

7.01.81	Nerve Graft with Radical Prostatectomy		
Original Policy Date:	June 1, 2016	Effective Date:	June 1, 2024
Section:	7.0 Surgery	Page:	Page 1 of 8

Policy Statement

- I. Unilateral or bilateral nerve graft is considered **investigational** in individuals who have had resection of one or both neurovascular bundles as part of a radical prostatectomy.

NOTE: Refer to [Appendix A](#) to see the policy statement changes (if any) from the previous version.

Policy Guidelines

Coding

See the [Codes table](#) for details.

Description

Nerve grafting at the time of radical prostatectomy, most commonly using the sural nerve, has been proposed to reduce the risk of postoperative erectile dysfunction.

Related Policies

- N/A

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

A nerve graft with radical prostatectomy is a surgical procedure and, as such, is not subject to regulation by the U.S. Food and Drug Administration (FDA).

Several nerve cuff products have been cleared for marketing by FDA through the 510(k) process. FDA product code: JXI. An example of a human tissue nerve graft product, the Avance® nerve graft (AxoGen), is regulated by FDA under 21 CFR, Part 1271 regulations for Human Cellular and Tissue-based Products (HCT/P).

Rationale

Background

Erectile Dysfunction

Erectile dysfunction is a common problem after radical prostatectomy. In particular, spontaneous erections are usually absent in men whose prostate cancer required bilateral resection of the neurovascular bundles as part of the radical prostatectomy procedure.

Treatment

A variety of noninvasive treatments are available, including vacuum constriction devices and intracavernosal injection therapy. However, spontaneous erectile activity is preferred by patients. Studies have reported results from bilateral and unilateral nerve grafts, the latter involving resection of 1 neurovascular bundle.

There has been interest in sural nerve grafting to replace cavernous nerves resection during prostatectomy. The sural nerve is considered expendable and has been extensively used in other nerve grafting procedures, such as brachial plexus and peripheral nerve injuries. As applied to prostatectomy, a portion of the sural nerve is harvested from 1 leg and then anastomosed to the divided ends of the cavernous nerve. Reports also indicate the use of other nerves (e.g., genitofemoral nerve) for grafting.

Literature Review

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to individuals and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms. To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

Nerve Grafting

Clinical Context and Therapy Purpose

Individuals with prostate cancer may undergo treatment with prostatectomy or prostate radiation therapy. Several studies have reported racial disparities among individuals with low-risk prostate cancer.¹ African American individuals enrolled in active surveillance programs have been shown to

have a higher risk of disease progression than White individuals. For African American individuals in the low-to-intermediate risk categories, there have been reports of increased risk of biochemical recurrence after treatment. While reasons for clinical disparities in this population are still being investigated, studies suggest that disparities in prostate cancer health outcomes can be minimized when health care access is equal.

The purpose of nerve grafting in individuals who have radical prostatectomy is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals who have radical prostatectomy with resection of neurovascular bundles.

Interventions

The therapy being considered is nerve grafting in association with radical prostatectomy.

Comparators

The relevant comparator is prostatectomy without nerve grafting.

Outcomes

The outcomes of interest are functional outcomes, quality of life, and treatment-related morbidity.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Review of Evidence

Randomized Controlled Trials

One RCT evaluating nerve grafting to reduce the risk of erectile dysfunction has been published; findings were reported by Davis et al (2009).² The trial included individuals ages 65 years or younger with normal self-reported baseline erectile function selected for a unilateral nerve-sparing radical prostatectomy with preservation of 1 neurovascular bundle. All patients had unilateral neurovascular bundle removal, and individuals were randomized to receive or not to receive sural nerve grafting after removal. The primary outcome was potency 2 years postsurgery, defined as the ability to have intercourse with or without erectile dysfunction medication. All patients received the same early erectile dysfunction therapy, including medication and mechanical devices. The investigators sought to detect an absolute difference of 20% between groups (graft, 60% potency rate vs no graft, 40% potency rate). A sample of 200 individuals was originally planned to provide 80% power. However, after 107 individuals were randomized, a preplanned interim analysis of evaluated individuals found similar potency rates between groups. The data monitoring committee stopped the trial based on its estimate of less than a 5% chance that additional recruitment would result in a significant difference between groups. Endpoint data were available for 66 individuals. Potency was achieved in 32 (71%) of 45 sural nerve graft individuals and 14 (67%) of 21 control individuals ($p=.78$). Trialists concluded that unilateral sural nerve graft did not result in an absolute improvement of 20% between groups, but that a smaller effect could not be ruled out. A limitation of the trial was that it was unblinded, which could have impacted self-report of potency because individuals knew the procedure they received.

Observational Studies

The literature also includes 2 retrospective cohort studies and 3 case series.^{3,4,5,6,7} The cohort studies are described below.

The cohort study by Kung et al (2015) included 38 patients who underwent nerve grafting after radical prostatectomy and a random sample of 53 control patients who had open prostatectomy without nerve grafting. Control patients had unilateral or bilateral nerve-sparing prostatectomy or non-nerve sparing prostatectomy. Complete urinary incontinence, no erectile capacity at baseline, and follow-up data less than 12 months were study exclusion criteria. Unilateral nerve grafting (n=29) and unilateral nerve-sparing (n=10) patients did not differ significantly between groups ($p>.05$) on various outcomes, including urinary continence, erections sufficient for sex, spontaneous erections, and use of erectile dysfunction medications. Bilateral nerve grafting (n=9) and bilateral non-nerve sparing (n=10) patients had similar outcomes ($p>.05$). This study lacked randomization and blinding, and subgroup analyses included small numbers of patients.

