



Louisiana

Nerve Graft in Association With Radical Prostatectomy

Policy # 00113

Original Effective Date: 06/05/2002

Current Effective Date: 05/16/2018

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers unilateral or bilateral nerve grafts in patients who have undergone resection of one or both neurovascular bundles as part of a radical prostatectomy to be **investigational**.*

Background/Overview

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. 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 use of other nerves (e.g., genitofemoral nerve) for grafting.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

A nerve graft with radical prostatectomy is a surgical procedure and, as such, is not subject to regulation by the U.S. 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 the 21 CFR Part 1271 regulations for Human Cellular and Tissue-based Products (HCT/P).

Centers for Medicare and Medicaid Services (CMS)

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

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Rationale/Source

One randomized controlled trial (RCT) evaluating nerve grafting to reduce risk of erectile dysfunction has been published; findings were reported in 2009 by Davis et al. The trial included men age 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 patients were randomized to receive or not 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 men was originally planned to provide 80% power. However, after 107 men were randomized, a preplanned interim analysis of evaluable patients 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. End point data were available for 66 patients. Potency was achieved in 32 (71%) of 45 sural nerve graft patients and 14 (67%) of 21 control patients ($p=0.78$). 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, because men knew the procedure they received, could have impacted self-report of potency.

The literature also includes 2 retrospective cohort studies and 3 case series. The cohort studies are described below.

A 2015 cohort study by Kung et al 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 ($p>0.05$) 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 ($p>0.05$). 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. 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

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biased study findings: the nerve grafted and bilateral nerve sparing patients reported higher baseline function than the unilateral nerve sparing group.

SUMMARY OF EVIDENCE

For individuals who have radical prostatectomy with resection of neurovascular bundles who receive nerve grafting, the evidence includes 1 RCT, cohort studies, and case series. Relevant outcomes are functional outcomes, quality of life, and treatment-related morbidity. The RCT did not find that unilateral nerve grafting was associated with a statistically significant improvement in potency rates at 2 years postsurgery. Cohort studies also did not result in better outcomes with nerve grafting. The evidence is insufficient to determine the effects of the technology on health outcomes.

References

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Policy History

Original Effective Date: 06/05/2002

Current Effective Date: 05/16/2018

05/16/2002 Medical Policy Committee review

06/05/2002 Managed Care Advisory Council approval

06/24/2002 Format revision. Coverage eligibility unchanged.

06/01/2004 Medical Director review

06/15/2004 Medical Policy Committee review. Format revision.

06/28/2004 Managed Care Advisory Council approval

08/02/2006 Medical Director Review

08/09/2006 Medical Policy Committee approval. Format revisions, references and rationale/source updated. Coverage eligibility unchanged.

06/13/2007 Medical Director Review

06/20/2007 Medical Policy Committee approval. Policy updated with literature search. No change to policy statement. Sural removed from title.

06/04/2009 Medical Director Review

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06/17/2009 Medical Policy Committee approval. No change to coverage.
06/03/2010 Medical Policy Committee approval
06/16/2010 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/02/2011 Medical Policy Committee review
06/15/2011 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/14/2012 Medical Policy Committee review
06/20/2012 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/06/2013 Medical Policy Committee review
06/25/2013 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
04/02/2015 Medical Policy Committee review
04/20/2015 Medical Policy Implementation Committee approval. Updated rationale /source. Coverage eligibility unchanged.
08/03/2015 Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
04/07/2016 Medical Policy Committee review
04/20/2016 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017 Coding update: Removing ICD-9 Diagnosis Codes
05/04/2017 Medical Policy Committee review
05/17/2017 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
05/03/2018 Medical Policy Committee review
05/16/2018 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 05/2019

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT)[®]†, copyright 2017 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	64999
HCPCS	No codes

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ICD-10 Diagnosis	C61, D78.81, D78.89, E89.810-E89.811, E89.89, H59.011-H59.019, H59.032-H59.039, H59.091, H59.093, H59.099, H59.811-H59.819, H59.88, H95.811-H95.819, H95.88-H95.89, M96.89, N52.02-N52.03, N52.1, N52.2, N52.31-N52.39, N52.8, N52.9, N98.1-N98.8, Z90.721-Z90.722, Z90.79
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*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 - 1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
 - 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 - 3. Reference to federal regulations.

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