Prior Authorization Review
Panel MCO Policy Submission

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Type of Submission – Check all that apply:
- [ ] New Policy
- [X] Revised Policy*
- [ ] Annual Review – No Revisions

*All revisions to the policy must be highlighted using track changes throughout the document. Please provide any clarifying information for the policy below:

CPB 371 Brachytherapy

This CPB has been revised to state that brachytherapy for bone metastases is considered experimental and investigational.

Name of Authorized Individual (Please type or print):
Dr. Bernard Lewin, M.D.

Signature of Authorized Individual:

Revised 04/12/2018
Policy

Aetna considers brachytherapy (also known as interstitial radiation, intracavitary radiation, internal radiation therapy) medically necessary for the following conditions:

- Breast cancer (such as the MammoSite Radiation Therapy System (Proxima Therapeutics, Alpharetta, GA)
- Esophageal cancer
- Eye tumors (e.g., choroidal melanoma; small retinoblastomas (i.e., less than 15 mm in diameter and less than 8 mm in thickness)
- Genitourinary cancers other than bladder cancer (including penile cancer, prostate cancer, urethral cancer)
- Gynecologic cancer (cervical, endometrial, vaginal or vulvar)
- Head and neck cancers (including buccal mucosa cancer, lip cancer, mouth cancer, nasopharyngeal cancer, salivary gland cancer, soft palate cancer, tonsillar fossa/pillar cancer)

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.*
- Respiratory and digestive tract cancers (including lung cancer (for palliation of obstructive symptoms due to intraluminal tumor), pelvic recurrence of colorectal cancer, pleural mesotheliomas, rectal (anal) cancer)
- Skin cancer, where surgical resection and photon or electron beam techniques are contraindicated
- Soft tissue sarcomas
- Stenotic obstruction post lung transplantation refractory to other treatments such as balloon dilation, laser debridement, or stent placement.

Aetna considers brachytherapy experimental and investigational for all other indications including the following (not an all-inclusive list) because its effectiveness for indications other than the ones listed above has not been established.

- Bladder cancer
- Bone metastases
- Brain tumors
- Leukemia
- Lymphoma
- Multiple myeloma
- Palmoplantar pustulosis
- Pancreatic cancer
- Prevention and treatment of keloids
- Subfoveal choroidal neovascularization secondary to age-related macular degeneration
Aetna considers electronic brachytherapy experimental and investigational for breast cancer and all other indications (e.g., non-melanoma skin cancer) because its effectiveness has not been established.

Aetna considers endovascular/intravascular brachytherapy to reduce re-stenosis following percutaneous renal angioplasty, percutaneous femoropopliteal angioplasty/peripheral vascular disease experimental and investigational because its effectiveness has not been established.

The combination of brachytherapy and external beam radiation therapy (ProstRcision) has not been proven to be more effective than other established alternatives for the treatment of prostate cancer.

Notes:

Brachytherapy may be used in conjunction with surgery. Tumors close to critical structures that can not be resected with adequate surgical margins may also be treated by interstitial brachytherapy.

Brachytherapy may be used either alone or in combination with external beam radiation.

For brachytherapy via radioembolization of the liver, see

CPB 0268 - Liver and Other Neoplasms: Treatment Approaches
(../200_299/0268.html)
Background

Brachytherapy is a type of radiation therapy in which the radiation device is placed within or close to the target site, in contrast to teletherapy which uses a device removed from the patient. With brachytherapy, a radiation source, in the form of seeds, ribbons or capsules, is placed directly into or near a cancerous tumor inside the body. It may also be known as internal radiation, implant radiation or interstitial radiation therapy. By placing the radioactive sources in or near the tumor, a higher dose of radiation is delivered to a smaller part of the body; thereby reducing the dose to surrounding healthy tissues. In general, any solid tumor that is sufficiently localized may be treated by interstitial brachytherapy. A variety of radioactive isotopes are employed in brachytherapy including lower energy sources usually for permanent implantation such as Palladium-103 and Iodine-125, as well as higher energy sources such as Iridium-192, Gold-198, and Cesium-137, which, except for Gold-198, are used for limited periods of time via after loading catheters.

Traditionally, brachytherapy has been employed in the treatment of gynecologic tumors (uterine cervix and endometrium) employing Radium-226 (Ra-226), Cobalt-60 (Co-60), and Cesium-137 (Cs-137). Similarly, therapy of oropharyngeal tumors...
may require interstitial brachytherapy, such as radium needles, Cs-137 or Iridium-192 (Ir-192) in selected carcinomas of the lip, nasal vestibule or floor of mouth lesions, radium in oral tongue cancers, Gold-198 (Au-198) seeds or Ir-192 ribbons or catheters for base of tongue lesions (3) or tonsillar malignancies (radon or gold seeds). In pelvic recurrences of colorectal tumors or in anal or bile duct cancers, interstitial Ir-192 or Iodine-125 (I-125) boosts may be combined with external beam radiation therapy (EBRT). In superficial bladder tumors, penile cancers and small tumors of the female urethra, interstitial implantation with Ra-226, Cs-137 or Ir-192 may be necessary.

Interstitial brachytherapy is indicated for stages A2 and B prostatic cancer and for malignant brain tumors. A variety of other tumors have been treated by this technique, including ophthalmic malignancies of the choroid or retina, hepatocellular carcinomas, unresectable esophageal cancers, pulmonary malignancies, as well as an adjunct to surgical treatment of neoplasms in varying anatomic locations, when tumors attached or adjacent to critical structures can not be completely excised or resected with adequate surgical margins.

Breast brachytherapy treatment delivers radiation via a balloon catheter following lumpectomy to the space left after the cancerous tumor is removed and to the tissue directly surrounding the cavity. By delivering radiation to the area directly surrounding the original tumor, radiation exposure is minimized to the rest of the breast and other organs. Examples of delivery systems include, but may not be limited
to, the MammoSite Radiation Therapy System (RTS), the CONTURA Multi-Lumen Balloon (MLB) Catheter and the SAVI applicator, a single-entry device that allows physicians to customize radiation treatments based on individual-specific anatomy.

The MammoSite Radiation Therapy System (Proxima Therapeutics, Alpharetta, GA) is an alternative to interstitial brachytherapy with either seeds or needles to treat the intact breast lumpectomy site. With the MammoSite technique, the lumpectomy cavity is dilated by a balloon and a single high-dose radiation source is positioned within the central portion of the balloon to deliver a uniform dose to the walls of the lumpectomy cavity. Although the MammoSite technique may offer a more uniform dose distribution over older techniques of interstitial brachytherapy implants, it has not been shown to offer any appreciable improvement in dosimetry over conventional external beam radiation. The primary justification for breast brachytherapy is a lack of patient compliance with conventional post-operative external beam radiotherapy. The MammoSite offers the convenience of a short course of treatment, usually 10 high-dose radiation applications done twice-daily over 5 days. By contrast, external beam radiotherapy usually requires 5 to 7 weeks of treatment post-operatively. Another system that has been cleared by the Food and Drug Administration (FDA) for interstitial breast brachytherapy is the MammoTest Breast Biopsy System (Fischer Imaging Corporation, Denver, CO).
Electronic brachytherapy (EBT) is radiotherapy that reportedly uses a high dose rate, low energy x-ray source to apply brachytherapy to the cancerous site. Purportedly, EBT is utilized to provide intracavity, interstitial or surface brachytherapy. Examples include, but may not be limited to, the Axxent Electronic Brachytherapy System and the INTRABEAM system. EBT has been developed to offer advantages over standard radioactive brachytherapy in the areas of radiation safety both to the patient as well as the personnel administering the treatment. The Axxent Electronic Brachytherapy System uses disposable miniature X-ray radiation sources to deliver electronically generated ionizing radiation directly to tumor beds. Electronic brachytherapy is intended to minimize exposure of the patient's healthy tissue to unnecessary radiation. Electronic brachytherapy uses X-ray energy to allow more flexibility than radioisotope-based brachytherapy systems that are currently in use. Electronic brachytherapy does not require a heavily shielded environment, so that it has potential for use in a broad array of clinical settings. The Axxent Electronic Brachytherapy System was cleared for use in breast cancer by the FDA based on a 510(k) application. Electronic brachytherapy has potential for use in administering high-dose rate brachytherapy for breast cancer (BCBSA, 2007; CTAF, 2006). However, there is insufficient evidence in the peer-reviewed published medical literature comparing outcomes of EBT with standard radioisotope-based brachytherapy.
In an observational, non-randomized, multi-center study, Beitsch et al (2010) evaluated EBT as a post-surgical adjuvant radiation therapy for early stage breast cancer. This study included women aged 50 years or more with invasive carcinoma or ductal carcinoma in situ, tumor size less than or equal to 3 cm, negative lymph node status, and negative surgical margins. The end points were skin and subcutaneous toxicities, efficacy outcomes, cosmetic outcomes, and device performance. In this interim report, 1-month, 6-month, and 1-year follow-up data were available on 68, 59, and 37 patients, respectively. The EBT device performed consistently, delivering the prescribed 34 Gy to all 69 patients (10 fractions/patient). Most adverse events were grade 1 and included firmness, erythema, breast tenderness, hyper-pigmentation, pruritus, field contracture, seroma, rash/desquamation, palpable mass, breast edema, hypo-pigmentation, telangiectasia, and blistering, which were anticipated. Breast infection occurred in 2 (2.9 %) patients. No tumor recurrences were reported. Cosmetic outcomes were excellent or good in 83.9 % to 100 % of evaluable patients at 1 month, 6 months, and 1 year. The authors concluded that this observational, non-randomized, multi-center study demonstrated that this EBT device was reliable and well-tolerated as an adjuvant radiation therapy for early stage breast cancer. These findings are limited by the length of follow-up, and longer follow-up data are needed.