The second cohort study, published by Namiki et al (2007), included 113 patients: 19 had unilateral nerve-sparing plus sural nerve graft, 60 patients had unilateral nerve-sparing with no grafting, and 34 patients had bilateral nerve-sparing surgery.⁴ Function was assessed using validated questionnaires and, at 2 years, no difference in sexual function scores was found between the unilateral nerve graft and bilateral nerve-sparing patients. At 3 years, similar percentages of patients in the unilateral nerve graft (25%) and bilateral nerve-sparing (28%) groups considered their sexual function as fair or good. Urinary function returned to baseline continence in the unilateral nerve graft and bilateral nerve-sparing groups at 6 months and in the unilateral nerve-sparing group at 12 months. Baseline sexual function differed between groups, which could have biased study findings; the nerve grafted and bilateral nerve-sparing patients reported higher baseline function than the unilateral nerve-sparing group.

Supplemental Information

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Clinical Input From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 4 academic medical centers while this policy was under review in 2008; no input was received from physician specialty societies. Input from the 4 centers agreed that this procedure is considered investigational.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

National Comprehensive Cancer Network

The National Comprehensive Cancer Network guidelines on the treatment of prostate cancer (v.4.2023) states: "Replacement of resected nerves with nerve grafts has not been shown to be beneficial" for recovery of erectile function after radical prostatectomy.¹

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials

A currently unpublished trial that might influence this review is shown in Table 1.

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
<i>Unpublished</i>			
NCT01770340	Nerve Grafting With an Allograft During Radical Prostatectomy - Extended Follow-up in a Prospective Randomized Trial	30	Jul 2020 (terminated)

NCT: national clinical trial.

References

1. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer. Version 4.2023. https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed February 9, 2024.
2. Davis JW, Chang DW, Chevray P, et al. Randomized phase II trial evaluation of erectile function after attempted unilateral cavernous nerve-sparing retropubic radical prostatectomy with versus without unilateral sural nerve grafting for clinically localized prostate cancer. *Eur Urol*. May 2009; 55(5): 1135-43. PMID 18783876
3. Kung TA, Waljee JF, Curtin CM, et al. Interpositional Nerve Grafting of the Prostatic Plexus after Radical Prostatectomy. *Plast Reconstr Surg Glob Open*. Jul 2015; 3(7): e452. PMID 26301141
4. Namiki S, Saito S, Nakagawa H, et al. Impact of unilateral sural nerve graft on recovery of potency and continence following radical prostatectomy: 3-year longitudinal study. *J Urol*. Jul 2007; 178(1): 212-6; discussion 216. PMID 17499797
5. Rabbani F, Ramasamy R, Patel MI, et al. Predictors of recovery of erectile function after unilateral cavernous nerve graft reconstruction at radical retropubic prostatectomy. *J Sex Med*. Jan 2010; 7(1 Pt 1): 166-81. PMID 19686422
6. Siddiqui KM, Billia M, Mazzola CR, et al. Three-year outcomes of recovery of erectile function after open radical prostatectomy with sural nerve grafting. *J Sex Med*. Aug 2014; 11(8): 2119-24. PMID 24903070
7. Souza Trindade JC, Viterbo F, Petean Trindade A, et al. Long-term follow-up of treatment of erectile dysfunction after radical prostatectomy using nerve grafts and end-to-side somatic-autonomic neurotaphy: a new technique. *BJU Int*. Jun 2017; 119(6): 948-954. PMID 28093890

Documentation for Clinical Review

- No records required

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	55840	Prostatectomy, retropubic radical, with or without nerve sparing
	55842	Prostatectomy, retropubic radical, with or without nerve sparing; with lymph node biopsy(s) (limited pelvic lymphadenectomy)
	55845	Prostatectomy, retropubic radical, with or without nerve sparing; with bilateral pelvic lymphadenectomy, including external iliac, hypogastric, and obturator nodes
	64910	Nerve repair; with synthetic conduit or vein allograft (e.g., nerve tube), each nerve
	64911	Nerve repair; with autogenous vein graft (includes harvest of vein graft), each nerve
	64912	Nerve repair; with nerve allograft, each nerve, first strand (cable)
	64913	Nerve repair; with nerve allograft, each additional strand (List separately in addition to code for primary procedure)
	64999	Unlisted procedure, nervous system
HCPCS	None	

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
06/01/2016	BCBSA Medical Policy Adoption
06/01/2017	Policy revision without position change
06/01/2018	Policy revision without position change
06/01/2019	Policy revision without position change
06/01/2023	Policy reactivated. Previously archived from 06/01/2020 to 05/31/2023.
06/01/2024	Annual review. No change to policy statement. Policy guidelines and literature review updated.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT (No changes)	
BEFORE	AFTER
<p>Nerve Graft with Radical Prostatectomy 7.01.81</p> <p>Policy Statement:</p> <ul style="list-style-type: none"> I. Unilateral or bilateral nerve graft is considered investigational in individuals who have had resection of one or both neurovascular bundles as part of a radical prostatectomy. 	<p>Nerve Graft with Radical Prostatectomy 7.01.81</p> <p>Policy Statement:</p> <ul style="list-style-type: none"> I. Unilateral or bilateral nerve graft is considered investigational in individuals who have had resection of one or both neurovascular bundles as part of a radical prostatectomy.