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MEDICAL PHYSICS

Recommendations for intraoperative mesh brachytherapy: Report of AAPM Task Group No. 222

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Disclosure Statement
The Chair of the Task Group 222 of Recommendations for intraoperative mesh brachytherapy has reviewed the required Conflict of Interest statement on file for each member of Task Group 222 of Recommendations for intraoperative mesh brachytherapy and determined that disclosure of potential Conflicts of Interest is an adequate
management plan. Disclosures of potential Conflicts of Interest for each member of Task Group 222 of Recommendations for intraoperative mesh brachytherapy are found at the close of this document.

Abstract

Mesh brachytherapy is a special type of a permanent brachytherapy implant: it uses low-energy radioactive seeds in an absorbable mesh that is sutured onto the tumor bed immediately after a surgical resection. This treatment offers low additional risk to the patient as the implant procedure is carried out as part of the tumor resection surgery. Mesh brachytherapy utilizes identification of the tumor bed through direct visual evaluation during surgery or medical imaging following surgery through radiographic imaging of radio-opaque markers within the sources located on the tumor bed. Thus, mesh brachytherapy is customizable for individual patients. Mesh brachytherapy is an intraoperative procedure involving mesh implantation and potentially real-time treatment planning while the patient is under general anesthesia. The procedure is multidisciplinary and requires the complex coordination of multiple medical specialties. The preimplant dosimetry calculation can be performed days beforehand or expediently in the operating room with the use of lookup tables. In this report, the guidelines of American Association of Physicists in Medicine (AAPM) are presented on the physics aspects of mesh brachytherapy. It describes the selection of radioactive sources, design and preparation of the mesh, preimplant treatment planning using a Task Group (TG) 43-based lookup table, and postimplant dosimetric evaluation using the TG-43 formalism or advanced algorithms. It introduces quality metrics for the mesh implant and presents an example of a risk analysis based on the AAPM TG-100 report. Recommendations include that the preimplant treatment plan be based upon the TG-43 dose calculation formalism with the point source approximation, and the postimplant dosimetric evaluation be performed by using either the TG-43 approach, or preferably the newer model-based algorithms (viz., TG-186 report) if available to account for effects of material heterogeneities. To

comply with the written directive and regulations governing the medical use of radionuclides, this report recommends that the prescription and written directive be based upon the implanted source strength, not target-volume dose coverage. The dose delivered by mesh implants can vary and depends upon multiple factors, such as postsurgery recovery and distortions in the implant shape over time. For the sake of consistency necessary for outcome analysis, prescriptions based on the lookup table (with selection of the intended dose, depth, and treatment area) are recommended, but the use of more advanced techniques that can account for real situations, such as material heterogeneities, implant geometric perturbations, and changes in source orientations, is encouraged in the dosimetric evaluation. The clinical workflow, logistics, and precautions are also presented.

KEYWORDS
brachytherapy, dosimetry, mesh, surgery

1 | INTRODUCTION

In many surgical situations such as breast lumpectomy, head-and-neck (H&N) tumor removal, and lung sublobar resection, adjuvant therapy in the form of radiation therapy (RT) is considered after surgical resection of a malignant tumor to treat residual gross or microscopic disease that may still be present in the surgical bed or close to the surgical margins. Interstitial implantation of radioactive seeds with a short half-life in the form of a low-energy, low-dose-rate (LDR) permanent brachytherapy implant is often an attractive option because of its quick deployment and low radiation exposure to clinicians. Implantation is performed during the same procedure as the surgical resection when the additional risk (such as foreign object reaction) to the patient is minimal and the brachytherapy is anticipated to be beneficial. Mesh brachytherapy is a special type of a permanent implant that contains radioactive seeds in an absorbable mesh sutured to the tumor bed after surgical resection of the gross tumor. The mesh can be prepared manually using absorbable sutures containing radioactive seeds or as a preloaded mesh in a sterile package obtained from a commercial vendor. Implant procedures can be performed in a minimally invasive manner by using advanced endoscopic techniques, or they can be performed during an open surgical procedure. Because of radio-opaque markers within the sources, radiographic imaging of mesh brachytherapy provides indirect visualization of the tumor bed and positioning relative to the patient's anatomy. Thus, it is especially suited for tailoring subsequent compensation or boost therapy to individual patients. Mesh brachytherapy is carried out in an operative setting requiring complex coordination of a highly skilled team of surgeons, radiation oncologists, medical physicists, and additional required health personnel that entails considerable preplanning and often requires intraoperative dosimetric modifications of the preplan in the operating room (OR). These complex cases are challenging to perform with the time limitations of a patient being under general anesthesia. This report presents guidelines of the American Association of Physicists in Medicine (AAPM) regarding the physics aspects of mesh brachytherapy.

The AAPM has approved the following charges for Task Group (TG) 222:

1. review the steps in mesh brachytherapy procedures,
2. describe the treatment planning and dosimetric aspects of the procedures,
3. recommend dosimetric parameters useful for specifying and evaluating the treatments,
4. provide recommendations for quality management unique to the procedures, and
5. recommend a definition for medical events involving these procedures.

Consequently, this report is organized into sections dedicated to covering these charges. Section 2 provides an educational background on the mesh brachytherapy procedure and dose evaluation. Section 3 describes the commissioning tasks, treatment planning, radiation safety precautions, and dosimetric parameters associated with the procedure. Section 4 addresses quality standards and provides an example workflow and fault tree analysis (FTA) for the procedure. Section 5 discusses the influence of radionuclide half-life on postimplantation exposure rates. Toward clarifying the scope, this report focuses on LDR radionuclide-based brachytherapy sources and does not consider intraoperative procedures using high-dose-rate (HDR) brachytherapy sources. Section 6 summarizes the report recommendations.

At the time of TG-222 formation, the Nuclear Regulatory Commission (NRC) definition of a medical event was dose based and the TG intended (charge 5) to present recommendations as the NRC definition was not appropriate for medical events involving mesh

brachytherapy. However, during the course of the TG-222 report development, the NRC revised the medical event definition to be based upon source strength and not dose, and obviated the need for TG-222 to develop recommendations specific to mesh brachytherapy.

The current report has been reviewed and approved by the AAPM and presents the recommended clinical practice standards for the medical physics community. This report clarifies AAPM expectations of medical physicists or their designees for how the planning and execution of the brachytherapy mesh procedure should be performed. Vendors and manufacturers of associated commercial equipment, instruments, and materials should consider this report toward improving partnership with the medical physics community. Although specific equipment, products, instruments, and materials are used as examples in this report to describe the specific circumstances, such identification does not imply recommendation or endorsement by the AAPM, nor imply that the identified device is necessarily the best available.

Terminology used in this report emulates that used in other AAPM TG reports where *shall* or *must* are used when the task is required by a regulatory agency, whereas the term *should* is used when it is expected that institutional customization for adoption of a procedure associated with mesh brachytherapy will guide the manner in which a particular task is performed. The term *recommend* is used when it is expected that the procedure will be followed as described. There may be instances where other issues, techniques, resources, or priorities could result in it being in the best interests of safety and efficacy to deviate from these specific recommendations.

2 | BACKGROUND

2.1 | Intraoperative mesh brachytherapy

Brachytherapy using absorbable sutures and meshes containing radioactive seeds has been in practice for several decades.[1] Surgical resection plays an important role in reducing tumor burden for some locally advanced and recurrent malignancies such as nonsmall cell lung cancer (NSCLC), sarcoma, and H&N cancers. The clinical data also indicate that the postoperative residual disease may require adjuvant therapies. Among all treatment modalities, brachytherapy is a conformal and cost-effective adjunctive therapy option. However, traditional brachytherapy seed implants can be difficult when large irregular volumes are to be treated following surgery. Irregular target shapes deter use of a catheter-based implant, which may cause significant inhomogeneous dose regions or undertreatment zones because catheters or needles are relatively rigid. To overcome this problem, mesh brachytherapy has been developed. Mesh brachytherapy involves the weaving of evenly spaced radioactive seeds in premade strands within a mesh device to provide a conformal radiation treatment to the target (i.e., surgical bed) as defined *in situ* by the surgeon and authorized user (AU).[1] Conformity is obtained due to the implant geometry and the low-energy radiation.

Although the current report examines lung mesh brachytherapy in detail, other anatomic sites are also included for comprehensive application of this modality. The basic techniques and preparatory steps are relevant for all anatomic sites, and certain aspects for each specific anatomic site require special attention. Site-specific implementation details were not included due to their adaptability from the lung example and to keep the length of the report manageable. Treatment of other anatomic sites such as the pelvis, H&N, spine, breast, brain, and various thoracic locations has substantially increased in recent years.[2–13]

Special considerations for lung mesh brachytherapy in comparison to other anatomic sites are the dramatically different geometries of the deflated lung when implanted compared to the inflated lung, the comparably lower density of lung tissue where model-based dose calculation algorithms (MBDCAs)[14] are needed to account for heterogeneity corrections, and lower attenuation by the lung tissue compared with solid tissue that potentially increases exposure rates to staff and family members.

2.2 | Mesh brachytherapy of lung cancer

Lung interstitial brachytherapy began in 1941 and used ^{222}Rn seeds.[15] Hilaris and Martini reported a 20-year follow-up on patient survival using this technique, which evolved from using ^{222}Rn and ^{192}Ir to ^{198}Au and ^{125}I seeds.[16] Radioactive sources in absorbable sutures as carriers were introduced in 1974 by Palos et al[17] and Martinez et al[18] at the Stanford University Hospital as a novel method for precise placement of sources in tumor bed. This technique was refined over the years and expanded to other cancer types.[19] Several vendors provide various kinds of stranded seeds containing ^{125}I, ^{103}Pd, or ^{131}Cs for weaving into meshes. LDR lung-mesh brachytherapy provides an option for patients with compromised physiological function reserve. This relatively simple procedure can be performed during a sublobar resection (wedge resection or segmentectomy) without adding much time to the overall operation.[20] It offers the possibility of improved local control.[20,21]

The efficacy of intraoperative mesh brachytherapy in NSCLC was evaluated in two trials. The first randomized trial by the American College of Surgeons Oncology Group (ACOSOG), Z4032 (a randomized phase III

study of sublobar resection vs. sublobar resection plus brachytherapy in high-risk patients with NSCLC, 3 cm or smaller in tumor size), was activated in January 2006 and completed accrual in January 2010.[22,23] Though the retrospective institutional trials demonstrated the benefit of intraoperative brachytherapy,[24] this prospective phase III study was not powered to detect small differences in local recurrence rates at 5-year follow-up. The recurrence rates of observed results were 14% without brachytherapy versus 17% with brachytherapy.[22] Also, no observed significant differences in overall survival were found at 5-year follow-up (61% without brachytherapy vs. 56% with brachytherapy).[22] The main limitation of this trial was that it was underpowered to determine statistical significance of the differences observed. The advancement of thoracic surgery technique, particularly using video-assisted thoracic surgery, was highlighted for improved local control for sublobar resection without brachytherapy compared to the prior studies in the 1990s. Negative margins were often achieved with this advanced thoracic surgical technique. Therefore, that study did not recommend routine intraoperative brachytherapy for sublobar resection. The second clinical trial by ACOSOG, (Z4099/RTOG 1021) a randomized phase III study of sublobar resection ± brachytherapy) versus stereotactic body RT in high-risk patients with Stage I NSCLC, was activated in 2011 and terminated early in 2013 due to low accrual (only 11 patients followed out of 400 initially sought).[24] Clinical outcome data have not been reported.

