Name of Policy:  
Nerve Graft in Association with Radical Prostatectomy

Policy #: 370  
Category: Surgery  
Latest Review Date: December 2013  
Policy Grade: B

Background/Definitions:  
As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. The technology must have final approval from the appropriate government regulatory bodies;
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;
3. The technology must improve the net health outcome;
4. The technology must be as beneficial as any established alternatives;
5. The improvement must be attainable outside the investigational setting.

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. In accordance with generally accepted standards of medical practice; and
2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient’s illness, injury or disease; and
3. Not primarily for the convenience of the patient, physician or other health care provider; and
4. 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 that patient’s illness, injury or disease.
**Description of Procedure or Service:**
Nerve grafting to replace cavernous nerves resected at the time of radical prostatectomy is proposed to reduce the risk of erectile dysfunction after this surgery. The sural nerve is most commonly used in grafting.

Erectile dysfunction is a common problem after radical prostatectomy. In particular, spontaneous erections are usually absent in patients whose extent of prostate cancer requires 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 one 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 used extensively 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 one 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.

**Policy:**
**Unilateral or bilateral nerve graft does not meet** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage and is considered investigational in patients who have undergone resection of one or both neurovascular bundles as part of a radical prostatectomy.

*Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the members' contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.*

**Key Points:**
After an initial literature search was performed in 2001, the policy was updated regularly with a literature review using MEDLINE. Most recently, the literature was searched from October 2012 through October 2013.

**Following is a summary of the literature to date:**
The first randomized controlled trial (RCT) that evaluated nerve grafting was published in 2009 by Davis et al. Eligibility criteria included age 65 or younger, normal self-report baseline erectile functions, and scheduled for a unilateral nerve-sparing radical prostatectomy with preservation of one neurovascular bundle. All patients had the other neurovascular bundle removed, and patients were randomly assigned to receive or not receive sural nerve grafting.
after its removal. The primary outcome was potency two years post-surgery, defined as the ability to have intercourse with or without erectile dysfunction medication. The investigators estimated that the control group would have a 40% potency rate and powered the study to detect an absolute difference of 20% between groups. All patients received the same early erectile dysfunction therapy including medication and mechanical devices. A sample size of 200 was originally planned to provide 80% power. However, after 107 patients were randomly assigned, a pre-planned interim analysis of evaluable patients found similar rates of potency in the two groups; the Data Monitoring Committee estimated that there was less than a 5% chance that there would be a significant difference between groups with additional recruitment and the trial was stopped early. When data collection ended, endpoint data were available for 66 patients who had either achieved potency or had been followed up for two years without potency. Potency was achieved in 32 of 45 (71%) sural nerve graft patients and 14 of 21 (67%) control patients (p=0.78). The authors concluded that unilateral sural nerve graft did not result in an absolute improvement of 20% in the rate of potency but that a smaller effect cannot be ruled out. A limitation of the study was that it was non-blinded, which could have impacted self-report of potency.

Other than the Davis et al study, the published literature consists of case series. When the initial literature search was performed, the largest available series included 23 men with a mean of 23-month follow-up. This study, by Kim et al, included men with clinically localized, but high-volume prostate cancer such that bilateral resection of the neurovascular bundles was considered necessary. Before surgery, all men reported spontaneous erection. The results were compared to a group of 12 men who were potent preoperatively and had undergone prostatectomy with bilateral nerve resection but who declined nerve graft placement. Of the 23 men undergoing nerve grafting, six (26%) had spontaneous, medically unassisted erection sufficient for sexual intercourse. An additional six men (26%) reported 40% to 60% spontaneous erection that was insufficient for intercourse; four of these patients were able to have intercourse using sildenafil. Therefore, a total of ten of the 23 patients were able to have intercourse, either spontaneously or with pharmacologic therapy. A total of 11 men had no clinical response even with the use of sildenafil. Not unexpectedly, all outcomes were significantly better compared to the control group. Side effects of the sural nerve donor site, which included incisional pain and a sensory deficit along the lateral aspect of the foot, were considered tolerable. The authors noted improvement 8 to 12 months postoperatively and accelerated improvement at 12 to 18 months postoperatively.

Subsequent literature searches identified additional case series. The largest published series and those with the longest follow-up are described below:

In 2007, Namiki et al published a series in Japan with three-year follow-up. A total of 113 patients were evaluated: 19 patients with unilateral nerve sparing plus sural nerve graft, 60 patients with unilateral nerve sparing but no grafting, and 34 patients with bilateral nerve-sparing surgery. Sexual function was assessed with validated questionnaires, and at two years there was no difference between the nerve-grafted and the bilateral nerve-sparing patients with regard to sexual function scores. At three years, 25% and 28% of patients in the nerve-grafted and bilateral nerve-sparing groups, respectively, considered their sexual function as fair or good. Urinary function returned to baseline in the nerve-grafted and bilateral nerve-sparing groups at six months and in the unilateral nerve-sparing group at 12 months. Differences in
sexual function were present at baseline with the nerve-grafted and bilateral nerve-sparing patients reporting higher baseline function than the unilateral nerve-sparing group.

