Clinical Policy Title: Brachytherapy of coronary arteries

Clinical Policy Number: 04.02.04

Effective Date: January 1, 2016
Initial Review Date: September 16, 2015
Most Recent Review Date: October 21, 2015
Next Review Date: September, 2016

Related policies:

CP# 05.02.02 Brachytherapy for localized prostate cancer
CP# 05.02.07 Brachytherapy for cancers other than prostate

ABOUT THIS POLICY: Arbor Health Plan has developed clinical policies to assist with making coverage determinations. Arbor Health Plan’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by Arbor Health Plan when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Arbor Health Plan’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Arbor Health Plan’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Arbor Health Plan will update its clinical policies as necessary. Arbor Health Plan’s clinical policies are not guarantees of payment.

Coverage policy

Arbor Health Plan considers the use of brachytherapy for coronary arteries intervention to be clinically proven and, therefore, medically necessary when the following criteria are met:

I. When used as an adjunct to percutaneous coronary intervention (PCI) for treatment of in-stent restenosis in a native coronary artery bare-metal stent (BMS).
II. To treat in-stent restenosis in grafted coronary vessels - that is, saphenous vein grafts (SVGs).

Limitations:

All other uses of brachytherapy for coronary arteries intervention are not medically necessary, including the use of drug-eluting stents (DES), because it is considered experimental, investigational or unproven.
Intravascular coronary brachytherapy is considered investigational for other applications, including, but not limited to:

- Managing initial lesions or treating restenosis in native or grafted coronary vessels without stents.
- As an alternative to stent placement to reduce the risk of or treat restenosis of native vessels or SVG at an unstented site of a prior PCI.
- Treating in-stent restenosis in SVG grafts using radioactive sources, excluding those that emit gamma radiation.

**Alternative covered services:**

Repeat PCI without brachytherapy surgery.

**Background**

Intracoronary brachytherapy is an established therapy. It is currently the only interventional procedure proven to effectively reduce the restenosis rates, after intervention of long and diffuse in-stent restenosis. For this indication, brachytherapy can be regarded as the current treatment of choice. Randomized studies yield promising results for bypass interventions, or interventions in small vessels or diabetic patients. These findings may encourage the decision to perform a percutaneous, transluminal intervention in these high-risk members. In clinical practice, implantation of new stents in combination with brachytherapy procedures should be avoided when possible.

Recurrent coronary stenosis occurs in 20 to 30 percent of patients in whom stents have been implanted for the treatment of obstructive lesions. When it occurs within the stent, it is referred to as in-stent re-stenosis.

In any case, the combined anti-aggregatory therapy should be conducted sufficiently long enough to minimize the danger of late stent thrombosis. Under this treatment, the expected thrombosis rates are within the range of placebo-treated members. The length of the radiation source should be sufficient to cover the entire interventional injury length to avoid recurrent edge stenosis. De novo lesions are currently not a routine indication for intracoronary brachytherapy. Although intracoronary brachytherapy may effectively reduce restenosis rates in sufficiently irradiated de novo lesion segments, de novo lesions should be treated only within controlled studies. The current available data with a follow-up period of up to five years show that intracoronary brachytherapy is, for the mid-term, a safe and effective therapy for the reduction of restenosis, after coronary interventions.

Revascularization of obstructed arteries due to coronary artery disease (CAD) may be accomplished by PCI with balloon angioplasty, a minimally-invasive procedure in which a catheter with an inflatable balloon at the tip is inserted into the lumen of the artery and inflated, dilating the area of blockage. Coronary stents are implanted in most members during PCI, resulting in lower rates of restenosis compared to balloon angioplasty alone. Several DES have been developed to minimize the incidence of restenosis, and represent approximately 70 – 90 percent of stent implantations. The choice of stent (bare metal vs. drug-eluting)
depends on various factors, including lesion location and morphology, patient characteristics, and the patient’s ability to adhere to the extended period of dual antiplatelet therapy, required for DES.

In-stent restenosis continues to be a significant problem with bare metal stents (BMS), and is thought to be caused by neointimal hyperplasia within the stent. Several mechanical treatments of in-stent restenosis were attempted, including balloon re-dilation, removal of in-stent hyperplasia by atherectomy and repeated bare metal stenting. Brachytherapy was introduced as a method to treat in-stent restenosis by the delivery of gamma or beta radiotherapy, via a catheter-based system. Brachytherapy affects the proliferation of smooth muscle cells that are responsible for restenosis, and may be used to treat in-stent restenosis of native coronary arteries and SVGs. The role of brachytherapy has diminished, however, and DES have emerged as the preferred method of treatment for in-stent restenosis. Although brachytherapy may still play a role in the treatment of selected members.