A detailed review of clinical outcomes of lung mesh brachytherapy is presented in a report by the American Brachytherapy Society (ABS).[20] Consensus guidelines for thoracic brachytherapy of lung cancer are provided on imaging technique, pretreatment evaluation, postoperative treatment planning, patient suitability, disease stage, brachytherapy prescription dose and fractionation, and mesh brachytherapy in combination with external-beam RT (EBRT).[20] However, the report was silent on the influence of tissue and brachytherapy device material heterogeneities on prescriptive goals and clinical guidance. The current report (Section 2.4) examines potential of MBDCAs to account for radiological effects that are beyond the TG-43-based approach. These issues and other details for clinical implementation are discussed in the AAPM TG-186 report.[25]

2.3 | Mesh brachytherapy of other clinical sites

Mesh brachytherapy can be applied at several different anatomic sites. Locally advanced and recurrent malignancies at various anatomic sites often require adjuvant RT to achieve tumor control; mesh brachytherapy can be an option in these situations. Below are examples of considerations that should be taken for other clinical sites including brain, H&N, and soft tissue.

2.3.1 | Brain cancers

Mesh brachytherapy is used as adjuvant therapy after brain metastases resection. The safety, feasibility, and efficacy were evaluated in a Phase I/II study.[26] Implants were planned based on preoperative data of tumor size and an in-house nomogram; planned dose was 80 Gy to a 0.5-cm depth from the resection cavity surface. All patients underwent neurosurgical lesion resection. At the time of resection, ^{131}Cs stranded seeds (Isoray Medical, Inc., Richland, WA, USA) were implanted and adjusted in real time to the intracavitary volume of the resected metastasis. The ^{131}Cs stranded seeds (1.0-cm interseed spacing) were delivered in strings of 10 seeds per strand, subsequently cut into smaller lengths to fit the nomogram, and placed as a permanent volume implant along the cavity in a tangential pattern to maintain 0.7-cm to 1.0-cm spacing between seeds. As a result, the cavity interior was lined in a pattern resembling barrel staves. The strands were then covered with an absorbable material to prevent seed migration and dosimetric variation. Some hemostatic materials were used to line the cavity to limit geometric shrinkage and further prevent seed migration. Within 2 days of the implant, the patient received a computed tomography (CT) scan to determine the source positions and the implanted dose distribution. Comparing the surgery plus ^{131}Cs with stereotactic radiosurgery, surgery + whole brain RT (WBRT), and WBRT alone, the surgery plus ^{131}Cs was similarly effective as other treatment modalities; however, surgery + ^{131}Cs was more cost-effective.[27] After failure of prior irradiation of brain metastases, reirradiation with intraoperative ^{131}Cs brachytherapy implants provided durable local control and limited risk of radionecrosis.[28]

Intraoperative brachytherapy is an option for patients with a good performance status and recurrent brain tumors, who received prior full dose RT. In a single-institution prospective study, all patients underwent re-resection just prior to implant. Due to their prior RT, all were prescribed 60 Gy at 0.5 cm.[29] Seeds were encased in a biocompatible carrier material, which was gelatin-based or collagen-based. The implantation added 12–20 minutes to the total procedure time. Postimplant CT and magnetic resonance imaging (MRI) were acquired on all patients, and postimplant dosimetry was performed. No seed migration was observed, and the postimplant treatment plans had excellent concordance with the preimplant treatment plans. No postoperative complications or operative bed recurrences were observed.[29]

2.3.2 | Head & neck cancers

Mesh brachytherapy has been increasingly used in treating H&N cancers. H&N cancers are typically squamous cell carcinoma, which clinically present as a rapidly growing tumor. In general, there are many neighboring organs-at-risk (OARs) located in the vicinity of H&N cancers. The target lesion of H&N cancers can include one or multiples of the following lesions: lip, tongue, floor of mouth, base of the tongue, oral cavity (mucosa), tonsillar region, soft palate, oropharynx, nasopharynx, and superficial lesion. The OARs include salivary glands, mandible and masticatory muscle, spinal cord, and major blood vessels. The sequelae to RT are xerostomy, osteoradionecrosis, fibrosis, trismus, and prior radiation. In the past, brachytherapy was used for local control, whereas EBRT was used for regional control. In the early 20th century, brachytherapy with ^{226}Rn in a flat applicator was used for treatment of lip cancer.[30] Before HDR treatments were available, interstitial brachytherapy implants were often used in the form of LDR brachytherapy with several different sources as historically available: ^{226}Ra, ^{60}Co, ^{198}Au, and ^{192}Ir.[31] Before intensity-modulated RT (IMRT) techniques were available, dose distributions from two-dimensional (2D) and three-dimensional (3D) planning in EBRT were not highly conformal. Therefore, LDR brachytherapy techniques were considered a standard-of-care for monotherapy or as a combined treatment with surgery for achieving local control. With the advent of IMRT techniques, including tomotherapy and most recently volumetric modulated arc therapy (VMAT), the ease of delivering complex dose distributions has reduced the need for brachytherapy. Although high control for locoregional tumors was traditionally a primary goal for management of H&N cancers, treatment with IMRT also strived for organ function preservation. Conventional LDR interstitial techniques (planar implants) followed the Paris system and the ICRU 58 reporting standards.[32] Later, pulsed dose rate (PDR) and HDR ^{192}Ir techniques equivalent to the LDR technique were added; this new updated approach focused on dose-fractionation schemes and treatment-selection criteria between brachytherapy alone versus adjuvant approaches using PDR or HDR techniques.[3] In addition, the guidelines on general quality assurance and physics aspects were added to improve the accuracy in interstitial implant, treatment planning, and delivery in the 3D image-based treatment planning and afterloading delivery.[3]

The clinical benefits of mesh brachytherapy have been shown by Pham et al,[4] who reported feasibility and efficacy of reirradiation using a ^{131}Cs mesh technique following surgical salvage for recurrent H&N cancer. The median overall and disease-free survivals were 15 and 12 months, respectively; comparable to other brachytherapy modalities for recurrent H&N cancer using HDR ^{192}Ir temporary implants and LDR ^{125}I permanent implants.[5–7] Pham et al[4] also reported that OR staff radiation exposure rates from ^{131}Cs were four times higher from H&N patients than from lung patients for the small cohort (4 vs. 24 patients),[8] likely because tissue attenuation was less and surgery time was longer. ^{131}Cs dose rapidly falls off due to its lower average energy (0.03 MeV) photons compared to ^{192}Ir (0.4 MeV) and thereby provides improved normal tissue sparing.

2.3.3 | Soft tissue sarcomas

Mesh brachytherapy has also been used to treat soft tissue sarcomas (STSs). STSs are rare tumors that present treatment challenges to achieve local control while preserving function and quality of life. High local recurrence rates occur after macroscopically complete resection, so the use of additional treatment modalities is necessary to improve the outcomes.[9] For patients with extremity STS, postoperative external beam irradiation significantly ($p = 0.0001$) reduced the 10-year death rates due to local recurrence from 24% (17/71) to 1.4% (1/70).[9] These rates were comparable to amputation and significantly better than wide excision alone.[9] Adjuvant RT in the form of ^{192}Ir brachytherapy delivered via temporary catheters implanted intraoperatively after resection improved local control rates in extremity STS compared to surgery alone.[10] Wide margins during resection of extremity STS and placement of brachytherapy catheters are relatively common for reducing the recurrence rate.

Deep cavity STSs involving the chest, abdomen, pelvis, retroperitoneum, and trunk typically present with a relatively large size, rendering treatment challenging. Furthermore, although wide margins are common during resection of extremity STS, achievement of the same wide margins of resection for deep cavity STS is limited by the potential morbidity of multivisceral resection. It is reported that the efficacy of EBRT and HDR brachytherapy is limited by the irregular contour of deep cavity tumor beds as well as the close proximity of vital structures.[33] Furthermore, attempts to deliver brachytherapy via catheters in deep cavities have resulted in serious toxicities, discouraging this practice.[11,12]

Mesh brachytherapy in the form of permanent ^{125}I sources embedded in an absorbable mesh provides an alternative RT delivery approach for irregularly shaped deep tumor beds. Fairweather et al[13] reported a study involving 46 patients. Those patients were treated for primary ($n = 8$, 17%) or recurrent ($n = 38$, 83%) deep cavity STS (median follow up 35 months); 74% received EBRT for STS or a prior presentation. In-field recurrences were observed in nine patients (19.5%). The cumulative incidences of in-field, regional, and distant

recurrences at 5 years were 26.3%, 54.2%, and 54.1%, respectively. The 5-year overall-survival rate was 47.2%, and median survival was 44 months. Twenty-two patients (48%) experienced complications: 11 patients (24%) developed Grade 3 or 4 complications requiring percutaneous intervention ($n = 6$) or reoperation ($n = 5$) at a median of 35.5 days. There were no postoperative deaths. They concluded that the local, in-field recurrence rates were relatively low in this high-risk population; ^{125}I mesh brachytherapy appeared effective, and it should be used with caution since 24% developed complications requiring intervention.[13]

2.4 | Dose calculation methods

Standard patient dose calculation practices for mesh brachytherapy involve approximations. With the volume at risk for recurrence being determined intraoperatively, treatment planning may consist of a source-strength lookup table to determine the seed spacing and source strength for a grid-pattern mesh implant. Traditionally, these lookup tables assumed a planar implant with regularly spaced seeds, are typically prescribed to a central dose point located 0.5 cm from the implant plane, and use the one-dimensional (1D; point source) approximation of the TG-43 formalism,[34] which is an acceptable standard for dose calculations of LDR seeds.[34–38] However, the 2D line-source approximation should be used for cases where stranded sources are aligned in a known orientation. Postimplant dosimetric evaluation is also typically performed using the TG-43 formalism for source locations determined from postimplant CT images. In comparison with the real treatment conditions, the TG-43 formalism assumes an infinite homogeneous water environment with no interseed attenuation, and ignores heterogeneous anatomy, for example, lung anatomy or bony structures, potentially producing inaccurate dosimetric results.[39] Patient-treatment geometries involve tissues that differ in atomic composition and mass density from water. At the low energies of photons emitted from LDR seeds, radiological parameters (mass energy absorption and attenuation coefficients) differ significantly between the treated tissues and water. On this basis, material heterogeneities are expected to affect dosimetry for mesh brachytherapy.[25,40,41] The AAPM recommends evaluating treatment quality with postimplant planning using the TG-43 model and the best available MBDCAs that correct for tissue heterogeneities,[34,37,38] as described in the AAPM TG-186 report.[25] Plans for both algorithms should be saved for immediate and later evaluation.

