preparative centrifuge and rotors
- refrigerator
- fume hood
- speed-vac
- ice machine

Additional resources are available in the microscopy/tissue processing/imaging room, including:
- light microscopes
- two fluorescent microscopes with real-time CCD cameras
- microtomes
- cryotome
- Leica TP1020 tissue processing station

The University of Utah Health Science (UUHS) Core

These laboratories, located on upper campus, which is a five-minute walk from the engineering campus, include facilities and staff focused on research involving:
- Biostatistics
- Cell imaging/fluorescence microscopy
- DNA sequencing and peptide synthesis
- Electron microscopy and flow cytometry
- Mass spectrometry and proteomics
- Microarray and protein interactions
- Genomics/metabolomics/bioinformatics

Equipment pertinent to this proposal and available on a fee-for-use basis include:
- several Olympus FluoView laser scanning confocal microscopes (FV300 Olympus IX81, two FV300-xy stage Olympus IX70, two FV1000 Olympus IX81), each capable of three fluorescence channels and transmitted light imaging
- high-throughput confocal imager with liquid handling and environmental controls (Pathway 885 from BD Biosciences)
- Affymetrix, Nimblegen and Agilent platforms for microarray analysis
- ABI 3730XL high throughput Capillary Electrophoresis
two ABI PRISM® 7900HT Real-Time detection instruments with 96 and 384-well plate capability, Biomek FX with Span-8 and 96 head, Velocity11 Vprep Station with 96 head
analytical ultracentrifuges
peptide synthesizer, oligonucleotide synthesis, automated DNA & protein sequencing
transmission and scanning electron microscopy
two upgraded 5-Color FACScan analyzers, FACS Vantage SE High Speed Cell Sorter
Genetix QArray Mini piezo microarray spotter

Also housed in the UUHS Core is a mass spectrometry facility that includes several high performance mass spectrometers and a Dual-Energy X-Ray absorptiometry instrument.

University of Utah Temporal Bone Lab
There is no plan in the proposed project to use these facilities, but they are listed here as a contingency. The University of Utah Temporal Bone Lab is a fully functional, state of the art temporal bone lab. There are twelve drilling stations with electric drills, microscopes and micro instruments. With cadaveric material available through the University Department of Anatomy, we are able to perform surgical approaches to the temporal bone, including that for cochlear implantation.

Utah Microfabrication Laboratory Overview
The College of Engineering Microfabrication Facility at the University of Utah is a multi-purpose cleanroom facility with approximately 5300 sq. ft. of laboratory floor space which provides the clean environment necessary for semiconductor materials and device research, micromachining, microfabrication, and semiconductor materials systems research. The laboratory has equipment for the deposition of materials (i.e., sputtering, electron beam evaporation, thermal evaporation, plasma enhanced chemical vapor deposition, low pressure chemical vapor deposition of polySi and Si-nitride), photolithography (e.g., Cr-on-glass and emulsion mask making, photoresist spinners and coaters, hot plates, ovens, mask aligners, design stations), an atomic force microscope (AFM), test / characterization / inspection equipment, and many other planar processes necessary for micro system research and characterization. Complete mask making facilities include an Electromask TRE Criss-Cross pattern generator with step and repeat camera and environmental control for repeatable high performance. The laboratory also has B & P solid state diffusion furnaces, annealing furnaces, and wet/dry oxidation furnaces.

Recently installed is a new dual-chamber high vacuum sputtering system from TM Vacuum. The TMV Super Series SS-40C-IV Multi Cathode Sputtering system is configured with:
- Dual-chamber with independently cryopumped load lock
- Base pressure 2x10^-7 torr, sputtering pressure controlled using gas flow combined with a foreline butterfly valve.
- Six cathodes configured for variations of sequential or simultaneous sputtering or reactive sputtering / configurable with any of the fitted power supplies. One cathode is permanently fitted with a ~60in^2 ITO target.

Some Laboratories Affiliated in micro- and nano-scale Science and Engineering
1. Utah Microfabrication Laboratories: Sputtered and e-beam deposited thin films, including ITO and dielectrics. CVD, PECVD, LPCVD systems. Diffusion furnaces. Photolithography and etch systems including electronic visions EV-420 contact/proximity aligner and Oxford Instruments RIE. CAD-Laser micromachining system (Nd-YAG laser / 1064nm) and dicing saws. Wet benches including electroplating and bulk micromachining baths. K&S gold wire bonder, Disco wafer dicing saw,
2. SEM Lab: Hitachi S-3000 LV-SEM / EDS / BSE and crystal orientation imaging systems.
3. TEM Lab: JEOL 2000FX II high-resolution electron microscope with EDXS attachment capable of detecting down to Boron. Accessories include high and low temperature in situ straining stage, double tilt holder suitable for crystallographic analysis. Peripheral equipment for electrolytic foil preparation as well as ion milling of thin foils is also available.
4. X-ray Lab: Siemens D5000 X-ray diffraction unit with facility (Rigaku/Bede) to perform double crystal diffraction analysis is available for diffraction analysis, if needed.
5. Metallography Lab: Allied HiTec sample polishing capability for precision parallel lapping and cross-sectioning. Precision parallel lapping and CMP. Various metallographic scopes, fume hood, hardness testing, 1000X optical microscopy with differential interference contrast and digital micrography.
6. Metrology lab with Dektak stylus profilometry, Nikon Optical comparator, and Digital Instruments Dimension 3000 AFM (100x100x2 micron scan field) with tapping & contact mode, STM, MFM, and nanoMAN also possible. Reliability characterization by electrodynamic four-point cyclic bending fixture.
7. Microtomography Lab: MicroCT, a MicroSystem characterization instrument developed in the Metallurgy department utilizing highly focused X-rays to provide 3-D internal rendering of MicroSystems at resolution of 5-20 microns.
8. Sonix Scanning Acoustic Tomography system for use in detecting bulk material voids, interfacial delaminations, and cracks.
9. CADE lab: SUN Solaris machines to run Finite element analysis (FEA). Also available: Intellisuite MEMS design and modeling software, and CADENCE layout software, Pro/ENGINEER.
10. 50 Educational licenses for ANSYS 6.0 to perform computer modeling and simulation.
11. Access to Utah High Performance Computing Center (UHPC) where extensive high speed computational hardware as well as several materials simulation software packages are available.

Detailed Equipment List
Micromachining Section:
CAD-Laser micromachining system (Nd-YAG laser / 1064nm)
KOH bulk Si etching
Electrodeposition (Cu, Ni)
Precision polishing/planarization (Allied Hi-Tech)
Slow-speed diamond saw (Allied Hi-Tech)
programmable silicon dicing saw (Disco)

Lithography Section:
Backside mask aligner: Electronic Visions EV-420, 350nm-450nm illumination, alignment resolution – 1 um frontside, 2 um backside, class 100 enclosure.
Electromask TRE Criss-Cross Pattern Generator and 5x, 10X stepper, in Class 100 environmentally-controlled chamber.
Artworks DXF & GDSII s/w converter
Dry bench / Headway Spin coater
Dry bench / Headway Spin coater
Mask aligners (2x Kasper Instruments)
Spin coater Karl Suss CT62 covered spin chamber
Lindberg BlueM curing oven
supporting hot plates

Diffusion Section:
Canary furnace stack– wet oxide, boron, LPCVD polysilicon, LPCVD nitride
Thermco Products MiniBrute Phos-diffusion, metal annealing
Thermco Pacesetter II (3") Boron diffusion 1050C gate ox, phos drive
Lindberg Diffusitron Mark IV heavy Duty Boron diffusion, wet/dry ox
Lindberg 4" tube furnaces (3x)

Dep Section:
TM-Vacuum Sputtering system: ITO target, Au, Ag, Al, Pt, Cr, Ni, Ti, Ti/W, Cu, W
Denton e-beam evaporator DV-SJ/20C, 4 targets manual. Materials available:
Sputt: Denton Discovery 18, 3 targets, 2 rf sources. Targets: SiO2, Si3N4, Au, Ag, Al, Pt, Cr, Ni,
Ti, Ti/W, Cu, W
MRC Sputtersphere (under refurb).
CHA Thermal Evaporator
PECVD: Oxford Plasmalab 80 Plus. Source gases: nitrogen, nitrous oxide, methane, ammonia,
silane
Canary furnace stack—wet oxide, boron, LPCVD polysilicon, LPCVD nitride
PECVD: MVS systems inc.
PlasmaLab (SiH4, O2, N2, N2O, H2)
APOMVPE systems (3x Custom OMVPE reactors)

Etch Section:
RIE – Plasma technology (SF6, NH3, CF4, BCL3, Cl2, C2H6, O2, N2, H2)
Oxford Plasmalab 80 Plus. Etch gases: Cl2, CF4, O2, SF6, H2, Ar2, Cl2

Characterization Section:
Spectroscopic ellipsometer: Woollam V-VASE auto-angle with autocompensator, spectral range
310nm – 1700nm. Vertical sample mounting.
Microscope – Olympus SZ-ET stereo zoom 2-18X by 20X
Microscope Nikon Optiphot 88 (5, 10, 40,60,100x) w/ digital camera and monitor, linewidth
measurement, image capture
Tencor P-10 Profilometer
Surface profiler Dektak III
Microscope Nikon Optiphot 88 (5, 20, 40, 100x) w/ digital camera
Gaertner Ellipsometer (HP computer)
Manual probe station
Plotter
Capacitance meter,
Function generator
Power supply
HP 4145A parameter analyzer
LeCroy 9350A 500MHz Oscilloscope
Tek Curve tracer
Digital Instruments AFM (Dimension 3000 (100x100x2 micron scan field) with tapping, contact,
STM, MFM, nanoMAN modes.
Hitachi LV-SEM (affiliated)
JEOL STEM (affiliated)
XRD (affiliated)
CV-Plotter
ALLIED HI-TECH Parallel lapping and precision polishing tools
Electrodynamic 4-pt cyclic bending apparatus with variable frequency and waveform, load or
displacement control

Packaging Section:
Wirebonder (wedgebonder)
Wirebonder (gold ball bonder)
Microautomation Dicing saw #1006 (2x)
Disco programmable dicing saw

Supporting Equipment:
Wet benches
Ecosys guardian burnbox for effluent
Wet Chemistry (three benches)
Laminar flow work benches
Fisher scientific FS20H ultrasonic bath
Whatman hotplate stirrer
Thermolyne 1400 benchtop furnace
Wet bench
D.I. water plant

Vanderbilt University

The extensive resources of Vanderbilt University (VU) and the Vanderbilt University Medical Center (VUMC) provide the ideal scientific environment in which the proposed project will flourish. The research team at Vanderbilt is led by co-I Webster, who conducts research at the intersection of engineering and medicine, and holds a joint appointment in the Vanderbilt School of Engineering (VUSE) Mechanical Engineering department and the VUMC Otolaryngology department. VUMC consistently ranks among the top 15 health care facilities in the United States. Laboratories at both VUSE and VUMC will be used in this research.

VUSE Laboratory
Medical & Electromechanical Design Laboratory: Prototyping, benchtop and testing, and computational simulation and analysis will be carried out in the Medical & Electromechanical Design (MED) Laboratory in the Vanderbilt Mechanical Engineering Department. Directed by PI Webster, the MED lab consists of a 1200 sq. ft. dedicated research space, to which students and the PI have 24-hour access, 7 days per week. The MED lab is equipped with computational equipment (high-end networked PCs), electrical fabrication/test equipment (e.g. oscilloscopes, multimeters, etc.), and mechanical fabrication equipment (e.g. powered and manual hand tools). The MED lab is also equipped with both optical (MicronTracker H3-60, Clarion, Inc.) and magnetic (Aurora, Northern Digital, Inc.) position and orientation tracking systems, a number of custom-built surgical robots and haptic interface devices, and a variety of motion control systems (e.g. Galil DMC-1886) and force sensors (e.g. ATI-NANO17). The Vanderbilt Medical Center (and all VU facilities mentioned below) are located within a 5-minute walk of the MED laboratory.

Clinical Facilities at VUMC
Vanderbilt University Hospital and The Vanderbilt Clinic consistently rank among the premier health care facilities in the United States; it is a principal referral center for physicians and patients throughout the region. The hospital has over 30,000 admissions and over 570,000 outpatient visits annually.
Temporal Bone Laboratory
The Department of Otolaryngology-Head and Neck Surgery programs are housed in a new facility (opened May 2005), the Vanderbilt Bill Wilkerson Center, a 136,000-square foot building in Medical Center East. The clinical space is approximately 45,000 net square feet. There are 24 state-of-the-art exam rooms. Within this building is a state-of-the-art temporal bone dissection laboratory with twelve operative stations occupying 1500 square feet. Each station has a surgical stand, operating microscope, surgical drill, and irrigation system. Storage facilities for temporal bones and cadaver heads are available. The phantom and in vitro studies will take place in this laboratory.

Computer-Assisted Otologic Surgery Laboratory
Also within the Vanderbilt Bill Wilkerson Center is the 1000 square-foot Computer-Assisted Otologic Surgery Laboratory. Contained within this lab are two Polaris infrared position trackers (Northern Digital, Waterloo, Ontario, CA), a MicronTracker visible-light position tracker (Claron Technology Inc, Toronto, Ontario, CA), a XarTrax steerable laser system (Traxtal, Inc, Toronto, Canada), two robots—a Mitsubishi RV-3S (Mitsubishi Electric & Electronics USA, Inc., Cyprus, CA) and a Motoman YR-SV035 (Motoman, Inc., West Carrollton, OH), an Acu-Rite III, xyz positioning system (Acu-Rite Companies Inc., Jamestown, NY), and two surgical stations with electric and pneumatic drills, surgical microscopes (Carl Zeiss AG, Oberkochen, Germany), and associated instrumentation.

Mechanical Engineering Manufacturing Facilities
The fabrication facilities of the Vanderbilt Mechanical Engineering department are also available and accessible to faculty and students for use in this project, including traditional and CNC milling machines and lathes, a 2D laser CAM (Kern 52 Series Laser Table), and a Rapid Prototyping Machine (Stratisys, Dimension SST). Also available are other standard shop machines including a vertical milling machine, lathe, drill press, and band saw. Additionally, the School of Engineering at Vanderbilt houses two multi-axis CNC machines, in addition to three multi-axis CNC machines housed by the University.

Otology Machine Shop: An additional fabrication facility is located across the hall from the otology labs for rapid design modifications, and we will use this facility for initial benchtop component and device experimental accuracy verification. This shop is equipped with an Ameritech CNC Jr. Milling Machine (Brousard Enterprises Inc., Sante Fe Springs, CA), a FARO Gage-Plus measuring system (FARO Technologies, INC., Atlanta, GA), a Delta tabletop band saw (Delta Tools, Jackson, TN), a Delta belt sander (Delta Tools, Jackson, TN), a Wilton tabletop drill press (WMH Tool Group, Inc., Elgin, IL), a tool cabinet, a metal stock shelf, and workbenches. In addition, an electronics shop of approximately 100 square feet will support the fabrication of circuits to be used in research projects. Equipment includes a waveform generator, DSO, and soldering stations.

Computer Resources
All personnel have desktop or laptop PCs with adequate printers and internet access. Statistical Software (SPSS, SYSTAT) for PCs is leased through Vanderbilt University, with SAS and BMD available on the university mainframe. Word processing (Word) and spreadsheet (Excel) software is available, and Sigma Plot and Power Point are used for graphic displays. Matlab access is likewise leased through the Vanderbilt University with wide availability throughout the departments.
**Offices**
Adequate office space is available in our facilities for all project staff. Office facilities include the necessary telephone, photocopy, and fax services. Secretarial support is available for tasks such as photocopying, scheduling of patients, and correspondence.

**Oregon Health and Science University**

**OHSU Laboratory for Temporal Bone Anatomy and Skull Base Surgery**  
Located on the OHSU Medical School campus, the laboratory is fully equipped for temporal bone and skull base dissection. Within the lab, there are eight dissection stations that are equipped with a dissecting microscope, a high-speed electronic drill and suction-irrigation set up. The lab is outfitted with contemporary audio-visual equipment for photodocumentation, video recording and teaching purposes. In addition, the lab has dedicated microdissection instruments for otologic and skull base surgery. Endoscopic equipment and a stereotactic navigation system is available in the lab for use as well.