Ahmad et al (2010) compared treatment plans for patients treated with EBT using the Axxent System as adjuvant therapy for early stage breast cancer with treatment plans prepared
from the same computed tomography (CT) image sets using an Ir-192 source. Patients were implanted with an appropriately sized Axxent balloon applicator based on tumor cavity size and shape. A CT image of the implanted balloon was utilized for developing both EBT and Ir-192 brachytherapy treatment plans. The prescription dose was 3.4 Gy per fraction for 10 fractions to be delivered to 1 cm beyond the balloon surface. Iridium plans were provided by the sites on 35 of the 44 patients enrolled in the study. The planning target volume coverage was very similar when comparing sources for each patient as well as between patients. There were no statistical differences in mean % V100. The percent of the planning target volume in the high-dose region was increased with EBT as compared with Iridium (p < 0.001). The mean maximum calculated skin and rib doses did not vary greatly between EBT and Iridium. By contrast, the doses to the ipsilateral lung and the heart were significantly lower with eBx as compared with Iridium (p < 0.0001). The total nominal dwell times required for treatment can be predicted by using a combination of the balloon fill volume and planned treatment volume (PTV). This dosimetric comparison of EBT and Iridium sources demonstrated that both forms of balloon-based brachytherapy provide comparable dose to the planning target volume. The authors concluded that EBT is significantly associated with increased dose at the surface of the balloon and decreased dose outside the PTV, resulting in significantly increased tissue sparing in the heart and ipsilateral lung. This was a dosimetric comparison study with no clinical data on health outcomes.
Njeh and colleagues (2010) noted that breast conservation therapy (BCT) is the procedure of choice for the management of the early stage breast cancer. However, its utilization has not been maximized because of logistics issues associated with the protracted treatment involved with the radiation treatment. Accelerated partial breast irradiation (APBI) is an approach that treats only the lumpectomy bed plus a 1 to 2 cm margin, rather than the whole breast. Hence, because of the small volume of irradiation, a higher dose can be delivered in a shorter period of time. There has been growing interest for APBI and various approaches have been developed under phase I to III clinical studies; these include multi-catheter interstitial brachytherapy, balloon catheter brachytherapy, conformal external beam radiation therapy and intra-operative radiation therapy (IORT). Balloon-based brachytherapy approaches include Mammosite, Axxent EBT and Contura, hybrid brachytherapy devices include SAVI and ClearPath. The authors reviewed the different techniques, identifying the weaknesses and strength of each approach and proposed a direction for future research and development. It is evident that APBI will play a role in the management of a selected group of early breast cancer. However, the relative role of the different techniques is yet to be clearly identified.

Ivanov et al (2011) reported 1-year results and clinical outcomes of a trial that utilizes EBT to deliver IORT for patients with early-stage breast cancer. A total of 11 patients were enrolled on an institutional review board (IRB)-approved protocol. Inclusion criteria were patient age
greater than 45 years, unifocal tumors with
infiltrating ductal or ductal carcinoma in situ
(DCIS) histology, tumors less than or equal to 3
cm, and uninvolved lymph nodes. Preloaded
radiation plans were used to deliver radiation
prescription dose of 20 Gy to the balloon
surface. The mean time for radiation delivery
was 22 mins; the total mean procedure time was
1 hr 39 mins. All margins of excision were
negative on final pathology. At mean follow-up
of 12 months, overall cosmesis was excellent in
10 of 11 patients. No infection, fat necrosis,
desquamation, rib fracture or cancer recurrence
has been observed. There was no evidence of
fibrosis at last follow-up. The authors concluded
that IORT utilizing EBT is emerging as a feasible,
well-tolerated alternative to post-surgical APBI.
They stated that further research and longer
follow-up data on EBT and other IORT methods
are needed to establish the clinical efficacy and
safety of this treatment.

Bhatnagar and Loper (2010) reported their initial
experience of EBT for the treatment of non-
melanoma skin cancer. Data were collected
retrospectively from patients treated from July
2009 through March 2010. Pre-treatment biopsy
was performed to confirm a malignant
cutaneous diagnosis. A CT scan was performed
to assess lesion depth for treatment planning,
and an appropriate size of surface applicator
was selected to provide an acceptable margin.
An high-dose rate (HDR) EBT system delivered a
dose of 40.0 Gy in 8 fractions twice-weekly with
48 hours between fractions, prescribed to a
depth of 3 to 7 mm. Treatment feasibility, acute
safety, efficacy outcomes, and cosmetic results
were assessed. A total of 37 patients (mean age
of 72.5 years) with 44 cutaneous malignancies were treated. Of 44 lesions treated, 39 (89 \%) were T1, 1 (2 \%) Tis, 1 (2 \%) T2, and 3 (7 \%) lesions were recurrent. Lesion locations included the nose for 16 lesions (36.4 \%), ear 5 (11 \%), scalp 5 (11 \%), face 14 (32 \%), and an extremity for 4 (9 \%). Median follow-up was 4.1 months. No severe toxicities occurred. Cosmesis ratings were good to excellent for 100 \% of the lesions at follow-up. The authors concluded that the early outcomes of EBT for the treatment of non-melanoma skin cancer appear to show acceptable acute safety and favorable cosmetic outcomes. They stated that long-term follow-up is in progress to further assess efficacy and cosmesis.

Guidelines on squamous cell skin cancer from the National Comprehensive Cancer Network (NCCN, 2016) state that "[t]here are insufficient long-term efficacy and safety data to support the routine use of electronic surface brachytherapy." NCCN guidelines on basal cell carcinoma (NCCN, 2016) has a similar statement.

In a multi-center clinical study, Dickler et al (2010) evaluated the success of treatment delivery, safety and toxicity of EBT in patients with endometrial cancer. A total of 15 patients with stage I or II endometrial cancer were enrolled at 5 sites. Patients were treated with vaginal EBT alone or in combination with external beam radiation. The prescribed doses of EBT were successfully delivered in all 15 patients. From the first fraction through 3 months follow-up, there were 4 common toxicity criteria (CTC) grade 1 adverse events and 2 CTC grade II adverse events reported that were EBT-
related. The mild events reported were dysuria, vaginal dryness, mucosal atrophy, and rectal bleeding. The moderate treatment related adverse events included dysuria, and vaginal pain. No grade III or IV adverse events were reported. The EBT system performed well and was associated with limited acute toxicities. The authors concluded that EBT shows acute results similar to HDR brachytherapy. They stated that additional research is needed to further assess the clinical efficacy and safety of EBT in the treatment of endometrial cancer.

The American Society for Therapeutic Radiology and Oncology (ASTRO) Emerging Technology Committee's report on EBT (Park et al, 2010) stated that "advantages of EBT over existing technologies are as yet unproven in terms of efficacy or patient outcomes". The report explains the impact of clinical use of electronic brachytherapy could be far-reaching, and if used improperly, potentially harmful to patients. The report explains that electronic brachytherapy is currently an unregulated treatment delivery modality for cancer therapy, with minimal clinical data available from small single institution studies, none with significant follow-up. It also noted that there are currently no accepted calibration standards for EBT. Thus, there can be large uncertainties associated with absorbed dose measurement at low energies.

Furthermore, the report stated that the effects of EBT on tumor and normal tissues are not yet well understood, given the paucity of clinical studies.
Published data on electronic brachytherapy comes from studies which are small, mostly single center studies with limited follow-up. Much of this evidence is from low-quality retrospective studies. Other evidence comes from dosimetric planning studies rather than studies reporting actual clinical outcomes. The TARGET-A study is an exception in that it is a large, multi-center prospective study (Vaidya et al, 2011). This study, however, did not employ direct comparisons between electronic brachytherapy and established methods of high-dose rate brachytherapy using radioactive isotopes.

Eaton (2015) noted that in the last decade, EBT has emerged as an attractive modality for the treatment of skin lesions and intra-operative partial breast irradiation, as well as finding wider applications in intra-cavitary and interstitial sites. These miniature x-ray sources, which operate at low kilo-voltage energies (less than 100kV), have reduced shielding requirements and inherent portability, so can be used outside the traditional realms of the radiotherapy department. However, steep dose gradients and increased sensitivity to inhomogeneities challenge accurate dosimetry. Secondly, ease of use does not mitigate the need for close involvement by Medical Physics Experts and consultant oncologists. Finally, the authors stated that further studies are needed to relate the more heterogeneous dose distributions to clinical outcomes. They stated that with these provisos, the practical convenience of EBT strongly suggests that it will become an established option for selected patients, not only
in radiotherapy departments but also in a range of operating theaters and clinics around the world.

Avila and colleagues (2009) assessed the short-term safety and feasibility of epiretinal strontium-90 brachytherapy delivered concomitantly with intra-vitreal bevacizumab for the treatment of subfoveal choroidal neovascularization (CNV) due to age-related macular degeneration (AMD) for 12 months. A 3-year follow-up is planned. In this prospective, non-randomized, multi-center study, 34 treatment-naïve patients with predominantly classic, minimally classic and occult subfoveal CNV lesions received a single treatment with 24 Gy beta radiation (strontium-90) and 2 injections of the anti-vascular endothelial growth factor (VEGF) antibody bevacizumab. Adverse events were observed. Best corrected visual acuity (BCVA) was measured using standard Early Treatment Diabetic Retinopathy Study (ETDRS) vision charts. Twelve months after treatment, no radiation-associated adverse events were observed. In the intent-to-treat (ITT) population, 91 % of patients lost less than 3 lines (15 ETDRS letters) of vision at 12 months, 68 % improved or maintained their BCVA at 12 months, and 38 % gained greater than or equal to 3 lines. The mean change in BCVA observed at month 12 was a gain of 8.9 letters. The authors concluded that the safety and effectiveness of intra-ocular, epiretinal brachytherapy delivered concomitantly with anti-VEGF therapy for the treatment of subfoveal CNV secondary to AMD were promising in this small study population.
They stated that long-term safety will be assessed for 3 years. This regimen is being evaluated in a large, multi-center, phase III study.