MBDCAs can account for radiation transport and energy deposition in segmented nonwater media more accurately than the TG-43 formalism, and have the potential to calculate more accurate dose distributions for brachytherapy.[25] MBDCAs used for mesh brachytherapy dose calculation and treatment planning systems (TPSs) include semianalytic path-length correction, Monte Carlo (MC), collapsed cone, discrete ordinates, and others.[25] A working group of the AAPM, ESTRO, and the Australasian Brachytherapy Group is expanding upon the TG-186 Report[42] to provide new guidance for clinical adoption of MBDCAs.

Several published studies in recent years describe application of MBDCAs toward improving dose calculations for mesh brachytherapy implants.[39,43–46] Yang and Rivard[39] performed simulations using the MCNP radiation transport code[47] for an idealized anatomic model of the chest volume to investigate the dosimetric effects of tissue heterogeneities for permanent mesh implants of the lung. They concluded that the AAPM TG-43 formalism overestimates planning target volume (PTV) doses by a few percent in a homogeneous water medium, but significantly underestimates doses to bone and healthy tissues.

In addition to material assignments, CT artifacts can affect mesh brachytherapy dose calculation accuracy. Sutherland et al[43,44] used a segmented and voxelized patient model from CTs for six patients implanted with ^{125}I lung meshes, performing MC simulations using the EGSnrc user-code BrachyDose.[48] As the CT data contained streak artifacts due to the presence of radio-opaque markers within the sources, metallic artifact reduction (MAR) techniques were developed and explored. With up to 40% differences in D_{90} observed between uncorrected and MAR-corrected phantoms, they concluded that MAR correction is necessary for accurate application of MBDCAs for lung mesh brachytherapy.[44,45] Calculations based on the TG-43 formalism[34,37] underestimated PTV dose by up to 36% for D_{90} for some of six patients with larger volumes containing higher proportions of healthy lung tissue.[43]

Sutherland et al later used the virtual patient models to consider doses to treatment volumes and OARs (ipsilateral lung, aorta, and heart) for ^{103}Pd, ^{125}I, and ^{131}Cs seeds as well as point sources using BrachyDose and a patient CT-derived computational phantom.[46] For treatment volumes and OARs, up to 40% variation with source energy and dose differences between MC and the TG-43 formalism were found. They concluded that MBDCAs should be used for selecting prescription doses, comparing clinical endpoints, and studying radiobiological effects for lung mesh brachytherapy.[46]

The TG-43 algorithm may over- or underestimate the dose based on the exact anatomy; thus, no simple correction scheme exists and users are recommended to use MBDCAs because they can better approximate the real situation. When using MBDCAs, lookup tables made using TG-43 methods can serve for preimplant planning purposes. It is expected that a better estimation of administered dose will come from the MBDCA results.

3 | IMPLEMENTATING A MESH BRACHYTHERAPY PROGRAM

Establishing an intraoperative mesh brachytherapy program in the clinic is similar to establishing other new intraoperative brachytherapy programs such as for prostate, brain, and breast permanent interstitial implants, with a few considerations specific to the unique characteristics of mesh implant sites such as lung, H&N, pelvis, and breast. Many aspects are common to treatment of any anatomic site, and include licensing, source ordering, preimplant and postimplant treatment planning, surgical placement, and radiation safety. However, nuances for treatment of a particular anatomic site must be considered. Treatment regimens are customized, even for a specific patient by customization of the mesh size and positioning, and by consideration as a boost if EBRT is also employed. Mesh geometries are also highly variable across anatomic sites: some organs, like the lung, will drastically change dimensions after implantation and other sites, such as pelvic sidewall or gynecological implants, will remain fairly fixed. Further, some anatomic sites such as the pelvis will be less sensitive to the dosimetric assumption of water equivalence.

Before implementation of the program, the institution's brachytherapy team should conduct discussions that include the following topics:

1. selection of radionuclide (^{125}I, ^{103}Pd, or ^{131}Cs), including its preparation and calibration;
2. choice of the mesh type: standard template versus custom-made in the OR, including mesh preparation and surgical implantation procedures;
3. pros and cons of low-tech versus high-tech methods, such as lookup tables versus image-based evaluation of target for treatment-planning estimations, and ability to cover the target (and potential coverage beyond tumor bed) if the tumor bed is measured accurately, yet surgical placement is somewhat offset;
4. choice of imaging modalities (CT, kV imaging, ultrasound, etc.) for the procedure;

definition of the tumor bed, target volume and what characterizes a good implant, for example, that 95% of prescription dose covers 90% of the PTV;

1. dosimetry considerations, including the prescription volume, area, or point(s), TPS commissioning, preimplant treatment planning and posttreatment dose assessment, and algorithm(s) to be used;
2. day-of-implant considerations, including source strength, physical configuration, radiation safety, and patient release criteria;
3. implant geometry, including mesh size, use of standard or custom mesh, appropriate coverage;

TABLE 1 Energies and half-lives for radionuclides used in permanent mesh brachytherapy implant.[37,38]

Radionuclide	Mean energy (keV)	Half-life (day)
^{125}I	28.37	59.41
^{103}Pd	20.74	16.99
^{131}Cs	30.38	9.69

4. method of performing and how to execute the postimplant dosimetric evaluation.

These items are discussed in greater detail in the following sections.

3.1 | Radionuclide Selection

Although ^{125}I sources were utilized for the early mesh implants, both ^{103}Pd and ^{131}Cs seeds have been incorporated in recent years.[4,20,36,49,50] The primary characteristics of each of these radionuclides can provide options for a mesh implant (Table 1).

All three radionuclides have proven effective in the treatment of prostate cancer and are capable of sparing adjacent organs and vessels when implanted with appropriate source strengths and spatial distributions. However, the radiosensitivity of adjacent tissues and the presence of voids and less attenuating structures are considerations when selecting the radionuclide. Due to its lower energy, ^{103}Pd irradiates less normal tissue. Yet, the resultant dose distribution will be more sensitive to the implant geometry. Additionally, lower energy does not always translate to lower radiation exposure rates to personnel. This may be of particular significance in the protracted hospital stay of patients most likely to be candidates for mesh brachytherapy. The radiobiological relationship of tumor response and tissue recovery will also be dependent on the radionuclide selection, largely driven by the half-life for permanent implantation.

3.2 | Stranded versus mesh configurations

Using lung mesh brachytherapy as an example, in the early practice of mesh brachytherapy, the source array was fabricated in the OR by the AU or physicist suturing the stranded seeds into the mesh material for a predetermined number of strands and seed spacing. Once the procedure became accepted on the basis of a comfortable workflow, source vendors started to produce meshes with stranded seeds already sutured to the mesh at the proper strand- and seed-spacing

TABLE 2 Available brachytherapy source models for permanent mesh implant that meet the AAPM dosimetric prerequisites for brachytherapy sources (last updated on 1 January 2019)

Manufacturer, model	Strandable	Available in both strand and mesh
I-125		
Best, 2301	yes	no
IsoAid, IAI-125A	yes	no
Theragenics, AgX100	yes	yes
Pd-103		
Best, 2335	yes	no
CivaTech, CS10	yes	yes
IsoAid, IAPd-103A	yes	no
Theragenics, 200	yes	yes
Cs-131		
Isoray, CS-1 Rev2	yes	yes

Best: Best Medical International Inc., Springfield, VA; IsoAid: IsoAid, LLC, Port Richey, FL; Theragenics: Theragenics, Corp., Buford, GA; CivaTech: CivaTech Oncology, Inc., Durham, NC; Isoray: Isoray Medical, Inc., Richland, WA.

as developed by Allegheny Hospital.[35] Brachytherapy sources that have met the AAPM dosimetric prerequisites[51,52] are available from several manufacturers in mesh brachytherapy configurations (Table 2). When seeds fabricated in a mesh substrate are not available, stranded seeds may be woven into a mesh carrier in the OR. Either method requires delivering the mesh assembly for implant in a sterile form. In addition, mesh implants have been performed just using seeds in strands that are fixed individually to the surgical site without a mesh carrier. Because the source layout with two or more strands not in mesh is similar to the mesh-style implant, a similar procedure should be followed. Advantages of a manufacturer-assembled mesh over one prepared in the OR by the radiation oncologist or other hospital staff include lower radiation exposure, less preparation time in the OR, higher design accuracy of the finished product, and independent QA documentation. An advantage of manually preparing a mesh (or suturing stranded seeds) in the OR is the just-in-time customization of the mesh based on the postresection geometry. For premanufactured and custom-made meshes, to reduce personnel radiation exposure, a sterilized dummy mesh (without radioactivity but with the same geometry and properties as the standard clinical mesh) can be ordered. This allows the surgeon to trim, practice, and check with the dummy mesh to ensure that the shape and size of the mesh conforms with the desired surgical bed or target volume. Although manufacturer-assembled mesh products can be trimmed before implantation, care should be taken to avoid cutting through a source capsule to cause radiocontamination.