**Located adjacent to the lab is the OHSU Body Donation Program**  
This provides anatomic material for the medical school anatomy course. Both fresh and fixed cadaveric material is readily available for use in anatomic studies through the program. The staff oversees the maintenance of the lab as well as the appropriate handling of cadaveric material used in the lab.
### RESEARCH & RELATED Senior/Key Person Profile (Expanded)

#### PROFILE - Project Director/Principal Investigator

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<th>Middle Name: J</th>
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**Credential, e.g., agency login:** JAKEABBOTT

**Project Role*: PD/PI

**Other Project Role Category:**

**Degree Type:** PhD, Mechanical Engineering

**Degree Year:** 2006

**Attach Biographical Sketch***: JakeAbbott_NIH_biosketch1009467275.pdf

**Attach Current & Pending Support:**

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#### PROFILE - Senior/Key Person

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**Credential, e.g., agency login:**

**Project Role*: Other (Specify)

**Other Project Role Category:** Co-I

**Degree Type:** PhD, Mechanical Engineering

**Degree Year:** 1991

**Attach Biographical Sketch***: TimAmeel_NIH_biosketch20131009466885.pdf

**Attach Current & Pending Support:**

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Funding Opportunity Number: PA-13-302 . Received Date: 2013-11-05T18:59:56.000-05:00
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A. Personal Statement

The goal of this project is to demonstrate that magnetic guidance of cochlear implants can be used to make the surgical insertion consistently less traumatic than the current paradigm of manual insertion by reducing insertion forces and forces on the basilar membrane, and to develop a method to safely remove the magnet after the insertion is complete, such that the patient may undergo future MRI scans.

My responsibility as PI on this project is first and foremost to coordinate the efforts of the various co-Is, postdocs, and graduate students to achieve the project's goals. I have assembled a skilled team to accomplish the proposed work, each providing complimentary expertise. It is important that the various groups stay in constant contact so that effort is neither wasted nor duplicated, and the project is always moving forward toward the project's specific aims. My lab will lead the tasks related to magnetic guidance during insertion and magnet removal after insertion. The magnetic-manipulation system is based upon the spherical permanent magnet manipulator (SPMM), which is a patent-pending device developed in my lab. The SPMM will enable the magnet to be moved relative to the patient in an inherently safe fashion; it is truly an enabling technology that will allow the proposed research to proceed quickly.

My expertise in robotics was initially formed during my PhD work at Johns Hopkins, where my research focused on control architectures for telemanipulation systems (e.g., da Vinci). I performed three-years of postdoctoral work at ETH Zurich, where I conducted research in magnetic manipulation of microrobots. My principal contribution was the OctoMag system, which comprises eight stationary electromagnets designed to surround a patient's head and manipulate an intraocular microrobot for targeted drug delivery to the retina. The system was the first to demonstrate five-degree-of-freedom dexterous manipulation of a fully untethered device, and we were awarded the Best Manipulation Paper award at the 2010 IEEE International Conference on Robotics and Automation, which is the premier international robotics conference. I have been a faculty member at the University of Utah for the past five years. My group has continued to explore the ways that magnetic fields can be used to control in vivo medical devices, including tethered devices such as cochlear implants, and untethered devices such as capsule endoscopes. Under the support of my NSF CAREER Award, a significant focus of my group’s effort has been the use of a single strong permanent magnet moved dynamically around the workspace (i.e., the patient) to perform manipulation, as opposed to the typical approach of surrounding the workspace with electromagnets (e.g., OctoMag, Magnetecs) or permanent magnets at a far distance (e.g., Stereotaxis). My fundamental conjecture is that such systems will be capable of better performance than existing systems at less cost.

Groundwork for the current proposal was laid through exciting and fruitful collaborations with co-Is Warren and Webster. I have been working with Dr. Warren for the past three years on this project, and we have already published/submitted four papers together, the results of which are described in the Research Statement. I have informally collaborated on a number of projects over the years with co-I Webster (since our time in graduate school at Johns Hopkins, where we often contributed to each other’s work). Dr. Webster has a related project with Rob Labadie, MD, at Vanderbilt University; our long-term goal is to combine the two efforts into a single minimally invasive cochlear-implant surgical system, but for the time being, the projects are independent.
B. Positions and Honors

Positions and Employment

1999-2001 Graduate Research Assistant, Department of Mechanical Engineering, University of Utah, Salt Lake City, UT
2002-2005 Graduate Research Assistant, Department of Mechanical Engineering, Johns Hopkins University, Baltimore, MD
2005-2008 Postdoctoral Research Associate, Institute of Robotics and Intelligent Systems, ETH Zurich, Zurich, Switzerland
2008-present Assistant Professor, Department of Mechanical Engineering, University of Utah, Salt Lake City, UT
2011-present Adjunct Assistant Professor, School of Computing, University of Utah, Salt Lake City, UT

Other Experience and Professional Memberships

1997-present American Society of Mechanical Engineers (ASME)
2003-present Institute of Electrical and Electronic Engineers (IEEE)
2007 Session Co-Chair, IEEE Int. Conf. Robotics and Automation: Medical Microrobots
2007 Local Organizing Committee, IEEE/ASME Int. Conf. Advanced Intelligent Mechatronics
2008 Local Organizing Committee, Robotics Science and Systems Workshop on Underwater Robotics at the Microscale
2008 Session Chair, IEEE/RSJ Int. Conf. Intelligent Robots and Systems: Videos
2008 Program Committee, IEEE Int. Conf. Biomedical Robotics and Biomechatronics
2009 Attendee, Winter School on Medical Robotics and Computer-Integrated Interventional Systems
2009 Session Chair, IEEE/RSJ Int. Conf. Intelligent Robots and Systems: Medical Robotic Systems
2010 Associate Editor, IEEE Int. Conf. Robotics and Automation
2011 Session Co-Chair, IEEE/RSJ Int. Conf. Intelligent Robots and Systems: Micromanipulation
2012 Associate Editor, IEEE Int. Conf. Robotics and Automation
2012 Member, Second Roadmapping Workshop on US Medical and Healthcare Robotics
2013 Associate Editor, IEEE Int. Conf. Robotics and Automation

Honors

1999 Outstanding Senior, Utah State University Mechanical Engineering Class of 1999
2005 Teaching Assistant of the Year, Department of Mechanical Engineering, Johns Hopkins University
2005 Finalist, Best Student Paper Award, Haptics Symposium
2008 Finalist, Best Paper Award, IEEE Int. Conf. Biomedical Robotics and Biomechatronics
2008 Finalist, Best Student Paper Award, IEEE Int. Conf. Biomedical Robotics and Biomechatronics
2008 Research featured on BBC News Click: Looking Ahead to Tiny Technology.
2009 Research featured on Euronews: Honey, I Shrunken the Endoscopy
2009 Interviewed on Utah Public Radio Science Questions: Robotic Surgery
2010 Finalist, Best Medical Robotics Paper Award, IEEE Int. Conf. Robotics and Automation
2010 Finalist, Best Video Award, IEEE Int. Conf. Robotics and Automation
2010 Best Manipulation Paper Award, IEEE Int. Conf. Robotics and Automation
2011 Outstanding Teaching Award, University of Utah Department of Mechanical Engineering, 2010-2011 Academic Year
2013 Best Poster Award, Hamlyn Symposium on Medical Robotics
C. Selected peer-reviewed publications

Most relevant to current application (in order of relevance)


Additional recent publications of importance to the field (in chronological order)

D. Research Support

Ongoing Research Support

**NSF IIS-0952718**  Abbott (PI)  04/01/10-03/31/15  $499,793

CAREER: Nonuniform-Magnetic-Field Control of Medical Microrobots
The major goal of this grant is to use dipole fields generated by permanent magnets to control medical devices. The results of this award are being utilized in the current proposal.

**Given Imaging**  Abbott (PI)  08/26/13-02/25/14  $28,000

Exploration of Magnetic Capsule Endoscopy using a Single Permanent Magnet
The major goal of this grant is to perform proof-of-concept experiments in a cadaver pig, based upon results already demonstrated in a phantom. The project uses the same spherical permanent magnet manipulator (SPMM) being utilized in the current proposal.

**NASA NNX13AL46H**  Abbott (PI)  08/01/13-07/31/17  $272,000

Modular Magnetic Mobile Manipulators for Microgravity Environments
The major goal of this grant is to develop a microgravity manipulation system based on omnidirectional electromagnets, which were originally developed with the support of NSF IIS-0952718.

**Intuitive Surgical**  Abbott (PI)  01/01/13-12/31/13  $50,000

Intuitive Telemanipulation System for Retinal Microsurgery
The major goal of this grant is to develop a robotic system to assist with epiretinal membrane peeling.

**Intuitive Surgical**  Abbott (PI)  01/01/14-12/31/14  $50,000

Microforceps Capability for the Retinal-Microsurgery Telemanipulation System
This is an extension of the previous year of support that will enable us to add the capability to actuate microforceps to the robotic system developed in the first year of support.

**U. Utah Research Foundation**  Raeymaekers (PI)  01/01/13-12/31/13  $56,372

Nitinol Ring-Capsulotome for Cataract Surgery
The major goal of this grant is to develop a disposable cutting tool used during cataract surgery.
Role: Co-PI. Responsible for 33% of the project.

**NSF NRI-0952718**  Hollerbach (PI)  09/01/12-08/30/15  $908,999

NRI: Small: Robotic Treadmill Therapy for Lower Spinal Cord Injuries
The major goal of this grant is to use the Treadport immersive locomotion interface for gait rehabilitation.
Role: Co-PI. Responsible for 29% of the project.

Completed Research Support

**U. Utah Research Foundation**  Abbott (PI)  06/01/11-05/30/12  $28,000

A Wearable Robotic Arm-Swing Device for Improved Gait Rehabilitation
The major goal of this grant was to generate preliminary results for the use of a robotic device to aid in proper arm-swing during gait rehabilitation. Results were used to obtain NSF NRI-0952718.
BIOGRAPHICAL SKETCH
Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. DO NOT EXCEED FOUR PAGES.

NAME
Timothy A. Ameel

POSITION TITLE
Professor and Chair, Department of Mechanical Engineering, University of Utah

eRA COMMONS USER NAME (credential, e.g., agency login)
TIMAMEEL

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE (if applicable)</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Montana State University, Bozeman, MT</td>
<td>B.S.</td>
<td>1975</td>
<td>Mechanical Engineering</td>
</tr>
<tr>
<td>Montana State University, Bozeman, MT</td>
<td>M.S.</td>
<td>1977</td>
<td>Mechanical Engineering</td>
</tr>
<tr>
<td>Arizona State University, Tempe, AZ</td>
<td>Ph.D.</td>
<td>1991</td>
<td>Mechanical Engineering</td>
</tr>
</tbody>
</table>

A. Personal Statement
In the proposed work, a permanent magnet will be attached to the tip of a cochlear implant (CI) using paraffin wax, and then resistively heated after the surgical insertion is complete, such that the magnet can be removed from the patient’s cochlea. I will lead the portion of the project involving heat-transfer analysis associated with the detachment process, with a focus on (1) mitigating risk to the cochlea and (2) ensuring the magnet will be successfully detached from the CI. This task will require the design of the heating system, including lead wires for power supply and tethering, and magnet, adhesive, and coating material selection. The heat-transfer analysis will incorporate all three heat transfer modes, including conduction within the implant and convection to the small annular space surrounding the implant. Given the small scale of the proposed system, I am uniquely qualified to carry out the numerical and experimental modeling efforts. My research focuses on the engineering science of microscale fluid dynamics and convection heat transfer, with nearly 100 manuscripts in the area. One of my areas of expertise is in slip-regime convection. My experimental work has emphasized the characterization of microchannel flow and convection. Geometric scales in the proposed heat transfer and fluid analysis are of similar, or perhaps an order of magnitude larger, than the scale of published experimental studies. Heat-exchanger analyses have focused on the effects of thermal interaction with the ambient, an inherent condition at small scales. Other work, not yet published, that is directly applicable to the proposed project has focused on the thermal heating of paraffin wax for phase change and subsequent expansion for application in a refreshable Braille reader with a tactile-based display assistive system. The experience gained on the thermal modeling of paraffin wax will be applicable to the modeling tasks specific to Aim 2.

B. Positions and Honors.

Positions and Employment
2009-present Professor and Chair, Dept. of Mechanical Engineering, University of Utah, Salt Lake City, UT
2001-2009 Associate Professor, Dept. of Mechanical Engineering, University of Utah, Salt Lake City, UT
2006 Visiting Professor, Division of Thermodynamics and Applied Refrigeration, Royal Institute of Technology, Stockholm, Sweden,
1996-2001 Assistant Professor, Dept. of Mechanical Engineering, University of Utah, Salt Lake City, UT
1992-1996 Assistant Professor, Dept. of Mech. & Ind. Engineering, Louisiana Tech University, Ruston, LA
1991-1992 Instructor, Dept. of Mechanical & Aerospace Engineering, Arizona State University, Tempe, AZ
1991-1992 Instructor, Engineering Sciences Department, Mesa Community College, Mesa, AZ
1985-1991 Teaching Assistant/Graduate Research Assistant, Dept. of Mechanical and Aerospace Engineering, Arizona State University, Tempe, AZ
1980-1985 Director of Skiing/Head Men’s Ski Coach, Dept. of Athletics, University of Wyoming, Laramie, WY
1978-1980 Research Engineer, Dept. of Mechanical Engineering, Montana State University, Bozeman, MT
1977-1978 Design Engineer, Drapes Engineering, Great Falls, MT
1975-1977 Graduate Research Assistant, Dept. of Mechanical Engineering, Montana State University, Bozeman, MT
Other Experience and Professional Memberships (partial list)

1992-present  American Society of Mechanical Engineers (ASME)
1996-present  American Society of Engineering Education (ASEE)

2008-2010  Reviewer, NSF Review Panels (3)
2009-2011  Reviewer, Fulbright Scholar Proposals, Council for International Exchange of Scholars and the U.S. Department of State
2009  Program Reviewer, Department of Mechanical Engineering, University of Nevada, Reno, NV

Honors

2006  Fulbright Scholar Award, Council for International Exchange of Scholars and the U.S. Department of State
2004  Outstanding Teaching Award, College of Engineering, University of Utah
2002  College Teaching Award (Top 15%), Heat Transfer
1998  Ralph R. Teetor Educational Award, Society of Automotive Engineers
1996  1995-96 Sigma XI Researcher of the Year, Louisiana Tech University
1985  Coach of NCAA National Championship Ski Team, University of Wyoming

C. Selected peer-reviewed publications.

**Most relevant to current application (in order of relevance)**


**Additional recent publications of importance to the field (in chronological order)**


**D. Research Support**

**Ongoing Research Support**

1. IGERT: Nanobiosensors, Nanomaterials, and Microfluidics, NSF, $3,200,000, 08/01/09 – 07/31/14, Co-PI, no salary support.

**Completed Research Support (related projects)**


2. Design Based Spiral Learning Curriculum, NSF, $200,000, May 2009 – May 2012, Co-PI.

3. Convective Flow Boiling in Microchannels, Fulbright Scholar Award, Council for International Exchange of Scholars and the United States Department of State, 130,000 SEK (~$18,000), Aug. – Dec. 2006, PI.


A. Personal Statement

The goal of this project is to demonstrate that magnetic guidance of cochlear implants can be used to make the surgical insertion consistently less traumatic than the current paradigm of manual insertion by reducing insertion forces and forces on the basilar membrane, and to develop a method to safely remove the magnet after the insertion is complete, such that the patient may undergo future MRI scans.

My responsibility will be to demonstrate that magnetic guidance of a cochlear implant results in less trauma to the cochlea than traditional insertion techniques in a guinea pig model. There has been a great interest in minimizing implant trauma for patients with residual hearing wishing to use a combined electric and acoustic stimulation.

