Healthy Blue

Clinical UM Guideline

Subject:	Intravascular Brachytherapy (Coronary and Non-Coronary)		
Guideline #:	CG-THER-RAD-07	**Publish Date:**	12/16/2020
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Description

This document addresses the use of intravascular brachytherapy. Intravascular brachytherapy is a technique that utilizes gamma or beta radiation to treat stenoses occurring at the site of a prior stent (that is, in-stent restenosis). Intravascular brachytherapy has been studied primarily in the coronary arteries but also in the femoropopliteal system. This document addresses intravascular brachytherapy in the coronary arteries and also in non-coronary vessels such as the femoropopliteal system.

Clinical Indications

Medically Necessary:

Intravascular coronary brachytherapy, also called intracoronary brachytherapy, is considered **medically necessary** as a treatment of in-stent restenosis.

Not Medically Necessary:

Intravascular coronary brachytherapy is considered **not medically necessary** for all other uses not specified above as medically necessary, including, but not limited to, the following:

- As an initial treatment of coronary artery disease to prevent de novo stenosis either within or adjacent to stent placement
- Repeat intracoronary brachytherapy

Non-coronary intravascular brachytherapy is considered **not medically necessary** for the treatment or prevention of stenosis or restenosis in blood vessels, including, but not limited to, the femoropopliteal vessels.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. 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.

Intravascular Coronary Brachytherapy
When services may be Medically Necessary when criteria are met:

CPT	
77770	Remote afterloading high dose rate radionuclide interstitial or intracavitary brachytherapy, includes basic dosimetry, when performed; 1 channel [when specified as coronary intravascular brachytherapy]
77771	Remote afterloading high dose rate radionuclide interstitial or intracavitary brachytherapy, includes basic dosimetry, when performed; 2-12 channels [when specified as coronary intravascular brachytherapy]
77772	Remote afterloading high dose rate radionuclide interstitial or intracavitary brachytherapy, includes basic dosimetry, when performed; over 12 channels [when specified as coronary intravascular brachytherapy]
92974	Transcatheter placement of radiation delivery device for subsequent coronary intravascular brachytherapy
ICD-10 Procedure	
02700T6-02734TZ	Dilation of coronary artery, with radioactive intraluminal device [by number of arteries and approach; includes codes 02700T6, 02700TZ, 02703T6, 02703TZ, 02704T6, 02704TZ, 02710T6, 02710TZ, 02713T6, 02713TZ, 02714T6, 02714TZ, 02720T6, 02720TZ, 02723T6, 02723TZ, 02724T6, 02724TZ, 02730T6, 02730TZ, 02733T6, 02733TZ, 02734T6, 02734TZ]
ICD-10 Diagnosis	
T82.855A-T82.855S	Stenosis of coronary artery stent

When services are Not Medically Necessary:
For the procedure and diagnosis codes listed above when criteria are not met or for the diagnoses listed below, or for situations designated in the Clinical Indications section as not medically necessary.

ICD-10 Diagnosis	
I25.10-I25.9	Chronic ischemic heart disease

Non-coronary Intravascular Brachytherapy
When services are Not Medically Necessary:
For the following procedure and diagnosis codes; or when the code describes a procedure designated in the Clinical Indications section as not medically necessary.

CPT	
77770	Remote afterloading high dose rate radionuclide interstitial or intracavitary brachytherapy, includes basic dosimetry, when performed; 1 channel [when specified as non-coronary intravascular brachytherapy]
77771	Remote afterloading high dose rate radionuclide interstitial or intracavitary brachytherapy, includes basic dosimetry, when performed; 2-12 channels [when specified as non-coronary intravascular brachytherapy

77772	Remote afterloading high dose rate radionuclide interstitial or intracavitary brachytherapy, includes basic dosimetry, when performed; over 12 channels [when specified as non-coronary intravascular brachytherapy]
93799	Unlisted cardiovascular service or procedure [when specified as transcatheter placement of radiation delivery device for non-coronary intravascular brachytherapy]

ICD-10 Diagnosis

I70.0-I70.92	Atherosclerosis
T82.856A-T82.856S	Stenosis of peripheral vascular stent

Discussion/General Information

Intravascular brachytherapy (IVB) involves the temporary placement of radioactive substances, usually in the form of a thin catheter filled with radioactive seeds, a radioactive wire, or a balloon coated or filled with radioactive material, into previously cleared vessels at the site of restenosis. When used to treat lesions in the coronary arteries, IVB is referred to as intravascular coronary brachytherapy (ICB). Radiation reduces the proliferation of the vessel's smooth muscle cells, preventing or delaying long-term occurrence of restenosis.