3.3 | Source preparation and calibration

In accordance with federal and state regulations, the process for source preparation is as follows. The package containing the sources is received, surveyed, and wipe tested, and then the sources are inventoried in accordance with federal and state regulations. As stated in the AAPM TG-56 report,[53] every institution practicing brachytherapy should have a system to measure source strength with secondary traceability for all source types used in its practice. Because of its capability for direct traceability to the National Institute of Standards and Technology (NIST) for source strength, the AAPM recommends use of a well-type ionization chamber for assaying sterile source assemblies or additional nonsterile loose seeds from the same lot.[54,55]

Based on the AAPM Low Energy Brachytherapy Source Calibration Working Group Report,[55] mesh brachytherapy users should either measure at least 10% of the total number of strands using a strand calibration coefficient or should order extra nonsterile loose seeds and perform measurements on at least 10% of the total number of sources. Sometimes, all the received sources are stranded, so users should carefully extract seeds from the strand for measurement if a strand calibration coefficient is not determined. If the source strength on the vendor certificate is verified (within 5%)[55] of the mean of the measured seeds, then the sources to be implanted are inferred to be the same as the measured seeds. If a difference more than 5% is observed after reperforming the measurements, the physicist should contact the vendor and notify the radiation oncologist toward deciding how to proceed. Some seed vendors may provide more than one calibration certificate if the sources to be implanted are from a different batch than the loose seeds to be measured.

New types of directional brachytherapy sources may also be calibrated with specific care.[56] One example is the CivaSheet source. A custom source holder for a single CivaSheet source (i.e., a CivaDot) is available from Standard Imaging, Inc. (Middleton, WI, USA) for the HDR 1000 Plus reentrant well-type air ionization chamber. Clinical physicists shall have the combination of their well chamber and the insert calibrated to obtain an Accredited Dosimetry Calibration Laboratory (ADCL) or NIST-traceable independent measurement of source strength.[57]

3.4 | Mesh preparation and surgical implantation

The spatial distribution within the mesh must be determined prior to implantation, either by manually measuring the seed spacing in the suture or by autoradiography

TABLE 3 The 2016 ABS dose recommendations for LDR thoracic mesh brachytherapy[20]

Radionuclide	Monotherapy	Boost or Reirradiation
^{125}I	100–125 Gy	50–80 Gy
^{103}Pd	80–125 Gy	50–80 Gy
^{131}Cs	80–100 Gy	50–80 Gy

It is recommended that the prescription of mesh brachytherapy should include the prescription dose, radionuclide, and treatment volume (simply being the treatment depth and area size).

of the stranded seeds or mesh. Two millimeter is the tolerance. If more than a 2-mm difference is found, then the measured or average spacing should be used for dose calculation. Once the mesh is fabricated or the premade mesh removed from its shielded container, it is presented to the surgeon for implantation. In a sterile environment, the surgeon secures the mesh along the surgical resection site where the tumor was removed. The mesh can also be directly placed if it is an open surgical resection. Radioactive sources must be counted in each phase, including total seeds ordered and brought to the OR before implant, seeds implanted after implant, and seeds remaining after the procedure. A mobile C-arm can be used for postimplant imaging to count implanted seeds and to create a permanent record. After documenting the number of seeds implanted and not implanted, any remaining seeds should be transported back to a secured storage for decay and for updating the inventory log for further disposal. Once the surgical procedure is complete and the patient has been removed from the OR, the room and any equipment and instruments used in the procedure shall be surveyed with a Geiger–Müller (GM) counter or scintillation detector to locate and account for any potential missing seeds. A record of the survey results shall be retained according to federal and state regulations. Clinicians participating in the implantation procedure should wear leaded gloves and use a portable L-block shield when handling the sources if they find that it would be beneficial for their radiation protection yet not impede dexterity and prolong the exposure time.

3.5 | Treatment planning and dosimetric aspects

3.5.1 | Prescription

Dose recommendations vary for differing radionuclides because of half-life and photon energy. For lung cancer, the ABS recommends the prescription doses shown in Table 3 (prescribed at 0.5 cm from the mesh plane) for the three commonly used LDR radionuclides for mesh brachytherapy. The ABS has not made mesh brachytherapy official recommendations for other anatomic sites, in general, ^{125}I mesh can be prescribed to deliver a dose of 85–150 Gy to the minimum peripheral dose.[58,59]

3.5.2 | TPS commissioning

The brachytherapy TPS should be commissioned by a physicist following the guidelines below:[58]

1. Select a brachytherapy TPS approved by the U.S. Food and Drug Administration (or take responsibility to create your own). Some TPSs have been successfully used in many brachytherapy procedures such as prostate, eye plaque, gynecological, and breast seed implants. Their accuracy and suitability have been verified by many users.
2. Verify the dosimetry model parameters for each radioactive source model for both the line-source and point-source dose-calculation algorithms. To minimize dosimetric variability, for TG-43 algorithm the verification should include comparison with consensus brachytherapy dosimetry data, as found in the AAPM Brachytherapy Source Registry, whenever available (including the most recent updates, supplements, and errata).[36,59–61] The physicist ensures that the entered data and calculation results for a sample case have been fully reviewed, validated (3% tolerance), and approved for clinical brachytherapy. When the data are entered (or evaluated if entered by the manufacturer), the data density (i.e., radial and angular distances between neighboring points) should be carefully examined. High-resolution grids are preferred with less than 2 mm spacings recommended in the source vicinity when closer than 1 cm. This is because the TPS performs interpolation and large errors can occur close to the implant where the dose rates are highest.
3. Verify the TPS functionality and accuracy by performing calculations at some known points with single and multiple sources. The line-source approximation should be used if the source orientation can be reasonably determined from imaging (less than 2 mm voxels) and source-to-source positioning restrictions (stranding) or a directional source is utilized. Furthermore, TPS dose calculation accuracy depends on the implementation of a specific algorithm with appropriate parameterization, the dose calculation grid, and the veracity of the output mechanisms such as DICOM-RT dose files. If an MBDCA algorithm is used, a comparison to TG-43 should be completed and documented as a part of its due commissioning process.[25] Comparing the results at several locations with another independent TPS or published data can facilitate TPS commissioning for the specific source and clinical application.
4. Learn the coordinate system and source strength units used in the TPS. The source locations will be entered into a mesh arrangement. The intersource

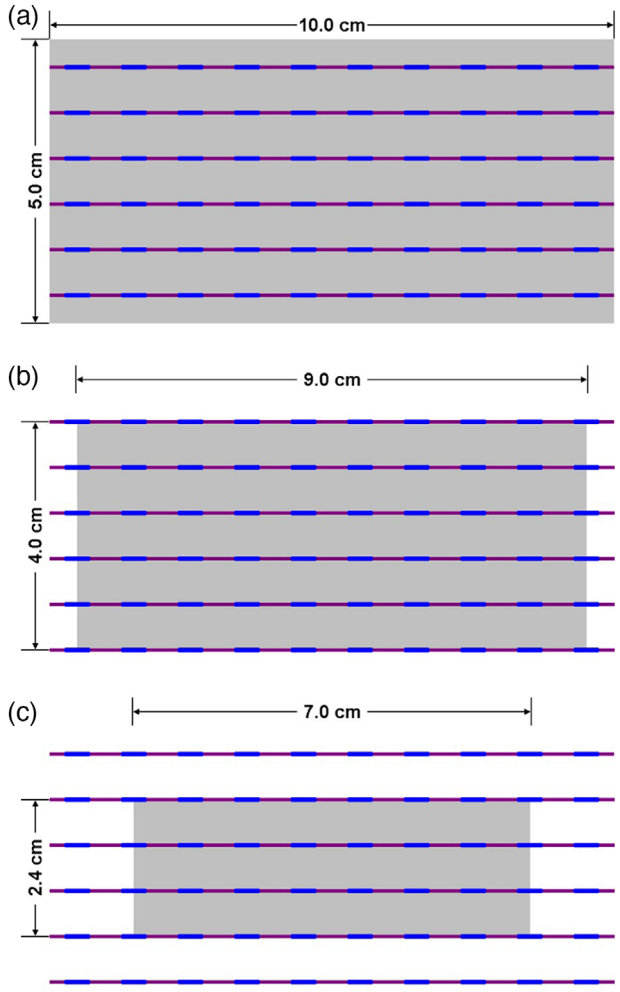

FIGURE 1 Alternative techniques used for implant treatment volume coverage with a mesh implant used by different groups. Each of the six horizontal strands has 10 seeds (blue), 1.0-cm seed-to-seed distances within each strand, and 0.8 cm spacing between rows or strands as overlaid on the variable CTV treatment area (gray). Upper: The CTV is 5.0 cm × 10.0 cm with the diagram corresponding to Table 4 as similar to Stewart et al[20] and Parashar et al for ^{131}Cs.[8] Middle: The CTV is 4.0 cm × 9.0 cm with the diagram corresponding to Table 5 from the study of Johnson et al for ^{125}I.[36] Lower: The CTV is 2.4 cm × 7.0 cm where a multimillimeter margin expansion is delivered around the CTV. The same size mesh is implanted in all three instances. However, the approach taken in the lower images provides increased margins around the treatment area, due to differences in target volume coverage goals and penetration depth for differing radionuclides

distance (center-to-center) along a strand is typically 1.0 cm with the distance between the strands (rows) ranging from 0.5 to 1.5 cm.

5. Create a series of mesh plans covering a wide range of target sizes (i.e., surgical beds) in square or rectangular shapes with requisite margin expansions (Figure 1). For each plan, create a series of reference points that are located on a plane that is 0.5 cm away from the mesh and along the central axis of the mesh pattern. If available, volumetric dose metrics (e.g., D_{90}, D_{100}, V_{95}, V_{100}) should be used for dose reporting instead of a series of simple reference points.
6. Create an array of lookup tables extracted from the mesh plans. Graph the lookup table data to aid in detecting data input errors and aid in planning. For a permanent implant, the source strength needed for all mesh sizes (1 to 20 cm in 1-cm increments) and shapes (square and rectangular) can be calculated. Based on the commonly used suture spacing and available source strengths, lookup tables can be made (e.g., Table 4). Because these tools potentially can affect all associated patients for the treatment modality, each individual value of these lookup tables should be checked by a qualified second physicist or dosimetrist, then formally approved by the brachytherapy team. For preimplant treatment planning, the TPS can serve as an independent dose calculation check for the lookup tables, and the lookup tables can serve as an independent dose calculation check of the TPS for postimplant treatment planning.