My expertise in guinea pig auditory physiology and anatomy began in 2004 when our laboratory developed and evaluated resorbable ventilation tubes. In collaboration with Glenn Prestwich, a medicinal chemist at the University of Utah, we later developed a modified hyaluronic hydrogel for middle ear packing and tympanic membrane perforation repair. Currently, much of our work is focused on understanding the pathophysiology of cytomegalovirus induced (CMV) hearing loss, a leading case of pediatric hearing loss. We have developed both guinea pig and murine models for CMV induced labyrinthitis. We have been able to demonstrate in utero transplacental transmission of guinea pig (gp) specific CMV to newborn pups and congenital hearing loss by auditory brainstem response and distortion product otoacoustic emission testing. We have also demonstrated gpCMV DNA in the cochlea by PCR analysis. In our murine model, we have shown elevated ABR thresholds in 4 week old infected pups and GFP expression of the virus in the spiral ganglion and scala tympani 7 days after inoculation. My laboratory will perform the auditory brainstem response threshold testing and temporal bone processing for the Hartley nonpigmented guinea pigs undergoing cochlear implantation under magnetic guidance. My laboratory also has experience with the surgical techniques, auditory testing and temporal bone histology in guinea pigs. As co-director of the pediatric hearing assessment clinic, the only multidisciplinary clinic of its kind in Utah, I have had a long established and profound interest in pediatric hearing loss. This novel approach to cochlear implantation has widespread and important ramifications for hearing preservation and rehabilitation.

B. Positions and Honors

Positions and Employment

<table>
<thead>
<tr>
<th>Year</th>
<th>Title</th>
<th>Institution and Location</th>
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<tbody>
<tr>
<td>1996–2002</td>
<td>Assistant Professor</td>
<td>Loyola University Medical Center, Dept. of Otolaryngology, Head and Neck Surgery and Pediatrics, Chicago, IL</td>
</tr>
<tr>
<td>2002</td>
<td>Associate Professor</td>
<td>Loyola University Medical Center, Department of Otolaryngology, Head and Neck Surgery and Pediatrics, Chicago, IL</td>
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<tr>
<td>2002–2008</td>
<td>Associate Professor</td>
<td>University of Utah, Division of Otolaryngology--Head and Neck Surgery and Pediatrics, Salt Lake City, UT</td>
</tr>
<tr>
<td>2009–Present</td>
<td>Professor</td>
<td>University of Utah, Division of Otolaryngology--Head and Neck Surgery and Pediatrics, Salt Lake City, UT</td>
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</table>
Division chief for Pediatric Otolaryngology, Primary Children’s Medical Center
2012-Present  Section chief- Pediatric Otolaryngology, University of Utah, Salt Lake City, UT

Honors
1986  Sims Scholar
1986  Phi Beta Kappa
1986  Honors with Distinction (Physics)
1996  First Place - Scientific Poster Presentation for Canadian Academy of Otolaryngology-Head and Neck Surgery
1996  First Place - Fellowship Presentation, Percy Ireland Research Competition, Toronto, Ontario, Canada.
1997  First Place - Charles F. Ferguson Clinical Research Award, American Society of Pediatric Otolaryngology
2001  Medtronic Xomed Award for Excellence in Clinical Research
2006  Second Place. Charles F. Ferguson Clinical Research Award, American Society of Pediatric Otolaryngology
2009  Third Place Poster Presentation ASPO

Federal Government Public Advisory Committee(s)
2006- present  Newborn Advisory Committee on Infant Hearing (Utah)
2011  NIH Ad hoc reviewer (NIDCD)

C. Selected peer-reviewed publications (In chronological order). Selected from over 50 publications.

Most relevant to current application (in order of relevance)

Additional recent publications of importance to the field (in chronological order)


**D. Research Support**

**Ongoing Research Support**

<table>
<thead>
<tr>
<th>Industry Supported Clinical Trial</th>
<th>Harris (PI)</th>
<th>12/1/2013-11/30/2014</th>
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<tbody>
<tr>
<td>Otonomy, Inc.</td>
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<td></td>
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<tr>
<td>Phase 3 study of Oto-201</td>
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<td></td>
</tr>
<tr>
<td>This is a prospective, randomized, double-blind multicenter phase 3 study of Oto-201 given as a single intratympanic injection for intraoperative treatment of middle ear effusion in pediatric subjects requiring tympanostomy tube placement</td>
<td></td>
<td></td>
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<tr>
<td>Role: Co-Principal Investigator</td>
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<table>
<thead>
<tr>
<th>E.W.&quot;Al&quot; Thrasher Award</th>
<th>Sadhasivam (PI)</th>
<th>03/20/2013-2/28/2015</th>
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<tbody>
<tr>
<td>Predicting Perioperative Opioid Adverse Effects and Personalizing Analgesia in Children</td>
<td></td>
<td></td>
</tr>
<tr>
<td>This is a multicenter pharmacogenetic study to determine the association between specific genotypes [as defined by a pattern of Single Nucleotide Polymorphisms (SNPs) influencing responses to pain and pain medication] and the phenotype, defined by pain perception, analgesic effect and side effects in response to a fixed dose of morphine in children following adenotonsillectomy (T &amp; A).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Role: Co-Principal Investigator</td>
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<table>
<thead>
<tr>
<th>Triological Society Research Career Development Award</th>
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<tbody>
<tr>
<td>Congenital Cytomegalovirus Induced Hearing Loss in a Murine Model</td>
<td></td>
<td></td>
</tr>
<tr>
<td>The goal of this proposal is to use this <em>murine</em> model of CMV infection to characterize the mechanism behind SNHL.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Role: Principal Investigator</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Interdisciplinary Grant</th>
<th>Park/Meier (PIs)</th>
<th>07/01/2012-06/30/2014</th>
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</thead>
<tbody>
<tr>
<td>University of Utah</td>
<td></td>
<td></td>
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<tr>
<td>Biomarkers for Congenital CMV Infection</td>
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<td></td>
</tr>
<tr>
<td>The goal of this proposal is to determine whether Th1 cytokine responses are expressed in infants with c-CMV infection but not in those with postnatal (&gt;3 weeks of age) infection.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Role: Principal Investigator</td>
<td></td>
<td></td>
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</table>

**Completed Research Support**

<table>
<thead>
<tr>
<th>American Academy of Otolaryngology Vaccination For CMV SNHL</th>
<th>Park (PI)</th>
<th>07/01/2010-06/30/2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>The goal of this proposal is to assess the protective effect of preconceptual gB vaccination to mediate protection against SNHL in a guinea pig model</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Role: Principal Investigator</td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Deafness Research Foundation Antiviral CMV Treatment</th>
<th>Park (PI)</th>
<th>07/01/2010-06/30/2012</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>
The goal of this proposal is to evaluate the potential efficacy of ganciclovir against labyrinthitis in a guinea pig model.
Role: Principal Investigator

American Academy of Otolaryngology Park/Patel (PIs) 07/01/2011-12/31/2011
Murine Model Of CMV

The goal of this proposal is to develop on hearing model for CMV induced labyrinthitis.
Role: Principal Investigator

Natl Organization for Hearing Research Foundation Park (PI) 05/01/2009-12/31/2010
Guinea Pig Model for CMV Induced SNHL

The goal of this proposal is to improve the guinea pig model for CMV induced sensorineural hearing loss.
Role: Principal Investigator

American Society of Pediatric Otolaryngology Park (PI) 07/01/2005-06/30/2006
Development of Biofilm Resistant Ventilation Tubes

The goal of this proposal is to develop a resorbable ventilation tube that demonstrates biofilm resistance properties.
Role: Principal Investigator

STTR Grant Prestwich (PI) 09/01/2004-08/31/2005
NIH NIDCD
Crosslinkable Hydrogels for Tympanic Membrane Repair
The goal of this proposal is to develop cross-linkable hydrogels materials to enhance tympanic membrane repair.
Role: Co-Investigator

Interdisciplinary Seed Grant Park (PI) 07/01/2003-06/30/2004
University of Utah
Development of an Animal Model for Resorbable Ventilation Tubes
The goal of this proposal is to develop a in vivo animal model for resorbable ventilation tube placement.
Role: Principal Investigator

American Society of Pediatric Otolaryngology Park (PI) 07/01/2001-06/30/2002
Role of Ropivicaine in Adenotonsillectomy Outcomes
The goal of this proposal is to evaluate the potential efficacy of intraoperative ropivacaine injection for adenotonsillectomy pediatric patients in a randomized clinical trial.
Role: Principal Investigator
**BIOGRAPHICAL SKETCH**

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.

Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

<table>
<thead>
<tr>
<th>NAME</th>
<th>POSITION TITLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Webster III, Robert James</td>
<td>Assistant Professor of Mechanical Engineering</td>
</tr>
<tr>
<td>eRA COMMONS USER NAME</td>
<td>Assistant Professor of Otolaryngology</td>
</tr>
<tr>
<td>websterrj</td>
<td>Assistant Professor of Neurological Surgery</td>
</tr>
</tbody>
</table>

**EDUCATION/TRAINING** *(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)*

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE (if applicable)</th>
<th>YEAR(s)</th>
<th>FIELD OF STUDY</th>
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<tr>
<td>Clemson University</td>
<td>B.S.</td>
<td>1997-2002</td>
<td>Electrical Engineering</td>
</tr>
<tr>
<td>Johns Hopkins University</td>
<td>M.S.</td>
<td>2002-2004</td>
<td>Mechanical Engineering</td>
</tr>
<tr>
<td>Johns Hopkins University</td>
<td>Ph.D.</td>
<td>2004-2007</td>
<td>Mechanical Engineering</td>
</tr>
</tbody>
</table>

**A. Personal Statement**

The goal of this proposal is to enable better hearing with cochlear implants by magnetically guiding implant insertion to reduce intracochlear trauma.

My responsibility as Co-I on this project is to translate benchtop results into a clinic-ready system for cochlear implant magnetic guidance, and perform cadaver validation studies.

My expertise in robotics, medical device design, and image guided surgery was initially forged during my doctoral work at Johns Hopkins, where I was trained in the Engineering Research Center for Computer Integrated Surgical Systems and Technology headed by Russell Taylor. During my doctoral work I invented, patented, and developed two different steerable needle designs, one of which was subsequently licensed to Intuitive Surgical, Inc. My work on the first of these (bevel-based steering) was the core technical foundation for successful NIH R21 (#EB003452) and subsequent R01 (#EB006435) grants. In 2008 I joined the faculty of Vanderbilt University and established the Medical & Electromechanical Design Laboratory, which I direct. Here, my work on the second needle steering design (the Active Cannula) became the foundation of an NSF project (#0651803), NIH R21 (#EB011628 – Webster PI), NIH SBIR (R44 #CA134169), and NIH R01 (EB017467) on which I am PI. A second thrust of my current research program is image guidance where I am Co-I on a NIH project (#R01 CA162477) for guidance in abdominal soft tissues. A third major thrust of my research program is image-guided cochlear implant surgery, where I am a Co-I on a NIH R01 (#DC10184) on applying microstereotactic frames to pediatric populations for percutaneous cochlear implantation, and PI on an R01 for robotic acoustic neuroma surgery. In view of the overall impact of my work on the field of medical robotics, I received the NSF CAREER award (#IIS-1054331) and the 2011 IEEE Volz award.

Groundwork for the current proposal has been laid through my collaboration with Dr. Rob Labadie and others in the Vanderbilt department of Otolaryngology which have led to me being joint appointed in the department. Labadie and I collaborate particularly closely; we are both Co-Is on each other’s R01s and some of my students sit full time in Labadie’s lab. I have also worked closely with Dr. Abbott dating back to graduate school, where we were members of the same laboratory and regularly solved challenging problems together. The current proposal leverages my experience in building clinically-ready systems for inner-ear surgery and with Dr. Abbott’s exceptional theoretical and practical experience in magnetic guidance of surgical robots.

**B. Positions and Honors (selected)**

**Positions and Employment**

1998: Nuclear Power Plant Intern, Plant Vogtle, GA
1998-2001 Telecommunications Engineer (Co-op), Adtran, Huntsville, AL
2001 Visiting Scholar, Savannah River Site, SC
2002 Undergraduate Research Assistant, Clemson University, Clemson, SC
2006 Visiting Scholar, Scuola Superiore Sant'Anna, Pisa, Italy
2004-2006 Teaching Assistant, Johns Hopkins University, Baltimore, MD
2002-2007 Graduate Research Assistant, Johns Hopkins University, Baltimore, MD
2008-present Assistant Professor, Mechanical Engineering, Vanderbilt University, Nashville, TN
2011-present Assistant Professor, Otolaryngology, Vanderbilt University, Nashville, TN
2013-present Assistant Professor of Neurological Surgery, Vanderbilt University, Nashville, TN
2013-present Assistant Professor of Electrical Engineering, Vanderbilt University, Nashville, TN

Other Experience and Professional Memberships
1997-present Institute of Electrical and Electronics Engineers (IEEE), and Mechatronics, Communications, Power, and Robotics & Automation societies.
2000-present Tau Beta Pi (Engineering Honor Society)
2000-present Eta Kappa Nu (Electrical Engineering Honor Society)
2005-2007 CISSRS Student Computer Integrated Surgery Society
2005-present Washington Computer Aided Surgery Society (WashCAS)
2005-present Medical Image Computing and Computer-Assisted Intervention Society
2010-present SPIE Image-Guided Procedures, Robotics, and Modeling Conference Committee Member
2010-present ASME Dynamic Systems and Controls Robotics Technical Committee Member
2010-present IEEE BioRob Conference Associate Editor
2013-present IEEE/RSJ Int'l Conf. on Intelligent Robots and Systems Associate Editor

Honors
1997-2002 Dixon Fellow
1997-2002 Calhoun Honors Scholar
1997-2002 Scholarships: IPTAY, CU, Square D, ADTRAN, AFCEA, Mallette, FEEA
1999-2002 Most Outstanding Electrical Engineer in Class, Clemson University (3 yrs)
1999 Fourth Place, IEEE Piedmont Student Paper Competition
2002 Most Outstanding Undergraduate Engineer, Clemson University
2002 First Place, IEEE Piedmont Student Paper Competition
2002 Tau Beta Pi Fellowship
2002 National Defense Science and Engineering Graduate Fellowship
2003 National Science Foundation Fellowship
2003 Best Project, Advanced Computer Integrated Surgery
2006 Best Presentation, Computer Integrated Surgical Systems and Technology Center
2006 IROS Best Paper Finalist: “Toward Active Cannulas: Miniature Snake-Like Surgical Robots”
2007 Damon Runyon-Rachleff Innovation Award Semifinalist
2009 Best Poster Award: ASME Design of Medical Devices Conference (three in five competition)
2010 Vanderbilt School of Engineering Best Student Paper of the Year Award (to my student)
2011 Best Poster Finalist: ASME Design of Medical Devices Conference (three in five competition)
2011 National Science Foundation CAREER Award
2011 IEEE Volz award for PhD thesis impact on the field during the two years following publication
2012 Best Medical Robotics Paper Finalist, IEEE International Conf. on Robotics and Automation
2012 Best Poster Award: ASME Design of Medical Devices Conference (three in five competition)
2013 Best Medical Robotics Paper Finalist, IEEE International Conf. on Robotics and Automation
2013 Best Poster Award: ASME Design of Medical Devices Conference (three in five competition)

C. Selected peer-reviewed publications (Selected from over 100 peer-reviewed publications)

Most relevant to the current application


Additional recent publications of importance to the field (in chronological order)


D. Research Support

Ongoing Research Support

NSF CAREER #IIS-1054331 Webster (PI) 7/1/11-6/30/16 $400,000
Lifesaving Robotic Tentacles

The major goal of this proposal is to explore the basic science of continuously flexible robots of various architectures, including tendon-actuated, concentric tube, and magnetically-actuated robots, and to study algorithms to endow these robots with intelligent behaviors.

