Effect of Polymerization Methods on Peripheral Nerve Regeneration

Ziya Baghmanli, MD; Melanie G Urbanchek, PhD; Benjamin Wei, MD; Bong Sup Shim, PhD; Kristoffer B Sugg, MD; David C Martin, PhD; William M Kuzon,Jr, MD, PhD; Paul S Cederna, MD

Objective: 3,4 polyethylenedioxythiphene (PEDOT) is a conductive polymer being tested for neural-machine interfaces. Two polymerization methods were described: dry (yields highly conductive, stiff product), wet (yields less conductive, soft product). We tested for the effects of dry and wet PEDOT on regenerating nerves. Our goal is to optimize conduction within an interface while preserving nerve viability.

Methods: A 15 mm rat peroneal nerve gap was reconstructed with various materials (n=8 per group): Sham, Autograft, Decellularized nerve (DN), dry PEDOT polymerized on DN (dry PEDOT), wet PEDOT polymerized on DN (wet PEDOT) and Gap (gap not reconstructed). After 90 days of recovery, nerve specimens were obtained and histologically assessed using qualitative techniques [1] and quantitative analysis. Nerve quantitative data were: neural area (m2), percent neural area (%), axon counts, and axon density (axon/m2). EMG and muscle force were also measured.

Results: All nerves successfully regenerated under the influence of PEDOT. Dry PEDOT had high action potential velocity, but lower muscle force, nerve rating and neural area than autograft. Wet PEDOT demonstrated similar histological outcomes as the sham, although action potential velocity and muscle force were lower. Additionally, wet PEDOT showed better histological outcomes than dry PEDOT, as neural area and axon density were similar to autograft, the gold standard (Tables 1and 2).

Conclusion: Peripheral nerve regeneration occurs in the presence of PEDOT. Favorable histological outcomes with wet PEDOT indicate some advantages. Mechanical obstruction to axonal sprouting and elongation by dry PEDOT is a possible explanation for the poorer histology outcomes. However, dry PEDOT afforded faster conduction. Based upon these results, we conclude that wet PEDOT is qualitatively and quantitatively superior to dry PEDOT, though the cost is some compromise in conductivity.

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Table 1: Statistical Summary of Quantitative Nerve Histology classified by Reconstruction type.

	Surgical Groups					
	Sham	Autograft	Decellular Nerve	Dry PEDOT	Wet PEDOT	Gap
Rat Number	n=8	n=8	n=8	n=8	n=8	n=8
Axon Count	877±461	863±297	552±256	169±240†	190±10†	0
Neural Area (μm^2)	15168.2±5639.3	9408.9±5191.2	4442.3±2809.9	998.2±1380.3†	1288.7±815.4	0
Axon Density ($1/\mu m^2$)	0.019±0.005	0.022±0.012	0.011±0.008	0.003±0.004*†	0.004±0.002	0
Percent of Neural Area (%)	3.48±1.0	2.13±0.75	9.03±0.63	1.68±0.24*†	2.73±0.8*†	0
Nerve histology grade	6±0	9.2±1.9 *	12.8±2.6 * †	20.5±1.4 *†‡	pending	22.0±0 *†‡

Values listed are mean ± SD, $p<0.05$, * indicates difference vs. Sham, † indicates difference vs. Autograft, ‡ indicates difference vs. Decellular Nerve.

Table 2: Statistical Summary of Muscle Force, Motor Action Potential Velocity and Nerve Histology Grade classified by Reconstruction type.

	Surgical Groups

	Sham	Autograft	Decellular Nerve	Dry PEDOT	Wet PEDOT	Gap
Number of Subjects	n=8	n=8	n=8	n=8	n=8	n=8
Maximum isometric tetanic force (mN)	3119.3± 570.7	1591.7±520.2 *	783.1± 685.6*	232.2± 210.9*†	82.1± 60.2*†	0
Action potential velocity (m/s)	13.41± 2.68	13.85± 3.77	9.31± 1.46*†	19.75± 2.85*†‡	5.73± 0.91*†§	0

Values listed are mean ± SD, $p<0.05$, * indicates difference vs. Sham, † indicates difference vs. Autograft, ‡ indicates difference vs Decellular nerve, § indicates difference vs. dry PEDOT