In a multi-center, randomized, active-controlled, phase III clinical trial, Dugel et al (2013) evaluated the safety and effectiveness of epi-macular brachytherapy (EMBT) for the treatment of neovascular AMD. A total of 494 participants with treatment-naïve neovascular AMD were enrolled in this study. Participants with classic, minimally classic, and occult lesions were randomized in a 2:1 ratio to EMBT or a ranibizumab monotherapy control arm. The EMBT arm received 2 mandated, monthly loading injections of 0.5 mg ranibizumab. The control arm received 3 mandated, monthly loading injections of ranibizumab then quarterly injections. Both arms also received monthly as needed (pro re nata) re-treatment. Main outcome measures were the proportion of participants losing fewer than 15 ETDRS letters from baseline VA and the proportion gaining more than 15 ETDRS letters from baseline VA. At 24 months, 77 % of the EMBT group and 90 % of the control group lost fewer than 15 letters. This difference did not meet the pre-specified 10 % non-inferiority margin. This end-point was non-inferior using a 20 % margin and a 95 % confidence interval (CI) for the group as a whole and for classic and minimally classic lesions, but not for occult lesions. The EMBT did not meet the superiority end-point for the proportion of participants gaining more than 15 letters (16 % for the EMBT group versus 26 % for the control group): this difference was statistically significant (favoring controls) for occult lesions, but not for predominantly classic and minimally classic
lesions. Mean VA change was -2.5 letters in the EMBT arm and +4.4 letters in the control arm. Participants in the EMBT arm received a mean of 6.2 ranibizumab injections versus 10.4 in the control arm. At least 1 serious adverse event occurred in 54% of the EMBT arm, most commonly post-vitrectomy cataract, versus 18% in the control arm. Mild, non-proliferative radiation retinopathy occurred in 3% of the EMBT participants, but no case was vision threatening. The authors concluded that the 2-year effectiveness data do not support the routine use of EMBT for treatment-naive wet AMD, despite an acceptable safety profile. They stated that further safety review is needed.

Ashida and Chang (2009) stated that since the curved linear array echo-endoscope (linear EUS) was developed in the 1990s, EUS has evolved from EUS imaging, to EUS-guided fine needle aspiration (FNA), and now to EUS-guided fine needle injection, giving EUS even wider application. This advancement has brought "interventional EUS" into the pancreato-biliary field. Interventional EUS for pancreatic cancer includes delivery of contrast agents, drainage/anastomosis, celiac neurolysis (including ganglion neurolysis), radiofrequency ablation, photodynamic therapy, brachytherapy, as well as delivery of a growing number of anti-tumor agents. Al-Haddad and Eloubeidi (2010) noted that coupled with FNA, EUS provides high accuracy for the diagnosis and staging of pancreatic cancer. Novel EUS-based techniques have emerged as a safe minimally invasive alternative to the surgical or radiological approaches. By allowing better pain control, delivering anti-tumor therapies or draining
obstructed bile ducts, such techniques hold a big promise to improve the quality of life of patients with unresectable pancreatic cancer.

Guidelines from the National Comprehensive Cancer Network (NCCN, 2016) on pancreatic cancer state that intraoperative radiation therapy (IORT) is delivered by external beam radiation therapy (IOERT) or HDR brachytherapy (HDR-IORT). IORT is generally delivered as a single fraction or in combination with adjuvant or neoadjuvant chemoradiation. The NCCN pancreatic cancer guidelines state that "the role of IORT is controversial and should only be performed at specialized centers. It is sometimes used in cases where surgical resection may result in close or involved margins."

The Alberta Health Services’ clinical guideline on “Penile cancer” (2012) listed brachytherapy as a management option for Tis, Ta N0 M0 (Stage 0); T1 N0 M0 (Stage I); as well as T2 N0 M0 (Stage II) and T3 N0 M0 (Early Stage III) penile cancers.

Mattiucci et al (2014) explored the role of radiotherapy in the extra-hepatic bile duct carcinoma, and examined if and when radiotherapy could be effective for this group of patients. These investigators performed a systematic review of recently published literature. Recent studies using radiotherapy with survival data, resection rates and quality of life data were analyzed. There are no randomized trials regarding the treatment of extra-hepatic cholangiocarcinoma. The bulk of available studies suggested that in some cases radio-chemotherapy can be used as adjuvant therapy. Radiotherapy could also have a role in
unresectable cholangiocarcinoma: external radiotherapy or intraluminal brachytherapy, alone or in combination, could improve the outcome in selected patients. Finally, radiotherapy, and in particular intraluminal brachytherapy, could be used as a palliative treatment to improve the quality of life and in controlling symptoms. The authors concluded that the role of radiotherapy in extra-hepatic cholangiocarcinoma remains undefined due to the lack of randomized trials or otherwise properly controlled studies.

Wiedmann and colleagues (2005) noted that carcinoma of the biliary tree are rare tumors of the gastro-intestinal tract with a rising incidence during the last years. Biliary neoplasms are classified into intra- and extra-hepatic cholangiocarcinoma (Klatskin tumor, middle and distal extra-hepatic tumors), gallbladder cancer, and ampullary carcinoma. Transformation of normal into malignant bile duct tissue requires a chain of consecutive gene mutations, similar to the adenoma-dysplasia-carcinoma-sequence in colon cancer. Abdominal ultrasound, combined non-invasive magnetic resonance cholangiography/tomography (MRC/MRT), and facultatively endoscopic retrograde cholangiography (ERC) for unclear diagnosis, represent the gold standard for primary diagnosis. For ampullary carcinoma, endosonography and endoscopic biopsy are the diagnostic tools of choice. Cure is attainable only by formal curative radical surgical resection. Increasing surgical radicality within the last years enabled clearly improved 5-year survival rates. In contrast, there has been no clinical benefit for adjuvant and neoadjuvant
therapies. For palliation, bile duct stenting and photodynamic therapy are established methods. Radio- and chemotherapy should be reserved for clinical studies. New therapeutic approaches include brachytherapy, the use of modern chemotherapeutics, COX-2- and tyrosine kinase-receptor-inhibitors.

Also, the NCCN's clinical practice guideline on “Hepatobiliary cancers” (Version 2.2013) does not mention the use of brachytherapy for gallbladder carcinoma. Furthermore, an UpToDate review on “Treatment of advanced, unresectable gallbladder cancer” (Mehrotra, 2014) states that “For locoregionally advanced unresectable disease with or without obvious metastatic disease, guidelines from the National Comprehensive Cancer Network (NCCN) suggest 5-FU-based chemotherapy with radiation therapy, palliative chemotherapy, supportive care alone, or participation in a clinical trial as appropriate options for patients with an unresectable tumor without obvious metastatic disease”. The review does not mention brachytherapy.

Intravascular brachytherapy has been investigated as an adjunct to angioplasty of the femoropopliteal segment to reduce the risk of restenosis. Mitchell et al (2012) noted that re-stenosis is a fundamental weakness of percutaneous femoropopliteal angioplasty (PTA). The potential of endovascular brachytherapy (EVBT) to reduce re-stenosis has been evaluated in randomized clinical trials (RCTs), but no pooled analysis has been undertaken. These investigators performed a systematic review to identify RCTs in which PTA
alone was compared to PTA plus EVBT. The Pubmed and Medline databases, American Heart Association OASIS database and conference proceedings from the Peripheral Vascular Surgery Society and Vascular Society of Great Britain and Ireland were searched. Eligible studies were RCTs comparing PTA to PTA plus EVBT in human subjects with at least 1 clinical outcome reported (re-stenosis, complications, patency). Study quality was assessed by the Jadad score. Random-effects modeling was used to generate pooled effect size estimates. A total of 6 trials (687 patients) were identified.

Endovascular brachytherapy reduced 12-month re-stenosis rates (pooled odds ratio 0.50; 95% CI: 0.301 to 0.836; p = 0.008). The benefit disappeared by 24 months. The short-term risk of new lesions elsewhere in the treated artery was significantly increased by EVBT (pooled odds ratio 8.65; 95% CI: 2.176 to 34.391; p = 0.002).

The authors concluded that while limited by the small sample sizes in the included trials, this analysis suggests that the early benefit of EVBT is counter-balanced by the increased risk of new lesions and the lack of medium- to long-term reductions in re-stenosis risk. Based upon the best available evidence, EVBT can not be recommended for routine clinical use.

