AAPM recommendations on medical physics practices for ocular plaque brachytherapy: Report of task group 221

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The American Association of Physicists in Medicine (AAPM) formed Task Group 221 (TG-221) to discuss a generalized commissioning process, quality management considerations, and clinical physics practice standards for ocular plaque brachytherapy. The purpose of this report is also, in part, to aid the clinician to implement recommendations of the AAPM TG-129 report, which placed emphasis on dosimetric considerations for ocular brachytherapy applicators used in the Collaborative Ocular Melanoma Study (COMS). This report is intended to assist medical physicists in establishing a new ocular brachytherapy program and, for existing programs, in reviewing and updating clinical practices. The report scope includes photon- and beta-emitting sources and source:applicator combinations. Dosimetric studies for photon and beta sources are reviewed to summarize the salient issues and provide references for additional study. The components of an ocular plaque brachytherapy quality management program are discussed, including radiation safety considerations, source calibration methodology, applicator commissioning, imaging quality assurance tests for treatment planning, treatment planning strategies, and treatment planning system commissioning. Finally, specific guidelines for commissioning an ocular plaque brachytherapy program, clinical physics practice standards in ocular plaque brachytherapy, and other areas reflecting the need for specialized treatment planning systems, measurement phantoms, and detectors (among other topics) to support the clinical practice of ocular brachytherapy are presented. Expected future advances and developments for ocular brachytherapy are discussed. [https://doi.org/10.1002/mp.13996]
Key words: commissioning, ocular brachytherapy, plaque brachytherapy, quality management, treatment planning

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1. INTRODUCTION

Melanoma is the most common primary intraocular cancer; it arises from the uveal layer, which is comprised of the choroid, ciliary body, and iris (from posterior to anterior). Historically, treatments have relied on enucleation; however various treatment options include external beam radiotherapy (EBRT) with photons (from a megavoltage linear accelerator[1–3] or Gamma Knife®-^{60}Co [4–6]); EBRT with charged particles using protons[7–9] or helium ions[10] (from high-energy cyclotrons); or ocular brachytherapy (see TG-129 report for a brief review of different treatment modalities).[11] Compared with brachytherapy, protons have demonstrated inferior clinical outcomes.[12] Intraocular tumor brachytherapy was first pioneered in the 1930s using a radon seed.[13] Treatments with other radionuclides including ^{60}Co, ^{106}Ru/^{106}Rh, ^{125}I, ^{103}Pd, ^{198}Au, ^{90}Sr/^{90}Y, and ^{131}Cs in the plaque sources have also been reported.[14–26] Modern plaques typically utilize low-energy photon-emitting brachytherapy seeds (^{125}I, ^{103}Pd, ^{131}Cs) assembled inside a gold alloy or stainless steel backing, or beta particle-emitting (^{106}Ru,^{90}Sr) silver plaques.[11]

The Collaborative Ocular Melanoma Study (COMS) was initiated in 1985 as a multi-institution clinical trial that provided a standardized approach for tumor diagnosis, plaque design, and ^{125}I plaque dosimetry.[27] The COMS medium tumor study demonstrated that plaque brachytherapy offers equivalent tumor control to enucleation while preserving the eye in addition to the possibility of vision retention.[28] While the standardized plaques of the COMS trial have been widely adopted for ocular brachytherapy (particularly in North America),[29–31] many other plaque types are used worldwide, including various designs containing photon-emitting brachytherapy sources. In Europe, there is a tradition for administering beta-emitters like ^{106}Ru/^{106}Rh following the pioneering work of Lommatzsch and colleagues,[15,32,33] and others.[26,34–41] Table I presents an overview of some plaque models in the scientific literature. Figure 1 presents two depictions of ocular brachytherapy, one for a beta plaque within an artist's rendition of ocular anatomy [Fig. 1(a)] and the other for a COMS plaque within a voxelized computational model of the eye [Fig. 1(b)].

Table I demonstrates the range of radionuclides that are currently used worldwide for ocular brachytherapy. Widely used low-dose rate (LDR) photon-emitting brachytherapy seeds include ^{125}I (mean photon energy E_γ = 28 keV and half-life $t_{½}$ = 59.4 days),[61] ^{103}Pd (E_γ = 21 keV, $t_{½}$ = 17.0 days),[62] and ^{131}Cs (E_γ = 30 keV, $t_{½}$ = 9.7 days).[63] A high-energy LDR photon-emitting source is ^{198}Au (E_γ = 0.4 MeV, $t_{½}$ = 2.3 days).[64] The beta-emitter is ^{106}Ru/^{106}Rh where ^{106}Ru ($t_{½}$ = 371.5 days) decays to ^{106}Rh[65] via beta decay with spectral maximum and mean energies of 39.4 and 10.0 keV, respectively. ^{106}Rh ($t_{½}$ = 30.1 s) then decays to stable ^{106}Pd via beta decay with spectral maximum and mean energies of 3.54 and 1.41 MeV, respectively.[66] This latter disintegration contributes therapeutically.

Due to the small size of the eye (outer diameter ~25 mm), dose distributions are generally highly sensitive to the assumptions underlying dose calculations, and accurate eye plaque dosimetry is critical for determining the location and incidence of potential side effects.[67] For photon-emitting plaques, dose calculations have historically been performed while assuming a homogeneous water environment medium and neglecting the effects of the plaque geometry (in addition to the non-water equivalent patient). However, the low-energy photons emitted from radionuclides used for eye plaque brachytherapy and the high effective atomic number (Z_{eff}) of plaques result in dose distributions that are sensitive to the presence of non-water media in the treatment region.[11] The use of many different plaque designs (Table I) with varying dosimetric effects (including some that were not characterized prior to clinical use) presents challenges for accurate dosimetry. Beta-emitting plaques do not have widely adopted standardized methods analogous to the TG-43 protocol for computing three-dimensional dose distributions. Both photon and beta-emitting plaques have no U.S. Food and Drug Administration (FDA) or Conformité Européene (CE) approved commercial software packages that perform dose calculations that take into account the non-water media of the plaque and/or patient. Recent work towards the adoption of model-based dose calculation algorithms (MBDCA) for brachytherapy is very important and relevant for ocular brachytherapy;[68] there is a need for advanced treatment planning systems (TPSs) to evaluate doses to tumor and normal critical ocular structures.

TABLE I. A partial list of plaque models represented in the literature. Plaques are grouped by type and their name or the institution where they are used. The media for the backing and insert (or seeds' fixative — if no insert) are indicated. Source shape indicates whether the activity is within a seed or plated/distributed, with radionuclide(s) indicated (based on publications; however, other radionuclides may be used in practice). References are restricted to those describing the plaque model or radiological physics aspects.

Type	Plaque name or Institution	Backing	Insert (fixative)	Source shape	Radionuclide(s)	Notes	Selected references
COMS	COMS plaques	Gold alloy	Silicone polymer	Seed	^{125}I, ^{103}Pd, ^{131}Cs	–	[27,42]
COMS backing, non-standard insert	New York Eye Cancer Center	Gold alloy	(Acrylic)	Seed	^{125}I, ^{103}Pd, ^{131}Cs	–	[43,44]
	Seed-guide plaques	Gold alloy	0.3 mm gold alloy	Seed	^{125}I, ^{103}Pd	–	[45]
Modified COMS	Mayo Iris plaques	Gold alloy	Silicone polymer	Seed	^{125}I, ^{103}Pd	Annular; 180°, 270°, 360° spans	[46]
	Finger's slotted plaques	Gold alloy	(Acrylic)	Seed	^{125}I, ^{103}Pd	Slots for optic nerve	[47]
Slotted plaques	USC slotted plaques	Gold alloy	Not reported	Seed	^{125}I	Individual collimating slots for sources	[48]
Gold alloy custom plaques	OSU-Nag	Gold alloy	Not reported	Seed	^{125}I, ^{131}Cs	Optional notch for optic nerve	[49,50]
	Helsinki University Central Hospital	Gold alloy	Silicone polymer	Seed	^{125}I	Optional notch for optic nerve	[51]
	Cliniques Universitaires St-Luc	Gold alloy	Resin	Seed	^{125}I	Optional notch for optic nerve	[52]
	Wills Eye Hospital	Gold alloy	Not reported	Seed	^{125}I	Shape adapted to treatment	[53]
	St. Erik Eye Hospital	Gold alloy	(Silicone glue)	Seed	^{125}I	–	[54]
	Essen University Hospital	Gold alloy	Not reported	Seed	^{125}I	Grooves for seeds	[55]
Stainless Steel backing	ROPES	Stainless steel	Acrylic	Seed	^{125}I, ^{103}Pd	–	[56]
	New South Wales Hospital, Sydney	Stainless steel	Acrylic	Seed	^{125}I	Shape adapted to treatment	[57]
Acrylic plaques	British Columbia Cancer Agency, Canada	Acrylic	Dental wax	Seed	^{198}Au	–	[21]
Beta plaques	^{106}Ru-Eye Applicator, Eckert & Ziegler BEBIG	Silver	–	Plated on hemispherical shell	^{106}Ru/^{106}Rh	16 various sizes and shapes	[58]
Mixed radionuclide plaques	Binuclide plaque, University Hospital Essen, Germany	Gold alloy, silver	Silicone polymer	Plating on hemispherical shell & seeds	^{106}Ru/^{106}Rh & ^{125}I	Prototype, only one size	[59]

ROPES = Radiation Oncology Physics and Engineering Services.

