High-Frequency Nerve Block for Chronic Postamputation Pain after Traumatic Amputations: Subgroup Analysis from the QUEST Study

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OBJECTIVE: To determine whether traumatic amputation etiology impacted results from the QUEST study evaluating high-frequency nerve block (HFNB) therapy for chronic phantom limb and residual limb pain.

CONCLUSIONS: Outcomes with HFNB therapy were similar in traumatic and dysvascular amputation subgroups. Use of HFNB therapy may support return to duty in traumatic amputee soldiers by alleviating acute and daily pain and improving quality of life.

INTRODUCTION

- Combat-related traumatic amputation is associated with high rates of phantom limb pain, widespread tissue and nerve damage, and high incidence of symptomatic neuromas and residual limb pain[1–3]
  - US VA/DoD guidance recently highlighted the lack of research available to guide treatment decisions for pain treatment in lower limb amputees[4]
- HFNB is an approved on-demand therapy for chronic intractable phantom limb pain and residual limb pain in lower limb amputees
  - The QUEST study evaluating HFNB met its primary endpoint;[5] HFNB therapy was also associated with significant reductions in acute pain, daily pain, and opioid use and significantly improved pain-related quality of life over 12 months[6]
- The QUEST study did not exclude participants based on amputation etiology; therefore, any potential impact of traumatic amputation on QUEST outcomes has not been evaluated

MATERIALS AND METHODS

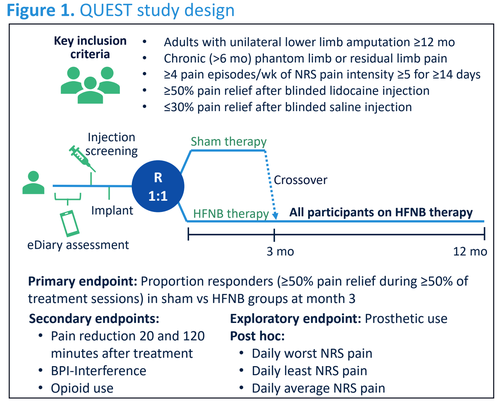
Study design

- The QUEST study design has been previously described[5,6] (**Figure 1**)
- Eligible participants were implanted with the Altius Direct Electrical Nerve Stimulation System (Neuros Medical); participants were instructed to activate their devices on-demand when they felt pain to deliver therapy for 30 minutes

Assessments and analyses

- Participants used an eDiary to record: pain levels (numerical rating scale [NRS], 0-10; 0=‘no pain’; 10=‘pain as bad as you can imagine’) before and 30 and 120 minutes after treatment; daily worst, least, and average NRS pain levels; opioid use/day; and prosthetic use
- Brief Pain Inventory (BPI) Interference with Activities of Daily Living (0-10; 0-’does not interfere’ and 10=‘completely interferes’) was completed at clinic visits at specified time points
- All analyses assessed consistency of treatment results rather than treatment effectiveness; *P*-values represent comparison of subgroups to each other at each time point
- Prespecified subgroup analysis of the primary endpoint was assessed using the Breslow-Day test
- All 12-month outcomes report post hoc subgroup analyses using combined data from all participants with dysvascular vs traumatic amputations (regardless of initial randomization)
- Acute pain relief (difference between NRS pain scores before and 30 and 120 minutes after treatment) comparisons were generated using a generalized estimating equation model; all other outcomes used an analysis of variance model

Figure 1. QUEST study design



Eligible participants received device implantation after completing 4 weeks of eDiary entries confirming pain severity and frequency and after successful injection screening. ADL, activities of daily living; BPI, Brief Pain Inventory; HFNB, high-frequency nerve block; NRS, numerical rating scale.

RESULTS

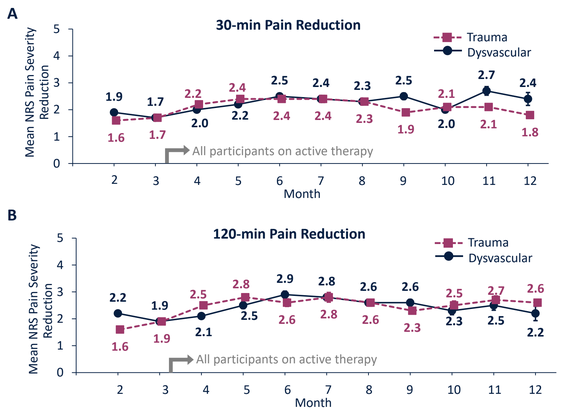
Responder rate at month 3 (primary endpoint)

- Of 170 participants included in the primary endpoint, 72 (42%) had a traumatic amputation, 71 (42%) had a dysvascular amputation, and 27 (16%) reported other etiology*
  - Amputation etiology subgroups were equally distributed between treatment and control arms
- The proportion of responders was greater in the treatment arm vs the control arm for all three subgroups (trauma, 16% [6/37] vs 6% [2/35]; dysvascular, 26% [9/35] vs 11% [4/35]; other, 46% [6/13] vs 0% [0/15]); there was no effect of amputation etiology on the primary endpoint (*P*=0.192)