3.5.3 | Preimplant treatment planning

Preimplant treatment planning with the aid of lookup tables is straightforward and can be adapted for a range of source strengths. The surgical procedure may include tumor debulking in addition to placement of the brachytherapy mesh implant, and it will deform (sometimes substantially) the anatomy and resultant images used for treatment planning comparing to the image obtained before the procedure. The available source strength from vendors may not be a limiting consideration for deciding the operation date because the seed spacing can be adjusted by vendors in a premade mesh to accommodate the available source strength for achieving the prescription dose and target coverage. Early dosimetric analysis for interstitial implants using ^{125}I brachytherapy sources was originally based on relationships to ^{222}Rn seeds, as this form of treatment evolved in the 1960s at what is now the Memorial Sloan Kettering Cancer Center. The refinement of dosimetric parameters for both ^{125}I and ^{103}Pd through the subsequent decades is chronicled in the series of TG-43 reports from the AAPM,[34] including adjustment of the NIST standard incorporating the wide-angle free-air chamber and the TG-43 dose calculation formalism.[37] Recommended dose prescription considerations were also published by the AAPM for interstitial application of sources containing these two radionuclides. Dosimetric uncertainties for prostate implants were addressed in the AAPM TG-64 report,[60] but these were mainly related to implant geometry and are not as relevant for the mesh technique.

TABLE 4 Example of mesh geometry and prescription dose. A lookup table for the model CS-1 Rev2 ^{131}Cs seed (Isoray Medical) planar implants for 10 seeds per strand (covered length of 9.5 cm), assuming 1.0 cm seed center-to-seed center spacing along the strands, 1.0 cm between the strands, and 0.5 cm treatment depth (adapted from Refs. 8 and 20). $V_{100\%}$ is the volume covered by 100% of the prescription dose

Prescription dose (Gy)	Covered width (cm)	$V_{100\%}$ (cm^3)	Source strength (U)
100	1.9 (two strands)	14.66	3.25
	3.8 (four strands)	32.02	2.70
	5.8 (six strands)	46.34	2.40
80	1.9 (two strands)	14.66	2.60
	3.8 (four strands)	31.94	2.15
	5.8 (six strands)	47.58	1.95
60	1.9 (two strands)	14.66	1.95
	3.8 (four strands)	31.78	1.60
	5.8 (six strands)	46.94	1.45

When preparing preimplant treatment plans using lookup tables for a specific patient, the guidelines below should be followed:

1. Establish the prescription dose, source configuration, and prescription paradigm such as the line-source formalism or for isodose volumetric coverage.
2. Estimate the treatment volume, decide the source model, number of sources, and source strength.
3. Determine a process for preimplant treatment planning such as using lookup tables or image-based evaluation of the target for preimplant treatment planning estimations.[36]
4. Decide mesh implant geometry and select an implant convention.[61] There are several conventions to implant meshed seeds onto a surgical excision bed (Figure 1,). In one convention (Figure 1a), the seeds' center-to-center area (plus ~0.5 cm on each side) defines the treatment area.[20] In a second convention (Figure 1b), the surgical excision area is defined and covered by the seeds' center-to-center mesh area.[36] A third approach (Figure 1c) is to have a generous margin and with the source area covering a clinical target volume (CTV) with a PTV expansion. In light of the recommendations provided in the current report, the physicist should generate lookup tables based on a particular convention agreed upon by the AU and physicist.
5. Identify a mesh size and source row spacing for the selected implant geometry by using the lookup table based on the measured source strength and target volume. Ensure that the entire tumor bed is covered. When the tumor bed is irregular in shape, ensure that a rectangular mesh size covers the tumor bed dimensions. If the treatment area and available source strengths do not fit precalculated source row spacing, a new spacing would be calculated by a physicist or their designate. Lookup tables can be interpolated for intermediate mesh sizes.

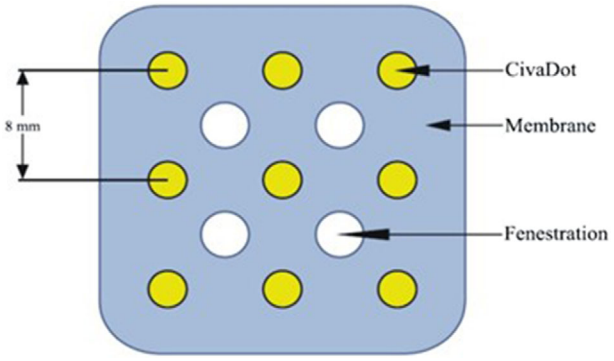

FIGURE 2 A schematic diagram of a sample CivaSheet array with nine buttonlike CivaDot sources[57]

6. Prepare a preimplant treatment plan. The plan should be prepared and signed by the physicist or qualified personnel supervised by the physicist.
7. Independently verify the plan by a second physicist (or a trained dosimetrist if first approved and signed by a physicist). The plan should contain information such as plan type, mesh size, tumor size, radionuclide, source strength, source-to-source spacing in strand, strand-to-strand distance, size checked from the lookup table, tumor margin, and so on.

Instead of placing seeds in a mesh, CivaSheet, which provides a distinctly different geometry and source configuration, populates buttonlike ^{103}Pd sources in a rectilinear grid as shown in Figure 2. Example lookup tables are provided in Ref. [41].

3.5.4 | Postimplant dosimetric evaluation

Postimplant dosimetric evaluation provides an indication of treatment quality and is therefore very important. Unlike for prostate implants where the timing for

postimplant dosimetry is dependent on edema and choice of radionuclide,[62] postimplant imaging for 3D dosimetric evaluation should occur after the operation is completed and the patient is stable, usually more than 2 h after the surgery. Some patients are imaged the next day or even the next week to stabilize; this is equally fine as long as a hospital protocol is followed. Volumetric imaging such as CT is used for postimplant dosimetric evaluation using the AAPM TG-43 formalism or an MBDCA algorithm. Because the sources might cause artifacts, CT having metal-artifact reduction functionality is desired. To permit evaluation of the high-dose gradients around the implant, imaging should provide accurate source localization (all implanted sources can be located) for dose reconstruction. This may require high mAs (depending on machine) and high-resolution CT slice thickness on the order of 1 mm with even finer in-plane resolution through patient positioning in a narrow field-of-view. Although a scan with 2–3 mm slice thickness may prevent seeds from appearing on multiple slices and help to quickly identify source locations, for dosimetric evaluation, a smaller slice thickness is preferred for accurate dosimetric evaluation (e.g., knowing the source orientations and using the 2D TG-43 dose calculation formalism) and tissue delineation. If brachytherapy is performed in conjunction with EBRT, one CT should be performed to permit precise implant localization with a small field of view, and a different CT scan with lower resolution with a large field of view to allow fusion with an EBRT treatment course. With modern CT, it is possible to use a high-resolution scan to generate a second low-resolution image through reconstruction. The registration and fusion of brachytherapy and EBRT images and dose should not just rely on the patient geometry because of anatomic deformation due to surgical resection and implantation of the brachytherapy device. Other factors are identifiable sources, surgical clips, and vascular structures. Further confounding the combination of dose summation of EBRT and brachytherapy is the biological effectiveness of their differing dose rates, energy, and linear energy transfer (LET).

Postimplant dosimetric evaluation for mesh brachytherapy requires entry of the implanted source strength into the TPS, identification of the implanted sources in the patient geometry, and consideration if there is a medical event due to potential migration of sources outside of the implanted PTV (see Section 3.6.5).[35] If volumetric dose coverage is not evaluable (for example, if a CT scan is not possible due to the patient being too large or the patient has a life support system), dose to two points-of-interest located at the geometric center of the implant (placed 0.5 cm above and 0.5 cm below the approximated mesh plane) is averaged to calculate an estimate of the delivered dose. If volumetric imaging is used, the CTV should be defined by the resection boundary plus the suspected subclinical disease and the prescription depth. The PTV may be considered as the CTV plus a 0.5-cm margin with the mesh technique or a 0.7-cm margin with the double strand technique.[20] Dosimetric metrics (e.g., D_{90}, D_{100}, V_{95}, V_{100}) should be documented. For LDR ^{125}I, ACOSOG Z4099/RTOG 1021 recommends that at least 90% of the CTV should be covered by 95% of the prescription dose.[24] Although absolute doses will differ due to half-life, it is expected that ^{125}I and ^{131}Cs coverage metrics will be similar given their similar photon energies.

3.5.5 | Dosimetric parameters useful for mesh brachytherapy

Dosimetric parameters recommended by the AAPM TG-137 report for prostate permanent LDR brachytherapy,[62] such as prescription dose D_p, doses covering 90% and 100% of target volume (D_{90}, D_{100}), percentages of target volume covered by 90% and 100% of prescription dose (V_{90}, V_{100}) can be used for mesh brachytherapy to assess correlations of clinical outcomes and administered dose distributions. If the OARs are delineated, the maximum dose received by 2, 1, and 0.1 cm^3 (i.e., D_{2cc}, D_{1cc}, $D_{0.1cc}$) should be calculated.[70,71] The following parameters are considered to be useful in mesh brachytherapy:

1. source strength unit is U, prescription dose D_{Rx};
2. target coverage parameters, D_{90}, D_{100}, V_{90}, V_{100}; and
3. D_{2cc}, D_{1cc}, $D_{0.1cc}$ for each OAR.