Ocular plaque brachytherapy requires a highly trained multi-disciplinary clinical treatment team. As of today, no other commonly performed brachytherapy procedure discharges the patient following implantation, with the expectation that s/he will return for surgical removal of the plaque within a few days to achieve the prescribed implant duration. Thus, special challenges exist for preparing a robust quality management program for an ocular plaque brachytherapy treatment program. While COMS set standards for a specific set of plaques,[69] the study is closed, and these standards are not applicable to all the medical devices (both photon and beta plaques) included in this report. Consequently, the current report outlines aspects of a quality management program necessary for the consistent and safe delivery of ocular plaque brachytherapy.

In 2012, the report of American Association of Physicists in Medicine (AAPM) and American Brachytherapy Society (ABS) TG-129 was published.[11] It focused on the standardized COMS plaques using ^{125}I and ^{103}Pd to provide guidance on treatment planning and quality management for the clinical medical physicist. The 2014 ABS consensus guidelines for plaque brachytherapy of uveal melanoma and retinoblastoma complement this work and focus on clinical (rather than physics) aspects.[67] There are no analogous reports specific to beta (^{106}Ru) plaques; the closest analogue for these reports is ISO 21439 (2009) on clinical dosimetry of beta ray sources for brachytherapy.[70] The current report extends the scope of TG-129[11] to encompass plaques of general design, including both photon- and beta-emitting sources to reflect the devices used worldwide for ocular brachytherapy. The scope of this report is limited to plaques used for treatment of malignant disease, for example, the use of a ^{90}Sr plaque for post-surgical pterygium removal is not considered.[71] While generalized descriptions are used in this report, the scope of TG-221 is

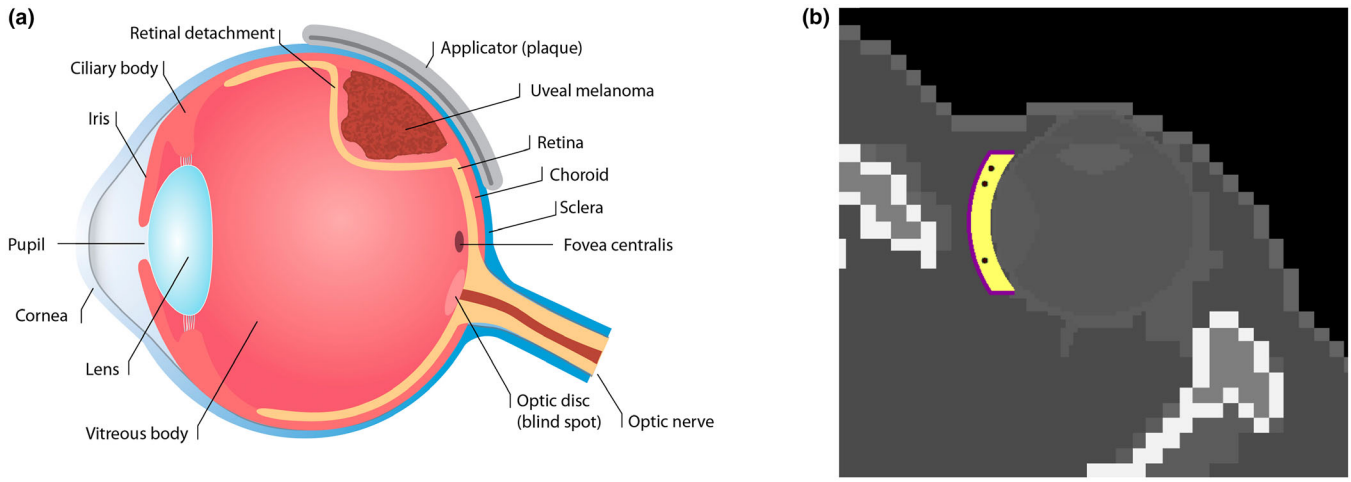

FIG. 1. Depictions of ocular brachytherapy: (a) ^{106}Ru eye applicator in an artist's representation of eye anatomy (image courtesy Eckert & Ziegler BEBIG GmbH) and (b) Collaborative Ocular Melanoma Study plaque within a voxelized eye/patient model (courtesy of Lesperance et al., Ref. 60).

limited to ocular plaque brachytherapy with a specific emphasis on medical physics practices.

TG-221 was approved with the following charges:

1. provide considerations for non-COMS plaques with respect to TG-129 dosimetry recommendations and recent dosimetry advancements,
2. recommend quality management practice standards for ocular plaque brachytherapy, and
3. provide a framework for a generalized commissioning process and discuss considerations for site-specific clinical physics practice standards for ocular plaque brachytherapy.

All the approved charges are addressed in the current report in the following sections:

Section 2 presents a review of dosimetric studies for photon and beta-emitting plaques, and describes many plaque models appearing in the literature. Section 3 covers topics related to quality management/quality assurance (QA) of an ocular plaque brachytherapy program: radiation safety, source calibration, applicator commissioning, medical imaging, and treatment planning. Each Section 3 subsection indicates the current status of research and clinical practice to provide the background and rationale for the TG-221 recommendations. The significant recommendations of TG-221 are pulled together in Section 4. A discussion of future considerations appears in Section 5. These recommendations reflect the guidance of the AAPM for its members. The European Society for Radiotherapy and Oncology (ESTRO) Advisory Committee on Radiation Oncology Practice (ACROP) committee has reviewed these recommendations and found that they conform to European practice standards. Lacking specific recommendations for ocular brachytherapy, ESTRO endorses these recommendations for potential use by its members, except where noted below. Identification of commercial products within this report does not imply recommendation or endorsement by the AAPM or ESTRO, nor does it imply that these products are the most suitable or best for these purposes.

2. REVIEW OF DOSIMETRIC STUDIES FOR VARIOUS PLAQUE MODELS

Studies of dosimetry for eye plaque brachytherapy are difficult due to the short distance scales coupled with steep dose gradients; these factors, in addition to the wide variety of plaque models available (Table I), illustrate why development of a comprehensive understanding of dosimetry for eye plaque brachytherapy has been a challenge. Various dosimetric studies have been performed for different eye plaque models with an assortment of radionuclides and seed models. Dosimetric measurements have utilized thermoluminescent dosimeters (TLDs),[48,55,72–78] diodes,[73,79–81] radiographic film,[82,83] radiochromic film,[48,73,84,85] plastic scintillators,[86–88] polymer gel,[89] small ion chambers,[73] alanine,[73] and diamond detectors.[73] Currently, optically stimulated luminescent detectors have not been used to characterize eye plaque dose distributions, potentially due to the size of the detector (7 mm diameter; 0.2 mm thickness). The appropriate detector size is generally $\leq$ 2 mm in diameter and $\leq$ 0.5 mm thickness. In addition, dosimetry calculations include the TG-43 approach and superposition,[74,90–94] Monte Carlo simulations,[46,56,60,72,95–102] discrete-ordinates calculation methods,[103,104] and collapsed cone convolution.[105,106] These studies generally demonstrate the sensitivity of dose distributions to plaque design and source choice, and the considerable differences between doses calculated for sources in homogeneous water, that is, the TG-43 approach[107,108] and delivered or measured doses.

2.A. Photon-emitting sources

This section reviews dose distributions and treatment planning publications for commonly used photon-emitting

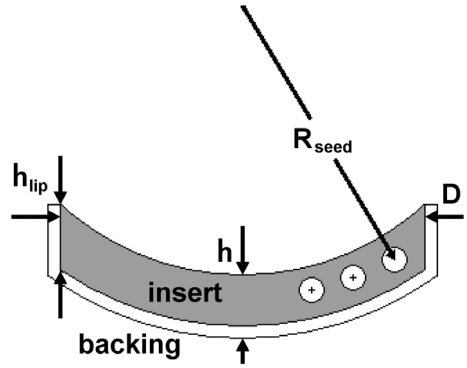

FIG. 2. Visualization of a generalized ocular brachytherapy plaque with photon-emitting seeds. Plaque designs can vary considerably (Table I) with different distances of seeds from the center of the eye (R_{seed}), plaque heights (h), collimating lip heights (h_{lip}) if a lip is present, and diameter D. In addition, seeds may be held within the plaque by an insert or may be affixed to the backing with a fixative.

plaques (Fig. 2), with summaries grouped according to "type" corresponding to entries in Table I. While COMS plaques are briefly discussed to provide context, the reader is referred to the AAPM TG-129 report for a comprehensive analysis.[11] Table II provides a high-level summary focused on some of the dosimetric studies cited herein to complement the presentation and assist readers in seeking further information.

2.A.1. COMS plaques

Collaborative Ocular Melanoma Study plaques are the most widely used, studied, and dosimetrically characterized. Historically, the COMS study used plaques with ^{125}I sources only and diameters between 12 and 20 mm. More recently, COMS plaques in a smaller size (i.e., 10 mm) and in a larger size (i.e., 22 mm) have been adopted.[11] Furthermore, ^{103}Pd and ^{131}Cs are being used as sources in these plaques. Previous studies of COMS dosimetry include Monte Carlo simulations by Melhus and Rivard with MCNP5[97] and by Thomson et al. with BrachyDose.[96,98] The 10 to 22 mm COMS plaques fully loaded with ^{125}I, ^{103}Pd, or ^{131}Cs sources showed average dose reductions at 5 mm depth of 11%, 19%, and 9%, respectively, relative to MC simulation of corresponding seeds in water.[97] Rivard et al.[109] compared doses for 16 mm COMS eye plaques containing ^{125}I or ^{103}Pd sources using three brachytherapy TPSs and two Monte Carlo (MC) codes. They reported that a prescription dose of 85 Gy at a depth of 5 mm (computed assuming a homogeneous water environment, that is, TG-43 approach) actually delivers 76 Gy for ^{125}I (model 6711 seed) and 67 Gy for ^{103}Pd (model 200 seed) assuming a water equivalent infinite patient.[109]

2.A.2. COMS plaque backing with non-standard insert

COMS plaques may be used in a non-standard way: for example, the gold alloy plaque backing alone with no Silastic insert and seeds directly affixed to the plaque backing,[44] with a very thin reusable seed-guide insert,[45] or with non-uniform loading to improve homogeneity of the dose distribution.[110] In 2005, Astrahan et al.[45] reported a dosimetry study that used the Plaque Simulator© treatment planning system (Eye Physics, LLC, Los Alamitos, CA) to calculate dose distributions for the COMS plaque backing with the 0.3 mm thick

TABLE II. Overview of the dosimetric studies discussed in Section 2.A for diverse plaque models containing photon-emitting brachytherapy seeds.