A study by Secin et al had five-year follow-up. The authors reported results on 44 consecutive patients who underwent bilateral nerve grafting from 1999 to 2004 at Memorial Sloan-Kettering Cancer Center. The overall five-year recovery of erectile function was 34%, and the rate of consistent function was 11%. None of a number of variables (e.g., age, type of nerve [sural, genitofemoral, ilioinguinal], comorbidities) was significantly associated with recovery of postoperative erectile function.

Sim et al reported on two-year results in 41 patients who received unilateral sural nerve grafts following radical prostatectomy when one neurovascular bundle was resected. In this series, recovery of erectile function was reported for 63% of patients (based on 24 of 38 patients). This study also reported on erectile function on another group of patients who had unilateral resection at the same institution but without a nerve graft. In this group, which was older and was not matched on key characteristics to the group who received a nerve graft, the erectile function was 26.5% (13 of 49).

A recent case series reviewed the records of 131 men who had unilateral nerve grafts after radical prostatectomy with unilateral neurovascular bundle resection. Men who had prior radiation or hormonal treatment were excluded. Another eligibility criterion was satisfactory erections presurgery as assessed by a five-point scale (1=full erections; 2=diminished erections, but routinely sufficient for sexual intercourse; 3=partial erections occasionally satisfactory for intercourse; 4=partial erections unsatisfactory for intercourse; and 5=no erections). A total of 49 men received sural nerve grafts, 79 received genitofemoral nerve grafts and 3 received ilioinguinal nerve grafts. Recovery of erections was evaluated at each follow-up visit according to the five-point scale (also called five levels). The median patient age was 58.7 years, and the median follow-up was 37 months. According to actuarial analysis, the 5-year probability of recovering erections of level three or better was 46%. The probability of recovering erections of at least level two or level one was 34% and 12%, respectively.

2012 Update
There are no new articles in the peer-reviewed literature that would change this policy statement. This procedure remains not covered.

2013 Update
There are no new articles in the peer reviewed literature that would change this policy statement. This procedure remains not covered. There is a new clinical trial underway: Nerve Grafting With an Allograft During Radical Prostatectomy - Extended Follow-up in a Prospective Randomized Trial (NCT01770340): This single-blind study includes 60 patients with prostate cancer. Patients have been randomized to receive radical prostatectomy with or without implantation of an allogenic nerve graft. The primary outcome is erectile function and follow-up is at least 24 months postsurgery. The expected date of final data collection is January 2014.
Summary
Nerve-grafting, most commonly using the sural nerve, at the time of radical prostatectomy has been proposed to reduce the risk of postoperative erectile dysfunction. Only one randomized controlled trial that evaluated sural nerve grafting with radical prostatectomy has been published, and this study did not find that unilateral sural nerve grafting was associated with a statistically significant improvement in potency rates two years post-surgery. An additional randomized, controlled trial (RCT) is underway and results are expected in 2014. Due to the negative findings of this study, and the lack of other controlled studies evaluating unilateral or bilateral nerve grafting, the technique is considered investigational.

Physician Specialty Society and Academic Medical Center Input
In response to requests, input was received from four academic medical centers while this policy was under review in 2008; no input was received from physician specialty societies. 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. Input from these four centers agreed that this procedure is considered investigational as adopted in the policy in May 2008.

Technology Assessments, Guidelines, and Position Statements
The 2013 (V.4) National Comprehensive Care Network (NCCN) prostate cancer guideline states that replacement of resected nerves has not been shown to be beneficial for recovery of erectile function after radical prostatectomy.

Key Words:
Genitofemoral Nerve Graft, Prostatectomy, Sural Nerve Graft

Approved by Governing Bodies:
N/A

Benefit Application:
Coverage is subject to member’s specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Home Policy provisions apply
FEP: Special benefit consideration may apply. Refer to member’s benefit plan. FEP does not consider investigational if FDA approved. Will be reviewed for medical necessity.
Pre-certification requirements: Not applicable
**Current Coding:**

CPT Codes:  
- **64999**  
- **55840 – 55845**  

Unlisted procedure, nervous system  
Radical retropubic prostatectomy, code range

**References:**


**Policy History:**

Medical Policy Group, March 2011 (2)  
Medical Policy Administration Committee, March 2011  
Available for comment April 4 – May 18, 2011  
Medical Policy Group, October 2012 (2): 2012 Updates to Key Points and References  
Medical Policy Panel, December 2012  
Medical Policy Panel December 2013

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member’s plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield’s administration of plan contracts.