

Supplementary Materials

Regenerative neurotization in breast reconstruction: biomaterials, nerve guidance, and emerging strategies for sensory restoration

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Supplementary Tables

Supplementary Table 1. Search strategy

Database	Key Search Terms	Results
PubMed	("breast reconstruction" OR "postmastectomy reconstruction") AND (neurotization OR reinnervation OR "nerve regeneration" OR "sensory recovery")	162
Web of Science	("breast reconstruction") AND (neurotization OR "nerve regeneration" OR "sensory restoration") AND (biomaterial* OR "nerve conduit" OR scaffold*)	102
Scopus	("breast reconstruct" OR "DIEP flap" OR "TRAM flap") AND (neurotization OR "nerve coaptation" OR "sensory recovery") AND (biomaterial OR scaffold* OR conduit*)	90
ScienceDirect	("breast reconstruction" OR "postmastectomy reconstruction") AND (neurotization OR reinnervation OR "nerve regeneration" OR "sensory recovery")	347
EMBASE	("breast reconstruct" OR "DIEP flap" OR "TRAM flap") AND (neurotization OR "nerve coaptation" OR "sensory restoration") AND (biomaterial OR scaffold* OR conduit*)	94
TOTAL		795

DIEP: Deep inferior epigastric perforator; TRAM: transverse rectus abdominis myocutaneous.

Supplementary Table 2. Study summary

Author (Year)	Country	Study Type	Sample Size	Reconstruction Type	Neurotization Technique	Assessment Method	Follow-up	Key Finding
Alston <i>et al.</i> (2025) [50]	USA	Prospective comparative	60	Gender-affirming mastectomy	Targeted reinnervation via direct repair or allograft	NAC Quantitative sensory tests + PROs	12 months	Better outcomes after direct repair vs. allograft.
Aristizábal <i>et al.</i> (2025) [37]	Multi	SR + meta-analysis	495 breasts (352 subgroup)	DIEP, LTP, TRAM	Direct nerve coaptation	SWM testing	10-77 months	Neurotized flaps showed superior tactile recovery.
Beugels <i>et al.</i> (2019) [43]	Netherlands	Prospective cohort	81	DIEP flap	End-to-end intercostal coaptation	SWM testing	15-17 months	Neurotized flaps achieved better sensory recovery.
Beugels <i>et al.</i> (2021) [36]	Netherlands	Prospective cohort	125	DIEP flap	Coaptation to third intercostal nerve	SWM testing	Postoperative	Nerve coaptation improved sensory recovery.
Bijkerk <i>et al.</i> (2020) [46]	Netherlands	Within-patient cohort	15	DIEP / LTP	Direct nerve coaptation	SWM testing	~19 months	Innervated flaps showed better protective sensation.
Blondeel <i>et al.</i> (1999) [41]	Belgium	Comparative cohort Double-blind	104	DIEP and TRAM	Intercostal nerve repair	Multimodal sensory testing	~20 months	Nerve repair accelerated and enhanced recovery.
Bubberman <i>et al.</i> (2024) [27]	Netherlands	RCT (preliminary/interim results)	41	DIEP flap	Intercostal nerve coaptation	SWM + PSSD + thermal	24 months	Innervated flaps showed better tactile and thermal recovery.
Chinta <i>et al.</i> (2025) [52]	USA	Randomised comparative	14 surgeons	Cancer/gender-affirming mastectomy	Nerve Tape sutureless coaptation	Neurorrhaphy quality grading	Intraoperative	Nerve Tape: faster repair (1.79 vs. 5.20 min) and higher acceptable repair rate (92% vs. 69%).
Djohan <i>et al.</i> (2020) [67]	USA	Prospective cohort	13	Implant-based	Processed nerve allograft to NAC	PSSD testing	Months	Early sensory restoration feasibility demonstrated.
Momeni <i>et al.</i> (2021) [40]	USA	Prospective registry	59	Abdominal free flaps	Allograft bridging	SWM testing	>=12 months	Allograft neurotization enhanced protective sensation.
Parand <i>et al.</i> (2024) [38]	Multi	SR + meta-analysis	12 studies	DIEP, TRAM, VRAM	Various coaptation techniques	SWM + PSSD	Variable	Neurotized flaps consistently showed superior recovery.

Peled and Peled (2019) [33]	USA	Prospective case series	16	Implant-based (NSM)	NAC neurotization using allograft	Two-point discrimination	≥ 3 months	Combined nerve preservation and grafting maintained sensation.
Puonti <i>et al.</i> (2011) [44]	Finland	Prospective cohort	40	TRAM flap	Neural anastomosis with thoracic nerves	Quantitative sensory testing	Long-term	Neurotized TRAM flaps showed improved recovery.
Temple <i>et al.</i> (2006) [66]	USA	RCT (blinded assessor)	27	TRAM flap	Intercostal nerve repair	SWM + temperature tests	~ 16 months	Innervated TRAM flaps showed improved recovery vs. non-innervated.
Vartanian <i>et al.</i> (2021) [47]	USA	Comparative review	640	DIEP, TRAM, others	Direct nerve coaptation	Multimodal sensory testing	Variable	Neurotization improved postoperative sensation vs. spontaneous recovery.

SR: Systematic review; MA: meta-analysis; NAC: nipple-areola complex; PROs: patient-reported outcomes; DIEP: deep inferior epigastric perforator; LTP: lateral thigh perforator; TRAM: transverse rectus abdominis myocutaneous; SWM: Semmes-Weinstein monofilament; RCT: randomized controlled trial; PSSD: pressure-specified sensory device; VRAM: vertical rectus abdominis myocutaneous; NSM: nipple-sparing mastectomy.