NIH R01 #DC012593 Webster (PI) 2/15/13-2/14/17 $1,456,393
Safe, Rapid Access to the Internal Auditory Canal for Acoustic Neuroma

The major goal of this project is to design and experimentally validate a bone-attached parallel robot for mastoidectomy. The robot will be designed to ensure safe drilling to the internal auditory canal.
<table>
<thead>
<tr>
<th>Grant Number</th>
<th>PI</th>
<th>Start Date</th>
<th>End Date</th>
<th>Funding</th>
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<tbody>
<tr>
<td>NIH R01 #EB017467</td>
<td>Webster (PI)</td>
<td>7/1/13</td>
<td>5/30/17</td>
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<tr>
<td>Robotic Natural Orifice Skull Base Surgery</td>
<td>Webster (PI)</td>
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<tr>
<td>NIH R01 #DC010184</td>
<td>Labadie (PI)</td>
<td>9/1/09</td>
<td>8/31/13</td>
<td>$2,970,077</td>
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<tr>
<td>Pediatric Percutaneous Cochlear Implantation: Clinical Validation and Implementation</td>
<td>Labadie (PI)</td>
<td>7/1/2012-6/30/2017</td>
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<td>NIH R01 #DC008408</td>
<td>Labadie (PI)</td>
<td>7/1/2012</td>
<td>6-30/2017</td>
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<tr>
<td>Clinical Validation and Testing of Percutaneous Cochlear Implantation</td>
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<td>NIH R44 #CA134169</td>
<td>Burdette (PI)</td>
<td>8/1/08</td>
<td>7/31/13</td>
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<td>Precisely Shaped Acoustic Ablation of Tumors Under 3D Ultrasound Image Guidance</td>
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<td>Fluid-Powered Surgery &amp; Rehabilitation via Compact, Integrated Systems</td>
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<td>Clinical Translation of Deformation Compensation for Image-Guided Liver Surgery</td>
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<tr>
<td>Curvilinear Brain Surgery: Hope for Inoperable Patients</td>
<td>Webster (PI)</td>
<td>5/1/13-4/31/15</td>
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<td>VISE Seed Grant</td>
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<td>6/30/13</td>
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<td>NSF CPS 1239355</td>
<td>Valdastri (PI)</td>
<td>12/1/12-11/30/16</td>
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<td>CPS: Synergy: Integrated modeling, analysis and synthesis of miniature medical devices</td>
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Completed Research Support

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<td>6/1/10</td>
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<td>Reaching inaccessible anatomy percutaneously via multi-lumen steerable needles</td>
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</table>
BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. DO NOT EXCEED FOUR PAGES.

NAME
Frank M. Warren, III, MD

POSITION TITLE
Assistant Professor of Otolaryngology, School of Medicine

eRA COMMONS USER NAME (credential, e.g., agency login)
WARRENF

EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)

<table>
<thead>
<tr>
<th>INSTITUTION AND LOCATION</th>
<th>DEGREE</th>
<th>MM/YY</th>
<th>FIELD OF STUDY</th>
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<tr>
<td>Tufts University, Medford, MA</td>
<td>BS</td>
<td>1989-92</td>
<td>Biology</td>
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<tr>
<td>Oregon Health Sciences University, Portland, OR</td>
<td>MD</td>
<td>1995-99</td>
<td>Medicine</td>
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<td>Oregon Health Sciences University, Portland, OR</td>
<td>Intern</td>
<td>1999-00</td>
<td>Surgery</td>
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<tr>
<td>Oregon Health Sciences University, Portland, OR</td>
<td>Resident</td>
<td>2000-04</td>
<td>Otolaryngology</td>
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<tr>
<td>Vanderbilt University Medical Center, Nashville, TN</td>
<td>Fellow</td>
<td>2004-06</td>
<td>Neuro-Otology</td>
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</table>

A. Personal Statement

The goal of this project is to demonstrate that magnetic guidance of cochlear implants can be used to make the surgical insertion consistently less traumatic than the current paradigm of manual insertion by reducing insertion forces and forces on the basilar membrane, and to develop a method to safely remove the magnet after the insertion is complete, such that the patient may undergo future MRI scans.

My responsibility as co-Investigator on this project is to add technical expertise from the point of view of a cochlear implant surgeon. I will help in the tasks related to magnetic guidance during insertion and magnet removal after insertion. I have already contributed to the development of the two scala tympani phantoms that the lab has produced, and also performed the surgical dissections to harvest the cochlea from the temporal bone for cadaveric insertions. In addition, I will help analyze the histologic sections of the cochlea following insertions.

My expertise in cochlear implantation began with my fellowship training in neuro-otology (the subspecialty of ENT that just focuses on the ear). In addition to further training in ear surgery during this time, I also worked with Dr. Robert Labadie at Vanderbilt on his percutaneous cochlear implant project. Since that time, I have been a cochlear implant surgeon. I am currently the director of the OHSU cochlear implant program and performed over 100 cochlear implants last year. We have active research ongoing in clinical outcomes after cochlear implantation and I have published on several aspects of cochlear implantation as outlined below.

B. Positions and Honors.

Positions and Employment

2006-2010 Assistant Professor, University of Utah School of Medicine, Department of Surgery Otolaryngology-Head and Neck, Salt Lake City, UT

2010-Present Assistant Professor, Oregon Health and Science University, Department of Otolaryngology-Head and Neck Surgery, Portland, OR

Other Experience and Professional Memberships

None to report.

Honors

None to report.
C. Selected peer-reviewed publications

Most relevant to current application (in order of relevance)


Additional recent publications of importance to the field (in chronological order)


**D. Research Support.**

**Ongoing Research Support**
None to report.

**Completed Research Support**
None to report.
1. Project Director / Principal Investigator (PD/PI)

Prefix: Dr.
First Name*: JAKE
Middle Name: J
Last Name*: ABBOTT
Suffix:

2. Human Subjects

Clinical Trial? ☐ No ☐ Yes
Agency-Defined Phase III Clinical Trial?* ☐ No ☐ Yes

3. Permission Statement*

If this application does not result in an award, is the Government permitted to disclose the title of your proposed project, and the name, address, telephone number and e-mail address of the official signing for the applicant organization, to organizations that may be interested in contacting you for further information (e.g., possible collaborations, investment)?

☐ Yes ● No

4. Program Income*

Is program income anticipated during the periods for which the grant support is requested?  ☐ Yes ● No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

<table>
<thead>
<tr>
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<th>Anticipated Amount ($)*</th>
<th>Source(s)*</th>
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</table>
# PHS 398 Cover Page Supplement

## 5. Human Embryonic Stem Cells

Does the proposed project involve human embryonic stem cells?  ● No ○ Yes

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: [http://grants.nih.gov/stem_cells/registry/current.htm](http://grants.nih.gov/stem_cells/registry/current.htm). Or, if a specific stem cell line cannot be referenced at this time, please check the box indicating that one from the registry will be used:

**Cell Line(s):**

Specific stem cell line cannot be referenced at this time. One from the registry will be used.

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<th>Line 8</th>
<th>Line 9</th>
<th>Line 10</th>
<th>Line 11</th>
<th>Line 12</th>
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## 6. Inventions and Patents (For renewal applications only)

Inventions and Patents*: ○ Yes ○ No

If the answer is "Yes" then please answer the following:

Previously Reported*: ○ Yes ○ No

## 7. Change of Investigator / Change of Institution Questions

- Change of principal investigator / program director
  
  Name of former principal investigator / program director:
  
  Prefix:
  
  First Name*:
  
  Middle Name:
  
  Last Name*:
  
  Suffix:

- Change of Grantee Institution
  
  Name of former institution*:

Tracking Number: GRANT11521489

Contact PD/PI: ABBOTT, JAKE, J
# PHS 398 Modular Budget

## Budget Period: 1

| Start Date: 07/15/2014 | End Date: 07/14/2015 |

### A. Direct Costs

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<tr>
<th>Description</th>
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<tr>
<td>Consortium F&amp;A</td>
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### B. Indirect Costs

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<tr>
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<th>Indirect Cost Base ($)</th>
<th>Funds Requested ($)</th>
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<th>DHHS, Wallace Chan, 415-637-7820</th>
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### C. Total Direct and Indirect Costs (A + B)

| Funds Requested ($) | 357,536.00 |

---

Contact PD/PI: ABBOTT, JAKE, J
# PHS 398 Modular Budget

## Budget Period: 2

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## A. Direct Costs

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**Cognizant Agency**

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**Indirect Cost Rate Agreement Date**

04/22/2009

**Total Indirect Costs**

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## C. Total Direct and Indirect Costs (A + B)

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PHS 398 Modular Budget

**Budget Period:** 3  
**Start Date:** 07/15/2016  
**End Date:** 07/14/2017

### A. Direct Costs

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**Cognizant Agency**  
( Agency Name, POC Name and Phone Number)  
DHHS, Wallace Chan, 415-637-7820

**Indirect Cost Rate Agreement Date**  
04/22/2009

**Total Indirect Costs**  
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### C. Total Direct and Indirect Costs (A + B)

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# PHS 398 Modular Budget

**Budget Period:** 4  
**Start Date:** 07/15/2017  
**End Date:** 07/14/2018

## A. Direct Costs

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## B. Indirect Costs

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**Cognizant Agency**  
**DHHS, Wallace Chan, 415-637-7820**

**Indirect Cost Rate Agreement Date**  
04/22/2009

**Total Indirect Costs**  
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## C. Total Direct and Indirect Costs (A + B)

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PHS 398 Modular Budget

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<td>Direct Cost less Consortium F&amp;A*</td>
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<table>
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**Cognizant Agency**  
DHHS, Wallace Chan, 415-637-7820

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<table>
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## PHS 398 Modular Budget

### Cumulative Budget Information

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<tbody>
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<td>Section B, Total Indirect Costs for Entire Project Period ($)</td>
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<tr>
<td>Section C, Total Direct and Indirect Costs (A+B) for Entire Project Period ($)</td>
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<tr>
<td>Additional Narrative Justification</td>
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</table>
**Personnel Justification**

The research spans a five-year period. The justification of the personnel necessary to conduct the proposed research is provided below:

**Jake Abbott, PhD, Principle Investigator, average 2.1 calendar months (17% effort) in Years 1-5**

Dr. Abbott is an Assistant Professor in the Department of Mechanical Engineering. He will lead the portions of the project involving magnetic guidance for cochlear-implant insertion, and magnet attachment/detachment and removal. He will advise one PhD student in Year 1, one postdoc in Years 2-3, and another postdoc in Years 4-5. He will also coordinate the efforts of the other investigators. His group has already developed the spherical-permanent-magnet manipulator that will be used in the proposed research.

Dr. Abbott has eight years of research experience in the areas of surgical robotics and magnetic manipulation. During his postdoctoral research, he had a leading role in a group that made significant leaps in magnetic manipulation, including the smallest-ever magnetic swimming microrobot, and a system that enables manipulation of a submillimeter fully untethered microrobot for vitreoretinal procedures. He has published 68 peer-reviewed papers, and has five patents and patents pending, including those related to the technology and methods used in this proposal. At the University of Utah, he continues to explore methods for remote manipulation with magnetic fields. He is the recipient of the NSF CAREER Award for his work on the use of nonuniform magnetic fields for the control of medical devices, which forms the analytical foundation of the work proposed here. He currently has funded projects from Given Imaging to explore magnetic propulsion of capsule endoscopes using similar techniques to those used in this proposal, and from Intuitive Surgical to develop a telemanipulation system for retinal surgery.

The amount of effort he has budgeted here is limited only due to the constraints placed by the modular budget limit: the PI chose to budget slightly less salary than is typical in order to assemble a team with the expertise to successfully complete the proposed research. At two or more months of salary budgeted each year, this project will constitute 66% of his standard total research effort. Most of the PI's other active projects will be complete by the time of this award. The PI has included a letter from his Department Chair with a commitment that his teaching load will remain low (one course per semester) and that he has the option of buying out of his teaching commitment one semester each year, should his research demand more of his time. As an Early Stage Investigator, Dr. Abbott appreciates the importance of his successfully completing each of the project's specific aims, and he is fully committed to this project.

**Frank Warren, MD, Co-Investigator, average 1.15 summer months (9% effort) in Years 1-5**

Dr. Warren is an Assistant Professor in the Department of Otolaryngology-Head and Neck Surgery at Oregon Health and Science University. He will guide the project team on all clinical aspects of the project. He has collaborated with PI Abbott since the inception of the project proposed here. He will be actively involved in the planning of the research, and the dissemination of results. He will conduct the human cadaver temporal-bone insertions at Vanderbilt throughout the duration of the project. He will work with Dr. Park to conduct the in vivo guinea-pig insertions at Utah, and conduct the histologic examination, in Years 3 and 5. He has budgeted travel for multiple trips per year to Nashville and Salt Lake City.

Dr. Warren has been involved with studies of various interventions for hearing loss, including a study of stapes implants in temporal bone specimens, and a study investigating the feasibility of performing a percutaneous cochlear implant. He is currently the director of the OHSU cochlear implant program, and performed over 100 cochlear implants last year. He has active research ongoing in clinical outcomes after cochlear implantation and has published on several aspects of cochlear implantation.
Robert J. Webster III, PhD, Co-Investigator, 1 summer month (8% effort) in Years 1-5
Dr. Webster is an Assistant Professor in the Department of Mechanical Engineering, with a secondary appointment in the Department of Otolaryngology. He will oversee all activities at Vanderbilt related to this project. He will lead the portion of the project involving segmentation and processing of the scala tympani from CT scans, system integration and registration, and force-feedback control of cochlear-implant insertion. He will advise one PhD student. His group has already developed the automatic force-sensing insertion tool that will be used in the proposed research.

Dr. Webster’s work on bevel-based needle steering was the core technical foundation for successful NIH R21 (#EB003452) and subsequent R01 (#EB006435) grants. His work on "Active Cannula" became the foundation of an NSF project (#0651803), NIH R21 (#EB011628 – Webster PI), NIH SBIR (R44 #CA134169), and NIH R01 (EB017467) on which he is PI. He is Co-I on an NIH project (#R01 CA162477) for image guidance in abdominal soft tissues. In his work on image-guided cochlear implant surgery, he is a Co-I on a NIH R01 (#DC10184) on applying microstereotactic frames to pediatric populations for percutaneous cochlear implantation, and PI on an R01 for robotic acoustic neuroma surgery; neither of these projects has any overlap with the current proposal, as both project involve precise drilling and neither involve insertion. In view of the overall impact of his work on the field of medical robotics, he received the NSF CAREER award (#IIS-1054331) and the 2011 IEEE Volz award.

Tim Ameel, PhD, Co-Investigator, 1 calendar month (8% effort) in Years 2-5
Dr. Ameel is Professor and Chair in the Department of Mechanical Engineering at the University of Utah. He will lead the portions of the project involving heat-transfer associated with the magnet detachment process, and he will advise one PhD student.

The heat-transfer analysis of the proposed magnetic cochlear implant involves conduction within the implant and convection to the small annular space surrounding the implant. Dr. Ameel's research focuses on the engineering science of microscale fluid dynamics and convection heat transfer, with nearly 100 manuscripts in the area. He is an expert on slip-regime convection, and his experimental work has emphasized the characterization of microchannel flow and convection. His heat-exchanger analysis has focused on the effects of thermal interaction with the ambient, an inherent condition at small scales.

Albert Park, Senior Personnel, (0% effort)
Dr. Park is a Professor in the Department of Surgery, Division of Otolaryngology-Head and Neck Surgery, at the University of Utah, and Section Chief of Pediatric Otolaryngology at Primary Children's Medical Center. Although Dr. Park has not budgeted any effort, he has budgeted effort of his lab technician. His laboratory will perform the auditory brainstem response threshold testing and temporal bone processing for the Hartley nonpigmented guinea pigs undergoing cochlear implantation under magnetic guidance. His laboratory also has experience with the surgical techniques, auditory testing, and temporal bone histology in guinea pigs.

Dr. Park's work related to guinea pig auditory physiology and anatomy began in 2004 when his laboratory developed and evaluated resorbable ventilation tubes. Currently, much of his work is focused on understanding the pathophysiology of cytomegalovirus induced (CMV) hearing loss, a leading case of pediatric hearing loss. His group has developed both guinea pig and murine models for CMV induced labyrinthitis. They have been able to demonstrate in utero transplacental transmission of guinea pig (gp) specific CMV to newborn pups and congenital hearing loss by audity brainstem response and distortion product otoacoustic emission testing. They have also demonstrated gpCMV DNA in the cochlea by PCR analysis. In the murine
model, they have shown elevated ABR thresholds in 4-week-old infected pups and GFP expression of the virus in the spiral ganglion and scala tympani 7 days after inoculation.

Graduate Students (Two), 12 calendar months (100% effort) in Years 1-5
• One student will be advised by Dr. Abbott (PI) at the University of Utah in Year 1, and will focus on magnetic guidance of cochlear implants; this will be the student who has been involved with all of the preliminary work on magnetic guidance during cochlear-implant insertion, who is nearing completion of his PhD.
• One student will be advised by Dr. Ameel (co-I) at the University of Utah in Years 2-5, and will focus on the heat-transfer analysis associated with the magnet detachment process in the cochlea.
• One student will be advised by Dr. Webster (co-I) at Vanderbilt University, and will focus on registering the robotic and magnetic subsystems to the scala tympani, force-feedback control during cochlear-implant insertion, and experimental verification in human cadaver temporal bones.

