Expanded Outcomes from an International Registry Study on Processed Nerve Allografts in Upper Extremity Nerve Repairs

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The RANGER registry is an active database designed to collect outcomes data for processed nerve allografts (Avance® Nerve Graft, AxoGen) on sensory, mixed, and motor nerve repairs. The registry has continued to collect long-term follow-up and has expanded to include data from additional centers. Here we report on meaningful recovery of the expanded cumulative registry for injuries spanning 70 mm as compared to historical controls for nerve autograft and tube conduit.

Introduction

Processed nerve allografts (PNA) have been shown to be safe and effective option to repair nerve gap injuries in a growing number of clinical studies. The RANGER registry is an active database designed to collect outcomes data for processed nerve allografts (Avance® Nerve Graft, AxoGen) on sensory, mixed, and motor nerve repairs. The registry has continued to collect long-term follow-up and has expanded to include data from additional centers. Here we report on meaningful recovery of the expanded cumulative registry for injuries spanning 70 mm as compared to historical controls for nerve autograft and tube conduit.

Methods

The RANGER database was queried according to the following:

- Nerve repairs in the upper extremity using processed nerve allograft
- Motor outcomes from nerves repaired >150 days post organ injury
- Gaps ≤70 mm
- Partial transections
- Mixed nerves reporting sensory or motor function
- Less than 6 month of quantitative outcomes data

Reported sensory and/or motor assessments included:

- 2-point discrimination and/or Semmes-Weinstein Monofilament (SMWF) testing
- Range of motion and or muscle strength testing

Outcome data were incorporated into the MRC scale for sensory and motor function and comparisons made to historical literature

- Meaningful recovery was defined as ≥ S3 or M3
- Higher thresholds of recovery, defined as S3+M4 or greater, were evaluated in repairs reporting a minimum of 15 months of follow-up

Demographics, outcomes by nerve type and covariate analysis were performed to further characterize the sub-groups

Comparison to Historical Reference Literature

| Study                        | Nerve Injury Types | Test Article                          | Level of Recovery | Positive Outcomes
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<tr>
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<tbody>
<tr>
<td>Nerve Autograft Studies</td>
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<tr>
<td>Weber, et al., 2000</td>
<td>Sensory Nerves</td>
<td>Direct Repair and Autograft</td>
<td>≥S3</td>
<td>86%</td>
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<tr>
<td>Kim and Kline 2001-2006</td>
<td>Sensory and Mixed</td>
<td>Direct Suture and Autograft</td>
<td>≥S3/M3</td>
<td>67%</td>
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<tr>
<td>Frykman and Gramyk, 1991</td>
<td>Sensory Nerves</td>
<td>Autograft for Digital Nerve Injury</td>
<td>≥S3</td>
<td>70%</td>
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<tr>
<td>Frykman and Gramyk, 1991</td>
<td>Sensory Nerves</td>
<td>Autograft for Digital Suture and</td>
<td>≥S3/M3</td>
<td>70-75%</td>
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<td>Kallo, et al., 1993</td>
<td>Sensory Nerves</td>
<td>Autograft and Direct Repair</td>
<td>≥S3/M3</td>
<td>67%</td>
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<tr>
<td>Majczek et al., 2003</td>
<td>Sensory and Mixed</td>
<td>Autograft</td>
<td>≥S3/M3</td>
<td>60-80%</td>
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<tr>
<td>Donzelli et al. 1998</td>
<td>Sensory and Mixed</td>
<td>Autograft</td>
<td>≥S3/M3</td>
<td>65%</td>
</tr>
<tr>
<td>Rijks et al. 2005</td>
<td>Mixed Nerves</td>
<td>Autograft</td>
<td>≥S3+M4</td>
<td>51%</td>
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<td>Hollow Tube Conduit Studies</td>
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<tr>
<td>Wangensteen and Kalliaiinen</td>
<td>Sensory, Mixed</td>
<td>NeuraGen®</td>
<td>≥S3/M3</td>
<td>43%</td>
</tr>
<tr>
<td>Chiriac et al.</td>
<td>Digital</td>
<td>NeuraGen®</td>
<td>≥S3/M3</td>
<td>44%</td>
</tr>
<tr>
<td>Haug et al.</td>
<td>Digital</td>
<td>NeuraGen®</td>
<td>≥S3/M3</td>
<td>40%</td>
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<tr>
<td>Taras et al.</td>
<td>Digital</td>
<td>NeuraGen®</td>
<td>≥S3/M3</td>
<td>72%</td>
</tr>
<tr>
<td>Chiriac et al.</td>
<td>Median and Ulnar</td>
<td>NeuraGen®</td>
<td>≥S3/M3</td>
<td>8%</td>
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Horsetail: 3.7 (2.7-3.9) (P<0.001 vs M3, S3)

As reported, based on initial study parameters for a susceptible outcome.

Results

The current RANGER® registry has sufficient quantitative outcomes data on 360 repairs

- 311 sensory nerve injuries
- 49 mixed/motor nerve injuries
- Mean age was 43 ± 18 (18 – 81) years
- Mean gap length was 22 ± 14 (3 – 70) mm
- Mean follow up time of 11 months
- Meaningful recovery was observed in 84% of all repairs
- No related adverse events were reported
- Higher thresholds of recovery: 74% S3+/M4 or greater with mean follow-up 22 ± 8.9 (15 – 42) months

Sensory Nerve Outcomes

- Meaningful recovery in 85% of sensory nerves
- Recovery of static 2PD at 12 months was consistent across gap groups

Mixed/Motor Nerve Outcomes

- Meaningful recovery on 78% of mixed nerve repairs
- Recovery in laceration and complex injuries were consistent

Conclusions

- Processed nerve allografts continue to be a safe and reliable off-the-shelf option for the reconstruction of nerve deficits
- Meaningful recovery in 85% and 78% of sensory and mixed repairs
- Repairs with longer term follow-up demonstrated higher levels of recovery at 74%
- These results compare favorably to historical outcomes for autografts and exceed those for conduits
- The registry remains ongoing and will continue to expand to further collect outcomes data on processed nerve allografts