In a Cochrane review, Andras et al (2014) evaluated the effectiveness of, and complications associated with, intra-vascular brachytherapy (IVBT) for maintaining patency after angioplasty or stent insertion in native vessels or bypass grafts of the iliac or infrainguinal arteries. For this update, the Cochrane Peripheral Vascular Diseases Group Trials Search Co-ordinator searched their Specialised Register
Randomized controlled trials of the use of brachytherapy as an adjunct to the endovascular treatment of people with peripheral arterial disease (PAD) or stenosed bypass grafts of the iliac or infra-inguinal arteries versus the procedure without brachytherapy were selected for analysis. Two review authors independently assessed trial quality and 2 other review authors independently extracted the data. Adverse event information was collected from the trials. A total of 8 trials with a combined total of 1,090 participants were included in this review. All included studies used the femoro-popliteal artery. These investigators did not identify any studies that used the iliac arteries. All studies compared percutaneous transluminal angioplasty (PTA) with or without stenting plus IVBT versus PTA with or without stenting alone. No trials were found comparing IVBT to technologies such as drug eluting stents or balloons, or cryoplasty. Follow-up ranged from 6 months to 5 years. The quality of the included trials was moderate with concerns relating to the difficulty of blinding due to the nature of the procedures and the small sample sizes for some studies. Primary outcomes (patency or re-stenosis and need for re-intervention) were reported in the majority of the trials, but reporting at various time points and the use of multiple definitions of the outcomes by the included studies meant that not all data were available for pooling. The secondary outcomes were not reported in many of the included studies. For brachytherapy, cumulative patency was higher at 24 months (odds ratio (OR) 2.36, 95% CI: 1.36 to 4.10, n = 222, p = 0.002). A statistically significant
difference was found for re-stenosis at 6 months (OR 0.27, 95% CI: 0.11 to 0.66, n = 562, p = 0.004), 12 months (OR 0.44, 95% CI: 0.28 to 0.68, n = 375, p = 0.0002) and 24 months (OR 0.41, 95% CI: 0.21 to 0.78, n = 164, p = 0.007) in favor of IVBT. No difference was found after 5 years as measured in 1 study. The need for re-interventions was reported in 6 studies. Target lesion re-vascularization was significantly reduced in trial participants treated with IVBT compared with angioplasty alone (OR 0.51, 95% CI: 0.27 to 0.97, p = 0.04) at 6 months after the interventions. No statistically significant difference was found between the procedures on the need for re-intervention at 12 and 24 months after the procedures. A statistically significant lower number of occlusions was found in the control group at more than 3 months (OR 11.46, 95% CI: 1.44 to 90.96, n = 363, p = 0.02) but no differences were found at less than 1 month nor at 12 months after the procedures making the clinical significance uncertain. Ankle brachial index was statistically significantly better for IVBT at the 12 month follow-up (mean difference 0.08, 95% CI: 0.02 to 0.14, n = 100, p = 0.02) but no statistically significant differences were found at 24 hours and at 6 months. Quality of life, complications, limb loss, cardiovascular deaths, death from all causes, pain-free walking distance and maximum walking distance on a treadmill were similar for the 2 arms of the trials with no statistically significant difference found between the treatment groups. The authors concluded that the evidence for using peripheral artery brachytherapy as an adjunct to PTA to maintain patency and for the prevention of re-stenosis in people with peripheral vascular disease is
limited, mainly due to the inconsistency of assessment and reporting of clinically relevant outcomes. They stated that more data are needed on clinically relevant outcomes such as health related quality of life (HRQOL) or limb salvage and longer-term outcomes, together with comparisons with other techniques such as drug eluting balloons and stents; adequately powered RCTs, health economics and cost-effectiveness data are needed before the procedure could be recommended for widespread use.

Silverman et al (2014) stated that renal artery in-stent restenosis (RAISR) is not an infrequent occurrence and may be in part responsible for the failure of renal stents to improve clinical outcome. A variety of treatments have been used to restore patency, with mixed results. These include repeated percutaneous transluminal renal angioplasty (PTRA), repeated PTRA with bare-metal stents, and repeated PTRA with drug-eluting stents or covered stents. Endovascular brachytherapy has been proven effective in preventing recurrent neointimal hyperplasia in coronary bare-metal stents. This prompted this group of researchers to study the effect of EVBT on RAISR. From 2004 to 2012, a total of 21 patients (23 renal arteries) developed RAISR less than or equal to 30 months after the initial procedure and were subsequently treated with EVBT. Five patients had at least 1 prior PTRA for recurrent re-stenosis. Renal artery duplex scanning was performed as a baseline study within a few days of the EVBT and then every 6 months. All patients who had EVBT were concurrently treated by PTRA and EVBT on the basis of existing protocols. Patency of the
treated stents was evaluated by Kaplan-Meier survival curves. The average onset of the original RAISR was 11 ± 9 months (range of 2 to 30 months; median of 8 months). The initial technical success of combined PTRA and EVBT was 100%. Mean follow-up was 44 ± 18 months (range of 14 to 84 months). Of 5 patients who had PTRA before EVBT, 4 were available for long-term follow-up. These 4 patients had a combined total number of 5 PTRA before EVBT, with recurrent stenosis developing on average by 12 months. After EVBT, 3 stents were patent at 39, 48, and 65 months, and 1 stent re-stenosed at 42 months. This was the only patient in the entire series to develop re-stenosis after EVBT. The authors concluded that this retrospective experience with a relatively small number of patients undergoing concurrent EVBT/PTRA for recurrent stenosis in stents placed to treat atherosclerotic renal artery stenosis suggested that EVBT is safe and provided long-term freedom from recurrent stenosis. The findings of this small retrospective study (n = 21) need to be validated by well-designed studies.

In a retrospective case-series study, Marr et al (2015) described the results of patients with diffuse conjunctival neoplasms treated with radioactive phosphorus 32 (32P)-impregnated flexible brachytherapy film. This study was carried out between January 1, 2010, and January 1, 2013 at Memorial Sloan-Kettering Cancer Center, a tertiary referral center. It was conducted on 7 eyes of 6 patients treated for diffuse conjunctival squamous cell carcinoma, sebaceous carcinoma, or lymphoma that had recurrent or residual disease after primary
treatment. Patients underwent mapping biopsies and detailed conjunctival drawings to delineate the pathologic extent of the disease. The brachytherapy film used for treatment was the RIC Conformal Source Model 100 (RIC-100, RI Consultants). The RIC-100 is a flexible, thin (approximately 0.5 mm) film made of a polymer chemically bound to 32P. The radioactive 32P film was placed intraoperatively, allowed to stay in place until the prescription dose was reached, and then removed. The median dose at the prescription point (1 mm from the surface of the film) was 15 Gy (range of 5 to 17 Gy). Patients were tested for best-corrected visual acuity, recurrence-free survival, and adverse events scored by using the Adult Comorbidity Evaluation-27 scale. Between 2010 and 2013, 7 eyes of 6 patients were treated. The median age of patients was 70 years. All patients had a recurrent or persistent neoplasm. Four patients with squamous cell carcinoma, 1 with sebaceous carcinoma, and 1 with metachronous bilateral lymphomas were treated. The median treatment time was 19 minutes (range of 10 to 52 minutes). The median follow-up was 24.9 months (range of 3.1 to 38.2 months).

Recurrence-free survival 24 months after brachytherapy was 75 % (95 % CI: 19 to 89.1). Two moderate adverse events and 1 severe adverse event occurred. Visual acuity was stable or improved in 5 of the 7 eyes (i.e., better than 20/70 in the 5 patients who retained their treated eye). The authors concluded that the findings of this study showed the use of an intraoperative high-dose rate of 32P brachytherapy in selected cases of recalcitrant diffuse conjunctival neoplasms. They stated that
this technique offers a novel adjunct in the
treatment of these cancers; and further follow-
up and study are needed.

Collettini et al (2015) evaluated the clinical
outcome of CT-guided high-dose-rate
brachytherapy (CT-HDRBT) in patients with
unresectable hepato-cellular carcinoma (HCC).
Over a 6-year period, a total of 98 patients with
212 unresectable HCC underwent CT-HDRBT
applying a 192Ir source at the authors’
institution. Magnetic resonance imaging (MRI)
follow-up was performed 6 weeks after the
intervention and then every 3 months. The
primary end-point was local tumor control (LTC);
secondary end-points included progression-free
survival (PFS) and overall survival (OS). Patients
were available for MRI evaluation for a mean
follow-up of 23.1 months (range of 4 to 64
months; median of 20 months). Mean tumor
diameter was 5 cm (range of 1.8 to 12 cm).
Eighteen of 212 (8.5 %) tumors showed local
progression after a mean LTC of 21.1 months. In
all, 67 patients (68.4 %) experienced distant
tumor progression. The mean PFS was 15.2
months; 46 patients died during the follow-up
period. Median OS was 29.2 months. Actuarial
1-, 2-, and 3-year OS rates were 80, 62, and 46 %,
respectively. The authors concluded that CT-
HDRBT is an effective therapy to attain local
tumor control in patients with unresectable HCC.
They stated that prospective randomized
studies comparing CT-HDRBT with the standard
treatments like radiofrequency ablation (RFA)
and trans-arterial chemo-embolization (TACE)
are mandatory.
Denecke et al (2015) stated that TACE is established as bridging therapy of HCC listed for liver transplantation (LT). CT-guided brachytherapy (CTB) has not been evaluated as a bridging concept. These investigators compared CTB and TACE for bridging before LT in HCC patients. A total of 12 patients with HCC received LT after CTB (minimal tumor dose, 15 to 20 Gy). Patients were matched (CTB:TACE; 1:2) by sex, age, number and size of lesions, and underlying liver disease with patients who received TACE before transplantation. Study end-points were extent of necrosis at histopathology and recurrence rate after OLT. There were no significant differences between the CTB and TACE groups regarding Child-Pugh category (p = 0.732), AFP (0.765), time on waiting list (p = 0.659), number (p = 0.698) and size (p = 0.853) of HCC lesions, fulfilment of Milan-criteria (p = 0.638), or previous liver-specific treatments. CT-guided brachytherapy achieved higher tumor necrosis rates than TACE (p = 0.018). The 1- and 3-year recurrence rate in the CTB group was 10 and 10 % versus TACE, 14 and 30 % (p = 0.292). The authors concluded that these findings showed comparable or even better response and post-LT recurrence rates of CTB compared to TACE for treating HCC in patients prior to LT. They stated that CTB should be further evaluated as an alternative bridging modality, especially for patients not suited for TACE. They noted that CTB is a promising alternative to TACE.