Postdoctoral Researcher, 12 calendar months (100% effort) in Years 2-5
• One postdoc will be supervised by Dr. Abbott (PI) at the University of Utah in Years 2-3, and will focus on magnetic guidance during cochlear-implant insertion. This postdoc will most likely be the former PhD student that has been involved with all of the preliminary work on magnetic guidance during cochlear-implant insertion.
• One postdoc will be supervised by Dr. Abbott (PI) at the University of Utah in Years 4-5, and will focus on magnet attachment/detachment. This postdoc will have expertise in microfabrication.

Lab Technician, 1.25 calendar months (10% effort) in Years 3 and 5
Dr. Park (Senior Personnel) has budgeted his lab technician at 20% effort for 6 months in each of Years 3 and 5. This lab technician will conduct all of the non-surgical work associated with the guinea-pig experiments.
Consortium Justification

This project is a consortium of three domestic universities: the University of Utah, Vanderbilt University, and Oregon Health and Science University (OHSU). The University of Utah is the lead institution, with Jake Abbott as Principle Investigator. The research spans a five-year period, and conforms to a modular budget, with total direct costs of $250,000 per year. The cost breakdown by year and by institution is given in Table 1.

**Table 1: Consortium costs, rounded to the nearest $1,000**

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The following is a description of the personnel (with percent effort and responsibilities) at each institution. A more detailed description of project personnel can be found in the Personnel Justification document.

**University of Utah, $767,000 direct costs, $1,147,000 total costs**

- **Jake Abbott, PhD, Principal Investigator, average 2.1 calendar months (17% effort) in Years 1-5.** Dr. Abbott is an Assistant Professor in the Department of Mechanical Engineering. He will lead the portions of the project involving magnetic guidance for cochlear-implant insertion, and magnet attachment/detachment and removal. He will also coordinate the efforts of the consortium personnel. He will advise one PhD student in Year 1 (the PhD student who has done all of the preliminary work on this project, who is nearing graduation), one postdoc in Years 2-3 (most likely the current PhD student), and another postdoc in Years 4-5. The amount of effort budgeted by the PI is limited here only due to the modular budget: the PI chose to budget slightly less salary than is typical in order to assemble a team with the expertise to successfully complete the proposed research. At two or more months of salary budgeted each year, this project will constitute 66% of his standard research effort. Most of the PI’s other active projects will be complete by the time of this award. The PI has included a letter from his Department Chair with a commitment that his teaching load will remain low (one course per semester) and that he has the option of buying out of his teaching commitment one semester each year should his research demand more of his time.

- **Tim Ameel, PhD, Co-Investigator, 1 calendar month (8% effort) in Years 2-5.** Dr. Ameel is Professor and Chair of the Department of Mechanical Engineering. He will lead the portion of the project involving heat-transfer analysis associated with the magnet detachment process. He will advise one PhD student.

- **Albert Park, MD, Senior Personnel (0% effort).** Dr. Park is a Professor in the Department of Surgery, Division of Otolaryngology-Head and Neck Surgery, and Section
Chief of Pediatric Otolaryngology at Primary Children’s Hospital. Dr. Park’s lab has the expertise to conduct the guinea-pig experiments, including the ABR testing, surgery, and histology. Although Dr. Park has not budgeted any effort, he has budgeted his lab technician at 20% effort for six months in Years 3 and 5.

- **Lab Technician, 1.25 calendar months (10% effort), Years 3 and 5.** Dr. Park (Senior Personnel) has budgeted his lab technician at 20% effort for 6 months in each of Years 3 and 5. This lab technician will conduct all of the non-surgical work associated with the guinea-pig experiments.

- **Graduate Student, 12 calendar months (100% effort), Year 1.** One student will be advised by Dr. Abbott (PI), and will focus on magnetic guidance of cochlear implants; this will be the student who has been involved with all of the preliminary work on magnetic guidance during cochlear-implant insertion, who is nearing completion of his PhD.

- **Graduate Student, 12 calendar months (100% effort), Years 2-5.** One student will be advised by Dr. Ameel (co-I), and will focus on the heat-transfer analysis associated with the magnet detachment process in the cochlea.

- **Postdoctoral Researcher, 12 calendar months (100% effort), Years 2-3.** One postdoc will be supervised by Dr. Abbott (PI), and will focus on magnetic guidance during cochlear-implant insertion. This postdoc will most likely be the former PhD student that has been involved with all of the preliminary work on magnetic guidance on magnetic guidance during cochlear-implant insertion.

- **Postdoctoral Researcher, 12 calendar months (100% effort), Years 4-5.** One postdoc will be supervised by Dr. Abbott (PI), and will focus on magnet attachment/detachment. This postdoc will have expertise in microfabrication.

Vanderbilt University, $362,000 direct costs, $509,000 total costs

- **Robert Webster III, PhD, Co-Investigator (8% effort in Years 1-5).** Dr. Webster is an Assistant Professor in the Department of Mechanical Engineering and the Department of Otolaryngology. He will lead the portion of the project involving segmentation and processing of the scala tympani from CT scans, system integration and registration, and force-feedback control of cochlear-implant insertion. He will advise one PhD student. Dr. Webster has a number of related active NIH grants, but no project has any overlap with the proposed research: one project involves drilling safely to the cochlea, the other project is strictly about drilling mastoidectomies, and neither involves insertion of the electrode array.

- **Graduate Student, 12 calendar months (100% effort), Years 1-5.** One student will be advised by Dr. Webster (co-I), and will focus on registering the robotic and magnetic subsystems to the scala tympani, force-feedback control during cochlear-implant insertion, and experimental verification in human cadaver temporal bones.

Oregon Health and Science University, $121,000 direct costs, $186,000 total costs

- **Frank Warren, MD, Co-Investigator (9% average effort in Years 1-5).** Dr. Warren is a neuro-otologist and cochlear-implant surgeon that will guide the project team on all clinical aspects of the proposed research. He will conduct the human cadaver temporal-bone insertions at Vanderbilt. He will work with Dr. Park to conduct the in vivo guinea-pig insertions at Utah, and conduct the histologic examination. He has collaborated with Dr. Abbott on all of the preliminary work related to magnetic guidance of cochlear implants and development of anatomic and clinically accurate scala-tympani phantoms, frequently traveling to Utah since leaving Utah to join the faculty at OHSU.
# PHS 398 Research Plan
Please attach applicable sections of the research plan, below.

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Introduction to the Revised Application

We would like to thank the reviewers for their valuable feedback on our proposal. We appreciate the enthusiasm expressed for the “highly significant” goal of reducing intracochlear trauma during cochlear-implant (CI) insertion, the “highly innovative nature” of using magnetic guidance to accomplish this goal, and the “considerable praise voiced for the systematic research strategy that moves from phantoms to cadavers.” We also appreciate the constructive criticism from the reviewers, which was clearly given in the spirit of helping us improve our research strategy. We have taken the criticism seriously, and have worked diligently to gather new preliminary data and improve our research plan, including a new plan for micro CT scans of cadaver temporal bones to evaluate intracochlear trauma and final CI placement, and new in vivo guinea-pig experiments that will enable us to evaluate trauma using both auditory brainstem response (ABR) hearing tests and histology. We have made significant revisions throughout the proposal (emphasized in italics).

Multiple reviewers felt that the focus of the research should be on trauma reduction, rather than deeper insertion or improved CI performance; we have adapted our strategy to this end.

Multiple reviewers felt that limited cadaver testing raised concerns; we have now done some preliminary cadaver insertions that are promising, and we have segmented the scala tympani of cadavers CT scans, successfully demonstrating individual components that will be combined in the proposed work.

Reviewer 1 was concerned that all preliminary data were gathered using a 3:1 scale model, and was concerned that the methods might not scale down properly. We have moved to 1:1 scale scala-tympani phantoms, and have modified actual commercial CIs with magnetic tips (rather than using custom-made 3:1 scale mock-up CIs). The new data presented here are even more promising than the data provided in the original submission.

Reviewer 1 was concerned that insertion forces are not being correlated with damage, and that magnetic-guidance improvements are only relative to automatic insertion. Although the types of damage that occur with traditional insertions are well documented, it is not correlated with insertion force. That said, we have already demonstrated that we consistently achieve lower peak forces while the electrode is advanced off the stylet with our automated insertion tool than obtained by trained surgeons. We have also shown that magnetic guidance provides additional improvement. Our study will be the first to truly address the reviewer’s concern.

Reviewer 1 would have preferred to see a force-sensed CI tip, rather than a forced-sensed basilar membrane in a phantom. Although we agree this would be very desirable, to the best of our knowledge, the technology does not currently exist to embed a sensor with the desired resolution in such a small package size. Our method will measure the entire basilar-membrane force, which will be a conservative over-estimate of tip force.

Reviewer 1 was concerned by tether abrasion during magnet removal. As observed when using transparent phantoms, the tether is never put into significant tension when pulled slowly, since the detached magnet tends to move in the direction of a gentle tether force when it is vibrated. By adding in vivo guinea pig studies both with and without magnet removal, we will be able to quantify any damage due to CI insertion and magnetic removal independently. In addition, we have already successfully removed a spherical magnet from deep within a scala-tympani phantom using a completely open-loop (i.e., blind) magnetic method that rolls the magnet out without any tether, and found the method to be fast and robust. We include this method as an alternate strategy.

Reviewer 1 requested more description of our optical tracking system, which we have provided.

Reviewer 2 was concerned that multiple investigators had only budgeted “summer months.” Although this concept is typically only an accounting construct for engineering faculty, multiple investigators have changed their salary to “calendar months” to more accurately capture their commitment throughout the year.

Reviewer 2 was concerned that there was not sufficient expertise in radiological or histological evaluation of trauma. Although Dr. Warren is capable of doing this analysis himself, the addition of Dr. Park to this proposal significantly strengthens our team in this regard.

Reviewer 2 was concerned that real-time imaging is required for our magnetic guidance methods. To be clear, real-time imaging is not used in any of our preliminary studies. Imaging is only used to create the plan, which is then run open-loop during the insertion. In the proposed work, the image-based plans will be replaced by the CT-based plans discussed above (which have already been demonstrated in preliminary studies).

Reviewer 2 was concerned that the drop point of paraffin wax occurs at a dangerously high temperature. We have conducted experiments to prove that the drop point can be precisely controlled to safer temperatures.

Reviewer 3 was concerned about a lack of provisions to deal with possible inhomogeneity in the heat-transfer model. We have included more detail on our numerical model that will capture the various geometric, thermodynamic, and transport properties of the fluid-filled cochlea in the temporal bone, and that includes within-material inhomogeneity to account for factors like blood perfusion and the porosity of bone.
Specific Aims

As a cochlear implant (CI) is surgically inserted into the scala tympani, delicate intracochlear structures are often damaged, which can result in decreased implant effectiveness and loss of residual hearing, especially when the implant deviates into the adjacent scala vestibuli chamber via rupture of the basilar membrane, which occurs in approximately 33% of insertions. The goal of reducing surgical trauma is especially compelling given that electric acoustic stimulation, which is a relatively new treatment directed at individuals with a considerable amount of residual hearing in the low-frequency range, requires atraumatic insertions to preserve the patient’s residual hearing. The goal of this project is to demonstrate that magnetic guidance of CIs will reduce trauma relative to manual insertion. Magnetic guidance will be accomplished with an inexpensive clinical system based on proven robotic and magnetic technologies developed by the investigators.

Specific Aim 1: Magnetic Guidance for Improved CI Insertion

We will test the conjecture that magnetic guidance will reduce insertion forces and forces against the basilar membrane compared to manual insertions, using a CI with a magnet embedded in the distal tip.

- **Task 1-1**: Develop scala-tympani phantom with force-sensitive basilar membrane. Knowledge of force against the basilar membrane during insertion is critical yet currently unavailable.
- **Task 1-2**: Optimal placement of external magnet. Determine the location of the manipulator magnet relative to the patient’s head that optimizes the balance between control authority and safety.
- **Task 1-3**: Segmentation and registration of the scala tympani. The cochlea and scala tympani will be automatically segmented and registered relative to the robotic and magnetic subsystems. We will develop patient-specific automated trajectory planning algorithms that describe the location and desired orientation of the CI tip as a function of insertion depth. We hypothesize that magnetically guided CI insertions using patient-specific trajectory planning will result in less insertion trauma than magnetically guided insertions using an averaged trajectory.
- **Task 1-4**: Develop magnetic guidance algorithms. Separate algorithms will be developed to solve for the correct magnetic field magnitude and orientation as a function of insertion depth for the four combinations of precurved and free-fitting CIs with cochleostomy and round-window insertions, using the results of Tasks 1-2 and 1-3. Thorough experimentation will be done using phantom cochleae.
- **Task 1-5**: Develop real-time force controller. By utilizing the insertion force being measured in real-time in combination with the planned trajectories from Task 1-4, the method can be made safer and more robust to registration errors by detecting and quickly acting upon force rises that are imperceptible manually.
- **Task 1-6**: Reduce forces through high-frequency vibration. We will determine if low-amplitude high-frequency “dithering” provides additional benefits when combined with the results of Tasks 1-4 and 1-5.

Specific Aim 2: Safe Detachment and Removal of the Magnet

We will test the conjecture that the magnet can be safely removed after CI insertion, such that the patient would not be precluded from future MRI scans.

- **Task 2-1**: Attaching and detaching the magnet from the CI tip. We will develop a method to attach a magnet to the tip of a CI, forming a rigid connection for insertion, and allowing the connection to be broken after insertion. We will consider two methods, and determine which is most effective.
- **Task 2-2**: Ensure safe heating during magnet detachment. The detachment mechanisms of Task 2-1 result in heating near the distal tip of the CI. Heat-transfer modeling and analysis will be used to ensure that cochlear structures are not damaged by heating.
- **Task 2-3**: Safe removal of the magnet. After magnet detachment, the magnet will be gently removed from the cochlea using a tether and magnetic assistance. An alternate, tetherless plan is also proposed.

Specific Aim 3:

We will verify the methods developed in the first two aims in human cadaver temporal bones and guinea pigs.

- **Task 3-1**: Ex vivo human cadaver temporal bone experiments, with micro CT. Throughout the duration of the project, we will conduct insertion experiments in human cadaver temporal bones to verify that reduction of insertion force with magnetic guidance relative to manual insertion is similar to that observed in phantoms. Micro CT scans will be used to verify that the CI is not misdeployed, and that intracochlear structures such as the basilar membrane are not disrupted.
- **Task 3-2**: In vivo guinea-pig experiments, with ABR and histology. At the end of Specific Aim 1 and Specific Aim 2, we will conduct experiments on live guinea pigs and perform auditory brainstem response tests and histology to verify that trauma is reduced using magnetic guidance, relative to manual insertion.
1 Research Strategy: Significance

Approximately 1.5 million Americans three years of age or older are completely deaf in both ears [12], and 28 million suffer from some form of hearing loss [39]. Cochlear implantation is an FDA-approved treatment for sensorineural hearing loss, which accounts for 90% of all hearing loss. A cochlear implant (CI) is an array of electrodes embedded in silicone that is surgically inserted into the scala-tympani chamber of the cochlea to electrically stimulate the nerves responsible for hearing (Fig. 1).

As the CI is inserted into the scala tympani, delicate intracochlear structures are often damaged, which can result in decreased implant effectiveness and loss of residual hearing [2, 47, 56, 59, 60], especially when the implant deviates into the adjacent scala vestibuli chamber (via rupture of the basilar membrane), which occurs in approximately 33% of insertions [3, 17, 52]. Common causes of intracochlear trauma that can occur even during “successful” implantations include tip scraping [18], tip fold-over [44], and electrode-array buckling [8, 18] (Fig. 2).

Two major factors contribute to damage during insertion: surgical technique and CI design [47]. CIs are currently inserted manually, and there can be wide variability in force application. Multiple studies evaluating CI designs have included straight electrode arrays [1, 18, 54, 60], precurved electrode arrays [5, 18, 19, 54, 59, 60], and arrays with external positioners [19, 46, 53]. Different array designs result in varying amounts of intracochlear trauma during insertion. Studies have been conducted on the various insertion methods for stylet-based, precurved CIs, such as the standard insertion technique [8, 46, 53], the partial stylet withdrawal [8, 53], and the advance-off-stylet (AOS) technique [44, 46, 53]. AOS showed a notable decrease in forces for nearly the entire insertion procedure. However, advancing too early can cause the implant tip to fold-over, and late stylet removal can result in the implant contacting the scala-tympani outer wall, potentially causing damage. The variability in human cochlea dimensions poses a challenge when using these techniques, since the time during insertion when stylet removal should begin is patient-dependent.