Intravascular Coronary Brachytherapy
There are well-designed, randomized, clinical trials evaluating the effectiveness of brachytherapy using gamma or beta radiation for the management of coronary in-stent restenosis. The outcomes of these trials report that individuals receiving brachytherapy have statistically significant reductions in restenosis and in target lesion revascularization rates (Leon, 2001; Popma, 2002; Waksman, 2002a; Waksman, 2002b; Waksman, 2003), although long-term studies have reported late occurrences of restenosis (Grise, 2002; Maeder, 2008; Meerkin, 2002; Silber, 2005). While there was initial interest in IVB as a first-line treatment of stenoses, clinical trials have suggested that drug-eluting stents are preferred in preventing in-stent restenosis (Ellis, 2008; Oliver, 2008; Park, 2008). Restenosis following bare-metal stent implantation has a high recurrence rate (Holmes, 2008). Clinical trials show that the treatment of restenosis with drug-eluting stents after implantation of bare-metal stents results in better clinical outcomes such as improved event-free survival and reduced angiographic restenosis (Stone, 2006; Holmes, 2006).

Lu (2011) conducted a meta-analysis to compare the outcomes of drug-eluting stents versus ICB for in-stent restenosis. Twelve studies met study criteria and were reviewed; four trials were randomized and eight were nonrandomized. The mid-term follow-up period was 6 to 12 months. Target-vessel revascularization data showed an odds ratio of 0.44% suggesting the occurrence of target-vessel revascularization was significantly reduced by the use of drug-eluting stents. A subgroup analysis showed a difference in the result between the randomized trials and nonrandomized trials with a benefit shown in the drug-eluting stents versus no benefit in the nonrandomized trials. At mid-term follow-up, binary restenosis was found to have occurred in 13.9% of individuals treated with drug-eluting stents and 29.5% of those individuals treated with ICB. At the mid-term follow-up period, late lumen loss showed no significant effect of the use of drug-eluting stents in the randomized trials, but showed a significant reduction in the non-randomized trials. During the mid-term follow-up period, no differences were noted between drug-eluting stents and ICB in cardiac death, myocardial infarction and late stent restenosis. A long-term follow-up period of 24 to 36 months was recorded for target-vessel revascularization, cardiac death and myocardial infarction

(insufficient data was provided to perform long-term follow-up analysis for binary stenosis and late lumen loss). A significant difference was found for target-vessel revascularization (odds ratio: 0.61, 95% confidence interval [CI]: 0.43-0.86, P=0.005). There were no significant differences found between drug-eluting stents versus ICB for cardiac death and myocardial infarction. These findings suggest that the use of drug-eluting stents for in-stent restenosis when compared with ICB appears to be associated with reduced occurrences of target-vessel revascularization and binary restenosis, there may be a possible benefit from drug-eluting stents in late lumen loss reduction, but drug-eluting stents were not superior to ICB in reducing death or myocardial infarction.

In a 2018 retrospective review by Varghese and colleagues, 197 participants with recurrent drug-eluting stent in-stent restenosis underwent treatment with IVB compared to 131 participants who underwent routine percutaneous intervention (non-IVB group). The primary end point was major adverse cardiac events which was defined as a composite of target lesion revascularization, myocardial infarction, and all-cause mortality at 12 months. For all 328 participants treated for recurrent drug-eluting stent restenosis, immediate angiographic success was achieved and participants were discharged alive from the hospital. For those participants who underwent IVB there were no immediate periprocedural complications attributed to the use of the brachytherapy catheter. At 12 months, the major adverse cardiac events were lower in the IVB arm when compared to the non-IVB group (13.2% and 28.2%; P=0.01). Target lesion revascularization rates were lower in the IVB arm compared to the non-IVB group (17.8% and 29%; P=0.09). At the 12-month analysis, there were no significant differences between the groups noted in either death, myocardial infarction or stent thrombosis. The participants in this study represent a high-risk group for restenosis given the high prevalence of clinical risk factors. There are limitations to this study which includes its retrospective nature and follow-up time of 12 months. A long-term follow-up is needed to rule out concerns, such as late catch-up phenomenon and very late stent thrombosis. Even with the limitations, this study shows benefit of IVB by reducing restenosis and major adverse cardiac events.

Another retrospective study by Nakahama and colleagues (2018) reports the 10-year results of major adverse cardiac events in 680 participants treated with IVB for coronary in-stent restenosis. Major adverse cardiac events were defined as all-cause death, myocardial infarction, and target vessel revascularization. At 10-year follow-up, the rate of death was 25%, myocardial infarction was 22.4%, and target vessel revascularization was 48%. This study has limitations which include its retrospective design, it was a single center, and there was no standardized follow-up after IVB which raised the concern for varying medication administration and clinical care after treatment. However, the results appear to be similar with other studies which shows benefit for IVB for coronary in-stent restenosis.

A 2020 systematic review and meta-analysis was done by Megaly and colleagues. The authors reported on long-term outcomes of IVB in recurrent in-stent restenosis. There were five observational studies included which encompassed 917 participants. The primary outcome was target vessel revascularization with secondary outcomes including myocardial infarction and all-cause mortality. At 1 year after IVB, the incidence of target vessel revascularization was 17.5% and myocardial infarction was 3.1%. At 2 years after IVB, the incidence of target vessel revascularization was 26.7% and myocardial infarction was 3.9%. With a mean follow-up time of 24 ± 7 months, incidence of target vessel revascularization was 29.2%, incidence of myocardial infarction was 4.3%, and incidence of all-cause mortality was 7.3%. While this study has limitations including an observational, single-arm design without a control group, IVB is an effective treatment option for in-stent restenosis.