			Seeds[c]			Results[d]		
Reference	Plaque type[a]	Study method[b]	Radionuclide(s)	1	> 1	Homo.	Pl. Het.	Full Het.
[97]	C	MCNP5	^{125}I, ^{103}Pd, ^{131}Cs	X	X	X	X	
[96]	C	BrachyDose	^{125}I, ^{103}Pd	X	X	X	X	X
[98]	C	BrachyDose	^{125}I, ^{103}Pd	X	X	X	X	
[109]	C	MCNP5, BrachyDose, Plaque Simulator, TPS	^{125}I, ^{103}Pd		X	X	X	
[45]	CI	Plaque Simulator	^{125}I, ^{103}Pd	X	X	X	X	
[110]	C,CI	MCNP5	^{125}I, ^{103}Pd, ^{131}Cs		X	X	X	
[102]	C, CI, modC, SP, GC, SS	BrachyDose	^{125}I, ^{103}Pd, ^{131}Cs	X	X	X	X	X
[46]	modC	BrachyDose	^{125}I, ^{103}Pd		X	X	X	
[47]	modC	Plaque Simulator	^{125}I, ^{103}Pd		X		X	
[48]	C,SP	Plaque Simulator, TLD, radiochromic film	^{125}I		X		X	
[55]	GC	Manual calculation, TLD	^{125}I	X	X	X	X	
[51]	GC	Plaque Simulator	^{125}I		X	X	X	
[50]	GC,CI	MCNPX	^{125}I, ^{131}Cs	X	X		X	
[56]	GC	Plaque Simulator, Geant4	^{125}I	X	X	X	X	

[a]C, COMS; CI, COMS backing, non-standard insert; GC, Gold alloy custom plaques; modC, Modified COMS; SP, Slotted plaques; SS, Stainless Steel backing.
[b]Study method (calculation algorithm(s) and/or measurement approach): MCNP5, Monte Carlo N-Particle 5; MCNPX, Monte Carlo N-Particle X; TLD, thermoluminescent dosimeter.
[c]Radionuclide(s); 1, single seed in plaque; > 1, multiple seeds in plaque.
[d]Results obtained using following conditions: Homo: "homogeneous" water; Pl. het.: plaque heterogeneity; Full het.: plaque and patient tissues heterogeneity.

gold alloy seed guide. Doses for a 14 mm COMS plaque backing fully loaded with ^{125}I seeds were compared with the Silastic insert and with the seed guide (no Silastic); both dose distributions were normalized to achieve the same prescription dose at the tumor apex (5 mm from the inner sclera). The central axis had lower doses within the tumor by up to 10% with the seed guide compared with the Silastic insert.[45] In contrast, doses beyond the tumor were up to 11% higher with the seed guide (see Table II in Astrahan et al.[45]). Lesperance et al. modeled a 16 mm COMS Modulay plaque with (^{125}I, ^{103}Pd, or ^{131}Cs) single or multiple sources affixed to the backing with a thin layer of acrylic (no Silastic).[102] A single source at the plaque center is associated with a small dose enhancement near the plaque, and the opposite side of the eye from the plaque had dose reductions of 6% (^{103}Pd), 10% (^{125}I), and 12% (^{131}Cs) relative to the same source in homogeneous water.[102]

2.A.3. Modified COMS plaques

Modifications have been made to COMS plaques for specific indications: for example, the Mayo Clinic Rochester treats iris melanoma with a plaque where an inner lip surrounds a 10 mm diameter cut-out region at the plaque center and plaques span arcs of different possible lengths to conform with the tumor extent.[46] In 2010, Thomson et al. used the EGSnrc user-code BrachyDose to perform Monte Carlo simulations of the iris plaques containing ^{125}I or ^{103}Pd seeds; dose distributions were compared to TG-43 calculated doses and doses calculated for plaques representing those employed by Finger (brachytherapy seeds directly affixed to the COMS plaque backing with no Silastic insert)[44] and by Shields et al. (gold alloy backing with no collimating lip or insert).[53,111] Although doses calculated using the TG-43 approach were identical for any of the plaques containing the same configuration of seeds of the same type, actual dose distributions differed markedly from each other and from those calculated using TG-43.[46] The main effect of all considered plaque models is a dose reduction compared to TG-43-determined doses (within the eye and surrounding tissues) due to the plaque's presence. Dose reductions were most significant for the iris-modified COMS plaques which contain a Silastic insert: Plaques with a Silastic insert had dose reductions of 20–22% at the eye wall opposite the plaque whereas Finger and Shields group plaques at the same location had reductions of 5–10%.[46] The iris-modified COMS plaques have inner and outer collimating lips that substantially collimate radiation, sculpting dose distributions and reducing doses to critical structures and surrounding tissues; doses to ocular structures differed by up to 70% compared with TG-43 calculations.[46]

2.A.4. Slotted plaques

Astrahan et al. reported on both calculations (using an early version of Plaque Simulator) and measurements for prototype USC slotted plaques, which employ a gold alloy backing with ^{125}I seeds placed in individual collimating slots.[48] The collimating effect of the slots within the plaque was demonstrated qualitatively using radiochromic film.[48] Plaque Simulator calculation accuracy was demonstrated with TLD measurements. The authors[48] reported that the slotted plaque improved dose homogeneity within the tumor, reduced scleral dose more than COMS plaques, and reduced doses to normal ocular tissues. Lesperance et al. modeled a slotted plaque,[102] and confirmed differences in dose between the two calculation methods: the sclera received significantly reduced doses for ^{125}I, ^{103}Pd, and ^{131}Cs seeds; and the globe received significant collimation of radiation dose compared with TG-43 calculations and other plaque models.

2.A.5. Gold alloy custom plaques

Gold alloy plaques with shorter collimating lips than COMS plaques and no Silastic insert are employed for eye plaque therapy.[52,55] For example, plaques with sources affixed directly to the plaque backing by an adhesive are employed at the Cliniques Universitaires St-Luc (UCL), Brussels, Belgium.[52] Clinical treatment planning for UCL plaques is carried out using Plaque Simulator; dosimetry for these plaques has been validated by measurements made at the National Institute of Standards and Technology (NIST) using solid-water eye phantoms with TLDs and alanine detectors.[112] Lesperance et al.[102] modeled a similar plaque with a Modulay backing, a thin acrylic insert, and 1.5 mm long collimating lips: these plaques contained thirteen ^{125}I, ^{103}Pd, or ^{131}Cs seeds in a water phantom, and showed a dose enhancement near the plaque on its central axis relative to TG-43 calculations but a dose reduction at the opposite side of the eye of 8% (^{125}I), 5% (^{103}Pd), and 11% (^{131}Cs).

Some clinics treat with plaques consisting of a gold alloy backing and no collimating lip, e.g., the plaques used at Helsinki University Central Hospital in Finland[51] and the "Nag" plaques.[49] Zhang et al. compared dose distributions for 16 mm OSU-Nag and COMS (backing only; no Silastic insert) eye plaques using Monte Carlo simulations; doses to the sclera near the plaque were 10% for ^{125}I (^{131}Cs: 12%) higher and doses to the retina at the opposite side of the eye from the plaque were 6% for ^{125}I (^{131}Cs: 3%) lower for the OSU-Nag plaque than for the COMS (no Silastic insert).[50] Lesperance et al.[102] modeled a Modulay plaque with no collimating lip but with a Silastic seed carrier (representative of the plaques described by Puusari et al.[51]) loaded with thirteen seeds. They[102] reported that the ^{125}I, ^{103}Pd, and ^{131}Cs sources presented dose decreases for the plaque in water relative to TG-43 calculations of 2%, 6%, and 1% on the central axis near the sclera, respectively and 11%, 10%, and 13% at the opposite side of the eye to the plaque, respectively.