Acute pain relief over 12 months

- For the 164 participants included in the 12-month follow-up, distribution across initial treatment randomization (treatment vs control) by amputation etiology remained similar; the ‘other’ group was disregarded for the remaining outcomes
- Reductions in acute pain were similar between trauma and dysvascular subgroups through month 12 (P>0.05 for all time points; **Figure 2**)
  - At month 12, acute pain 30 minutes after treatment was reduced by ~27% on average in the trauma subgroup compared with before treatment initiation; at 120 minutes after treatment, pain reduction increased to ~34%

Figure 2. Acute pain reduction relative to before initiating a treatment session in trauma and dysvascular subgroups through month 12

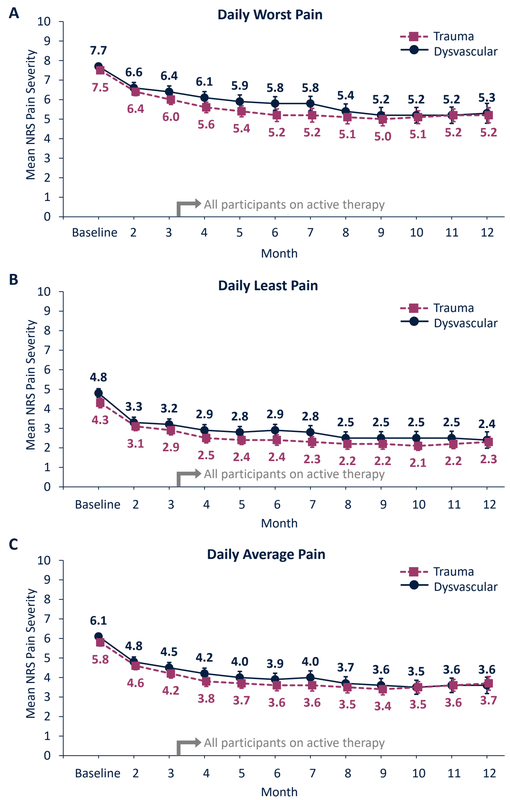


Data represent mean (SE) reduction in NRS pain severity scores at 30 (A) and 120 (B) minutes after treatment initiation relative to NRS pain severity scores before initiating treatment. Each time point represents the average change for each individual treatment session from the previous month. NRS, numerical rating scale.

Daily pain levels over 12 months

- Reported daily worst, least, and average pain levels similarly declined for both the trauma and dysvascular subgroups through month 12 (P>0.05 for all time points; **Figure 3**)
  - At month 12, daily worst, least, and average pain levels in the trauma subgroup were reduced relative to baseline by 31%, 47%, and 36%, respectively

Figure 3. Daily pain levels in trauma and dysvascular subgroups through month 12

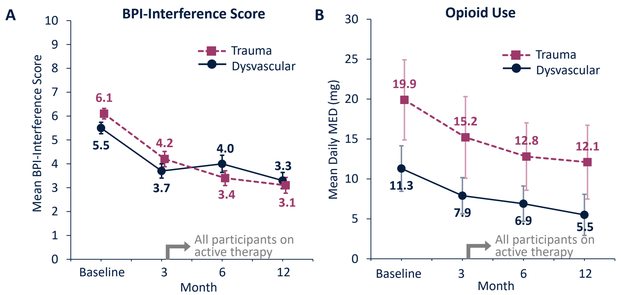


Data represent mean (SE) NRS daily worst (A), least (B) and average (C) NRS pain levels. Daily pain levels were calculated using the average from the 2-week period prior to each time point. NRS, numerical rating scale.

Pain-related quality of life and opioid use

- Mean BPI-Interference scores exhibited similar improvements (decreases) between trauma and dysvascular subgroups over the follow-up period (P>0.05 for all time points; **Figure 4A**)
  - At month 12, the trauma subgroup experienced a 49% improvement in pain-related quality of life relative to baseline
- Cumulative opioid use decreased in a similar fashion from baseline to month 12 in both the trauma and dysvascular subgroups (P>0.05 for all time points; **Figure 4B**)
  - At month 12, cumulative daily MED decreased by ~40% in the trauma subgroup relative to baseline

Figure 4. Pain-related quality of life and opioid use in trauma and dysvascular subgroups through month 12



Mean (SE) BPI-Interference scores (A) and cumulative opioid use (B) by amputation etiology. Daily MED were calculated as the average of the 2 weeks prior to each time point. BPI-Interference, Brief Pain Inventory Interference to Activities of Daily Living; MED, morphine equivalent dose.

Prosthetic use

- Baseline mean (SE) prosthetic use was 62.3 (4.74) and 69.5 (4.86) h/week for the trauma and dysvascular subgroups, respectively; at month 12 prosthetic use was similar between subgroups (trauma, 65.4 [5.95] h/week; dysvascular, 76.4 [6.50] h/week; P>0.05)

DISCUSSION

- In the QUEST study, acute pain relief, improvements in daily pain levels and pain-related quality of life, reductions in opioid use, and prosthetic use over 12 months were similar between amputation etiology subgroups and aligned with the statistically significant results from the full cohort[5,6]
- While QUEST was not designed to evaluate the effectiveness of HFNB therapy after combat-related amputation, these data suggest HFNB may benefit wounded amputee soldiers with chronic pain; future studies of HFNB for pain management in this population would complement the many rehabilitation options currently focused on functional outcomes

*One participant categorized as having a dysvascular amputation at baseline was reassigned to the ‘Other’ category before the 3-month time point.

REFERENCES:
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