It has been said that future CIs will need to address three widely accepted goals [44]: (1) reduced intracochlear damage during surgical insertion, (2) deeper insertion into the scala tympani to access lower frequency cochlear neurons, and (3) greater operating efficiency, defined as a reduction in the stimulus charge required to produce a comfortable loudness level. Due to the limitations of existing CIs, several research groups have developed experimental prototypes designed to achieve a perimodiolar position within the cochlea [36, 57, 58, 62], with some CIs actively bent or steered during insertion to minimize insertion trauma [7, 9, 64, 66]. Several previous studies have used insertion force measurement as a means to compare CI designs and evaluate insertion technique [1, 34, 43, 46, 48, 53, 63, 64, 66], with a decrease in insertion force believed to correspond to a decrease in trauma. Variability can be greatly decreased using robot-assisted insertion [21, 34, 48] and optimized path planning [64, 66], and robots enable insertion speed [63] and other desired parameter values [64, 65] to be more easily reproduced. However, CI designs that use mechanical means to achieve bending can increase the stiffness of the array as it is being inserted. If the array is not a good fit for the scala-tympani channel, or is misdirected down the channel, the increased stiffness could result in increased trauma.

The objective of this project is to test the hypotheses that magnetic guidance of CIs will reduce insertion forces and forces against the basilar membrane during surgery, and consequently reduce trauma, for both free-fitting and precurved CIs. Magnetic guidance will be accomplished with an inexpensive clinical system, based on combined proven technologies developed by the investigators. The goal of reducing trauma is especially compelling given that electric acoustic stimulation (EAS), which is a relatively new treatment directed at individuals with a considerable amount of residual hearing in the low-frequency range, is receiving greater interest. EAS combines electric stimulation of high frequencies with acoustic amplification of low frequencies, but it requires atraumatic cochlear-implant insertions to preserve the patient’s residual hearing for effectiveness. Unlike other proposed methods, our method will not add increased stiffness to the CI, and our method will be designed to work with existing
CIs already in clinical use with only minor modifications, some of which have already been done by our collaborators at MED-EL (see letter of collaboration). By reducing interaction forces between the CI and intracochlear structures, the results of our method will likely provide additional benefits related to deeper CI insertion and, in the case of precurved CIs, enabling tighter hugging of the modiolus since magnetic torque can be used to uncoil a CI with a tighter resting shape.

2 Research Strategy: Innovation

Our original magnetic-guidance concept was presented in [10], and in the original submission of this proposal. To achieve CI guidance, a small permanent magnet is located at the tip of the CI. A large actuator magnet located near the patient’s head is used to apply a magnetic field to the CI tip. As the CI is inserted, the actuator magnet is rotated slowly to apply torque to the tip of CI in order to bend it and direct it away from cochlear walls, and to keep it parallel to the scala-tympani channel to protect the basilar membrane, thus reducing the contact forces that cause trauma. The actuator magnet is also allowed to translate with one degree-of-freedom (1-DOF) to vary the distance between it and the patient to change the strength of the applied magnetic field acting on the CI tip. The CI insertion is synchronized with external-magnet movement in software. In a 3:1 scale prototype and scala-tympani phantom, we showed an approximately 50% reduction in insertion force throughout the insertion.

Since the original submission of this proposal, our group has made significant progress and invented new technology that will enable better and safer magnetic guidance at reduced cost. Our current system concept is illustrated in Fig. 3. An automatic CI insertion tool with real-time sensing of insertion force, developed by co-I Webster’s group, inserts the CI either by cochleostomy or round window. The magnetic actuation system consists of a spherical permanent magnet manipulator (SPMM) on a 1-DOF linear stage. The SPMM, recently invented by PI Abbott’s group, consists of a spherical magnet that can be instantaneously rotated about any axis using three motor-driven omniwheels whose axes are mutually orthogonal, which contact the spherical magnet and drive it with friction. An approximately 1:1 scale prototype SPMM has been constructed in the PI’s lab. The patent-pending SPMM is an enabling technology that reduces the need for a large, expensive, and potentially dangerous robotic manipulator to orient the magnet in space near the patient’s head, representing a significant improvement over our original concept. The linear stage is positioned to allow the SPMM to move toward/away from the patient’s head, but be physically incapable of touching the patient’s head for inherent safety. Manually operated lockable positioning arms are used to position the two devices. The entire system is registered to the patient using a commercial optical tracking system (Polaris Spectra).

The automatic CI insertion tool developed by co-I Webster’s group is shown in Fig. 4. It is equipped with sensors to intraoperatively monitor forces applied to the cochlea [48]. The tool uses the mechanism of [22, 42] with two linear piezoelectric motors for automatic AOS insertion. The motors have nanometer-resolution encoders that enable accurate closed-loop control of the speed and depth of insertion. The main linear motor is connected to a surgical forceps that are tightened to grip the proximal end of a CI and to advance it through a rigid guide tube into the scala tympani. AOS CIs are straightened before insertion by a stylet wire inserted into a central channel of the array. The second motor attaches to the exposed proximal end of the stylet wire, and halts the advancement of the stylet at the basal turn of the scala tympani. Further advancement of the main motor then causes the CI to deploy off of the stationary stylet, regaining its pre-curved shape. The tool is also suitable for use with non-AOS (free-fitting) CI designs, which would not require use of the second motor. To measure mN-range forces applied by the CI to the cochlea, we developed a flexure mechanism that suspends both motors from a rigid mounting. An arrangement of semiconductor strain gauges on flexures enables continuous monitoring of mN-range forces applied by the CI to the cochlea. Experiments performed with

![Figure 3: Concept for magnetically assisted cochlear-implant surgery. The external magnet manipulator is shown rotated by 180° to illustrate the functional components, but the three moving omniwheels will actually be on the opposite side so as not to potentially conflict with the insertion tool or the patient’s ear.](image)

![Figure 4: Automatic cochlear implant insertion tool already developed.](image)
a scala-tympani phantom indicate that use of an automatic insertion tool will result in lower peak forces on the cochlea during the AOS portion of insertion than those applied during traditional freehand insertions [34]. The automatic insertion tool executes highly repeatable insertion trajectories, allowing us to compare forces recorded with magnetic guidance to unguided insertions without the confounding influence of operator technique.

Magnetic guidance of cochlear implants is completely innovative; besides the PI’s preliminary studies, it has never before been attempted. Force sensing combined with robotic AOS CI insertion is also innovative; and was achieved for the first time in co-I Webster’s preliminary studies. The overall innovation in this proposal is amplified by the fact that it combines these two technological advancements toward improving patient hearing outcomes through the creation of a fully automated CI insertion system with the potential to achieve significant CI insertion trauma reduction.

3 Research Strategy: Approach
This project has three specific aims. The first aim will test the conjecture that magnetic assistance of CI insertion will reduce insertion forces and forces against the basilar membrane. We will consider both free-fitting CIs and precurved AOS CIs with permanent magnets embedded in the tips. We will develop a safe, inexpensive, and easy-to-use clinical system that implements the methods developed here. The second aim will test the conjecture that the magnet can be safely removed from the CI and from the cochlea after CI insertion. This aim is motivated by making the CI MRI compatible. The third aim will verify the methods of the first two aims in human cadaver temporal bones ex vivo, and guinea pigs in vivo. The ex vivo studies will verify that the methods developed here will result in a reduction in insertion forces and trauma in human cochleae. The in vivo studies, with hearing tests and histology, will demonstrate that trauma on delicate intracochlear structures is reduced using the methods developed here.

Specific Aim 1: Magnetic Guidance for Improved CI Insertion
Task 1-1: Develop Basilar-Membrane Phantom
To perform thorough experiments during the development of our proposed method, we must have accurate phantom cochleae, since cadaver experiments are both expensive and cumbersome and, as such, must be used sparingly. Phantoms available from CI manufacturers each have limitations in duplicating the anatomical and clinical constraints imposed upon CI insertions, making insertion experiments in these phantoms too easy. We had previously developed a scala-tympani phantom that was more anatomically accurate, and manufactured a 3:1 scale version [11]. In our original submission of this proposal, we proposed to make a 1:1 scale phantom that is more accurate in terms of both anatomy and clinical approach. In the time since our first submission, we have completed that work (Fig. 5), and we now have access to very accurate scala-tympani phantoms for both cochleostomy and round-window insertions [28].

In our preliminary work, we showed a significant decrease in insertion force using magnetic guidance, implying a net decrease in forces of the CI against the scala-tympani walls. However, it is conceivable that force of the tip against the basilar membrane actually increases due to magnetic attraction. We can analytically bound this force, and we hypothesize that it is not significant and will likely decrease with magnetic guidance because the field helps maintain tip alignment parallel to the walls.

To experimentally investigate this hypothesis, we will design a new phantom that has an instrumented “basilar membrane” (Fig. 6). The scala tympani will be modeled as an open channel that has collapsed to a plane. A Nano-dyne force sensor, which the PI has used previously for similar sensitive measurements [13], will be used to create a force-sensitive ceiling; the sensor has µN accuracy, which is more than sufficient to resolve the basilar forces. This new phantom loses some accuracy due to the loss of the full 3D spiral structure, but will provide valuable information that is currently unavailable by any means. By synthesizing experiments with both

Figure 5: Scala-tympani phantoms with MED-EL CI inserted [28].

Figure 6: A collapsed open-channel phantom with a force-sensitive ceiling to approximate the basilar membrane.
Figure 7: (a) When a magnet with dipole moment $\mathbf{M}$ rotates around the axis $\hat{\Omega}$ with $\mathbf{M}$ perpendicular to $\hat{\Omega}$, the field vector at any given position rotates around, and is perpendicular to, a constant axis (shown at various positions with large blue arrows). A representation of the ellipse traced out by the rotating magnetic field at the position $\mathbf{p}$ is shown. (b) A slowly rotating magnet is used to roll a magnetic sphere down a transparent tube. The actuator magnet’s position in space is held constant, but its axis of rotation is updated based on the position of the rolling sphere. Videos of this and other experiments can be seen on PI Abbott’s lab web page. (c) This concept enables us to move the position of the external magnet around the patient’s head to find the optimal location. At each position, there is a unique correct axis of rotation. Translation toward/away from the cochlea does not affect the solution. Magnets are depicted as rectangles rather than spheres for clarity.

Although we agree with previous reviewers that it would be desirable to place a force sensor directly at the tip of the CI, we believe that the technology does not currently exist in a small enough package to enable such a sensor to be incorporated with commercially available CIs and enable measurements with the resolution that we require. If such a sensor does become available, we would surely incorporate it into future designs. However, our proposed solution is conservative in that it measures the total force applied across the entire basilar membrane, which will be larger than that applied only at the tip of the CI (which is where actual membrane punctures typically occur).

Task 1-2: Determine Optimal Placement of the External Magnet

In our original conception of magnetic guidance of CIs, the external actuation magnet was placed such that its axis of rotation was co-axial with the modiolus. This puts a constraint on system design, and the attractive force pulls the magnet on the CI’s tip toward the external magnet and toward the basilar membrane, which is undesirable (although simulations and measurements of this attractive force are smaller than the force that has been shown to puncture the membrane [24], even making worst-case assumptions). Through the support of the PI’s NSF CAREER Award, we have significantly advanced that state-of-the-art in understanding ways in which a single controlled permanent magnet can be used to apply controlled force and torque to manipulate another smaller magnetic device [29–33, 41]. We have discovered a number of unintuitive and useful phenomena, and as a result, we can modify our original concept to enable magnetic guidance that is both more effective and safer. We have discovered that a rotating magnetic field can be created at any location in space about any desired axis, using an actuator magnet at any other location in space, and there is a unique axis-of-rotation at each location to achieve the desired rotating field ( [32, 33], Fig. 7(a)). We know that the method is quite robust to localization uncertainty (i.e., we do not need perfect knowledge of the patient’s modiolar axis to choose a near-optimal magnet location and axis), and misalignments of 10° have essentially no impact on performance [30]. We have also found that the magnetic force on the CI magnet, which is typically attractive, can be redirected by up to 90° away from the actuator if the magnet is allowed to move into non-co-axial positions [29]. Fig. 7(c) shows the co-axial position, as well as two alternate positions in which the external magnet is located in non-co-axial positions, with their necessary axes of rotation. With our new spherical permanent magnet manipulator (Fig. 3), all axes of rotation are equally easy to achieve. Certain positions are more desirable than others in that they allow the external magnet to get closer to the cochlea, and thus enable a smaller magnet to be used at the tip of the CI.

We will determine the optimal placement of the external magnet. We will start by taking CT scans of a human head and turning the surface of the head into a point cloud in which each point is described relative to the intersection of the patient’s modiolus and the basal turn of the cochlea. We will then simulate a spherical magnet touching each point and normal to the local surface described by neighboring points. For each external-magnet configuration, we will simulate the CI tip at locations/orientations that span the entire scala-typani. For each CI configuration, we will simulate the...
orientation of the external magnet at orientations that span its entire 360° range of motion. For each of these combinations of parameters, we will evaluate the worst-case (i.e., minimum) magnetic torque for control authority to guide the CI, and the worst-case (i.e., maximum) force component in the direction of the basilar membrane. The optimal placement will ultimately be chosen to maximize the ratio of magnetic torque to magnetic force in the direction of the basilar membrane: available magnetic torque is always desirable in that it is used to guide the CI through the scala tympani, and there will never be a significant torque component that would tend to bend the tip into the basilar membrane due to the phenomenon shown in Fig. 7(a); magnetic force is always undesirable in that we do not use it for CI guidance with our method, and our goal is to minimize interaction forces. After choosing the optimal magnet placement based on simulations, we will verify optimality by performing exhaustive and statistically significant insertion experiments in our various phantoms discussed previously. We will consider the magnet at the hypothesized-optimal location as well as surrounding locations. We will use both insertion force and basilar-membrane force as figures of merit. In both simulations and experiments, we will determine the sensitivity to alignment and positioning errors, quantify the amount of error that is acceptable, and determine if patient-specific magnet positioning is required or if the optimal magnet position for the “average patient” can be used across the population.

**Task 1-3: Segmentation and Registration of the Scala Tympani**

Before the surgery, the surgeon will manually select the location of the cochlea on the CT image set, indicating the apex, the cochleostomy or round-window entry point, and another point on the basal turn of the cochlea, as well as identifying the surface of the forehead of the patient in the scan. The scala tympani will then be segmented using existing methods [38] as shown Fig. 8 and registered to the selected cochlea points before the surgery, with the surgeon confirming the alignment. Then, in the operating room, the CT image space (and hence the cochlea model) will be registered to the patient using a standard brow scan with the optical tracking system (the procedure used on clinical image-guidance systems such as Brainlab system, which is widely clinically used). Since both the insertion tool and the magnetic manipulator will be optically tracked, the position of the magnet will be known relative to the cochlea and the insertion tool. We will use a Polaris Spectra optical tracker, which has a positional accuracy of 0.25 mm, leading to sub-degree angular accuracy. We will develop this clinic-ready procedure, as well as a modification for use in the cadaver experiments.

A set of instructions for how to adjust the magnetic manipulator will be output to a display screen so that the surgeon can move the magnet into place, in a manner conceptually similar to adjusting a standard stereotactic frame, with feedback from the display screen telling the surgeon how the final system arrangement should look with respect to the patient, what adjustments should be made, and when the adjustment has been correctly completed. Based on preliminary studies quantifying the robustness of our magnetic-field methods to misalignment and localization uncertainty [30], we will test the hypothesis that the optical tracking system and precise system registration will not actually be required for the final clinic-ready system. Rather, the surgeon will simply arrange the system as depicted on the display. A clinic-ready system that did not require an optical-tracking system would be significantly less expensive. The inherent-safe nature of the system will ensure that the magnet cannot contact the patient after the initial alignment by the surgeon. We will test our hypothesis by conducting phantom and cadaver experiments both with and without optical tracking, and will quantify the differences in terms of insertion force, basilar-membrane force, and trauma. Even if the actual contour of the patient-specific trajectory is not of great value over an average trajectory (e.g., when using the force-feedback controller of Task 1-5), the location of the cochlea and alignment of the scala tympani (i.e., the vector \( \mathbf{v} \) in Fig. 8) with respect to the external anatomy could be important.