2.A.6. Plaques with stainless steel backing

Plaques with stainless steel, rather than gold alloy, backings are used in clinical practice.[56,57] Granero et al. reported

on Monte Carlo and also Plaque Simulator calculations for the 15 mm ROPES plaque, which is comprised of an acrylic insert containing ten ^{125}I seeds within a stainless steel shell.[56] Monte Carlo simulations were performed for a plaque at the center of a 30 cm diameter water sphere and a simplified patient geometry consisting of a water head plus head-air interface, with the plaque placed at the eye's posterior. The authors[56] reported that the main dosimetric perturbation of the plaque was due to the stainless steel backing which collimates radiation; the acrylic insert was not found to significantly affect dose distributions. The effect of the air interface was generally not significant. Lesperance et al. modeled a plaque similar to the ROPES plaque[56] and that documented by Karolis et al.[57] for one seed at the center of the plaque.[102] They reported[102] that dose reductions for the plaque in water relative to TG-43 calculations were 11%, 6%, and 14% for ^{125}I, ^{103}Pd, ^{131}Cs sources, respectively, at the opposite side of the eye from the plaque.[102] These single-source dose reductions relative to TG-43 calculations are not as substantial as those for the COMS plaques (16%, 20%, and 18% for ^{125}I, ^{103}Pd, ^{131}Cs sources, respectively).[102]

2.A.7. Acrylic plaques

The British Columbia Cancer Agency has a unique practice: ^{198}Au seeds in acrylic plaques are used for ocular brachytherapy.[21] The acrylic plaques have a groove around the periphery where up to 22 ^{198}Au sources are embedded in dental wax; one or two central seeds are also optionally used. Treatment planning is carried out with in-house software using the energy-absorption build-up factor method (documented in Appendix B of the 1995 TG-43 report[107]). Point-source calculations using the energy-absorption build-up factor method and the particular parameter values used to model the ^{198}Au seeds give results that are within 5% of the 3D calculations [Spadinger, private communication to R. Thomson, 2012] based on TG-43 parameters published for the ^{198}Au seeds by Dauffy et al.[113]

2.A.8. Diverse plaque models considering patient heterogeneity effects and anatomy

The heterogeneity corrections described above focus on the plaque heterogeneity. A complete accounting of the delivered dose also needs to consider the effects of ocular media on dose distributions and/or variations in dose due to patient-specific ocular anatomy (as opposed to a stylized or generic eye model).

Thomson et al. reported that the dose decreases in the eye region due to the presence of orbital bone, and up to 8% differences in dose occurred in phantoms with eye tissue and air replacing the water.[96] Lesperance et al. developed a representative computational model of the human eye, including geometries and elemental compositions of ocular structures, and used it for Monte Carlo simulations of eye plaque brachytherapy with COMS[60] and other eye plaques.[102] Mass energy-absorption and attenuation coefficients of ocular media were found to differ from those of water by as much as 12% in the 20 to 30 keV photon energy range. For example, mass-energy absorption coefficients for the tumor tissue were up to 10% higher than those for water, while for scleral tissue they were up to 12% lower than for water. Doses from simulations of the plaque in the representative computational eye model showed considerable differences to doses for the heterogeneous plaque in homogeneous water or seeds in homogeneous water (i.e., TG-43 dose calculation formalism).

Tien et al quantified the dosimetric impact of incorporating CT-derived patient-specific models as opposed to the conventional stylized-standard model for treatment planning but approximating all patient tissues as water. They concluded that patient-specific modeling should be used for clinical planning, particularly for cases with <6 mm between the target and optic disk.[114]

2.B. Beta-emitting sources

Currently, Eckert & Ziegler BEBIG (Berlin, Germany) is the only manufacturer of beta radiation emitting ophthalmic applicators commercially available in Europe and North America. Sixteen ^{106}Ru ophthalmic applicators of different sizes and geometry are available to accommodate various tumor locations (including proximity to normal eye structures, e.g., optic nerve and iris). As shown in Fig. 3 the physical plaque diameter D is offered from 11.6 to 25.4 mm, the total plaque height H from 2.3 to 8 mm, and the radius of plaque curvature R from 12 to 14 mm. The distance from the edge of the encapsulated radioactivity to the physical edge of the plaque is approximately 0.75 to 1.0 mm, depending on plaque model. The core of the ^{106}Ru eye applicator is a foil coated with ^{106}Ru/^{106}Rh, which is encapsulated within pure silver (Fig. 3); the thin silver coating covering the radioactive surface is delicate and must be carefully handled, such as only by the edges with very light pressure. Commercially available ^{106}Ru plaques are limited to 50 sterilization cycles.

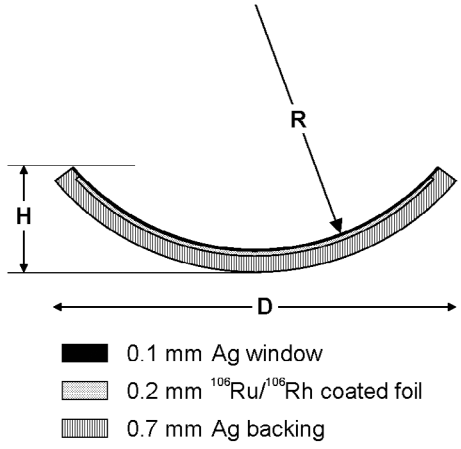

FIG. 3. Structure of ^{106}Ru ophthalmic applicators in sectionnal view. Nominal plaque dimensions are given by the inner radius R, total height H, and diameter D.

In addition, the ~1 yr half-life of ^{106}Ru restricts the useful life of the source, which is defined as 18 months in the instructions for use. After 12 months, the treatment team should assess the minimum dose rate to assure therapeutic dose delivery.[67]

The dose distributions of ^{106}Ru applicators have been measured with different detectors: radiochromic films,[84,115] a p-type silicon detector,[116] extrapolation ionization chambers,[73,115,117] magnetic resonance imaging of BANG polymer gel,[89] TLDs,[73] alanine pellets,[73] a small-volume ionization chamber,[73] a diode detector,[73] a diamond detector,[73] a scintillation dosimetry method,[88] and plastic scintillators.[73,87,118–121] Flühs et al developed dosimeters for beta sources based on plastic scintillators:[87] these detectors consist of a tissue-substituting scintillator probe, an optical fiber light guide, and a photomultiplier tube. With these detectors, a real-time three-dimensional (3D) dosimeter using a multichannel detector system has been developed for eye plaque dosimetry and dosimetric treatment optimization.

In 2001, Soares et al.[73] published an international comparison on the dosimetry of three beta-emitting ophthalmic applicators (planar applicators of ^{90}Sr/^{90}Y and ^{106}Ru/^{106}Rh, and a concave applicator of ^{106}Ru/^{106}Rh). The measurements involved radiochromic film, TLDs, alanine pellets, plastic scintillators, extrapolation ionization chambers, small fixed-volume ionization chambers, a diode detector and a diamond detector. The various methods yield absolute dosimetry results at a 1-mm reference depth with a relative standard deviation of measurement ranging from 10% to 14% depending on the source applicator. For depth-doses relative to 1 mm along the source axis at depths of 5 mm or less, the relative standard deviation of measurement was 3%–9% depending on the source applicator, dose gradient, and depth in phantom. Crucial to the proper interpretation of the measurement results was an accurate knowledge of the detector geometry, that is, sensitive volume and amount of insensitive covering material.

Kirov et al. developed a fast 3D dosimetry method based on the observation of scintillation light from an irradiated liquid scintillator volume serving simultaneously as a phantom material and as a dose detector medium.[88] This method was used for ^{106}Ru eye plaque dosimetry but was found to be inaccurate very near the periphery of the plaque and further than approximately 10 mm away (<10% central axis depth dose) from the plaque surface.[88] Eichmann et al.[121] developed a new measurement device with a plastic scintillator which can be used to measure the surface dose rate of ophthalmic applicators (at a small distance between the applicator and the detector). This device allows for a high density of measurement points in addition to complete and gapless coverage of the applicator. The uncertainty in the dose rate in terms of absorbed dose to water is <7%. This work has been extended to measure 3D dose distributions for a variety of brachytherapy source models.[122]

For theoretical absorbed dose to water calculation for ^{106}Ru plaques, the Monte Carlo method is considered the most accurate.[58,84,95,100] Cross et al.[95] performed an international comparative study (ICRU72[123]) that involved several independent users and a variety of MC codes (ACCEPT3.0, EGS4, MCNP4B, GEANT3) on the CCB type applicator. Some differences in calculated doses among the codes were found, and the authors attributed these differences to variable ability of the codes to model the geometry of the ^{106}Ru semi-spherical source. Mourtada et al. performed MC simulations for the ^{106}Ru CCB plaque placed on an eye model with a tumor and air-tissue interface for comparison with an external beam approach using protons.[100] Hermida-López et al. reported MC results using the PENELOPE-2008.1 code for 12 commercially available ^{106}Ru plaques and compared depth dose and lateral dose with a few plaque results published in the literature.[58] Similarly, Brualla et al. used PENELOPE to simulate dose distributions from two applicator models and project them onto tomographic scans of a patient's eye.[124] ICRU72 indicates that MC dose calculations for beta particle sources has an overall uncertainty on the order of 3–4% (k = 1).[123] The aforementioned MC results are for idealized sources with uniform radioactivity distributions. Actual sources may have non-uniformities in the radionuclide distribution that might influence relative depth dose profiles, and thus MC results that assume a uniform activity distribution should be used for guidance only and should not be used in place of dosimetry measurements.[70,125]

Other theoretical beta particle dose calculation methods include point-source kernel integration that has limitations near heterogeneities such as the plaque itself.[91] The patch source model has improved on the point-source kernel method and was implemented by Astrahan in the Plaque Simulator TPS via aggregating 300 to 1,000 overlapping "patch-like" source kernels (i.e., small disk-shaped sources) to determine dose to a point.[126]

In addition to ^{106}Ru, a few authors have reported use of ^{90}Sr-loaded plaques for treatment of choroidal melanoma.[23,127] Van Ginderdeuren et al. reported on 18 yr of experience using a modified epibulbar ^{90}Sr surface applicator sealed with 0.1 mm Pt;[127] a total of 98 eyes were treated with durations ranging from 0.5 h to over 3 h.

3. QUALITY MANAGEMENT & ASSURANCE PROCESSES FOR OCULAR PLAQUE BRACHYTHERAPY

A quality management program seeks to provide a comprehensive process for ensuring high-quality, safe, and patient-centered care. The process for establishing a quality management program includes detailed and documented QA, quality control (QC), and quality improvements (QI). Quality control is defined as the portion of quality management focused on fulfilling quality requirements, while QA is defined as the part of quality management focused on providing confidence that quality requirements have been fulfilled. While these concepts are very similar, the intent is for QC to focus on the outcome of the process, while QA provides a systemic review of the various steps in the process to mitigate errors and support quality. QI occurs after the process is reviewed and changes are implemented to improve the

reliability of the process. Many clinics practice QI by observing a process, implementing a change to improve the process, and then observing the outcome of the changed process to assure improvement.