3.6 | Radiation safety aspects

Complete documentation of the procedure from the prescription generation to the radiation exposure for the clinical personnel and members of the general population (including the potential for multiple radioactive implantation sites) is critical for the institution to demonstrate regulatory compliance. Federal regulations mandate the requirements of the records and the length of the time these records need to be made available for inspection. Users in Agreement States should also consult the federal regulations as they may become out of sync based on ongoing updates. Appropriate training on U.S. Department of Transportation regulations are required to dispose of or ship any unused source(s) back to the vendor.[63]

3.6.1 | Precautions for the inpatient stay

Based on 10 CFR 35.415, a patient who receives an operative mesh brachytherapy implant and cannot be discharged the same day from the hospital shall have a designated room that is visibly posted with a

"Radioactive Materials" sign and established visitor stay times and seating location in room if applicable. The facility shall have applicable emergency response equipment in case a seed becomes dislodged from the patient. Surgical patients may have tubes placed to facilitate fluid drainage from the surgical site. For the mesh brachytherapy patient, the tube or drainage receptacle potentially could contain a dislodged seed. Upon removal of drainage fluid, tube and receptacle, and bandages, these items should be surveyed with a GM counter or scintillator probe and cleared of any dislodged seed prior to disposal. Following discharge of the patient, the patient's room shall be surveyed and cleared of any potentially dislodged sources. The AU and radiation safety officer (RSO) shall be notified as soon as possible of any medical emergency or patient death in order for the AU to take some necessary measures for the patient, such as moving the patient to intensive care, explanting the seeds, reporting the event to NRC/State health department, and so forth.

It is recommended to hold training inservices for hospital personnel in departments outside of radiation oncology if they will care for implanted patients. Training on the principles of radiation safety (i.e., time, distance, and shielding) and the process of personnel exposure monitoring (i.e., personal radiation dosimeters) will help to create a knowledgeable team that is properly trained for working in the vicinity of patients having mesh brachytherapy implants.

3.6.2 | Patient release guidelines

NRC guidelines for patient release determination are based on three methods: (1) total contained activity, (2) measured dose rate 1 m from the patient, and (3) patient-specific calculated dose.[64] Method (1) is conservatively based on a 5 mSv dose limit, 25% occupancy factor, and there being no tissue present to attenuate the radiation. In method (2), the dose rate is measured at 1 m and compared to radionuclide-specific limits in the NUREG Guidance. Method (3) is based on patient-specific dose calculations to indicate that the maximum likely dose received by an exposed individual would not exceed 5 mSv with example calculations in Appendix U Supplement B of NUREG-1556, Vol. 9.[65]

3.6.3 | Patient discharge following mesh brachytherapy

Written instructions shall be provided to the patient,[65,66 and a] record of the basis for release authorization shall be kept in the hospital for 3 years[65,67] if either methods (2) or (3) of Section 3.6.2 are used for patient release. The written instructions shall include several aspects outlined in Appendix U.2.3.2 of the NUREG1556 Guidance. These instructions should be specific to the anatomic location of the permanent implant and include the name and phone number of the AU's facility.

When it is required to provide instructions to the patient, these should include the radionuclide, implant (typically the AU, physicist, and/or institutional RSO). These instructions should be explained to the patient prior to discharge or even prior to the implant. The importance of sharing this contact information with future caregivers must be conveyed as these patients often have future procedures and interventions, and they may present in an emergency department or even a different hospital. Release instructions shall be dealt with on a case-by-case basis because they are difficult to generalize for all possible situations.[68]

Recommended by this report, the records-of-release document kept on file should include patient identifiers, radioactive material implanted, total contained activity, source strength per seed, implant date, date/time and result of survey, survey instrument model and serial number with calibration date, and name of person who made the survey measurement.

Readers are referred to the NCRP Reports 155 and 161, which explain all issues in great depth and provide clear recommendations for patient management and radionuclide responsibilities.[69,70] Newer guidelines for addressing implanted and deceased patients are covered in the IAEA and CDC guidelines.[71,72] Physicists involved with mesh brachytherapy are advised to read through the references in this section to integrate practice guidelines into their clinic.

3.6.4 | Emergency procedure for leaking, lost, or dislodged sources

Emergency procedures need to be prepared to deal with sources exhibiting radioactive leakage, both upon receipt of the sources and during mesh fabrication. These procedures should include confinement and decontamination processes.[71,72] Patient and room surveys should be performed, including all personnel involved and equipment used. For patients with ^{125}I mesh implants, a patient bioassay may be required for the patient if it is suspected that an implanted source encapsulation might be compromised; in which case the RSO must notify the NRC or the Agreement State radiation control program.

3.6.5 | Medical events

A medical event in brachytherapy is defined in accordance with federal and state regulations,[73,74] and is defined in part based upon the implanted source strength (in the postimplantation portion of the

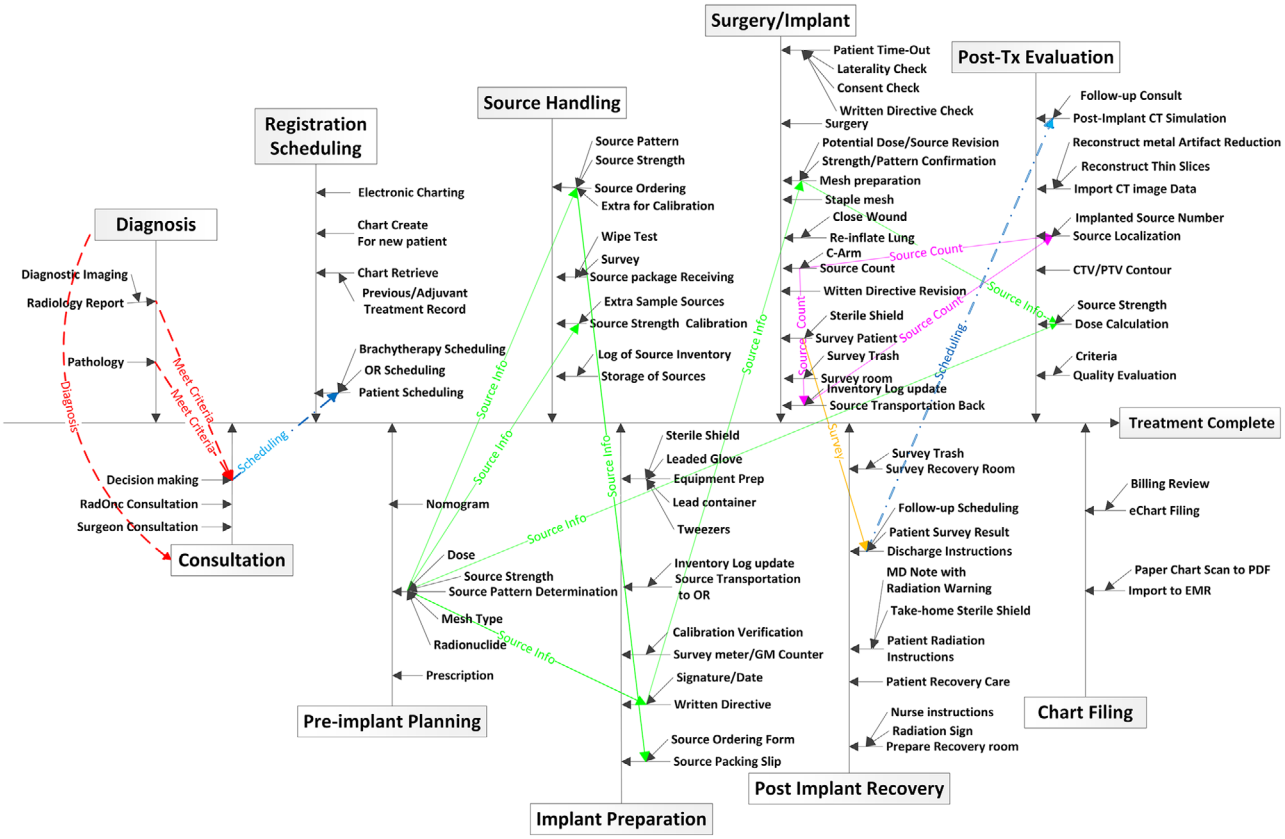

FIGURE 3 An example workflow for lung mesh brachytherapy following the AAPM TG-100 report guidelines.[76] The color scheme assigns red (diagnosis), green (source strength and pattern), yellow (source quantity), and blue (scheduling)

written directive, 20% or more of source strength being implanted outside the PTV) and not the dose delivered to prescription points.[75] Physicists practicing brachytherapy should be familiar with the definition of such an event specific to mesh brachytherapy. As mesh brachytherapy is based on the definition of the PTV and needed treatment margin beyond the physical mesh, the margin is identified through imaging obtained during postoperative dosimetry for implant evaluation.

4 | WORKFLOW AND QUALITY

The AAPM TG-222 recommends the following minimum tasks for intraoperative mesh brachytherapy:

1. implement methods for achieving compliance with the written directive,
2. verify with the AU positioning of the mesh at the intended location,
3. monitor quantitative dose coverage of the target volume(s), and
4. minimize radiation dose to staff and general public.

Through multidisciplinary collaboration, the physicist is responsible for establishing quality standards for mesh brachytherapy.

The workflow for mesh brachytherapy procedures shall be established and fully understood by all team members. An example workflow is shown in Figure 3. It is noted that the workflow details will vary across institutions depending upon available resources and their unique situations.

4.1 | Mesh brachytherapy workflow

To summarize, the typical workflow for mesh brachytherapy is as follows:

1. Source orders
   a. Either stranded seeds or sources already prefabricated in a mesh may be ordered. The ordering process for each is slightly different. In both cases, the number of sources ordered is based on tumor size, potential excision size, and predicted target tumor bed size. Radionuclide and prescription dose are determined by site and location. From this information, the source

strength, number of seeds, and configuration are determined (typically using a lookup table).
   b. Stranded seeds: Source strength, number of seeds, number of strands, and seed spacing within a strand need to be specified. For source strength verification, order an additional 5% of the total number or a minimum of five extra nonsterile loose seeds, whichever is fewer.[56]
   c. Seeds in premade mesh: Source strength, number of seeds, number of strands, seed spacing within a strand, and strand-to-strand spacing need to be specified. Verify source strength by ordering 5% of the total number or a minimum of five extra nonsterile loose seeds, whichever is fewer.[56]
   d. Verification of seed ordering: A process should be in place for a preimplant treatment-plan check that includes source strength, number of strands, seeds per strand, and configuration as based upon the written directive, which should be completed preceding the order.
2. Source receipt, surveying, and storage
   a. Sources should arrive in the clinic at least 1 day before the procedure, leaving enough time for handling, verification, and preparation.
   b. Upon receipt, survey and wipe test the package containing the sources as per NRC or Agreement State regulations.
   c. Source receipt should be documented in an inventory logbook, and the sources and logbook should be kept in a secure storage location.
   d. A survey meter, such as GM counter, needs to be available, functional, and have a valid calibration (i.e., date within 1 year with similar radiations and energies). A calibrated ionization-based survey meter may be used to survey the radiation exposure levels of the patient and OR staff at the end of the implant procedure and needs to be available to search for a misplaced seed in the OR.
   e. Verify source type, quantity, configuration, and source strength. Autoradiographs are performed for verifying the number of seeds and the interseed distance (if not provided by the manufacturer).
3. Source QA and Calibration. The steps and precautions are listed in Section 3.3.
4. Mesh preparation and handling: Seeds may arrive in a mesh or may need to be sewn onto a mesh for implantation. In the latter case, to minimize radiation exposure as well as to improve accuracy and efficiency, the physicist and participating physician (AU or surgeon) should be trained in the process.
   a. Simulating a sterile technique, dummy seeds (nonradioactive but the same size as the real seed) embedded within vicryl sutures should be sewn to a sheet of appropriately sized vicryl mesh with sutures and/or surgical clips at each end. Through a rehearsal with needed devices, radiation protection can be achieved by use of an optically transparent radiation shield behind which the mesh should be assembled with real seeds.
   b. If possible, develop a method to simulate mesh placement and suturing within the patient such as with video-assisted thoracoscopic surgery or a robotic system for suturing or stapling.
   c. If a premade mesh is not used, the strands should be stitched into the mesh following the lines drawn, whereas the suture containing the seeds is handled only with forceps. On the OR preparation table, the strand should be anchored on either side with a small staple, and any excess seeds in the strand should be carefully cut off and properly placed in a shielded container in the OR. All leftover seeds will be transported to the onsite decay storage or disposal facility using appropriate radiation protection guidelines, and proper documentation should be filed.
5. Implant procedure including radiation safety and supervision.
   a. Decide in advance on the role of participants for quality checks during the treatment and explain it to the relevant parties: surgeon, AU, physicist, and others.
   b. Identify the patient preceding the implant through two methods, and perform a timeout per institutional guidelines.
   c. Post radioactive materials signs on the OR entry door(s) before starting the procedure.
   d. Position the mesh at the target location and precisely suture it in place without puncturing a source.
   e. Verify and count seeds through imaging. If a seed is missing, the patient and all staff, equipment, supplies, and trash should not be cleared from the OR until the seed is found.
   f. Measure the exposure rate (mSv/h) from the patient at 1 m with a survey meter calibrated for the radionuclide photon energy.
   g. Survey all personnel involved in the procedure before leaving the OR.
   h. Survey the OR after removal of the patient to ensure that no seeds are present prior to clearing the OR and releasing it back for other use.
   i. Remove the radioactive materials signs from the OR entry doors following procedure completion.
6. Recovery room procedures
   a. The appropriate recovery room personnel should be notified of the mesh brachytherapy patient.
   b. If measurements made in the OR show that further radiation dose-related measurements and restrictions are necessary, radioactive materials

signs are posted in the recovery area while the brachytherapy patient is present.
   c. The recovery area (patient, bed, and associated devices) should also be surveyed. Radiation exposure levels and personnel restrictions should be documented and communicated to the appropriate staff. Staff should be educated beforehand and reminded how to handle drainage devices.
7. Hospital patient room procedures
   a. A radioactive materials sign with the 1-m dose rate is posted on the patient's room door.
   b. Restrictions are made based on the dose rate 1 m from the patient's body surface and at a visitor's sitting chair. The restriction may not be necessary if the measured levels are sufficiently low.
   c. As long as any drainage devices are in place, a dislodged seed may become loose in the room. Until the drainage devices are removed, they need to be surveyed prior to fluid and device disposal as does the patient linen and the trash.
8. Unused and recovered seeds should be counted, stored in a shielded container, and logged into storage in a secure location (e.g., hot lab). Any discrepancy of the total ordered seed number from the sum of unused or recovered seeds and the implanted seeds counted with C-arm imaging should be resolved.
9. A CT scan should be taken following surgical recovery to verify source count and for postimplant dosimetry.
10. Procedures for unforeseen events.
   a. In the unfortunate case where a seed may be compromised, then the lost or ruptured seed must be documented and verified by a physicist, RSO, or their designee.
   b. If some seeds could not be found from the postimplant CT imaging, seeds may have been lost during the procedure or migrated from the implant location to another site within the patient. A CT scout/topogram offers an extended spatial range to track lost seeds. Precautionary measures or remedy treatments based on the dosimetric report may be considered.
   c. Following surgery, an implant may be deemed poor from a dosimetric perspective (typically based on postimplant imaging). In this case, mitigating actions should be taken such as supplementing target dosage through EBRT or surgical explant of the device if warranted.
11. Most medical events result from human errors and unfamiliar technical barriers.[72] Two methods to reduce human errors and technical barriers that can be combined with other interventions are training of staff members and having written checklists for all procedures. A checklist and forms need to be followed for every patient and checked during the implantation procedure. A detailed checklist and forms based on the practical workflow should be created and should include the following items:
   a. patient identification;
   b. site and site verification;
   c. number of seeds received;
   d. number of seed-containing strands, ribbons, or meshes;
   e. number of seeds per strand, ribbon or mesh;
   f. number of seeds used;
   g. target size/dimensions;
   h. mesh dimension: predefined margin should be added to all directions from the target size. If physician preferred, the margin could be zero;
   i. unused seeds;
   j. results of patient radiation exposure survey performed after implantation; and
   k. survey results of OR after patient is moved out and body survey for participating surgical staff, and so forth.

4.2 | Example of FTA and general quality management

After the workflow is well understood by the involved personnel, failure mode and effect analysis (FMEA) should be performed by the team to identify which processes cause high risk among the possible failure modes.[76]

The following FTA was prepared for the case of mesh brachytherapy implantation as an example for the workflow presented in Figure 3, and possible general quality management procedures are suggested for each branch in the FTA. The fault tree began with the potential failure modes that would produce an incorrect dose distribution or patient side effect identified in the FMEA. The causes for each potential failure mode were investigated. Actions to address the potential failure modes can be to either eliminate the causes that can start propagation along the branch of the fault tree or to interrupt the failure progression by placing an intervention along the branch. Either method can be effective. Failures indicated in the three green boxes on the left of Figure 4 are solely of the physician or surgeon and are not considered further herein.

It is possible that some of the failures indicated in the example FTA could result in medical events based on the NRC definition of a medical event (10 CFR 35.3045) for permanent implant brachytherapy, which is generally accepted in Agreement States. In fact, most of the listed faults have potential to result in the administered source strength differing by greater than 20% from the postimplant written directive. For the total source strength administered outside of the treatment site exceeding 20% of the total source strength documented in the postimplantation portion of the written directive, this is

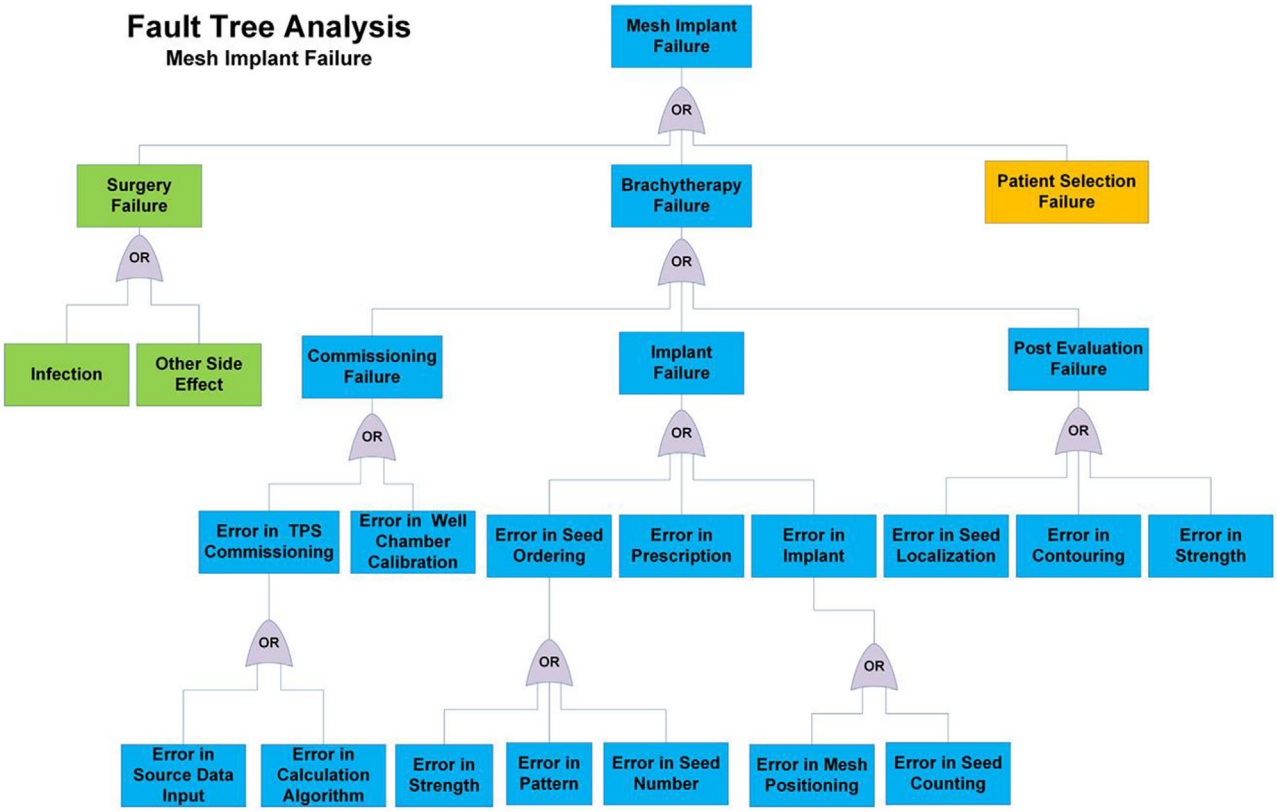

FIGURE 4 An example lung mesh brachytherapy FTA, proceeding from bottom to top. The color scheme assigns green for surgery, blue for brachytherapy, and yellow for patient selection. The ***OR*** symbol is a Boolean gate or logic operator

highly technique-dependent and requires both good surgical skill and accurate postimplant documentation. The other possibilities for a medical event include wrong radionuclide, patient, and treatment site as well as leaking sources that contribute over 0.5 Sv to an organ or tissue. Although these would be most likely caused by the actions pertinent to a specific patient, good-quality management relies on processes established during the commission phase that identify such potential failures and resultant medical events.