The American College of Cardiology (ACC)/American Heart Association (AHA)/Society for Cardiovascular Angiography and Interventions in their 2011 Guideline for Percutaneous Coronary Intervention, note that lower rates of restenosis occur with the use of drug-eluting stents when compared to bare-metal stents or vascular brachytherapy and does not recommend brachytherapy for the prevention of restenosis.

Intravascular Non-coronary Brachytherapy
IVB has also been studied as an adjunct to percutaneous transluminal angioplasty of the femoropopliteal system. While the greatest amount of clinical experience with IVB is in the coronary artery system, there are a number of important differences that preclude extrapolation of results from the coronary to the peripheral arterial system. There is greater anatomic variability in peripheral arteries than coronary arteries, such as length, diameter, thickness, curvature, and orientation. The larger size of peripheral arteries necessitates treatment with a high-energy gamma radiation source, rather than the beta radiation, which is more commonly used for the coronary arteries. Gamma radiation sources for IVB are not currently marketed in the United States, so it is unlikely that this procedure is commonly performed.

Studies have focused on IVB as both an adjunct to primary angioplasty or as a treatment of restenosis. One randomized trial enrolled 113 individuals with either de novo or restenotic lesions of the femoropopliteal system who underwent angioplasty with or without IVB (Wolfram, 2005). At 6-month follow-up, the restenosis rate was lower in the IVB group compared to the angioplasty group. However, by 5-year follow-up, there were no differences in the stenosis rate between the two groups. Diehm and colleagues (2005) reported on the results of a similarly designed trial enrolling 147 individuals. These authors also reported that the short-term improvements in restenoses associated with IVB were not maintained in the longer term.

Mitchell et al (2012) reported on a literature review and meta-analysis of randomized clinical trials for brachytherapy and restenosis following lower limb angioplasty. A total of six trials were identified (687 participants). All six trials reported 12-month data with respect to restenosis; 99/343 brachytherapy participants had restenosis at 12 months versus 147/344 control participants with restenosis at 12 months (pooled odds ratio 0.50; 95% CI, 0.301-0.836; p=0.008). At 24 months, three trials reported data regarding restenosis; 43/154 brachytherapy participants had restenosis versus 82/157 controls (pooled odds ratio 0.32; 95% CI, 0.02-1.621; p=0.17). Rates for re-intervention within 12 months were reported by four trials; 25/166 required re-intervention versus 41/171 controls (pooled odds ratio 0.53; 95% CI, 0.272-1.017; p=0.06). Three trials reported the development of a new stenosis in the irradiated artery within the first year, but it was outside the previously irradiated area (16/109 brachytherapy participants versus 3/115 controls; pooled odds ratio 8.65; 95% CI, 2.176-34.391; p=0.002). With small sample sizes in the trials, it is suggested that there is some early benefit of brachytherapy, but there is an increased risk of new lesions developing and there is a lack of long-term reductions in risk.

The American College of Cardiology Foundation (ACCF)/AHA guideline for the management of patients with peripheral artery disease (Gerhard-Herman 2016) does not include any recommendations for IVB of the femoropopliteal system.

Published in 2018, the Society for Cardiac Angiography and Interventions consensus guidelines for device selection in femoral-popliteal arterial interventions does not recommend brachytherapy for femoropopliteal revascularization due to lack of supportive data or failure to demonstrate significant advantages over currently available percutaneous transluminal angioplasty or stents.

Definitions

De novo: Something that is newly developed or was not previously present. In the context of this document, de novo refers to new stenotic lesions either in previously untreated vessels or vessels that have received prior ICB but at a new location adjacent to the existing lesion.

Intravascular brachytherapy: A type of medical therapy that involves the placement of a radioactive substance at the site of a previously cleared blood vessel. This therapy is intended to treat recurrences of vessel blockages.

Percutaneous transluminal angioplasty (PTA): A procedure for enlarging a narrowed vascular lumen by inflating and withdrawing through the stenotic region a balloon on the tip of an angiographic catheter. This may include positioning of an intravascular endoluminal stent.

Restenosis: A recurrence of narrowing or constriction.

Stenosis: A constriction or narrowing of a passage.

Stent: A wire mesh tube-like device used to prop open an artery after initial angioplasty.

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Websites for Additional Information

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Index

Brachytherapy, Intravascular Coronary
Brachytherapy, Intravascular Non-Coronary
Novoste™ Beta-Cath™ System

The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

History

Status	Date	Action
Reviewed	11/05/2020	Medical Policy & Technology Assessment Committee (MPTAC) review. Updated Discussion/General Information and References sections. Reformatted Coding section; clarified applicable diagnosis codes.
Reviewed	11/07/2019	MPTAC review.
Reviewed	01/24/2019	MPTAC review. Updated Discussion/General Information and References sections.
New	03/22/2018	MPTAC review. Initial document development. Moved content of THER-RAD.00003 Intravascular Brachytherapy (Coronary and Non-Coronary) to new clinical utilization management guideline document with the same title.