While these concepts may sound abstract, in practice they are very familiar to the field of medical physics. For example, an end-to-end test is an effective way to evaluate the outcome of a process; however, there are few end-to-end tests available to clinicians practicing brachytherapy. Irradiating an anthropomorphic phantom on a linear accelerator for review by an external auditor is an example of QC for external beam radiotherapy, but there is no current analog for brachytherapy. Assessments of the individual steps or components in the treatment process represent QA, and specific examples include independent measurement of source strength, assessment of dedicated imaging equipment, and treatment planning system verification. Each of the components in a process that were evaluated by QA support overall quality, but QC is still helpful toward examining the combination of all of the underlying processes.

Along these lines, quality investigations may be constructed to support eye plaque brachytherapy. In this section, separate discussions are presented to provide input, guidance, and suggestions to those looking to establish an ocular brachytherapy program with an associated quality management program. These discussions include radiation safety concepts, source calibration methodologies, ophthalmic applicator testing, TPS commissioning, and medical imaging considerations.

3.A. Quality management program

Quality delivery of radiation therapy is dependent on organizational aspects that go beyond QA tasks. This point is underscored in the AAPM TG-100 report in a generalized sense for radiation therapy.[128] Like other radiotherapy modalities, a formal quality management program should be established for ocular brachytherapy, as recommended in the TG-129 report,[11] and in the 2014 ABS consensus guidelines.[67] A quality management program should include an institution-specific process map or a process tree, as well as a fault tree analysis (FTA) and a failure modes and effects analysis (FMEA). Prospectively identifying potential problems through preparation of an FTA and FMEA will benefit both the patient and the institution. Process maps, FTA, and FMEA for COMS plaque treatments based on institutional experience have been presented.[129,130]

Figure 4 depicts an example of a process tree for an eye plaque brachytherapy program. The key events that occur for the brachytherapy procedure are indicated. The process tree should be developed to identify an exhaustive list of procedure-associated tasks, responsible parties, and sensitivities to errors. Through this analysis and preparation of a fault tree analysis, the process tree and the associated procedural quality should improve through an iterative process. While the example process depicted in Fig. 4 is for a photon-emitting plaque, the process tree may be adapted for ^{106}Ru sources. For example, a calibrated ^{106}Ru plaque already in inventory would not require steps 5, 6, and 7. Similarly, the use of ultrasound, transpupillary illumination or other placement techniques (within Step 10) would be specific to institutional practice, and the example process tree could be appropriately adapted to reflect different institutional practices.

Figure S1 is an example of a realistic clinical process tree. Figure 4 and/or Fig. S1 serve as a useful template, with specific steps and techniques varying for each institution. Additionally, the process tree and FMEA analysis of Lee el al. may serve as a guide.[130] While process maps, FTA, and FMEA may be applied by any institution to improve clinical practices, it is important to note that the application of the principles of AAPM TG-100[128] are not required by other professional societies at this time. For example, the AAPM TG-100 report[128] is currently being adopted in North America, while ESTRO has different recommendations and standards for quality management/ process improvement.

3.B. Radiation safety

Ocular brachytherapy relies on manual loading of plaques containing encapsulated radioactivity. After a process tree has been delineated (e.g., Fig. 4), the clinical treatment team should review the entire treatment process and assess the potential for radiation exposure and for the security of radioactive materials. The institution will generally be required to have a radioactive materials license, which may further govern the operational requirements. These guidelines shall be individually assessed for the institution, implemented as needed, and documented by the clinical treatment team. Considerations should include shipping and receiving of radioactive material, secure storage of radioactive material, guidelines for temporary implants of radioactive material, disposal of radioactive sources, radiation exposure limits to staff,[131,132] and radiation exposure limits to members of the public, among others.

Specific regulations and requirements will vary on a state-to-state basis in the United States and on a country-by-country basis in the European Union and elsewhere. Medical physicists or appropriate surrogates shall consult the pertinent governing agency to identify the applicable regulations, as some considerations below will not apply in some regions or countries. This report is not intended to replace or summarize specific regulatory requirements, nor is it inclusive of all potential radiation safety considerations.

3.B.1. Radiation workers and protective equipment

It is important for clinical staff to minimize exposure to radiation through appropriate use of ALARA practices (*A*s *L*ow *A*s *R*easonably *A*chievable — using time, distance, and shielding concepts). Manipulation of plaques, for example, source handling and/or loading, should be performed behind leaded glass using long handled forceps. Further use of protective equipment could be considered, for example, leaded glasses and/or shielded hoods. All radiation workers should

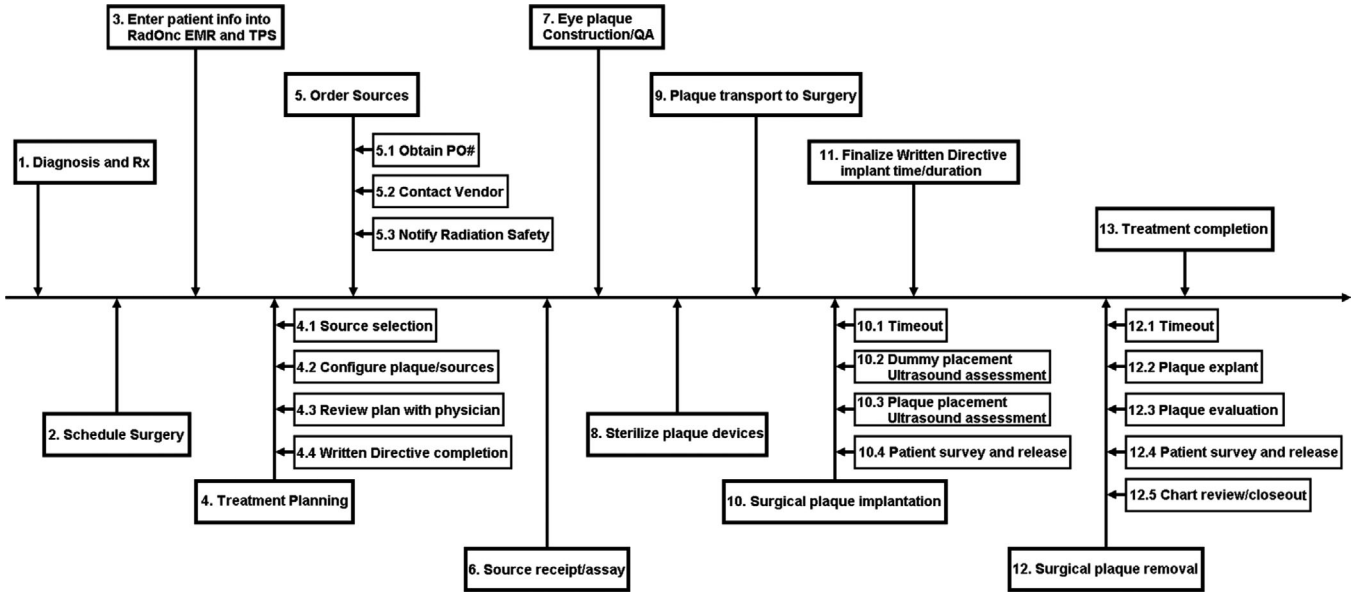

FIG. 4. An example process tree for an ocular brachytherapy program that highlights the main events of a procedure using photon-emitting sources at one institution. A similar process tree could be constructed for beta-emitting sources and/or other institutional practices. Events are ordered chronologically, proceeding from left to right. Rx, prescription; EMR, electronic medical record; PO#, purchase order number.

be provided personnel dosimeters including a ring badge to allow estimation of extremity dose for those handling the sources or radioactive plaques, and workers should receive regular training for source and radioactive plaque handling policies, pertinent regulatory requirements, and good practices. Any individual that may handle the radioactive plaque, even if it is within a shielded safe, should be properly trained. Furthermore, any medical professional that may care for a patient with implanted radioactive materials should receive appropriate and regular training, for example, nurses and environmental services staff. Written procedures for handling and transport of radioactive plaques should be available for each person involved at any point of the entire process.

Radiation workers need to have access to detection equipment capable of locating radioactivity and quantifying radiation fields and materials. Geiger-Müller tubes and NaI detectors may be used to identify low levels of radioactivity, and ionization chambers should be used to quantify radiation levels. Care should be taken to ensure that these detectors are available and calibrated per local standards for the low-energy sources typically used in ocular brachytherapy. To prevent contamination from a leaking source, the clinical treatment team should have access to and utilize a wipe testing system that is capable of detecting the minimum amount of loose radioactivity specified by governing regulations. Wipe tests may also be required for shipping and receiving of radioactive material. As noted above, all pertinent regulatory requirements should be reviewed and implemented to assure compliance with the governing regulations.

3.B.2. Radioactive materials work areas

Photon-emitting plaques should be loaded with sources in a dedicated room designated for handling radioactive materials. Depending on the radionuclide and proximity to non-radiation workers, it may be beneficial to use a shielded workspace. For both photon and beta plaques, work areas should be free of clutter and separate from high-traffic locations. In particular, source storage and handling areas should not be accessible to non-radiation workers. It is standard practice to perform a radiation survey of the room before and after source handling to detect potentially misplaced sources. Wipe tests can also be used to routinely survey work spaces, storage areas, and operating or procedure rooms. Work areas may have additional requirements regarding cleanliness/sterility, including tools used for plaque handling/assembly and the plaque components to be implanted. The clinical treatment team should consult with an expert trained in sterile processing services to evaluate proposed assembly areas. This consultation builds confidence that the assembled plaque can be clean and sterile leading up to the implant.

