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TITLE: Treating Intractable Post-Amputation Phantom Limb Pain with Ambulatory Continuous Peripheral Nerve Blocks

PRINCIPAL INVESTIGATOR: Brian M. Ilfeld, MD, MS

CONTRACTING ORGANIZATION: University of California, San Diego
La Jolla, CA 92093-8770

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Brian M. Ilfeld, MD, MS

E-Mail: bilfeld@ucsd.edu

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University of California, San Diego
Altman CTRI
9500 Gilman Drive,, MC 0898
La Jolla, CA 92093-0898

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13. SUPPLEMENTARY NOTES

14. ABSTRACT (brief – 200 words appro•.) of most significant finding during the research period.

This is a randomized, double-masked, placebo-controlled clinical trial. The results will not be available until the completion of enrollment and unmasking of treatment groups. Therefore, there are no results/findings to report at this juncture as we are still completing enrollment.

The tasks of the no-cost extension Year 6 encompassed finishing recruiting and enrollment as well as continuing data collection:

- 144 subjects enrolled to date for all centers—this is the full compliment of subjects—no further subjects will be recruited
- 58 subjects provided crossover treatment
- Amputee support group outreach, prosthetics groups outreach, and clinic outreach conducted and concluded
- Data collection ongoing for enrolled subjects
- Since we must keep the HRPO open while we complete data collection through October 2019, we have requested an additional no-cost extension year through December 24, 2019

15. SUBJECT TERMS

NONE LISTED

16. SECURITY CLASSIFICATION OF:			**17. LIMITATION OF ABSTRACT**	**18. NUMBER OF PAGES**	**19a. NAME OF RESPONSIBLE PERSON**
					USAMRMC
a. REPORT	**b. ABSTRACT**	**c. THIS PAGE**			**19b. TELEPHONE NUMBER** *(include area code)*
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Introduction:

This project is a randomized, double-masked, placebo-controlled, simultaneous parallel and crossover, human-subjects clinical trial to determine if ambulatory continuous peripheral nerve block (CPNB) is an effective treatment for intractable phantom limb pain following a traumatic limb amputation. There is currently no reliable treatment for phantom limb pain, which resolves in only 16% of cases. This is a multicenter trial at five collaborating sites: Walter Reed National Military Medical Center, Naval Medical Center San Diego, Veterans Affairs Palo Alto, Cleveland Clinic, and the University of California, San Diego. Subjects will have an e•isting upper or lower amputation and e•perience phantom limb pain at least 3 times each week for the previous 8 weeks. They will be randomized to receive one of two study solutions in a double-masked manner: either a local anesthetic (ropivacaine 0.5%) or placebo (normal saline). Catheters will be removed after 6 days of at-home infusion. Although not required, each subject has the option to return for the alternative treatment 4-16 weeks later (crossover infusion). The primary endpoint will be the difference in average phantom pain intensity at baseline and 4 weeks following the initial infusion as measured with the Numeric Rating Scale between treatment groups for the initial infusion. Secondary endpoints will involve intra- and inter-subject comparisons of additional measures of pain and health-related quality-of-life. This trial has a strong potential to identify the first reliably effective treatment for intractable phantom limb pain following a traumatic limb amputation.

Body:

Revised SOW (submitted with NCE request):

Funding Year:	**2013**			**2014**	**2015**	**2016-18**	**2019**
Months (Within Year):	**1-4**	**5-8**	**9-12**				
Register study on clinicaltrials.gov	x						
Initiate DSMB meetings	x						
DSMB meetings (every 6 months)		x	x	x	x	x	x
Report to medical monitor (every month)		x	x	x	x	x	x
Finalize protocol and study forms	x						
Hire/train research coordinators	x	x	x				
Site visits and training by UCSD coordinator	x						
Submit study to individual IRBs and USAMRMC	x	x					
Site visits and training by Principal Investigator		x					

Prepare data-entry platform at UCSD	x						
Send database letters (following IRB approval)		x	x	x	x	x	
Educate clinic contacts for referrals		x	x				
Order and prepare equipment	x	x					
Amputee support group outreach			x	x	x	x	
Advertising study in publications/websites			x	x	x	x	
Patient enrollment (following IRB approval)			x	x	x	x	
Interim analyses (at 25%, 50%, 75% enrollment)					x	x	
Quality assurance			x	x	x	x	x
Data collection & entry (Day 1 to Month 12)			x	x	x	x	x
Data cleaning and final statistical analysis							x
Abstract preparation							x
Full-length manuscript preparation							x
IRB closures at all enrolling centers							x
Final report to USAMRMC							x
Uploading results to ClinicalTrials.gov							x
Results sent to all enrolled subjects							x