In a phase I clinical trial, Mattiucci et al (2015) determined the recommended dose of endoscopically assisted high-dose-rate intraluminal brachytherapy (HDR-192Ir-ILBT) as a
palliative treatment of extra-hepatic biliary tract cancer. Patients with non-metastatic extra-hepatic biliary cancer with age less than 80 years, unsuitable for surgical resection or radiochemotherapy for co-morbidities or Eastern Cooperative Oncology Group (ECOG) greater than or equal to 2 or patients with age greater than or equal to 80 years were included. Patients underwent implantation of metal stents by endoscopic retrograde cholangiopancreatography followed by HDR-192Ir-ILBT. The initial dose of HDR-192-Ir-ILBT was 15 Gy. Three levels of dose were planned. At each dose level almost 3 patients were treated, and if no Grade 3 to 4 toxicity (considering as dose-limiting toxicity) was recorded, dose escalation was applied with 5 Gy increments until the maximum tolerated dose was established. A high dose Iridium-192 after loading system was used (Nucletron Microselectron HDR). From May 2007 to January 2010, a total of 18 patients underwent HDR-192Ir-ILBT, with 1 catheter in 12 patients and 2 catheters in 6 patients. Three levels of dose were planned: 15 Gy in 3 patients, 20 Gy in 9 patients, and 25 Gy in 6 patients with daily dose of 500 cGy per fraction. One patient at Dose Level II experienced acute toxicity (cholangitis) related to brachytherapy procedure, so the cohort was expanded. No patient of Level III had a dose-limiting toxicity and these researchers stopped at this dose level waiting to assess the late toxicity that has not yet appeared at the time of the analysis; 6 months and 1 year OS was 77 % and 59 %, respectively, with a median of 12 months. The authors concluded that the recommended dose was defined as 25 Gy in 5 fraction. It will be used in a phase II
study to better evaluate tumor and symptom control in patients with extra-hepatic biliary tract cancer.

Frakulli et al (2015) stated that non melanoma skin cancers (NMSC) of eyelid are uncommon. Many treatments approach are available with surgery being considered as the gold standard. Radiotherapy is an effective alternative in patients unfit for surgery. Brachytherapy might be a better therapeutic option due high radiation dose concentration to the tumor and rapid dose fall-off resulting in normal tissues sparing. In a systematic review, these researchers evaluated local control, toxicity, and functional cosmetic outcome of BT in NMSC of eyelid. A systematic search of the bibliographic databases PubMed, Scopus, and Cochrane Library from the earliest possible date through October 2015 was performed. Only studies published in English were included. A total of 6 articles fulfilled the selection criteria and were included in this review. Due to high risk of bias, all studies were classified to provide a low level of evidence (according to Scottish Intercollegiate Guidelines Network Classification). No RCTs or case control studies were founded. Brachytherapy was well-tolerated with acceptable toxicity and high local control rates (median of 95.2 %). Functional and cosmetic outcome were reported in 5 studies as acceptable good functional-cosmetic outcome (median of 100 %). The authors concluded that to-date, few evidences are available on the role of BT in eyelid NMSC, and they showed satisfactory results in terms of local control and functional cosmetic outcome. They stated that prospective controlled trials are needed.
**Keloids:**

Jiang and colleagues (2016) evaluated high-dose-rate brachytherapy in the treatment of therapy-resistant keloids and reported first results, with emphasis on feasibility and early treatment outcome. From 2009 to 2014, a total of 24 patients with 32 recurrent keloids were treated with immediate peri-operative high-dose-rate brachytherapy; 3 patients had been previously treated with adjuvant EBRT and presented with recurrences in the pre-treated areas. Two or more different treatment modalities had been tried in all patients and had failed to achieve remission. After (re-)excision of the keloids, a single brachytherapy tube was placed subcutaneously before closing the wound. The target volume covered the scar in total length. Brachytherapy was given in 3 fractions with a single dose of 6 Gy in 5 mm tissue depth. The 1st fraction was given within 6 hours after surgery, the other 2 fractions on the first post-operative day. Thus, a total dose of 18 Gy in 3 fractions was administered within 36 hours after the resection. The treatment was feasible in all patients. No procedure-related complications (e.g., secondary infections) occurred. A total of 19 patients had keloid-related symptoms before treatment like pain and pruritus; disappearance of symptoms was noticed in all patients after treatment. After a median follow-up of 29.4 months (range of 7.9 to 72.4), 2 keloid recurrences and 2 mildly hypertrophied scars were observed. The local control rate was 94 %. Pigmentary abnormalities were detected in 3 patients, and an additional 6 patients had a mild delay in the wound-healing process. The authors concluded that the early results of this
study proved the feasibility and the effectiveness of brachytherapy for the prevention of keloids. They stated that these findings also suggested that brachytherapy may be advantageous in the management of high-risk keloids or as salvage treatment for failure after EBRT. These preliminary findings need to be validated by well-designed studies.

Jiang and associates (2018) established a protocol of peri-operative interstitial HDR brachytherapy with 3 fractions of 6 Gy and achieved an excellent 2-year local control rate of 94% (In search of the optimal treatment of keloids: Report of a series and a review of the literature). This report was an update on the long-term results of prospective study. A total of 29 patients were included with a median follow-up of 5 years. From 2009 to 2015, 29 patients with 37 recurrent keloids were treated with peri-operative interstitial HDR brachytherapy; 3 patients had been previously treated with adjuvant EBT and presented with recurrences in the pre-treated area. Brachytherapy was given in 3 fractions with a single dose of 6 Gy in 5-mm tissue depth and covered the scar in total length. Follow-up visits were scheduled at 6 weeks, 3 months, 6 months, 1 year, and annually thereafter. Therapeutic outcome was assessed in terms of recurrence, acute and late complications, and cosmetic results. No procedure-related complications occurred. Improvement of keloid-related symptoms was noticed in all patients after treatment. After a median follow-up of 49.7 months (range of 7.9 to 91.9 months), 3 keloid recurrences and 2 hypertrophied scars were observed. The authors concluded that these findings suggested
that brachytherapy may be advantageous in the management of high-risk keloids, even after failure of EBT and other treatment procedures.

**Palmoplantar Pustulosis:**

Timemen et al (2016) noted that palmoplantar pustulosis (PPP) is a chronic pustular dermatitis of the palms and soles, which is frequently associated with significant pruritus and pain, often limiting daily activities. These researchers presented the case of a 36-year old man with severe PPP who had treatment failure with multiple medical therapies but showed marked improvement with high-dose rate brachytherapy. Brachytherapy has the advantage of providing a conformal dose distribution over complex curved surfaces, such as the foot and ankle. The authors concluded that their observations suggested that brachytherapy may be a therapeutic option for patients with severe, refractory PPP. This finding needs to be confirmed by further research.

**Retinoblastoma:**

An UpToDate review on “Overview of retinoblastoma” (Kaufman et al, 2016) states that “A variety of treatment options are available for children with retinoblastoma, including several "vision-sparing" therapies. The choice of treatment depends upon visual prognosis, tumor size and location, presence or absence of vitreous or subretinal seeds, and patient age. Standard therapeutic options include enucleation, external beam radiation therapy (RT), radioactive plaques (I-125 brachytherapy),...
cryotherapy, laser photo-ablation, and chemotherapy .... Following enucleation, adjuvant systemic chemotherapy or brachytherapy may be considered in patients with high-risk features to prevent metastatic disease (e.g., iris, ciliary body, massive choroidal, or scleral infiltration, and invasion of the optic nerve posterior to the lamina cribrosa) .... Radioactive plaque therapy (I-125 brachytherapy), which involves securing a radioactive plaque to the sclera at the base of the tumor, may be used as a primary treatment or as an adjunct to chemotherapy. The radiation dose is approximately 40 to 45 Gy delivered to the tumor apex. Children treated with brachytherapy usually have excellent visual outcomes if the tumor is not in the posterior pole, with measured vision 20/20 to 20/30 in more than one-half of cases. When used appropriately, brachytherapy as primary treatment can control approximately 90% of tumors. However, not all patients are candidates for brachytherapy, as the following factors must be taken into consideration including the tumor must be less than 15 mm in diameter and less than 8 mm thick”.

Brachytherapy is a constantly evolving field and the above recommendations are subject to modifications as new data become available.