**Potential Pitfalls and Backup Plans:** If registration via brow scan is not sufficiently accurate, we will instead mount the insertion tool directly to the patient’s skull using bone anchors and a microstereotactic frame as suggested in [48] (see [4, 26, 27, 37] for further information on this approach). The Vanderbilt group currently has two active R01 grants on this topic, one of which co-I Webster is a co-I on, and the other of which has
supported some of his graduate student’s research in this area. We do not suggest this method as “plan A” because it requires a CNC milling machine and trained machinist in the hospital. Although we have proven that these infrastructural elements are feasible in some hospitals, we prefer optical tracking since it is already widely deployed and relatively low in cost. If our cochlea model is not sufficiently accurate to account for patient-to-patient variability, we will use statistical atlas techniques to segment patient-specific cochlea geometry [38] (Fig. 8). This will enable us to determine patient-specific CI trajectories, which can be used to plan the motion of the system in cadaveric trials. We hypothesize that the methods of Task 1-4 and Task 1-5 will make this unnecessary.

**Task 1-4: Magnetic Guidance Algorithms**

We will develop magnetic planning algorithms that parameterize the optimal magnetic field orientation and magnitude as a function of CI insertion depth. We will consider both free-fitting CIs and pre-curved AOS CIs, as well as both cochleostomy and round-window insertions, with the four scenarios being treated independently. The magnetic field will be oriented such that it is orthogonal to the scala tympani at each location of the tip as the CI is inserted, in order to generate maximum torque (with the desired tip orientation parallel to the scala typanic). The magnitude of the magnetic field, which is set by controlling the distance between the external magnet and the cochlea, will be parameterized by insertion depth such that the CI tip is actually observed to be parallel to the scala tympani, using the transparent phantom. Once we have constructed a function that maps insertion depth to required magnetic-field magnitude, this function can be used with any scala-tympani plan, including those obtained from CT scans as described in Task 1-3. To be clear, the transparent phantom will be used to generate the plans, but real-time visual feedback is not required for our magnetic-guidance method.

We have very recently gotten a permanent-magnet distributor to start manufacturing magnets at our desired sub-millimeter scale at low cost to us, and we have gotten MED-EL (a leading CI manufacturer) to begin making free-fitting CIs for us with our magnets embedded in the tip (Fig. 10). All future experiments with free-fitting CIs will be of this type (see letter of collaboration).

In addition to using magnetic fields to coil a free-fitting CI, we will use magnetic fields to uncoil a pre-curved CI in combination with the AOS technique. We will use the Cochlear Nucleus Contour Advance (NCA) in all experiments; Cochlear is by far the largest clinical supplier of cochlear implants in the US, and co-Is Webster and Warren both have extensive experience with the NCA. With free-fitting CIs, the required torque increases as the CI is inserted, and thus the external magnet moves toward the head during the insertion. With pre-curved CIs, the maximum torque required to straighten the CI is through the initial straight portion of the scala tympani,
where tip fold-over is a major concern that can be overcome with magnetic guidance. As the insertion proceeds, the magnetic torque is reduced by moving the external magnet away from the head, allowing the CI to return to its natural curved shape. We will begin by modifying NCAs with a magnetic tip (e.g., Fig. 9), and then work with Cochlear to embed our small magnets in the tip of the NCA.

For all four insertion scenarios, we will evaluate the robustness of our method to registration errors, quantified by an increase in applied forces as a function of misalignment angle. The PI's group has found time after time with a variety of systems that magnetic manipulation methods are robust to localization and registration errors, and we hypothesize that this will hold true for magnetic guidance of CIs. This is due to the fact that magnetic torque is based on a vector cross-product, which is very insensitive to angular misalignment of up to 10°.

**Task 1-5: Real-time Force Control**

In insertion experiments described previously, insertions were pre-planned, and insertion-force data were gathered only for post-insertion analysis. By utilizing the insertion-force measurements in real-time, we will develop control algorithms that minimize insertion forces adaptively throughout the insertion, essentially allowing the CI to “feel in the dark”. At its essence, the method will function by inserting the CI a very small distance, monitoring the force rise (at a level that would be imperceptible by a surgeon manually), retracting the same small distance, making a small modification to the magnetic fields, and then repeating. Unexpected increases in force will be detected before they become problematic. We already have rudimentary force-feedback implemented, with an unintended rise in force being detected and acted upon in less than 1 ms. We hypothesize that incorporating real-time force-feedback algorithms with pre-planned trajectories will improve performance, making insertions more robust to registration and modeling errors, and adding a level of safety that is current not available with manual insertions.

**Task 1-6: Reducing Forces through High-Frequency Vibration**

In addition to the slowly varying field used to guide the tip of the CI via a significant bending torque, we will experiment with the superposition of higher-frequency magnetic fields (1–50 Hz) to induce a low-amplitude vibration in the CI’s distal tip in an attempt to further improve insertion. We will also consider vibration induced by the piezoelectric insertion tool on the proximal end. These sorts of “dithering” techniques are commonly used to inhibit sticking due to friction. We have conducted pilot studies with cadaver temporal bones that indicate tip vibration will likely be beneficial (Fig. 11). In the experiments, the external magnet was spun continuously at a variety of speeds as the CI was inserted, and at certain speeds we observed a reduction in insertion force, even though we were not causing any bulk deformation in the CI.

We do not intend to utilize vibration on its own, rather, it will be superimposed with the magnetic guidance of Task 1-4 and the force-feedback control of Task 1-5. All vibration studies will be completely experimental (i.e., no modeling component), and will be exhaustively conducted using phantom cochleae. To generate the higher-frequency magnetic fields, we will use an electromagnet located near the patient’s head. The field’s magnitude-frequency combinations that will be used will be well below the known safety limits of time-varying magnetic fields. We hypothesize that vibration will result in improved insertion, but our method does not hinge on vibration for success. If vibration of the CI is deemed to be of little additional value, or if additional trauma is observed, we will simply abandon vibration.

**Figure 10:** A custom commercially manufactured cylindrical NdFeB permanent magnet has been embedded in CIs by MED-EL engineers.

**Figure 11:** Round-window insertion of free-fitting MED-EL CI in cadaver temporal bones. Open-loop “blind” vibration, without any other magnetic guidance, reduces insertion forces in the final stage of the insertion. The effect appears to be both frequency and velocity dependent.
Aim 2: Safe Detachment and Removal of the Magnet

It is undesirable to leave a permanent magnet inside a patient’s cochlea. At best, it would create a large imaging artifact in an MRI scan, and at worst, it could be unsafe to have an MRI scan. Our goal in this aim is to detach and remove the magnet from the tip after insertion of the CI. This aim is completely independent of the first aim, particularly considering that there are currently a number of CIs in clinical use that are not MRI-compatible.

Task 2-1: Attaching and Detaching the Magnet from the CI’s Tip

We will develop a method to attach a magnet to the tip of a CI, forming a rigid connection for insertion, and allowing the connection to be broken after insertion. We will explore two approaches (Plans A and B), and determine which method is superior only after thorough analysis and experimentation.

Plan A: Attachment with Paraffin Wax and Detachment with Resistive Heating: In the first plan, the permanent magnet will be attached to the tip of the CI using paraffin wax to form a rigid connection during insertion. A fine insulated copper wire will be arranged in a “radiator” fashion in the paraffin-wax interface, rigidly attached to the magnet, with the two wire leads acting as the tether of the magnet. Electrical current will result in minor heating along the length of the tether, and significant heating at the “radiator” to heat the paraffin and release the magnet. The drop point (i.e., the temperature at which the wax significantly softens, which occurs at a significantly lower temperature than the melting point) can be controlled by the manufacturer, and paraffin can be manufactured to very high purity. Paraffin is inert (similar to the CI silicone), and has been used in the form of “bone wax” in ear surgery for many years (e.g., placed in the balance canals to occlude them for various vestibular disorders [51]).

The paraffin may not form a sufficiently robust connection with the CI silicone. If this is the case, we will develop a “crown” made of biocompatible material (e.g., titanium, platinum) on which the magnet will be attached, manufactured using known techniques such as microwire electrical discharge machining. This crown will be placed on the tip of the CI. The magnet will be released and removed, but the crown will remain on the CI. This design may be beneficial even if a direct paraffin-silicone connection is possible, since the crown design would effectively enable the crown-magnet-tether system to be an aftermarket product that could be attached directly to existing commercial CIs without any modification.

It is widely acknowledged that a 2°C rise in temperature can be tolerated by tissue with no adverse effects. Hyperthermia therapies (e.g., combined with chemotherapy) typically involve a temperature increase of 5–8°C, and thermoablation (direct cell death through heat) typically involves a temperature increase of 13°C. Taking these values into consideration, our primary goal is to tune the magnet release event (via the drop point of the wax) to occur at a temperature rise 2–5°C above body temperature. At this value, there is no risk to the surrounding tissue structure. It is allowable for the magnet and CI tip to have a slightly higher temperature rise, provided that the surrounding tissue only experiences a rise of a few degrees during the heating and magnet-removal process, but we will therefore need to better understand the heat-transfer mechanisms to the surrounding tissue: this is the topic of Task 2-2. We will also consider simply lowering the wax drop point to require less heating for release while still providing a sufficiently rigid connection during CI insertion. We have conducted experiments that blend pure paraffin wax with mineral oil.

![Figure 12: The drop point of paraffin wax can be controlled by blending with mineral oil.](image)

Plan B: Attachment with Solder and Detachment with Electrolysis: We will develop a mechanism inspired by Guglielmi Detachable Coils (GDCs), which are a standard treatment for brain aneurysms [20]. A GDC is made of platinum, and is rigidly soldered to a steel guidewire. The GDC, via the wire, is deployed into an aneurysm using a catheter, and then electrolysis is used to break the connection at the interface of the two metals: the wire is held at a low voltage relative to the patient’s body, which is grounded, and a very small current is induced, which results in the connection dissolving over the course of approximately 4 minutes, leaving the platinum coil unharmed, at which point the wire and catheter can be removed, leaving the GDC behind. The electrolysis rate is proportional to the current (e.g., half the current could be used, but it would take 8 minutes). No material is lost into the blood stream in this process.

In our GDC-inspired mechanism, the platinum portion will be directly attached to the CI tip as the “crown,” which will remain inside the patient, and solder joints will be made at one or more points to connect the magnet to the platinum. Each solder joint will require its own wire for the electrolysis process, but multiple joints can be dissolved simultaneously. These wires will also act as the tether(s) to remove the magnet after detachment. The method in this plan also generates...
electrical heating, but as a byproduct, not as the primary means of magnet release. Since heating is proportional to the square of current, simply reducing the current and allowing a little more time for release can have a large effect on heat generated.

Task 2-2: Ensuring Safe Heating During Magnet Detachment

Both of the detachment methods being considered involve some local electrical current at the magnet-CI interface. The release mechanisms proposed will subsequently transfer heat to the silicone support structure, the attachment material, and the surrounding fluid and tissue. A certain amount of heat is required to raise the temperature of the paraffin wax in Plan A, but if the heating effect is significant, device failure or tissue damage is possible. In Plan B, heat generation can be managed as needed at the cost of longer time for a complete release, but heat generation must still be understood for proper management.

Although other medical researchers have used a lumped capacitance method (LCM) [23] to make predictions of the heating effect of an electromagnet formed from copper wire [6,45,49,50], this simplification does not include conduction, convection, and radiation effects. To investigate the heating effect further, a preliminary finite element analysis (FEA) that includes conduction and convection effects was performed using ANSYS and compared against a basic LCM approach. A conducting coil was modeled as an annulus with outer and inner diameters of 1 and 0.5 mm, respectively, and the silicone cylinder was 0.5 mm in diameter with an overall length of 1 cm. Note that final CI and permanent-magnet dimensions will likely be different than those used in this preliminary analysis, and the results are only intended to show capability, trends, and issues for future study. A 0.5 A current was applied to the copper annulus with a resistance of 5 Ω. A convective boundary condition was applied to the outer surfaces with a heat transfer coefficient of $h = 15 \text{ W/K/m}^2$ and ambient temperature of 310 K. The temperature in the silicone near the copper heater (location of the maximum temperature) is presented as a function of time for the heating and cooling processes in Fig. 13. The current was applied for a time period of 60 s and then turned off to investigate the cool-down rate due to convection with two $h$ values. The $h$ effect on the cooling rate is significant, indicating that environmental effects are important. In a project involving a coil at the tip of a catheter, Roberts et al. [45] concluded that temperature rise will be approximately 1 °C/s since additional materials in contact with the copper wire (e.g., silicone and blood) have nearly the same energy storage capacity, but we cannot make that conclusion because the difference in energy storage capacity between copper and silicone is very significant at 300 K. Our preliminary FEA results indicate that simply assuming that the temperature will increase at 1 °C/s at the (arbitrary) simulated current of 0.5 A would underestimate the actual heating rate.

Thus, it is essential that an accurate thermal model of the system (CI and surrounding fluid and tissue) be developed to determine heating effects before experiments are performed. Model accuracy will be enabled by incorporating all heat-transfer modes and medium inhomogeneity. An existing open-source code (Uintah.utah.edu) developed at the University of Utah will be used for the advanced modeling efforts. Specifically, a fluid structure interaction algorithm that couples a traditional Implicit Continuous Eulerian (ICE) algorithm for the fluids with the particle-based Material Point Method (MPM) for the solids will be applied. The simplified FEA did not include radiation effects. The fluid flow around the CI can also be simulated, alleviating the need to assume a heat-transfer coefficient. These additional physics, including conduction in all systems, radiation, and fluid flow, will be included in the detailed model. Full parametric studies will be conducted with the computational model. Parameters to be studied include: magnet size; CI diameter; attachment material (properties, thickness); surface properties (absorptivity, emissivity) of silicone, nickel plating, the attachment material, and tissue; fluid type (properties); tissue perfusion rate; initial system temperature; and ambient temperature. Moreover, experimental work will be performed to validate the model. Embedded thermocouples at discrete locations will measure the transient temperature in the CI prototype during actual magnet-detachment tests. With a transparent scala-tympani phantom, thermal images of the CI prototype during magnet-detachment tests will allow spatial and temporal temperature validation. The computational and experimental thermal analyses will produce data that will enable CI design and the quantification of a detachment process that is safe and efficient.

![Figure 13: Temporal temperature response (emphasizing expected trends) for the coil model: (-) LCM, VH on; (+) FEA, VH on; (○) FEA, VH off, $h = 15 \text{ W/K/m}^2$; (●) FEA, VH off, $h = 1 \text{ W/K/m}^2$.](image-url)
Task 2-3: Removing the Magnet

Safe removal of the detached magnet will be accomplished through a combination of gently pulling the magnet with a tether and vibrating the magnet using alternating magnetic fields to reduce sticking. The alternating magnetic field will be generated in two ways: by quickly rotating the external magnet in an open-loop fashion, and by using the same electromagnet used for the high-frequency-vibration insertions studies. The concept of magnet removal with a precurved CI is depicted in Fig. 14(a). Because the CI hugs the modiolus, the detached tip can be removed along the outer wall by pulling gently on the attached tendon as the magnetic guidance system redirects the detached tip along the channel. The cross-sectional geometry of the scala tympani is such that a CI resting near the modiolus leaves sufficient space for the magnet to be nearly the same size as the CI's tip itself. As the magnet is removed, the channel enlarges and the tether shortens; as a result, peak retraction forces occur at the beginning of the retraction, as expected. In the case of free-fitting CIs, the CI rests against the outer wall of the scala tympani, and the magnet is retracted on the modiolar side, but with the tether pressing the magnet outward against the silicon of the CI, analogous to the CI itself.

We conducted a preliminary experiment to explore peak retraction force as a function of magnetic vibration induced in the tip, without any additional form of magnetic guidance (Fig. 14(c)). Our hypothesis was that vibration reduces friction, and a gentle tension on the tether creates a preferential direction of motion, such that the magnet wiggles out of the scala tympani. Thus, the force required to remove the tethered magnet is reduced. We found this to be the case, and observed a significant reduction in required retraction force. We will thoroughly explore this phenomenon, both in our phantom cochleae and in cadaver experiments. We will quantify the effect of vibration frequency, retraction speed, and field strength (regulated by changing the distance between the external magnet and the cochlea) on tether-retraction forces and basilar-membrane force.