The shielded container holding the radioactive plaque should be labeled with the patient name, plaque size/model, radionuclide(s), total source strength, and dates of application and removal. It is also good practice to include contact information in the event that the container is misplaced. Note that local regulations may provide specific requirements regarding labelling, and these requirements should be reviewed and adopted by the treatment team. In addition, maintaining a log is often necessary to track source and ophthalmic plaque movement. This record may be kept in the source room and would be updated to indicate when a source or radioactive plaque leaves the room and after it returns. The radioactive plaque is transferred by an authorized person from the storage room to the operating room or the sterilization department using a shielded container marked with appropriate radiation safety labels. The optimal shielded container is compatible with the sterilization process, for example, the container is

vented to allow steam or gas sterilization. It is important to keep in mind that regulations regarding security and storage of radioactive sources are applicable during sterilization. As such, a standard operating procedure should be defined and regular training given to personnel that may not be accustomed to handling radioactive material.

Prior to initiating the procedure, the implant team should perform a time out to verify the patient, the treatment site, and the procedure. Depending on the specific clinical practice and governing regulations, the radiation oncologist may be present to apply the plaque or oversee the placement. The clinical physicist, or their designate, may also attend the procedure to ensure conformance with the written directive and treatment plan, as well as to perform radiation surveys. After the implant is complete and the patient has left the operating room, the room and ophthalmologist's tools should be surveyed for radioactive contamination. The results of this survey should be appropriately documented. Items that entered the sterile field during the procedure need to be cleaned to remove biological contamination.

When the patient returns for plaque removal, the ophthalmologist will remove the plaque and place it in a shielded container. The subsequent steps will strongly depend on the type of radioactive implant, the practices around radioactive materials storage, and the practices around biologically contaminated materials. For an applicator loaded with encapsulated sources, the plaque and associated components can be surveyed for radioactivity and then sent for cleaning and sterilization. Due to biological contamination of the plaque, it may be preferable to extract the sources near the operating room and sterilization department to allow immediate biological cleaning of plaque components. For an applicator with integrated radioactivity (e.g., ^{106}Ru plaques), the plaque and source integrity are checked by visual inspection and wipe tested if necessary. For ^{106}Ru plaques, the source manufacturer recommends a specific wipe test procedure in their instructions for use.

The sources should be placed in a shielded container, returned to a radioactive materials storage area, and be prepared for storage or disposal. The collected sources are counted and their output may be checked before storage. If allowed by local regulations, sources to be used in a subsequent implant should be decontaminated and sterilized prior to implanting in another patient. An inventory log is generally kept to count sources going out of and coming into the storage area.[133]

Depending on the local governing regulations, end of useful life sources (photon seeds and ^{106}Ru applicators) may be decayed in storage, sent back to the vendor, or disposed of as radioactive waste. When the source strength of the seeds (photon plaques) and ^{106}Ru plaques is too low for treatment, the seeds or plaques should be disposed of in compliance with governing regulations. Depending on regulations governing radioactive waste, the sources may be allowed to decay-in-storage to background levels prior to disposal in the regular waste. For sources with longer half-lives, alternative disposal plans may be required.

3.B.3. Patient considerations

Prior to administering plaque brachytherapy, the patient should be provided information about radiological concerns related to the implant. These discussions should include radiation dose considerations for the patient, for close relations (e.g., family members), and members of the public. After plaque implantation, a radiation survey meter is used to survey the patient and to survey the operating room. Generally, no special radiological precaution is required and no shielding is necessary for the patient while the implant is in place. However, a high-Z eye patch may be worn to decrease radiation exposure near the patient while discharged.

In the inpatient setting, that is, when the patient is admitted to the hospital for the implant duration, the treatment team has direct oversight of radioactive material management. The inpatient team should receive annual training that minimally includes basic radiation safety principles, emergency procedures training, and review of pertinent regulatory issues. Local governing regulations and institutional practices will dictate whether personnel dosimeters are required for these workers, although it is recommended. In the outpatient setting, the clinical treatment team has to educate the patient regarding radioactive material management. It may be necessary to discharge the patient with an informational card that documents the radionuclide, source strength, and emergency contact information if the plaque is accidentally displaced. Policies and practices should be created to ensure that patients discharged with temporary radioactive implants can be managed within regulatory compliance.

3.B.4. Wipe test requirements for beta-emitting plaques

Wipe tests are required to localize loose beta-emitting radioactivity for ^{106}Ru sources. Unlike sealed photon-emitting sources that are generally encapsulated in a welded metal container, the active source material in a beta-emitting plaque is typically encapsulated under a delicate silver overlay. If a beta-emitting plaque appears damaged or discoloured during visual inspection, a wipe test should be performed. A wipe test should also be performed upon surgical removal to ensure the integrity of the protective layer. If the surgeon suspects that damage or leakage could have been caused by surgical instruments, s/he should immediately inform the clinical medical physicist or responsible health physicist present who should visually inspect the plaque. In addition, the surgical instruments and patient should be surveyed for radioactivity. Contamination should be removed and contained prior to releasing the patient, sterilizing the surgical equipment, and clearing the operating room to limit the spread of contamination. Before use in a subsequent patient, the clinical medical physicist shall repeat the standard acceptance tests (Section 3.D.1) to assure the plaque is suitable for clinical use.

3.C. Source calibration methodology

3.C.1. Photon-emitting sources

As recommended in the joint AAPM/ABS TG-129 report,[11] the AAPM Report 98 by Butler et al.,[134] and the European reports,[123,135,136] an in-house clinical medical physicist or his/her assigned designate needs to measure and document photon brachytherapy source strength preceding clinical use. Numerous AAPM reports state the need for this independent assay to be performed, including TG-40,[137] TG-56,[133] and TG-64.[138] Thus, in order to commission a photon-based ocular brachytherapy program, it is necessary to develop an in-house process for source calibration.

In the U.S., the recommended quantity for brachytherapy source strength (photon-emitting sources) is air kerma strength (S_K) with designated unit U, which has units of cGy h^{-1} cm^{-2}.[108] In Europe, the recommended quantity for source strength is the reference air kerma rate (RAKR), which is equivalent to air kerma strength and has units of Gy/s or μGy/h for LDR brachytherapy sources.[136,139] Generally, all brachytherapy sources marketed in North America have calibrations that are NIST traceable. In Europe, calibrations are traceable to a primary standard dosimetry laboratory (PSDL) or a secondary standard dosimetry laboratory (SSDL); a list of approved SSDLs is available at http://www-naweb.iaea.org/nahu/dmrp/SSDL. In the U.S., traceable calibrations are transferred via Accredited Dosimetry Calibration Laboratories (ADCLs), which are accredited by the AAPM. To assure traceability of the NIST calibration standard, source manufacturers are required to comply with recommendations of the AAPM Calibration Laboratory Accreditation Subcommittee.[140] Manufacturer compliance assures that accurate NIST-traceable calibrations are implemented in the U.S.

Measurements of brachytherapy source strength must be performed with a system that has *direct traceability* or *secondary traceability* to the NIST standard.[133] For a majority of institutions, traceability will be obtained through calibration of a traceable re-entrant well-type ionization chamber by an ADCL. Recommended quality assurance tests for well chambers are summarized in Table IV of the TG-56 report.[133] An alternate yet acceptable method as outlined in the TG-56 report[133] is for the user to obtain a source from the manufacturer having traceability to the NIST, and to calibrate the clinic well chamber or a dose calibrator. Dose calibrators have the advantage of being more sensitive than well chambers and insensitive to temperature and pressure variations, yet require regular demonstration of such insensitivity and use of a custom insert for reproducibly positioning single sources at the center of the collecting volume. Additional recommendations for QA of measurement instrumentation are in the AAPM TG-40 report.[137]

Once a local value for source assay is established, a procedure is needed for implant-specific considerations, which is based on the number of sources in the plaque. Butler et al.,[134] presented revised calibration recommendations of the TG-40 report[137] for low-energy photon-emitting sources in both sterile and non-sterile source assemblies. Butler et al. specified for loose sources that non-sterile assays should be performed on ≥10% of the order or 10 loose sources (whichever is larger). For sterile configurations, they recommended obtaining and assaying the lesser of 5% of the total order or five non-sterile sources from the same source activity batch. In addition, Butler et al.[134] updated the TG-40 report recommendations and provided the actions required when the local clinical medical physicist observes source strength differences from the manufacturer's assay. While the TG-138 report recommended using the assay value obtained by the clinical medical physicist instead of the value on the manufacturer calibration certificate because the associated uncertainty would be lower with a traceable calibration standard,[141] certain clinical workflows may not permit this in regular practice. Therefore, any of the prescribed/ordered, manufactured/delivered, or received/assayed values of source strength may be used as long as the average values all fall within 5% of each other.

In Europe, ESTRO booklet No. 8 also provides guidance for quality control of brachytherapy equipment.[136] The booklet describes methods for measuring source strength which use either re-entrant well-type ionization chambers for high- and low-energy sources or air ionization chambers for measurements of high-energy sources in air or solid phantoms. For comparisons between institutional measurements and the source strengths reported by the manufacturer, the booklet[136] recommends tolerances of 3% for the mean of a batch of sources and 5% for individual sources. Another European standard is Report 20 of the Netherlands Commission on Radiation Dosimetry (NCS).[135] This report recommended use of a re-entrant well-type ionization chamber for institutional measurements of brachytherapy source strength, and adopted the recommendations of the 2008 AAPM Report 98[134] for the number of sources to measure. In agreement with ESTRO booklet #8,[136] Report 20 recommends a tolerance of 3% between institutional measurements and the source strength reported by the manufacturer for the mean of a batch of sources. However, the NCS 20 Report explicitly excludes a tolerance for individual sources as long as the tolerance for the mean of a batch of sources is not violated.[135] This latter recommendation is stated as being based on the observation that variations in individual source strength have a limited influence on the dose distribution for a permanent prostate implant using ^{125}I. As the volumetric circumstances for prostate brachytherapy differ in comparison to ocular brachytherapy, the current report maintains that each individual source needs to be within the tolerance, and not just the mean of the batch of sources.