**Pancreatic Cancer:**

Han and colleagues (2017) evaluated the survival and pain relief outcomes of the I-seeds implantation brachytherapy in advanced pancreatic cancer patients. Literature search was carried out in multiple electronic databases
(Google Scholar, Embase, Medline/PubMed, and Ovid SP) and studies reporting I seeds implantation brachytherapy in pancreatic cancer patients with unresectable tumor were selected by following pre-determined eligibility criteria. Random effects meta-analysis was performed to achieve inverse variance weighted effect size of the OS rate after the intervention. Sensitivity and subgroups analyses were also carried out. A total of 23 studies (824 patients' data) were included in the meta-analysis. I-seeds implantation brachytherapy alone was associated with 8.98 [95 % CI: 6.94 to 11.03] months (p<0.00001) OS with 1-year survival of 25.7 ± 9.3 % (mean ± standard deviation; SD) and 2-year survival was 17.9 ± 8.6 % (mean ± SD). In stage IV pancreatic cancer patients, OS was 7.13 [95 % CI: 4.75 to 9.51] months (p < 0.00001). In patients treated with I-seeds implantation along with 1 or more therapies, OS was 11.75 [95 % CI: 9.84 to 13.65] months (p < 0.00001) with 1-year survival of 47.4±22.75 % (mean±SD) and 2-year survival was 16.97 ± 3.1 % (mean ± SD). I-seeds brachytherapy was associated with relief of pain in 79.7 ± 9.9 % (mean ± SD) of the patients. The authors concluded that survival of pancreatic cancer patients after I-seeds implantation brachytherapy was found to be 9 months, whereas a combined treatment with I-seeds brachytherapy and other therapies was associated with approximately 12 months' survival. The majority of patients who underwent I-seeds brachytherapy had their pain relieved. However, they stated that larger and better coordinated studies are needed to confirm the long-term effects of this brachytherapeutic regimen.
National Comprehensive Cancer Network’s clinical practice guideline on “Pancreatic adenocarcinoma) (Version 2.2016) stated that “IORT is delivered by external beam radiation therapy (IOERT) or high-dose rate brachytherapy (HDR-IORT). IORT is generally delivered as a single fraction or in combination with adjuvant or neoadjuvant chemoradiation. The role of IORT is controversial and should only be performed at specialized centers. It is sometimes used in cases where surgical resection may result in close or involved margins”.

Furthermore, the American Brachytherapy Society’s consensus report on “Intraoperative high-dose-rate brachytherapy” (Lloyd et al, 2017) as well as the American College of Radiology and the American Brachytherapy Society’s practice parameter on “The performance of low-dose-rate brachytherapy” (Viswanathan et al, 2017) do not mention brachytherapy as a therapeutic option for pancreatic cancer.

Wang and Yachimski (2018) noted that endoscopic ultrasound (EUS) and endoscopic retrograde cholangiopancreatography (ERCP) are the mainstays of interventional endoscopic practice; EUS occupies a central role in the diagnosis of pancreatobiliary neoplasms and offers a platform for a wide range of direct tumor therapies. Initial steps have demonstrated the feasibility of such applications in animal models and pilot studies. Larger clinical trials and incorporation of EUS-based therapies into co-operative cancer studies might demonstrate an impact in the clinical prognosis of patients with pancreatic cancer. ERCP plays
an important role in elucidating indeterminate biliary strictures and in treating patients with malignant biliary obstruction who are symptomatic or have borderline resectable or unresectable disease. ERCP-directed ablative therapies enable neoadjuvant and palliative intervention in patients with malignant biliary obstruction, in particular peri-hilar cholangiocarcinoma. The authors stated that additional comparative, multi-center studies are needed to better understand the safety and efficacy of endobiliary brachytherapy, photodynamic therapy, and radiofrequency ablation in patients with pancreatobiliary malignancies.

Skin Cancer:

Frakulli and colleagues (2015) stated that non-melanoma skin cancers (NMSC) of eyelid are uncommon. Many treatments approach are available with surgery being considered as the gold standard. Radiotherapy is an effective alternative in patients unfit for surgery; BT might be a better therapeutic option due to high radiation dose concentration to the tumor and rapid dose fall-off resulting in normal tissues sparing. These researchers evaluated local control, toxicity, and functional cosmetic outcome of BT in NMSC of eyelid. They performed a systematic search of the bibliographic databases PubMed, Scopus, and Cochrane Library from the earliest possible date through October 2015. Only studies published in English were included. A total of 6 articles fulfilled the selection criteria and were included in this review. Due to high risk of bias, all studies were classified to provide a low level of evidence.
(according to Scottish Intercollegiate Guidelines Network Classification). No RCTs or case control studies were founded. Brachytherapy was well-tolerated with acceptable toxicity and high local control rates (median: 95.2 %). Functional and cosmetic outcome were reported in 5 studies as acceptable good functional-cosmetic outcome (median: 100 %). The authors concluded that few evidences were available on the role of BT in eyelid NMSC, and they showed satisfactory results in terms of local control and functional cosmetic outcome. They stated that prospective controlled trials are needed.

Delishaj and associates (2016) evaluated the local control, toxicity, and cosmetic outcomes in NMSC treated with high-dose-rate BT (HDR-BT). In May 2016, a systematic search of bibliographic database of PubMed, Web of Science, Scopus, and Cochrane Library with a combination of key words of "skin cancer", "high dose rate brachytherapy", "squamous cell carcinoma", "basal cell carcinoma", and "non-melanoma skin cancer" was performed. In this systematic review, these investigators included randomized trials, non-randomized trials, prospective and retrospective studies in patients affected by NMSC treated with HDR-BT. The searches generated a total of 85 results, and through a process of screening, 10 publications were selected for the review. Brachytherapy was well-tolerated with acceptable toxicity and high local control rates (median: 97 %). Cosmetic outcome was reported in 7 studies and consisted in an excellent and good cosmetic results in 94.8 % of cases. The authors concluded that the treatment of NMSC with HDR-BT was effective with excellent and good cosmetics results, even
in elderly patients. The hypo-fractionated course appeared effective with very good local disease control. However, they stated that more data with large-scale randomized/prospective controlled trials and longer follow-up are needed to evaluate the safety and effectiveness of HDR-BT, and to compare it directly with external beam therapy as well as the differential cure rates of subtypes of basal cell carcinoma (BCC) versus squamous cell carcinoma (SCC).

Dou and co-workers (2016) treated BCC and SCC of the skin with the Freiburg flap applicator using a high-dose rate modality of an Elekta Flexitron or MicroSelectron for radiation delivery by compensating the dose deviation resulting from the incomplete scatter environment. Patients were selected to have lesions greater than or equal to 2 cm. A mask might be needed depending on special locations. The lesions on the eyelid and face presented in this research were, however, treated without a mask. Cutting the flap into a shape conformal to the target and attaching it to the mask were used in order to make the treatment reproducible. Patients were scanned with a Philips Big Bore Brilliant CT. A 1-cm margin was added to the lesion. An Elekta Oncentra Brachy treatment planning system Version 4.3 was used for treatment planning; 40 Gy in 10 or 8 fractions was prescribed to the 1-cm depth. The Freiburg flap was aligned and verified by CT scanning prior to treatment. Three patients with BCC and SCC of the skin were treated with the Freiburg flap applicator. Lesion sizes ranged from 2 cm to 6 cm in a maximum dimension. With treatment planning, these researchers made a dose correction for compensating the dose deviation resulting from
the incomplete scatter environment of the flap applicators exposed to air. The flap was also covered by a 4-cm bolus in order to obtain more back scattered radiation during treatment; 6-month follow-up showed a very good cosmetic result. The authors concluded that the Freiburg flap brachytherapy offered a non-invasive skin cancer treatment with a high skin dose delivered to the tumor while a low-dose sparing the surrounding health tissue. They stated that this approach is a promising alternative to skin cancer surgery or EBRT.

Likhacheva et al (2017) defined current patterns of care among radiation oncologists who use skin surface BT for the treatment of cutaneous SCC (cSCC) and BCC in academic and community settings. A 30-question electronic survey was administered to clinician members of the American Brachytherapy Society. The respondents were asked to provide details regarding their clinical practice and their approach to skin surface BT. A total of 16 surveys were returned. Among the respondents, aggregate experience varied from 8 to 1,800 cases. Most preferred BT over EBRT because of shorter treatment course, conformality of treatment for irregular or curved targets, and shallow dose deposition. A total of 60 % of respondents routinely estimated lesion depth via ultrasound before initiating treatment. Treatment margin on gross disease varied widely (range of 3 to 15 mm; median of 5 mm). Hypofractionation was the preferred dose schedule. Prescribed doses ranged from 30 Gy in 5fractions to 64 Gy in 32 fractions (EQD2, 40 Gy-65 Gy). There was a tendency to increase the number of fractions for larger targets, although
some used the same fractionation regardless of anatomic location or lesion size. There was no consensus on dosimetric constraints, and some respondents reported cases of severe toxicity, particularly when treating the pretibial skin. The authors concluded that this pattern of care study suggested that skin BT can be a convenient and safe tool for treatment of BCC and cSCC. Moreover, they stated that prospective trials and the development of expert consensus guidelines would be beneficial for optimizing skin surface BT and reducing practice variation.

**Interstitial Brachytherapy as a Salvage Treatment for Recurrent Spinal Metastases:**

Yao and colleagues (2016) examined the feasibility, safety, and effectiveness of CT-guided I-125 seed interstitial brachytherapy in patients with recurrent spinal metastases after EBRT. Between August 2003 and September 2015, a total of 26 spinal metastatic lesions (24 patients) were re-irradiated by this salvage therapy modality. Treatment for all patients was pre-planned using a 3-D treatment planning system 3 to 5 days before I-125 seed interstitial brachytherapy; dosimetry verification was performed immediately after seed implantation. Median actual D90 was 99 Gy (range of 90 to 176), and spinal cord median Dmax was 39 Gy (range of 6 to 110). Median local control (LC) was 12 months (95 % CI: 7.0 to 17.0). The 6- and 12-month LC rates were 52 % and 40 %, respectively. Median OS was 11 months (95 % CI: 7.7 to 14.3); 6-month and 1-, 2-, and 3-year OS rates were 65 %, 37 %, 14 %, and 9 %, respectively. Pain-free survival ranged from 2 to 42 months (median of 6; 95 % CI: 4.6 to 7.4).
Treatment was well-tolerated, with no radiation-induced vertebral compression fractures or myelopathy reported. Re-irradiation with CT-guided I-125 seed interstitial brachytherapy appeared to be feasible, safe, and effective as pain relief or salvage treatment for patients with recurrent spinal metastases after EBRT. The main drawbacks of this study included (i) the heterogeneity of the cohort of patients with respect to specific site and volume of the metastases, as well as the primary tumor type; (ii) it was a retrospective study with a relatively small sample size patients, and (iii) the study lacked a control group and had a relatively short follow-up time period. The authors stated that a multi-center, RCT with a long follow-up time is needed to verify these preliminary findings regarding the effectiveness of I-125 seed interstitial brachytherapy for recurrent spinal metastases after EBRT failure.