Potential Pitfalls and Backup Plans: In the event of unforeseen complications with our primary strategy, we will pursue an alternate strategy in which the same electromagnet used for high-frequency vibration during insertion and magnet removal is used to generate inductive heating to release the magnetic tip. This was our “Plan B” in our first submission of this proposal, but we believe that the new method of electrolytic detachment is more desirable for a number of reasons. With inductive heating, the copper wire interface at the paraffin wax is replaced by ferromagnetic material (e.g., permalloy) rigidly attached to the permanent magnet, and it is this material that is heated by a high-frequency magnetic field. In our previous submission, we included an extensive preliminary analysis of the required high-frequency magnetic fields compared against known safety standards (considering both peripheral nerve stimulation and cardiac fibrillation), and we found that the required heating would be possible at safe levels; this previous analysis is omitted in this submission due to space constraints. The tether, which is insulated copper wire in our primary strategy, is no longer required to conduct electricity, and is now Ultra-High-Molecular-Weight-Polyethylene (UHMWPE) fiber because of its accepted use in medical applications and its low coefficient of friction (0.05) [35]. Since the measured coefficient of friction between commercial CIs and the endosteum lining, conducted under wet conditions, is greater than 0.10 [25], any possible abrasion due to the tether should be less than the abrasion caused by the sliding of the CI during insertion, especially since the friction of UHMWPE is measured under dry conditions (ASTM D3108) [55], and likely overstates the tether’s friction coefficient while immersed in the fluid in the cochlea.

In the event that tether abrasion observed in the in vivo studies is the only problem with the primary strategy, we can embed the electrically conducting wires of Plan A or B inside the silicone CI, and use the UHMWPE tether to remove the magnet. We believe that a tether is inherently desirable, but an alternate strategy would allow magnet removal without a tether. If the cylindrical tip magnet is replaced with a spherical tip magnet, it can simply be rolled out of the cochlea after detachment. We have already successfully performed such a tetherless magnet removal from a 1:1 scale phantom using a 1-mm-diameter magnet in an open-loop “blind” fashion, and
finding it to be very robust and repeatable. The method is very similar to the rolling demo shown in Fig. 7(b), utilizing the phenomenon of Fig. 7(a). In our experiment, we inserted a small spherical magnet very deep into a scala tympani phantom, and quickly (\(\sim 3\) sec) rolled the magnet to the cochleostomy opening with no knowledge of the position of the magnet within the phantom, using only knowledge of the orientation of the modiolus.

### Aim 3: Ex Vivo and In Vivo Experimental Validation

**Task 3-1: Validation in Human Cadaver Temporal Bones**

In the final phases of Tasks 1-4, 1-5, 1-6, and 2-3, we will perform studies of cochlear insertion in human cadaver temporal bone specimens. Our hypothesis is that insertions will proceed similar to insertions in phantoms in terms of reduction of insertion force, and that there will be very little trauma to the inner-ear structures when compared to manual insertions. 10 cochleae will be used for each insertion scenario, including a manual-insertion control and a nonmagnetic automatic-insertion control. A mastoidectomy will be performed on the temporal bone to accommodate the insertion device and a cochleostomy or round-window opening will be made in the standard fashion for a cochlear implantation. The cochlea will be filled with saline solution to most closely simulate in vivo insertion conditions. For each trial, the electrode will be fully inserted into the cochlea as insertion forces are recorded. Following the insertion experiments, the CI will be left in place, and a micro CT scan will be made in the standard fashion for a cochlear implantation. The cochlea will be filled with saline solution to most closely simulate in vivo insertion conditions. For each trial, the electrode will be fully inserted into the cochlea as insertion forces are recorded. Following the insertion experiments, the CI will be left in place, and a micro CT scan will be used to assess if any inner-ear structures were damaged and if the CI deviated from the scala tympani. It has been shown that micro CT has sufficient resolution (down to 10 \(\mu\)m) to see soft tissues and resolve basilar-membrane disruption by a CI. We have access to micro CT at a rate of $25/hr, with 3/hr per bone estimated. The types of trauma that occur with traditional insertions are well documented in the literature (see Section 1), but are not typically correlated with insertion force measurements. Our work will contribute insight that is largely absent from the available literature.

**Task 3-2: In Vivo Guinea-Pig Experiments**

Hearing loss due to CI insertion trauma seems to have two components: (1) acute trauma to structures such as the basilar membrane, and (2) delayed destruction of hair cells that develop after the initial trauma. Since immediate post-insertion cochlea histology can only evaluate acute trauma, experiments with guinea pigs [14, 15] and rats [16] involving in vivo auditory brainstem response (ABR) measurements are being used in combination with post-mortem histology to evaluate both components of trauma-induced hearing loss. We believe that guinea-pig experiments, similar to those accomplished by Eshraghi et al. [14–16], have the required resolution to evaluate the effectiveness of our proposed strategies and represent the first attempt to use both histology and hearing loss metrics in evaluation of automated insertions of any kind.

At the end of Specific Aim 1 (Year 3), and again at the end of Specific Aim 2 (Year 5), we will conduct guinea-pig experiments, under IACUC approval, as follows. Four groups of Hartley non-pigmented guinea pigs will be used to test the four independent insertion cases. For each animal in these groups, one ear will be randomly chosen to be implanted using magnetic guidance, and the contralateral ear will serve as the manual-insertion control case. Prior to implantation, ABR testing, which is fully described in a publication by Park (Senior Personnel) [40], will assess each animal’s original residual hearing in each ear. In short, ABR measures the guinea pig’s hearing response in an acoustically isolated environment to clicks and tone bursts at various frequencies and various decibel levels, as measured by recording electrodes. Hearing loss will be defined as a 15-db increase in the required sound level to produce the same measured response prior to cochlear implantation. To assess hearing loss due to acute trauma, ABRs will be conducted immediately after implantation, which in Specific Aim 2 includes the extraction of the removable magnet. By comparing the ABR results immediately after implantation between Specific Aim 1 and Specific Aim 2, an assessment of the acute trauma due to magnet removal can be made. A final ABR will be conducted seven days after implantation to evaluate delayed, trauma-induced hearing loss.

Upon completion of the ABR studies, the animal will be euthanized, and the CI will be gently manually extracted from the cochlea. The temporal bone will then be harvested and fixed via perilymphic perfusion of buffered formalin solution through the oval window, followed by dehydration with an ascending series of alcohols (70–100% ethanol). Specimens will then be embedded in polymethylmethacrylate at 20°C with 100 \(\mu\)m serial sections made of all specimens. Histology slides will be examined by two researchers independently, grading the trauma using the scale described by Eshraghi et al. [14].

In order to evaluate the baseline trauma due solely to a cochleostomy procedure, an additional fifth group of guinea pigs will undergo “sham” surgery (i.e., a cochleostomy without electrode placement), with full ABR and histology evaluations. Finally, a sixth group of guinea pigs will act as a control, undergoing no form of surgery, but still undergoing full ABR and histology evaluations. We have budgeted for five guinea pigs in each of the six groups, in each year of experimentation.
Project Management
Jake Abbott (PI, University of Utah) will lead the portions of the project involving magnetic guidance, and magnet attachment/detachment and removal. He will also coordinate the efforts of the co-Is. Robert Webster (co-I, Vanderbilt University) will lead the portion of the project involving segmentation and processing of the scala tympani from CT scans, system integration and registration, and force-feedback control. Tim Ameel (co-I, University of Utah) will lead the portion of the project involving heat-transfer analysis associated with the magnet detachment process. Frank Warren, MD (co-I, Oregon Health and Science University) is a neuro-otologist and cochlear-implant surgeon that will guide the project team on all clinical aspects of the proposed research. He will conduct the human-cadaver insertions at Vanderbilt and analyze the micro CT scans post-insertion, and he will conduct the guinea-pig insertions at Utah and perform the histologic examination. Albert Park, MD (Senior Personnel, University of Utah) will provide the expertise required to conduct the in vivo guinea-pig experiments, including ABR and histologic examination. The project team will hold biweekly Skype meetings.

Hardware Development Tasks:
0-1 Construct two spherical-permanent-magnet manipulators based on prototype device in PI Abbott’s lab for use in Abbott and Webster labs (JA).
0-2 Construct automatic insertion tool based on device in co-I Webster’s lab for use in Abbott lab (RW).
0-3 Develop a graphical surgeon interface (RW, FW).

Specific Aim 1 Tasks:
1-1 Develop scala-tympani phantom with force-sensitive basilar membrane (JA, FW).
1-2 Optimal placement of external magnet (JA, FW).
1-3 Segmentation and registration of the scala tympani (RW, FW).
1-4 Magnetic guidance algorithms with both precurved and free-fitting CIs, for both cochleostomy and round-window insertions, using phantom cochleae (JA).
1-5 Develop real-time force controller (RW).
1-6 Explore high-frequency vibration, first magnetically, then with piezoelectric insertion stage (JA, RW).

Specific Aim 2 Tasks:
2-1-A Develop paraffin-wax attachment/detachment method (JA, TA).
2-2-B Develop electrolysis attachment/detachment method (JA, TA).
2-3 Modeling and experimentation to ensure safe heating in cochlea during detachment (TA, JA, FW).
2-4 Method for safe removal of magnet after detachment (JA, FW).

Specific Aim 3 Tasks:
3-1 Ex vivo human temporal bone experiments, with micro CT (FW, RW).
3-2 In vivo guinea-pig experiments, with histology (FW, AP, JA).

Plans for Future Research upon Completion
No in vivo human studies will be conducted in this project, but upon completion there will be copies of the developed clinic-ready system located at the University of Utah and Vanderbilt University, which will enable trials with animals and humans to be conducted simultaneously in multiple locations in future work. Since the total cost of a complete clinic-ready system will be approximately $40,000 (less if optical tracking is deemed unnecessary), it is also realistic that more copies could be constructed for more locations in future work (e.g., Oregon Health and Science University).

At Vanderbilt, Robert Labadie, MD and co-I Webster are developing methods to drastically reduce the invasiveness of the surgical procedure that prepares the patient for the CI insertion, currently supported under NIH R01 DC008408. Part of that work involves the use of nested sets of telescoping precurved Nitinol tubes to create “active cannulas” [61]. The method can be used for both cochleostomy and round-window CI insertions. In the future, such a device could deploy the magnetically guided CIs developed herein. Following the support of this award, our goal is to combine the results of the two projects to create an engineered system for next-generation minimally invasive CI surgery. However, the impact of the research herein does not hinge upon the combined future effort.
Vertebrate Animals

The proposed research will involve experiments with Hartley non-pigmented guinea pigs, as detailed in Task 3-2 in the Research Strategy document. However, the animal studies will not begin until approximately the end of Year 3 of the project. Because the exact involvement of animals is still indefinite, we will submit to the NIH awarding office detailed information and verification of IACUC approval prior to the involvement of animals, as described in PHS SF424.
References


References Cited


Consortium/Contractual Arrangement

The proposed research plan includes a consortium arrangement with Vanderbilt University and Oregon Health and Science University. The consortium arrangement is essential to the successful completion of the research plan.

Programmatic Arrangements
Dr. Robert Webster III is an Assistant Professor in the Department of Mechanical Engineering and the Department of Otolaryngology at Vanderbilt University. He has previously developed one of the subsystems that will be incorporated in the proposed system, and he has extensive experience in surgical robotics for inner-ear surgery. He will design a clinic-ready system, incorporating the magnetic-manipulation hardware and techniques developed in the PI’s lab with his own robotic and software subsystems.

Dr. Frank Warren is an Assistant Professor in the Department of Otolaryngology-Head and Neck Surgery at Oregon Health and Science University. He has collaborated with the PI for the past three years on the project proposed herein, beginning during his time as a faculty member at the University of Utah. Dr. Warren will guide the team on all clinical aspects of the project. Dr. Warren will make a week-long trip to Salt Lake City or Nashville to perform cochlea-phantom, human-cadaver, and live guinea-pig experiments. He will also conduct the analysis of the cadaver CT scans, and the histological analysis of the of the guinea-pig cochleae after the experiments (in collaboration with Dr. Albert Park at the University of Utah).

Fiscal Arrangements
Vanderbilt University and Oregon Health and Science University have each submitted a budget to the PI and the University of Utah detailing the resources required to carry out the proposed research. The amounts are presented in the Consortium Budget Justification. Similarly, the PI has come to an agreement with Dr. Webster and Dr. Warren regarding the cost of their services.

Administrative Arrangements
The PI will hold regular biweekly meetings with Dr. Webster and Dr. Warren via Skype. Throughout their ongoing collaboration, Dr. Webster and Dr. Warren have always been very generous with their time, and meetings can also be quickly scheduled on an as-needed basis. As technical milestones are met in the project, Dr. Warren will be kept apprised of the status, and his feedback will be solicited. Other administrative details will occur between entities via electronic communication.
Dear Dr Abbott,

MED-EL would like to support your study for incorporating small magnets in cochlear implant electrodes and using external magnets to guide the electrode in more precise and directed ways. We could supply you with scala tympani models to facilitate the evaluation of the electrode insertion and displacement using the external magnetic forces. We can also combine the small magnets that you have identified with our human electrode for in vitro and in situ studies.

It has been a pleasure to work with you and your supporting team (Dr Frank Warren, Mr Lisandro Leon). We are looking forward to further collaboration and we will be glad to supply you with the necessary silicone base electrodes for your study. From discussions with you, we anticipate fabricating approximately 10 magnetic electrodes per year for the study, which we can certainly provide.

I very much look forward to your results and we are happy to help with your research.

Kind regards,

Claude Jolly PhD
Director of Electrode Development/Research & Development
October 31, 2013

National Institute of Deafness and Other Communication Disorders
31 Center Drive, MSC 2320
Bethesda, MD 20892

Dear Sir or Madam:

I am a co-investigator on this proposal, but I also serve as the Chair of the Department of Mechanical Engineering, which is Dr. Abbott’s (PI) department. In my role as Chair, I can commit to keeping Dr. Abbott’s departmental duties to a minimum throughout the duration of the project, so that he has ample time to conduct the proposed research. This commitment comes in four forms: (1) Dr. Abbott will be limited to teaching no more than one course per semester. (2) Dr. Abbott will not be required to teach a course that he has not already taught, and thus, will not be required to develop any new courses. (3) Dr. Abbott’s committee duties will be kept to a minimum. (4) Dr. Abbott will have the option of buying out of his teaching obligations one semester per year.

Sincerely,

Tim Ameel, Ph.D.
Professor and Chair

Ph: (801) 585-0369, Fax: (801) 585-9826
email: ameel@mech.utah.edu
Date: November 5, 2013

Dear Jake,

This letter is to confirm my commitment and enthusiasm towards your grant application entitled: “Magnetic Guidance for Improved Cochlear-Implant Insertion.” As part of our collaboration, I will be more than happy to perform the auditory brainstem response threshold testing and temporal bone histology in guinea pigs undergoing cochlear implantation under magnetic guidance.

There is a great need to minimize implant trauma for patients with residual hearing wishing to use a combined electric and acoustic stimulation. The magnetic-manipulation system based upon the spherical permanent magnet manipulator (SPMM), developed in your laboratory is a novel approach that can reduce insertion forces on the cochlear basilar membrane. Our laboratory has extensive experience in guinea pig auditory physiology and histology. I very much look forward to continuing our collaboration on this project.

Kindest regards,

Albert Park, M.D.
Professor
Pediatric Otolaryngology

Otolaryngology-Head & Neck Surgery

Albert Park, M.D.
Professor of Pediatric Otolaryngology
Division of Otolaryngology-Head and Neck Surgery,
Department of Surgery
University of Utah School of Medicine/Primary Children’s Medical Center
Salt Lake City, UT 84113

Jake J. Abbott, Ph.D.
Assistant Professor, Department of Mechanical Engineering
Director, Telerobotics Lab
University of Utah
Data resulting from the proposed research will include CT scans from the human-cadaver studies proposed, and will include ABR and histology from the guinea-pig studies proposed, as well as the insertion data from those studies (which will include magnet-position data, cochlear-implant-position data, and insertion-force data, all with a common time stamp). Data will be disseminated primarily through publication in journals and conference proceedings.

Vanderbilt will store project information on a secure server, and provide access to other team members via a shared server repository as needed. All publications will be posted on Dr. Webster's lab website (http://research.vuse.vanderbilt.edu/MEDLab/). The PI posts PDFs of all of his publications on his lab website (http://www.telerobotics.utah.edu/index.php/Publications), which is kept up to date. The PI will also make sure that all publications are also submitted to the National Library of Medicine’s PubMed Central as required by the NIH Public Access Policy. The PI will also be happy to share all data by request, after allowing sufficient time to publish the results.