Recommendations for traceable measurements in Europe of source strength for photon-emitting brachytherapy sources need to be taken in context of the available calibration infrastructure. The PTB (Physikalisch-Technische Bundesanstalt; The National Metrology Institute) in Germany is the only calibration laboratory in Europe with a primary standard for low-energy photon-emitting sources. They provide direct calibration services of hospital well chambers for use in the clinic. The National Physical Laboratory (NPL) in the U.K.

offers calibration services, but these are based on a secondary standard. The majority of European countries have no available calibration services through their National Metrology Institutes (NMIs). This lack of calibration infrastructure is undesirable and is not likely to change within the foreseeable future. Two alternative calibration methods are available to European medical physicists. In the first alternative method, the facility purchases a manufacturer-calibrated seed with a traceable calibration certificate from the manufacturer. The medical physicist and staff calibrate the hospital well chamber against this manufacturer-calibrated seed. While this approach is readily available, it is undesirable in that calibrations of subsequent sources obtained by the hospital are not performed entirely independently of the manufacturer, and the manufacturer's calibration uncertainties are not minimal. A second alternative calibration method available to European medical physicists is to have their measurement equipment (i.e., re-entrant well-type ionization chamber) calibrated by the equipment manufacturer, who may collaborate with brachytherapy source suppliers. This approach usually involves sending the equipment to an outside certified laboratory. This approach is also readily available, but the calibrations may not fully comply with PSDL traceability requirements. If a clinic is not willing to send their equipment to a laboratory offering traceable calibrations for independent determination of source strength from the source manufacturer certificate, then the first alternative calibration method should be followed and documented.

The current report generally recommends following AAPM recommendations already established for low-energy brachytherapy seed calibrations as described in the following reports: TG-40,[137] TG-56,[133] TG-129,[11] and AAPM Report 98.[134] They are briefly summarized here. The current report recommends that each institution measure photon-emitting brachytherapy sources preceding clinical use. Measurement instruments should have calibrations traceable to a PSDL, be calibrated with a frequency of no more than 2 yr, and use the specific radiation quality that matches the sources to be measured. For non-sterile assays of loose sources, >10% of the order or 10 sources (whichever is larger) should be assayed. For sterile configurations, the lesser of 5% of the total order or 5 non-sterile sources from the same source strength batch should be assayed. Tolerances of 3% and 6% are recommended for the mean of a batch of sources and for individual sources, respectively.[134] Sterile preloaded ^{125}I plaques are available on the market. Clear guidance regarding source calibration for those plaques is available in TG-129.[11] TG-221 strongly encourages the assay of all sources used in an ocular implant. Because of the relatively small number of sources typically used, the relative dose contribution of a single source can become significant.

3.C.2. Beta-emitting sources

As for photon-emitting brachytherapy sources, AAPM recommendations imply that beta-emitting sources should be assayed also for dose output preceding clinical use. Historically, planar ^{90}Sr sources were calibrated in terms of surface absorbed dose rate. This fundamental difference with photon sources greatly complicates measurement procedures. Although the primary standard for these calibrations in the U.S. was at NIST[142] and most clinical calibrations were performed at the University of Wisconsin ADCL, the NIST primary standard is no longer supported. Beta-emitting plaques come with calibration values provided by the manufacturer, which have been compared with NIST values in a past survey.[143] Unlike photon sources, beta particle source strength is not specified in terms of S_K or RAKR. Hence, to characterize the strength of a beta-emitting plaque, clinicians should use the traditional source activity unit of contained mCi or MBq in treatment records. The output of a beta-emitting plaque should be described in terms of reference dose rate at a depth dependent on the source geometry. The contained source activity should be noted supplementary in treatment records.

Concave ^{106}Ru beta-emitting sources for treatment of ocular disease are calibrated in terms of absorbed dose rate at a reference depth of 2 mm in water. If measurements cannot be performed at this reference depth, clinical medical physicists may interpolate a value from measurements at various depths in appropriate phantoms. Extrapolation beyond the range of measurement is not advised. A small volume detector allows for precise localization and dose measurement in regions with steep dose gradients near the source, while minimizing perturbation of the beta particle radiation field. Considerations for such measurements are discussed in recommendations of international documents.[70,123,144]

Unfortunately there are significant barriers that challenge quantitative dose measurements of ^{106}Ru plaques in the clinical setting. For example, the plaque geometry precludes measurements with ionometric methods at clinically relevant distances; however, recent research by Hansen et al. has explored the use of a windowless extrapolation chamber to directly measure the output of a curved beta-emitting plaque.[145] Currently NPL offers the only available NMI primary calibration service for beta-emitting sources. The calibration service is performed using 5 mm diameter by 0.5 mm thick alanine pellets in stacks whose calibration is based on the NPL absorbed dose standard. Furthermore, there are no commercially available dosimetric eye phantoms or scintillator detectors to facilitate routine measurements of ophthalmic sources. These limitations substantially challenge the clinical medical physicist to validate the manufacturer calibration certificate. In many European clinical settings where these sources are used, clinical sites utilize the sources without independent source assay, which is in compliance with the GEC-ESTRO brachytherapy committee (GEC-ESTRO) standards for beta-emitting sources.

As stated in the AAPM TG-40 report,[137] sources without (inter)national standards should be calibrated using a local standard with traceability to a primary standard. Because the institution has responsibility to verify the manufacturer calibration, it is important to evaluate the dose rate and assess dose uniformity of the plaque independently. As noted in

Section 2.B, Soares et al. measured absolute dose at 1 mm from the source surface of selected beta-emitting applicators using a variety of detectors.[73] Several of these techniques are appropriate for developing a local standard, but many are utilized in the practice of EBRT and may be available to the clinical medical physicist. The recommendations of TG-167,[146] a joint report of the AAPM and GEC-ESTRO, may provide additional guidance toward establishing a local calibration or constancy standard.

Finally, it is the responsibility of professional societies, institutions, and clinicians to reach out to vendors to demand appropriate QA equipment for quantitative dose measurements of these sources/applicators. Similarly, these organizations and caregivers should demand a traceable calibration service from NMIs to assure a standard-of-care equivalent to that of other radiation therapy treatment modalities.

3.C.3. Historical remark on the calibration of ^{106}Ru eye plaques

Ocular brachytherapy applicators with ^{106}Ru/^{106}Rh were first used by Peter Lommatzsch in the 1960s.[32,33] Since then, they have been used widely by many ocular oncologists, mainly in Europe.[147] Until May 2002, ^{106}Ru eye plaques were provided by BEBIG with energy dose-rate values in mGy min^{-1}, which were based on the calibration of the NMI of the former German Democratic Republic, the Amt für Standardisierung, Messwesen und Warenprüfung. These measurements were carried out with a 2 mm diameter and 2 mm thick plastic scintillator: the stated uncertainty was 30%. However, differences exceeding a factor of two were observed relative to the manufacturer's stated dose-rate values on the plaque central axis.[118,125,148,149]

In May of 2002, BEBIG started delivering plaques with calibrations traceable to the NIST, which obtained dosimetric data using in-water measurements with plastic scintillator systems as small as 1 mm diameter and 0.5 mm thick, as well as in-phantom measurements with small TLDs (2 mm diameter and 0.4 mm thick), and thin radiochromic film (Model HD810).[70] The latter two systems were calibrated in terms of absorbed dose using ^{60}Co reference beams at 5 cm depth in water. From these Ru transfer standards, BEBIG used a plastic scintillator with 1 mm diameter and 1 mm thickness from 2002 to 2005, then transferred to a 1 mm diameter and 0.5 mm thickness plastic scintillator in 2005. The stated uncertainty of the manufacturer calibration was changed to 20%. A number of eye plaques tested in 2004 using a radiochromic film demonstrated homogeneous dose distributions in the planes perpendicular to the central axis of the plaque and good agreement with the manufacturer's calibration values.[119,120] Simultaneous with changing the reference calibration, BEBIG issued recommendations suggesting changes to the prescribed doses in the form of multiplication factors based on ratios of the former to the new NIST-based dosimetry.[150] Consequently, the doses reported in many clinical publications[32–34,39,40,151–153] were based on the now-known erroneous calibrations, and their reported dosimetry results need to be reevaluated. However, clinics using internally measured source output data may not be subject to these calibration errors, and thus the correction factor (a multiplier) may not be necessary. Physicists should clarify the origin of data used in clinical calculations to ensure use of the correction factor only when necessary. More information on this topic can be found in the ISO 21439 standard.[70]

3.D. Applicator commissioning

3.D.1. Physical characteristics

Accurate determination of dose delivery requires high-precision dimensional characterization of the eye plaque and ocular globe. Compared to other non-osseous tissues in the human body, the globe is a rigid structure. Its convex surface curvature is not constant among patients, nor uniform at various positions when considering a single globe. Conformity of the plaque concave surface to the globe's convex surface is crucial for the delivered dose to match the planned dose. For example:

a Some plaque designs have a contiguous semi-spherical surface (e.g., COMS Silastic™, or BEBIG beta-emitting plaques). If treating an eye that has a rounder surface (or smaller diameter) than the plaque was designed for, then points on the globe near the plaque center may receive the planned dose due to direct plaque contact. However, points near the plaque periphery may receive less than the planned dose due to the geometric offset.
b Some plaque designs (e.g., Eye Physics, LLC, Los Alamitos, CA) have a circular rim that permits insertion of the globe beneath the rim. If treating an eye that has a flatter surface (or larger diameter) than the plaque was designed for, then points on the optical globe near the plaque periphery may receive the planned dose due to direct plaque contact. However, points on the globe near the plaque center may receive less than the planned dose due to the geometric offset. Points at depth will be similarly subject to these effects. Due to the steep dose gradients of episcleral plaque brachytherapy, clinically significant deviations from the intended dose may result. Without sub-millimeter characterization of the plaque and globe, there is no way to address the dosimetric effects of this mechanical coupling.