Bone Metastases:

Wang and colleagues (2017) evaluated the safety and efficacy of I-125 seeds implantation in patients with bone metastases and assessed the QOL as an index for efficacy evaluation. The study enrolled 98 patients with 133 bone metastases from July 2010 to January 2016, who had undergone CT-guided brachytherapy with I-125 seeds. Brief pain inventory was administered to evaluate the degree of pain at the pre-operative (W0) and post-operative 2 weeks, 4 weeks, 8 weeks, 12 weeks, and 24 weeks (W2, W4, W8, W12, and W24). Drug use, QOL score, and complications were also assessed. Post-operative pain scores were significantly decreased and maintained for a
long-term. Numerical rating scale score at W0 was 7.3 ± 1.6, which was decreased to 4.5 ± 1.7 (p < 0.01), 3.7 ± 1.3 (p < 0.01), 2.5 ± 1.1 (p < 0.01), 1.9 ± 0.9 (p < 0.01), and 1.3 ± 0.5 (p < 0.01) at W2, W4, W8, W12, and W24, respectively. After standardized transformation, the dose of morphine for patients at W0 was 175.2 ± 24.5 mg, which was decreased to 91.2 ± 21.7 mg (p < 0.01), 89.4 ± 24.6 mg (p < 0.01), 89.4 ± 24.6 mg (p < 0.01), 72.8 ± 14.8 mg (p < 0.01), and 56.7 ± 11.3 mg (p < 0.01) at W2, W4, W8, W12, and W24, respectively. The efficiency reached 65.3 %, 85.1 %, 91.2 %, 95.2 %, and 92.7 % at post-operative W2, W4, W8, W12, and W24, respectively. QOL score at W0 was 17.4 ± 3.3, which increased to 23.2 ± 4.5 (p < 0.01), 28.6 ± 7.6 (p < 0.01), 43.2 ± 9.1 (p < 0.01), 45.6 ± 10.3 (p < 0.01), and 47.6 ± 9.8 (p < 0.01) at W2, W4, W8, W12, and W24, respectively. The authors concluded that brachytherapy with I-125 seeds was safe and effective for treating bone metastases, offering a potential alternative to EBT; QOL could be applied to evaluate the efficacy of I125 seeds implantation for treating bone metastases.

The authors stated that this study had several drawbacks, including the relatively small sample size and lack of EBRT control. Currently, multi-center-matched controlled studies of particle implantation and EBRT for treating bone metastases are underway. In addition, this study did not assess the dose control of particle implantation. They stated that further studies should be performed to examine the optimal means for reducing the high-dose region while ensuring the achievement of prescription dose.

Furthermore, UpToDate reviews on “Overview of
therapeutic approaches for adult patients with bone metastasis from solid tumors” (Yu and Hoffe, 2018), “Bone metastases in advanced prostate cancer: Management” (Sartor and DiBiase, 2018), and “Radiation therapy for the management of painful bone metastases” (Kachnic and DiBiase, 2018) do not mention brachytherapy as a therapeutic option.

Combined Endovascular Brachytherapy, Sorafenib, and Trans-Arterial Chemo-Embolization for Hepatocellular Carcinoma:

In a retrospective, single-center study, Zhang and colleagues (2017) evaluated the safety and efficacy of combined endovascular brachytherapy (EVBT), trans-arterial chemo-embolization (TACE), and sorafenib to treat hepatocellular carcinoma (HCC) patients with main portal vein tumor thrombus (MPVTT). This trial involved 68 patients with unresectable HCC or those who were unfit for liver transplantation and percutaneous frequency ablation according to the Barcelona Clinic Liver Cancer (BCLC) classification. All patients had Child-Pugh classification grade A or B, ECOG performance status of 0 to 2, and MPVTT. Patients received either EVBT with stent placement, TACE, and sorafenib (group A, n = 37), or TACE with sorafenib (group B, n = 31). The time to progression (TTP) and OS were evaluated by propensity score analysis. In the entire cohort, the 6-, 12-, and 24-month survival rates were 88.9 %, 54.3 %, and 14.1 % in group A, and 45.8 %, 0 %, and 0 % in group B, respectively (p < 0.001). The median TTP and OS were significantly longer in group A than group B (TTP: 9.0 months versus 3.4 months, p < 0.001; OS: 612.0x792.0
12.3 months versus 5.2 months, p < 0.001). In the propensity score-matched cohort, the median OS was longer in group A than in group B (10.3 months versus 6.0 months, p < 0.001). Similarly, the median TTP was longer in group A than in group B (9.0 months versus 3.4 months, p < 0.001). Multi-variate Cox analysis revealed that the EVBT combined with stent placement, TACE, and sorafenib strategy was an independent predictor of favorable OS (hazard ratio [HR] = 0.18, p < 0.001). The authors concluded that EVBT combined with stent placement, TACE, and sorafenib might be a safe and effective palliative option for MPVTT.

The authors stated that the major drawbacks of this study were the single-center retrospective design, which may affect the generalization of results, and small sample size. Further, cost-benefit analysis was not performed for the expensive procedures in this study, which may be a topic of interest to be covered in future studies.

CPT Codes / HCPCS Codes / ICD-10 Codes

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>19296</td>
<td>Placement of radiotherapy afterloading expandable catheter (single or multichannel) into the breast for interstitial radioelement application following partial mastectomy, includes imaging guidance; on date separate from partial mastectomy</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>---------</td>
<td>-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>+ 19297</td>
<td>concurrent with partial mastectomy (List separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>19298</td>
<td>Placement of radiotherapy afterloading brachytherapy catheters (multiple tube and button type) into the breast for interstitial radioelement application following (at the time of or subsequent to) partial mastectomy, includes imaging guidance</td>
</tr>
<tr>
<td>20555</td>
<td>Placement of needles or catheters into muscle and/or soft tissue for subsequent interstitial radioelement application (at the time of or subsequent to the procedure)</td>
</tr>
<tr>
<td>41019</td>
<td>Placement of needles, catheters, or other device(s) into the head and/or neck region (percutaneous, transoral, or transnasal) for subsequent interstitial radioelement application</td>
</tr>
<tr>
<td>+49327</td>
<td>Laparoscopy, surgical; with placement of interstitial device(s) for radiation therapy guidance (eg, fiducial markers, dosimeter), intra-abdominal, intrapelvic, and/or retroperitoneum, including imaging guidance, if performed, single or multiple (list separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>+49412</td>
<td>Placement of interstitial device(s) for radiation therapy guidance (eg, fiducial markers, dosimeter), open, intra-abdominal, intrapelvic, and/or retroperitoneum, including image guidance, if performed, single or multiple (list separately in addition to code for primary procedure)</td>
</tr>
<tr>
<td>55875</td>
<td>Transperineal placement of needles or catheters into prostate for interstitial radioelement application, with or without cystoscopy</td>
</tr>
<tr>
<td>55876</td>
<td>Placement of interstitial device(s) for radiation therapy guidance (eg, fiducial markers, dosimeter), prostate (via needle, any approach), single or multiple</td>
</tr>
<tr>
<td>55920</td>
<td>Placement of needles or catheters into pelvic organs and/or genitalia (except prostate) for subsequent interstitial radioelement application</td>
</tr>
<tr>
<td>57156</td>
<td>Insertion of a vaginal radiation afterloading apparatus for clinical brachytherapy</td>
</tr>
<tr>
<td>61770</td>
<td>Stereotactic localization, including burr hole(s), with insertion of catheter(s) or probe(s) for placement of radiation source</td>
</tr>
<tr>
<td>77316 - 77318</td>
<td>Brachytherapy isodose plan</td>
</tr>
<tr>
<td>77750</td>
<td>Infusion or instillation of radioelement solution (includes 3- month follow-up care)</td>
</tr>
<tr>
<td>77761 - 77763</td>
<td>Intracavitary radiation source application</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>77767-77768</td>
<td>Remote afterloading high dose rate radionuclide skin surface brachytherapy, includes basic dosimetry, when performed; up to lesion diameter over 2.0 cm and 2 or more channels, or multiple lesions</td>
</tr>
<tr>
<td>77770-77772</td>
<td>Remote afterloading high dose rate radionuclide interstitial or intracavitary brachytherapy, includes basic dosimetry, when performed; 1 - 12 channels</td>
</tr>
<tr>
<td>77778</td>
<td>Interstitial radiation source application, complex, includes supervision, handling, loading of radiation source, when performed</td>
</tr>
<tr>
<td>77789</td>
<td>Surface application of low dose rate radionuclide source</td>
</tr>
<tr>
<td>77799</td>
<td>Unlisted procedure, clinical brachytherapy</td>
</tr>
</tbody>
</table>

CPT codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0394T</td>
<td>High dose rate electronic brachytherapy, skin surface application, per fraction, includes basic dosimetry, when performed</td>
</tr>
<tr>
<td>0395T</td>
<td>High dose rate electronic brachytherapy, interstitial or intracavitary treatment, per fraction, includes basic dosimetry, when performed</td>
</tr>
</tbody>
</table>