DSMB: Data Safety Monitoring Board

UCSD: University of California San Diego

IRB: Institutional Review Board

USAMRMC: United States Army Medical Research and Materiel Command

Key Research Accomplishments:

We have completed enrollment with a total of 144 subjects. There are no study results to report at this time since this is a randomized, double-masked, placebo-controlled clinical trial; and, treatment group assignment will not be unmasked until the completion of data collection 1 year after the final subject was treated (October 2019).

Reportable Outcomes:

There are no reportable outcomes available at this time since this is a randomized, double-masked, placebo-controlled clinical trial; and, treatment group assignment will not be unmasked until the completion of data collection 1 year after the final subject was treated (October 2019).

Conclusion:
This is a randomized, triple-masked, placebo-controlled clinical trial that will remain masked until enrollment is completed and the final value for the primary endpoint has been collected. We are continuing enrollment; and, therefore, no results are available at this time.

References:
Non-applicable

Appendices:
None

Treating Intractable Post-Amputation Phantom Limb Pain with Ambulatory Continuous Peripheral Nerve Blocks

DM120032

PI: Brian Ilfeld, MD, MS **Org:** University California, San Diego **Award Amount:** $2,601,258

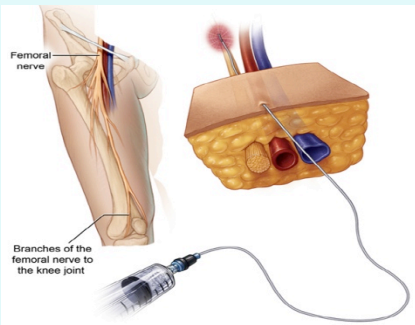
DMRDP

Study Aim

To determine if, following traumatic limb amputation, an ambulatory continuous peripheral nerve block is an effective treatment for intractable phantom limb pain

Approach

- A multicenter, randomized, triple-masked, placebo-controlled, crossover clinical trial
- A continuous peripheral nerve block is an infusion of local anesthetic (numbing medicine) bathing the peripheral nerve of an amputated limb through a catheter inserted through the skin
- Subjects will receive a 6-day infusion at home of either a local anesthetic or saline (a placebo) through their catheter(s)
- Primary endpoint: Phantom pain intensity at 4 weeks. Effects on phantom limb pain will be followed for one year
- They will have the option of returning 5 weeks later for the opposite treatment (local anesthetic or saline)
- Subjects will be followed for a total of 12 months



WOUNDED WARRIOR PROJECT

A continuous peripheral nerve block

Accomplishments: (1) 144 subjects enrolled with enrollment completed; (2) data collection and upload ongoing; (3) DSMB and Study Monitor reports/meetings continue; (4) a no-cost extension year has been requested since we cannot close the HRPO until all data is collected, which will occur October 2019

Timeline and Cost

Activities CY	13	14	15	16	17-18	19
Regulatory Approvals						
Prepare for Enrollment						
Subject enrollment						
Data/manuscript prep						
Budget $2.6-m	**$445k**	**$700k**	**$730k**	**$726k**	***NCE**	***NCE**

Updated: December 30, 2019 ** NCE: no-cost extension*

** Goals / Milestones **

CY13 Goal – Regulatory approvals and preparation for enrollment
- X Project approval from all center IRBs and USAMRMC
- X Prepare DSMB charter and initiate DSMB meetings
- X Prepare data-entry platform
- X Each center to prepare for initiation of protocol and enrollment

CY14 Goal – Begin enrollment
- X Amputee support group outreach and web-based advertisements

CY15 - 18 Goal – Complete enrollment

CY19 Goal – Complete enrollment, data collection, analysis and manuscript preparation
- ☐ Data cleaning and final statistical analysis
- ☐ Manuscript preparation and submission
- ☐ IRB/USAMRMC/DSMB final reports and closure

Budget Expenditure to date

Projected Expenditure: $2,601,258 Actual Expenditure: $2,595,000