Three brachytherapy devices received U.S. Food and Drug Administration (FDA) premarket approval (PMA). The Novoste™ Beta-Cath™ System (Novoste Corp., Norcross, GA) and the GALILEO™ Intravascular Radiotherapy System (Guidant Corp., Houston, TX) deliver beta radiation, while the Cordis Checkmate™ System (Cordis Corp., Miami, FL) delivers gamma radiation. Each operates in a similar fashion. A delivery catheter is placed in the coronary artery at the site of in-stent restenosis and a transfer device is connected to the catheter, delivering the radioactive seeds to administer radiation to the artery. After a specified period of time, the radioactive seeds are returned to the transfer device and removed. Although significant data was collected through the use of all of these devices, both the Checkmate and GALILEO systems have been discontinued by their respective manufacturers (2007), as DES are now most frequently used. The Beta-Cath System is now distributed by Best Vascular, Inc.

PCI may be indicated in the management of the following:

- Members with acute coronary syndrome (e.g., acute myocardial infarction, unstable angina).
- Members with a history of significant obstructive atherosclerotic disease.
- Members with restenosis of a coronary artery previously treated with an intracoronary stent or other revascularization procedure.
- Members with chronic angina.
- Members with silent ischemia.

Searches

Arbor Health Plan searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
• Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
• The Centers for Medicare & Medicaid Services (CMS).

We conducted searches on August 24, 2015. Search terms were: “brachytherapy, cardiac disease, DES, percutaneous transluminal coronary angioplasty, in-stent restenosis.”

We included:
• **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
• **Guidelines based on systematic reviews**.
• **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

A guideline update for following PCI published by the American College of Cardiology (ACC), American Heart Association (AHA) and the Society for Cardiovascular Angiography and Interventions (SCAI), (Smith et al. 2005), states that vascular brachytherapy is a successful treatment for restenosis occurring within stents, while other adjunctive therapies, such as the cutting balloon, rotary ablation, excimer laser and re-stenting show mixed results.

The ACC/AHA/SCAI guideline states that brachytherapy is a safe and effective treatment for in-stent restenosis (Class IIa recommendation). A Class IIa recommendation indicates that there is conflicting evidence and/or a divergence of opinion about the usefulness/efficacy of a procedure or treatment, but that the weight of evidence is in favor of usefulness/efficacy. No changes to this recommendation occurred in focused updates to the PCI guideline, published in 2007 and 2009.

The 2011 American College of Cardiology Foundation (ACCF)/AHA/SCAI PCI guideline, (Wijns et al.), does not include recommendations for brachytherapy. The guideline references studies demonstrating the superiority of DES over brachytherapy.

Guidelines on Myocardial Revascularization developed by The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS), state that currently, intracoronary brachytherapy is of very limited use: restenosis rates have declined and in-stent restenosis after BMS are treated by DES or coronary artery bypass graft (CABG).

The recent introduction of DES contributes a major breakthrough to interventional cardiology. Many large randomized clinical trials using DES show a remarkable reduction in angiographic restenosis and target
vessel revascularization, when compared with BMS. The results of these trials appear to be supported by
evidence from everyday practice and non-controlled clinical trials. However, the expanded applications of
DES, especially in treating complex lesions such as left main trunk, bifurcation, SVG or in-stent restenosis,
are still under evaluation with ongoing studies. With the availability of different types of DES in the market,
the issue of cost should not be a deterrent and DES will eventually be an economically viable option for all
members. The adoption of DES in all PCI may become a reality in the near future.

Prior to the widespread use of DES, in-stent restenosis following PCI was a significant clinical problem,
frequently resulting in the need for repeat revascularization procedures. Intracoronary brachytherapy was
shown to be an effective treatment for in-stent restenosis of native coronary arteries or SVG.

In recent years, brachytherapy procedures have decreased in frequency however, and DES emerged as the
treatment of choice, in the majority of cases. However, brachytherapy may still play a role in the treatment
of in-stent restenosis in selected members. There is insufficient evidence in the published medical literature
to demonstrate the safety and efficacy of brachytherapy for expanded indications, including treatment for
new stenosis of native coronary arteries and SVGs; restenosis of native coronary arteries and SVGs at the
unstented site of a previous PCI; or as primary prevention of restenosis after stent implantation for de novo
lesions. The use of brachytherapy for treatment of restenosis in a DES also remains investigational, as
medical efficacy has not yet been demonstrated.

SVGs are commonly used conduits for surgical revascularization of coronary arteries; however, they are
associated with poor long-term patency rates. Percutaneous revascularization of SVGs is associated with
worse clinical outcomes, including higher rates of in-stent restenosis, target vessel revascularization,
myocardial infarction and death compared with PCI of native coronary arteries. Use of embolic protection
devices is a Class I indication according to the ACC/AHA guidelines to decrease the risk of distal
embolization, no-reflow and periprocedural myocardial infarction. Nonetheless, these devices are
underused in clinical practice.

Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
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| Leter EM, et al. (2002) | Key points:  
Dosimetric comparison between high-precision external beam radiotherapy and endovascular brachytherapy for coronary artery in-stent restenosis.  
- Although the doses distributed throughout the heart were higher for high-precision EBRT compared to endovascular brachytherapy, they are expected to be clinically irrelevant when non-targeted major coronary arteries are not closely situated to the targeted vessel segment. |
<table>
<thead>
<tr>
<th>Citation</th>
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<tbody>
<tr>
<td>Oliver, et al. (2008)</td>
<td>Key points:</td>
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<td>A meta-analysis of randomized trials conducted assessing the outcome of Brachytherapy or drug-eluting stents for the treatment of in-stent restenosis.</td>
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<tr>
<td></td>
<td>• The analysis included 14 studies/3103 patients. Neither treatment had any effect on mortality or rate of myocardial infarction.</td>
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<td></td>
<td>• At intermediate follow-up, brachytherapy reduced the rate of revascularization, binary restenosis, and late loss compared to balloon angioplasty and selective bare metal stents alone.</td>
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<tr>
<td>C. Holmes, et al. (2008)</td>
<td>Key points:</td>
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<td></td>
<td>A randomized trial to evaluate the safety and efficacy of sirolimus-eluting stents (SES) (n=259), compared to vascular brachytherapy (VBT) (n=125) for treatment of in-stent restenosis, in a BMS.</td>
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<td></td>
<td>• At three years, survival free from TLR or TVR was significantly improved with SES; freedom from TLR was 81.0% for SES vs. 71.6% for brachytherapy, p=0.018; TVR was 78.2% for SES vs. 68.8% for brachytherapy, p=0.022.</td>
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<td>• Target vessel failure and major adverse cardiac events (MACE) improved with SES, but did not reach statistical significance. There was no statistically significant difference in definite or probable stent thrombosis between the two groups.</td>
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<td></td>
<td>• Five year follow-up of the Sirolimus in-stent restenosis (SISR) trial was published. There were no differences in safety or efficacy outcomes for treatment of BMS restenosis with SES vs. VBT.</td>
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<tr>
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<td>• There were no significant differences in survival free from TLR, TVR or major adverse cardiac events between the two groups.</td>
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<tr>
<td>Alli, et al. (2012)</td>
<td>Key points:</td>
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<td>A five year follow-up of the SISR trial was published by Alli et al. in 2012.</td>
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**Glossary**

**Coronary vascular brachytherapy** — Treatment for coronary in-stent restenosis, in which a catheter is placed inside blood vessels and sources are inserted and removed. Also known as interstitial radiation, intracavitary radiation or internal radiation therapy.

**Coronary restenosis** — Recurrent narrowing or constriction of a coronary artery following surgical procedures; performed to alleviate a prior obstruction.

**Drug-eluting stent (DES)** — A peripheral or coronary stent (a scaffold) placed into narrowed, diseased peripheral or coronary arteries that slowly releases a drug to block cell proliferation. This prevents fibrosis that, together with clots (thrombi), could otherwise block the stented artery, a process called restenosis.
Intensity-modulated radiation therapy (IMRT) — Technique that delivers precise therapeutic radiation to tumors while avoiding surrounding tissue.

Percutaneous coronary intervention (PCI) — A non-surgical procedure used to treat the stenotic (narrowed) coronary arteries of the heart found in coronary heart disease; also known as coronary angioplasty or simply angioplasty.

Restenosis — Pertains to an artery or other large blood vessel that has become narrowed, received treatment to clear the blockage and subsequently become renarrowed.

Scintigraphy — A diagnostic test used in nuclear medicine, wherein radioisotopes are taken internally (via radiopharmaceuticals) and the emitted radiation is captured by external detectors to form two dimensional images.

References

Professional society guidelines/other:


Peer-reviewed references:


Clinical trials:

Searched clinicaltrials.gov on August 27, 2015 using terms, brachytherapy and cardiac disease | Open Studies. Five studies found, one relevant.


CMS National Coverage Determinations (NCDs):

No NCDs identified as of the writing of this policy.

Local Coverage Determinations (LCDs):

Interventional Cardiology (L32603), 06/25/2015. Available at: https://www.cms.gov/medicare-coverage-database/details/lcddetails.aspx?LCDId=32603&ContrId=325&ver=40&ContrVer=1&SearchType=Advanced&CoverageSelection=Both&NCSelection=NCA%7cCAL%7cNCD%7cMEDCAC%7cTA%7cMCD&ArticleType=SA&D%7cEd&PolicyType=Final&s=All&KeyWord=Interventional+Cardiology&KeyWordLookUp=Doc&KeyWordSearchType=Exact&kq=true&bc=IAAAAABAAAAAAAA%3d%3d&. Accessed August 27, 2015.

Commonly submitted codes
Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

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<td>77785</td>
<td>Remote afterloading high dose radionuclide brachytherapy; 1 channel</td>
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<td>77787</td>
<td>Remote afterloading high dose radionuclide brachytherapy; more than 12 channels</td>
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<tr>
<td>92974</td>
<td>Transcatheter placement of radiation delivery device for subsequent coronary intravascular brachytherapy</td>
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<tr>
<td>996.03</td>
<td>Mechanical complication of coronary artery stent (restenosis)</td>
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<td>T82.857</td>
<td>Stenosis of cardiac prosthetic devices, implants and grafts</td>
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