Following are steps that can prevent some failures and improve overall safety:

1. Failures in proper TPS commissioning will affect all subsequent patient treatment plans and their evaluation. Quality management actions, such as quality controls and staff training, are required to catch critical failures early, prior to clinical use of the TPS. A second person can independently check the plan, and an independent dose calculation system can be used to verify the TPS dosimetry system.
2. Source strength is measured independently from the manufacturer certificate for verification using a system with instrumentation redundancy and ADCL calibrations.[56] This system should be set in place and tested preceding treatment of the first patient.
3. Seed ordering failure will potentially cause treatment postponement or even administering the incorrect dose. Two methods for staff to communicate with the source vendor should be used to specify the order, for example, using the plan itself and the written directive.
4. Failure to perform postimplant evaluation may not substantially affect the quality of care for the current patient. However, it will affect the collection of the implant quality data, which could indicate that therapeutic delivery was inadequate and that a modification for future patient care is necessary.
5. Plan review and plan approval by the physician can be an explicit step in quality management to catch potential errors.
6. Chart checks and independent checks of dose calculations by physicists or their designees can intercept potential errors before implantation. Preimplant treatment planning, such as with a lookup table or image-guided TPS, is handled or supervised by a physicist and should follow the same quality management principles as for postimplant treatment plan evaluation.

Note that the example quality management program described here is not an explicit recommendation, but is given to explain how physicists at a particular institution may adapt program elements to fit their workflow.

5 | DISCUSSION

The current report covers brachytherapy sources that have been used for mesh brachytherapy, but it, is of course, possible to use other radionuclides, extant, and new. Currently, there are three commercially available radionuclides (^{125}I, ^{103}Pd, and ^{131}Cs) used in mesh brachytherapy. From a radiation safety perspective, the key characteristics for different radionuclides are average photon energy and half-life (Table 1). In theory, the higher the energy of the emitted photons, for a given prescription dose, the higher the dose is expected to be delivered to adjacent tissues and organs. For the same accumulated dose, a higher initial dose rate can be expected for ^{131}Cs and ^{103}Pd (due to their shorter half-lives), which diminish more rapidly than ^{125}I. Similar exposure rates at 1 m from patients receiving permanent brachytherapy prostate implants were reported for ^{125}I and ^{103}Pd sources because the exposure rates were too small to observe differences.[77] Patients with H&N cancers may have even higher exposure rates than lung patients at their skin due to thinner tissue barriers between the mesh implant and patient external surface.

Due to its relatively high-energy photon emissions (0.4 MeV) and radiobiologically long half-life (74 days), LDR ^{192}Ir brachytherapy fell out of favor for permanent implantation about two decades ago.[78] Further, electronic brachytherapy (eBT) sources could also be utilized for treating diseases that are currently being treated with mesh brachytherapy. However, use of eBT X-ray sources to irradiate for several minutes in an intraoperative manner is beyond the scope of this report.

Pertinent developmental efforts on mesh brachytherapy include size reduction of the source capsule, which are advantageous for video-assisted thoracic surgery where the mesh is deployed through a small surgical opening instead of the traditional open surgical approach.[79,80] In comparison, open surgery increases time needed for postoperative healing and increases the likelihood for infection.[79,80] Toward embracing this approach for brachytherapy, yet principally intended for permanent prostate implantation, brachytherapy seeds were developed with thinner diameters (e.g., 0.05 vs. 0.08 cm) than conventional brachytherapy seeds.[92,93] Even though these sources were generally contained within a stranded configuration, their reduced size permits greater flexibility of a brachytherapy mesh and potentially smaller surgical entry with its associated advantages. Although there is no manufacturer that provides these thinner brachytherapy sources, AAPM and medical physicists welcome active brachytherapy source manufacturers to consider offering similarly thin sources similar to the model 9011 ThinSeed™, which was designed for interstitial brachytherapy and induced fewer artifacts on CT than the larger model 6711 counterpart.

Despite the assumption that sources need to be designed with isotropic radiation dose distributions, LDR brachytherapy seeds for permanent implantation have been developed with directional radiation emissions. These LDR brachytherapy sources have high-Z shields inside that result in directional radiation. Alternatively, directional radiation can be achieved through a specially designed applicator that uses conventional sources.[81,82] Investigators at the University of Wisconsin examined a prototype ^{125}I seed having an internal Au shield within the conventional titanium encapsulation.[83,84] This approach would have necessitated a keel to orient the seed to ensure that the shielding was aligned toward the critical structures and away from the clinical target. Special care should be taken when using directional sources as it is critical to ensure their correct orientation. A ^{103}Pd source (CivaSheet by CivaTech Oncology, Inc. Durham, NC, USA) has been developed with a 0.05-mm-thick Au shield to provide dosimetric directionality for preferentially irradiating the target while sparing critical structures, an approach not possible with isotropic seeds. Compared to the forward direction, dose reduction in the rearward direction from a single CivaDot source is reduced by factors of 276, 24, and 5.3 at radii of 0.1, 1, and 10 cm, respectively.[85] There are TPS brachytherapy dosimetry parameters for the CivaSheet, which was commissioned for early investigational clinical use in 2018.[41,85]

Designed to minimize high dose gradients, the GammaTile™ has been developed as a custom brachytherapy mesh with tissue located either about 0.1 cm or about 0.3 cm from the face of the tile. This permanent brachytherapy device comprises a bioabsorable collagen used to offset stranded ^{131}Cs seeds from direct contact with tissue in cranial implants.[86–88] The $(2\ \text{cm})^2$ tiled-device contains a 2×2 array of uniformly-spaced ^{131}Cs seeds.

As another innovative application,[56] brachytherapy seeds have been designed to elute concurrent chemotherapeutic drugs with their radiation emissions, albeit with different timing and spatial scales.[89,90] As applicable for mesh brachytherapy, the drug-eluting seeds (or spacers as the case may be) would need to have characteristics of selectivity and specificity for tumor types and sites to complement the brachytherapy radiation dose distribution as well as be compatible with the mesh and stranding materials comprising the implant device. Equally dramatic and without clinical demonstration are brachytherapy seeds with a dissolvable encapsulation for complete absorption following RT delivery.[91] Alternatively, brachytherapy seeds may contain paramagnetic materials that can provide local heating by combining hyperthermia and RT.[92] Given their potential for highly conformal treatments, these technologies show promise as areas of future research for mesh brachytherapy.

Research investigating the use of MBDCAs for mesh brachytherapy (reviewed in Section 2.4) has typically focused on lung treatments; however, further research is needed for other treatment sites to understand the site-specific implication of MBDCAs and consider if it is necessary to modify the size of prescription doses.[25] Advanced dose calculations may then be coupled to radiobiological models to enable comparisons of treatments with different radionuclides and other modalities toward improving treatment outcomes.[93]

6 | RECOMMENDATION SUMMARY

Physicists play a crucial role and should perform the following specific tasks when implementing a mesh brachytherapy program:

1. Examine the radioactive materials license to determine suitability for implementing a new mesh brachytherapy program or continuing an ongoing mesh-brachytherapy program to make appropriate license amendments if necessary (Section 3).
2. Prepare a quality management program that includes all direct stakeholders in its refinement. In addition to building processes, this includes building a workflow diagram and evaluating potential failure modes for each step from diagnosis to postimplant evaluation and follow-up (Section 4). The example workflow presented in Figure 3 can aid readers in developing their own workflow evaluation.
3. Commission and implement preimplant and postimplant treatment-planning methods to guide correct source ordering (Section 3).
4. Learn a specific implantation technique to deliver high-quality patient care (Section 3.5).
5. Estimate staff and public exposures before implementation of a mesh brachytherapy program for a specific anatomic site (Section 3.4).
6. Establish radiological safety procedures and provide proper training (Section 3).
7. Communicate the definition of a medical event with all stakeholders, and establish and promulgate an agreed-upon method for handling this (Section 3.6.5).
8. Follow the whole team-approved workflow during the implantation process to ensure implant accuracy according to the written directive and to follow good radiation safety practice and compliance (Section 3). Provide proper training for source handling and radiation safety to all involved staff; quantify the expected radiation exposures for all participants and establish radiological safety practices toward minimizing personnel exposure and promoting a safe and controlled work environment (Section 3.6.1).
9. Perform preimplant planning using the TG-43 dose calculation formalism with the point source approximation (Section 3.5.3).
10. Assay and evaluate sources from the same manufacturer lot (use sources from same lot for a single patient) preceding implantation (Section 3.3).
11. Utilize a written directive based on the implanted source strength, not target-volume dose coverage (Section 3.6.5).
12. Utilize a prescription based on table lookup of intended dose, depth, and treatment area (Section 3.5.1).
13. Calculate postimplant dosimetry with the AAPM TG-43 formalism with point source approximation (Section 3.5.4).
14. Perform dose estimates using an MBDCA (if available) for scientific evaluation of a given anatomic site and brachytherapy treatment modality (Section 2.4).
15. Evaluate treatment quality using target dosimetric metrics such as D_{90}, D_{100}, V_{95}, and V_{100} as well as dose and volume constraints to healthy tissues (Section 3.5.4).

CONFLICTS OF INTEREST

Before initiation of this report, all members of the TG 222 completed disclosure statements. These statements are maintained at the AAPM Headquarters in Alexandria, Virginia. The AAPM Therapy Physics Committee has reviewed these disclosures and determined that they do not present a conflict with respect to the TG members' work on this report.

1. The members of TG 222 of Recommendations for intraoperative mesh brachytherapy listed below attest that they have no potential Conflicts of Interest related to the subject matter or materials presented in this document: Wenzheng Feng, Elizabeth M. Carey, Sujatha Pai, Ravinder Nath, Yongbok Kim, Cynthia L. Thomason, and Hualin Zhang.

2. The members of TG 222 of Recommendations for intraoperative mesh brachytherapy listed below disclose the following potential Conflict(s) of Interest related to subject matter or materials presented in this document. Robert A. Hearn is an employee of Theragenics, Inc., and Dale E. Boyce was an employee of Isoray Medical, Inc. Mark J. Rivard has served as a consultant and received research funding from Varian Medical Systems, Inc., CivaTech Oncology, Inc., and Isoray Medical, Inc.

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