Other CPT codes related to the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>35471</td>
<td>Transluminal balloon angioplasty, percutaneous; renal or visceral artery</td>
</tr>
<tr>
<td>37224</td>
<td>Revascularization, endovascular, open or percutaneous, femoral, popliteal artery(s), unilateral; with transluminal angioplasty</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>-------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>75966</td>
<td>Transluminal balloon angioplasty, renal or other visceral artery, radiological</td>
</tr>
<tr>
<td></td>
<td>supervision and interpretation</td>
</tr>
</tbody>
</table>

HCPCS codes covered if selection criteria are met:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A9527</td>
<td>Iodine I-125, sodium iodide solution, therapeutic, per millicurie</td>
</tr>
<tr>
<td>C1715</td>
<td>Brachytherapy needle</td>
</tr>
<tr>
<td>C1716</td>
<td>Brachytherapy source, non-stranded, gold-198, per source</td>
</tr>
<tr>
<td>C1717</td>
<td>Brachytherapysource, non-stranded, high dose rate iridium-192, per source</td>
</tr>
<tr>
<td>C1719</td>
<td>Brachytherapysource, non-stranded, non-high dose rate iridium-192, per source</td>
</tr>
<tr>
<td>C2616</td>
<td>Brachytherapy source, non-stranded, yttrium-90, per source</td>
</tr>
<tr>
<td>C2634</td>
<td>Brachytherapy source, non-stranded, high activity, iodine-125, greater than 1.01</td>
</tr>
<tr>
<td></td>
<td>mCi (NIST), per source</td>
</tr>
<tr>
<td>C2635</td>
<td>Brachytherapysource, non-stranded, high activity palladium-103, greater than 2.2</td>
</tr>
<tr>
<td></td>
<td>mCi (NIST), per source</td>
</tr>
<tr>
<td>C2636</td>
<td>Brachytherapy linear source, non-stranded, palladium-103, per 1 mm</td>
</tr>
<tr>
<td>C2637</td>
<td>Brachytherapy source, non-stranded, ytterbium-169, per source</td>
</tr>
<tr>
<td>C2638</td>
<td>Brachytherapysource, stranded, iodine-125, per source</td>
</tr>
<tr>
<td>C2639</td>
<td>Brachytherapy source, non-stranded, iodine-125, per source</td>
</tr>
<tr>
<td>C2640</td>
<td>Brachytherapy source, stranded, palladium-103, per source</td>
</tr>
<tr>
<td>C2641</td>
<td>Brachytherapy source, non-stranded, palladium-103, per source</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>C2642</td>
<td>Brachytherapy source, stranded, cesium-131, per source</td>
</tr>
<tr>
<td>C2643</td>
<td>Brachytherapy source, non-stranded, cesium-131, per source</td>
</tr>
<tr>
<td>C2645</td>
<td>Brachytherapy planar source, palladium-103, per square millimeter</td>
</tr>
<tr>
<td>C2698</td>
<td>Brachytherapy source, stranded, not otherwise specified, per source</td>
</tr>
<tr>
<td>C2699</td>
<td>Brachytherapy source, non-stranded, not otherwise specified, per source</td>
</tr>
<tr>
<td>C9725</td>
<td>Placement of endorectal intracavitary applicator for high intensity brachytherapy</td>
</tr>
<tr>
<td>C9726</td>
<td>Placement and removal (if performed) of applicator into breast for radiation therapy</td>
</tr>
<tr>
<td>C9728</td>
<td>Placement of interstitial device(s) for radiation therapy/surgery guidance (e.g., fiducial markers, dosimeter), for other than the following sites (any approach): abdomen, pelvis, prostate, retroperitoneum, thorax, single or multiple</td>
</tr>
<tr>
<td>Q3001</td>
<td>Radioelements for brachytherapy, any type, each</td>
</tr>
</tbody>
</table>

Other HCPCS codes related to the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A4648</td>
<td>Tissue marker, implantable, any type, each</td>
</tr>
<tr>
<td>A4650</td>
<td>Implantable radiation dosimeter, each</td>
</tr>
</tbody>
</table>

ICD-10 codes covered if selection criteria are met:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C00.0 -</td>
<td>Malignant neoplasm of lip</td>
</tr>
<tr>
<td>C00.9</td>
<td></td>
</tr>
<tr>
<td>C05.1</td>
<td>Malignant neoplasm of soft palate</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>------------</td>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>C06.0</td>
<td>Malignant neoplasm of cheek mucosa</td>
</tr>
<tr>
<td>C08.9</td>
<td>Malignant neoplasm of major salivary gland</td>
</tr>
<tr>
<td>C09.0 - C09.1</td>
<td>Malignant neoplasm of tonsillar fossa and tonsillar pillar</td>
</tr>
<tr>
<td>C11.0 - C11.9</td>
<td>Malignant neoplasm of nasopharynx</td>
</tr>
<tr>
<td>C15.3 - C15.9</td>
<td>Malignant neoplasm of esophagus</td>
</tr>
<tr>
<td>C19</td>
<td>Malignant neoplasm of rectosigmoid junction [pelvic recurrence]</td>
</tr>
<tr>
<td>C20 - C21.8</td>
<td>Malignant neoplasm of rectum, anus and anal canal</td>
</tr>
<tr>
<td>C33 - C34.92</td>
<td>Malignant neoplasm of trachea, bronchus, and lung</td>
</tr>
<tr>
<td>C43.0 - C44.99</td>
<td>Melanoma and other malignant neoplasms of skin</td>
</tr>
<tr>
<td>C45.0</td>
<td>Mesothelioma of pleura</td>
</tr>
<tr>
<td>C50.011 - C50.929</td>
<td>Malignant neoplasm of breast</td>
</tr>
<tr>
<td>C51.0 - C55</td>
<td>Malignant neoplasm of vulva, vagina and uterus</td>
</tr>
<tr>
<td>C60.0 - C60.9</td>
<td>Malignant neoplasm of penis</td>
</tr>
<tr>
<td>C61</td>
<td>Malignant neoplasm of prostate</td>
</tr>
<tr>
<td>C68.0</td>
<td>Malignant neoplasm of urethra</td>
</tr>
<tr>
<td>C69.20 - C69.22</td>
<td>Malignant neoplasm of retina</td>
</tr>
<tr>
<td>C69.30 - C69.33</td>
<td>Malignant neoplasm of choroid [melanoma]</td>
</tr>
<tr>
<td>C78.0 - C78.2</td>
<td>Secondary malignant neoplasm of lung</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------</td>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>D02.20 - D02.22</td>
<td>Carcinoma in situ of bronchus and lung</td>
</tr>
<tr>
<td>D14.30 - D14.32</td>
<td>Benign neoplasm of bronchus and lung</td>
</tr>
<tr>
<td>D38.1</td>
<td>Neoplasm of uncertain behavior of trachea, bronchus and lung</td>
</tr>
<tr>
<td>T86.818</td>
<td>Other complications of lung transplant [stenotic obstruction post lung transplantation]</td>
</tr>
</tbody>
</table>

ICD-10 codes not covered for indications listed in the CPB:

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C25.0 - C25.9</td>
<td>Malignant neoplasm of pancreas</td>
</tr>
<tr>
<td>C67.0 - C67.9</td>
<td>Malignant neoplasm of bladder</td>
</tr>
<tr>
<td>C71.0 - C71.9</td>
<td>Malignant neoplasm of brain</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>--------</td>
<td>-------------------------------------------------------</td>
</tr>
<tr>
<td>D09.0</td>
<td>Carcinoma in situ of bladder</td>
</tr>
<tr>
<td>D30.3</td>
<td>Benign neoplasm of bladder</td>
</tr>
<tr>
<td>D33.0 - D33.2</td>
<td>Benign neoplasm of brain</td>
</tr>
<tr>
<td>D41.4</td>
<td>Neoplasm of uncertain behavior of bladder</td>
</tr>
<tr>
<td>D43.0 - D43.2, D43.4</td>
<td>Neoplasm of uncertain behavior of brain and spinal cord</td>
</tr>
<tr>
<td>D49.4</td>
<td>Neoplasm of unspecified behavior of bladder</td>
</tr>
<tr>
<td>D49.6</td>
<td>Neoplasm of unspecified behavior of brain</td>
</tr>
<tr>
<td>H35.30</td>
<td>Unspecified macular degeneration (age-related)</td>
</tr>
<tr>
<td>H35.3110 - H35.3194</td>
<td>Nonexudative age-related macular degeneration</td>
</tr>
<tr>
<td>H35.3210 - H35.3293</td>
<td>Exudative age-related macular degeneration</td>
</tr>
<tr>
<td>L40.3</td>
<td>Pustulosis palmaris et plantaris</td>
</tr>
<tr>
<td>L91.0</td>
<td>Hypertrophic scar [keloid]</td>
</tr>
</tbody>
</table>

The above policy is based on the following references:


31. Canadian Coordinating Office for Health Technology Assessment (CCOHTA).


35. BlueCross BlueShield Association (BCBSA), Technology Evaluation Center (TEC). Brachytherapy for the prevention of restenosis in peripheral arteries following PTA of the femoropopliteal system. TEC Assessment Program. Chicago IL: BCBSA; 2002;17(22).


Francisco, CA: CTAF; June 21, 2006. Available at:


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intersociety, multicenter brachytherapy trial. 

Comparison of tumor and normal tissue 
dose for accelerated partial breast 
irradiation using an electronic 
brachytherapy eBx source and an Iridium- 
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Accelerated Partial Breast Irradiation (APBI): 
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electronic brachytherapy for the treatment 
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American Society for Therapeutic Radiology 
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Committee report on electronic 

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AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number:
0371 Brachytherapy

There are no amendments for Medicaid.

www.aetnabetterhealth.com/pennsylvania  revised 04/12/2018