Nerve Graft in Association With Radical Prostatectomy

Policy #: 00113
Original Effective Date: 06/05/2002
Current Effective Date: 05/17/2017

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 extent of 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 nerve grafts; there are also reports of unilateral grafts when only 1 neurovascular bundle has been resected.

There has been interest in sural nerve grafting to replace cavernous nerves resected at the time of 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 are also being published using other nerves, such as the genitofemoral nerve.

FDA or Other Governmental Regulatory Approval
U.S. Food and Drug Administration (FDA)
A nerve graft in association 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)
No national coverage determination.

Rationale/Source
A single 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
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younger with normal self-report baseline erectile function who were scheduled for a unilateral nerve-sparing radical prostatectomy with preservation of 1 neurovascular bundle. All patients had unilateral neurovascular bundle removed, and patients were randomly assigned to receive or not 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 size of 200 was originally planned to provide 80% power. However, after 107 patients were randomly assigned, a preplanned interim analysis of evaluable patients found similar rates of potency 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 biased study findings: the nerve grafted and bilateral nerve sparing patients reported higher baseline function than the unilateral nerve sparing group.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 1.
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Table 1. Summary of Key Trials

<table>
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<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
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<td>Ongoing</td>
<td>Nerve Grafting With an Allograft During Radical Prostatectomy - Extended Follow-up in a Prospective Randomized Trial</td>
<td>60</td>
<td>Jan 2019</td>
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</table>

NCT: national clinical trial.

Clinical Input Received 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.

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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Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

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

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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. 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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