The TG-56 report recommends that applicator dimensions, integrity, and dosimetric properties be evaluated upon initial use, then annually thereafter.[133] Measurement of dimensions such as plaque diameter and depths can be made with a metric caliper for comparison to the manufacturer-reported dimensions. Agreement within 0.5 mm or better is expected based on the experience of the TG members. This tolerance is based on the measurement technique, and can be expected to be fixed for initial commissioning as well as annual checks of the plaque dimensions. For COMS-based plaques, the Silastic can be imaged with a flatbed scanner

and the dimensions and seed positions/orientations can be measured for agreement with the manufacturer-reported design within 0.2 mm and 10°. Note that the scanner may produce differing results along the detector axis, so rotating the Silastic 90° and repeating the measurement will obviate this effect. Plaque overall integrity is checked visually to identify any mechanical flaws or deviations from the manufacturer drawings. Visual inspections should be complemented with radiographic techniques, such as conducting a kV transmission test of plaque to assure functional shielding and reveal any non-visual issues. This is performed with fluoroscopy and radiographic film placed adjacent to the plaque. For pre-sterilized plaques available for rent, results of such tests can be requested from the manufacturer.

Most non-COMS applicators (photon and beta-emitters) are reusable, and efforts should be made to obtain complete understanding of their dimensions and the manner in which radiation is emitted.[154,155] For photon-emitting plaques, low-energy seeds are mechanically inserted into the plaque and secured with an adhesive, which can allow for a variety of component displacements.[156] For beta-emitting plaques, the electron-emitting radionuclide is part of the plaque design and not separable from the applicator. The clinical medical physicist should measure the applicator dimensions with a flatbed scanner or a digital camera, which will only validate results in a plane perpendicular to the plaque central axis (CAX). The effects of divergence or magnification should be considered. Other measurement systems, for example, a coordinate measuring machine, may also be used.[157] It is necessary to benchmark the measurement tool with calibrated distances on the sub-millimeter scale as those are needed for this task. With these dimensions in hand, comparison to a recognized standard may be a challenge since most of the plaque models included in this report do not have the requisite dimensions specified in the literature. For instance, only seed positions and orientations of the standard COMS plaques were included in the TG-129 report.[11] Constancy may be a more effective measure.

All sources and applicators should be examined for signs of wear or damage before and after use. Thorough cleaning and sterilization should be performed according to manufacturer specifications, when known. Physicists should identify the processes and make standard operating procedures for routine handling of plaque components. These considerations include cleaning plaque components, storage of plaque components, sterilization of assembled plaques, and storage of sterilized-assembled plaques prior to implant. Some components, such as the COMS Silastic insert, may pose challenges for reuse due to the porous nature of the material. Rubberized or elastomer components that cannot be properly and fully biologically decontaminated or cleaned prior to sterilization between patients should not be reused to minimize the risk for contamination (i.e., a condition of being actually or potentially in contact with microorganisms or tissue components).[158] The clinical treatment team should meet with a representative of the sterilization department to discuss the specifics of plaque assembly, sterilization, and decontamination. Due to the presence of radioactive materials, institutions should develop specific protocols for plaque construction in a clean area, plaque sterilization, handling of radioactive plaques during implantation and removal, plaque disassembly following an implant, and plaque cleaning prior to any subsequent implant. These policies should be formally approved and reviewed by all stakeholders at least annually and whenever there are changes to staff, components, or sterilization methods.

The integrity of plaques that contain seeds may be ensured on an ongoing basis with qualitative imaging or by checking that the assembled plaque is consistent with the expected or planned plaque. For example, one could perform a test in which the plaque is loaded with seeds and the loading consistency and pattern is checked annually by (for example) a reference image obtained by a magnified photocopy/scanned image of the plaque.[159]

Commissioning of ^{106}Ru eye applicators require a series of tests to be performed by the clinical medical physicist prior to clinical use. Most notably, each ^{106}Ru ophthalmic applicator has an engraved unique serial number, for example, CCB 1881, and the clinical medical physicist must check that the serial number engraved on the applicator and the serial number in the calibration certificate are identical. Subsequently, a visual inspection of the applicator must be carried out. A wet wipe test should be performed. The calibration certificate contains information on measured depth and surface dose rates, as well as contained radioactivity, which is needed for radiation safety, transportation, and other regulatory purposes.

3.D.2. Dosimetric measurements

Accurate dosimetry is important and hence a plaque's dose distribution should be validated by measurements made in clinical conditions. While measurements are challenging, some techniques and results have been reported in the literature. The ICRU Report 72 summarizes the different detectors and phantoms available for measurements with low-energy photons.[123] Dosimetric studies for various types of eye plaques have been reported (e.g., in Section 2 and references therein). TLDs have been used to measure the depth dose distribution along the transverse axis of a single seed in water equivalent phantom material.[55] A tissue-equivalent solid phantom material RE-1 (PTW-Freiburg, Freiburg, Germany) has been developed, and TLD measurements have shown that this material closely simulates the photon attenuation and scattering of the human eyeball for the ^{125}I spectrum.[160] A multichannel scintillator dosimetric device used with a special solid phantom and 16 tiny plastic scintillators allows the measurement of a 3D dose distribution of individual ^{125}I eye applicators prior to clinical use.[86] A silicon-pixelated detector operating in spectroscopy mode has been used for fast, real-time 3D dosimetric imaging of assembled eye plaques.[161] This prototype device can determine the dose distribution from plaques loaded with ^{125}I, and may be useful with other low-energy photon-emitting radionuclides such as ^{103}Pd and

^{131}Cs.[161] Measurements for dose-rate distribution of ^{125}I plaques as stipulated in the TG-129 report have used diodes,[79] X-Omat V radiographic film,[82] MD-55 radiochromic film,[48] and more recently GafChromic EBT3® film.[162]

^{106}Ru sources require the verification of source calibration discussed in Section 3.C.2, and TG-221 recommends that the clinical medical physicist take steps to verify the manufacturer-stated source uniformity and the relative depth dose profile, with the curve normalized at the reference point P_{ref}, using methods outlined in ISO 21439.[70] Specifically, the ^{106}Ru ophthalmic applicator manufacturer currently provides a certificate specifying the absorbed dose-rate curve as measured with a small plastic scintillator (diameter 1 mm, height 0.5 mm) in water on the ^{106}Ru ophthalmic applicator's central axis from 0.48 to 10 mm; and additional dose points may be measured or interpolated. As noted previously, extrapolation of measured data is not recommended, and estimates of scleral dose require a surface dose rate, which is challenging to obtain due to positional uncertainty and steep dose gradients.

Currently, only prototypes for measuring the dose distribution of a radioactive ophthalmic applicator although a number of systems have been described.[121,163] For example, an apparatus has recently been designed to guide a plastic scintillator detector across the applicator surface and has been used to determine the surface dose rate of ^{106}Ru applicators as well as ^{125}I plaques.[121] Similarly, depth-dose profiles have been measured using synthetic diamond and diode detectors.[163] Following these or similar examples, the clinical medical physicist can measure the dose distribution of ^{106}Ru ophthalmic applicator with small detectors (e.g., plastic scintillator or diamond detector) or alternatively, with radiochromic film. While radiochromic film could be used for qualitative assessments, the use of film to measure absolute dose rate will likely require construction of a phantom to accommodate a concave applicator. In addition to film measurements described by Soares et al.,[73] Trichter et al. described measurements using sensitive, thicker emulsion radiochromic films.[164] Heilemann et al. reported that a method using radiochromic film measurements for ^{106}Ru plaques could validate against MC simulation results as well as microdiamond and diode measurements.[165] Radiochromic films may be convenient as they can be calibrated in terms of absorbed dose to water using calibrated linac beams at reference depths in water.[166] Techniques used for other radionuclide sources may also provide helpful guidance. For example, Menon and Sloboda, and Deufel et al. described film-based measurements of beta-emitting applicators containing ^{90}Sr[167] and ^{32}P (EBT3),[168] respectively. Other detection systems include appropriately calibrated thin TLDs[73] and small plastic scintillators.[73,87,118] When evaluating these publications or performing similar measurements, it is critical for the investigator to consider the composition of detectors and phantoms, as they may not be radiologically equivalent to water.

Because of the inherent challenges described above, datasets from depth dose measurements with a scintillator and with radiochromic film are provided as examples of achievable accuracy in Figs. 5 and 6, respectively. Figure 5 provides scintillator-measured depth dose data acquired during acceptance testing in the University Hospital of Tübingen. Radiochromic film was used to characterize the depth dose curves displayed in Fig. 6, with the associated uncertainty budget for the measurement given in Table III. As mentioned in Section 2.B, published Monte Carlo results generally reflect an idealized source activity distribution and should not be used as a substitute for verifying source relative depth dose profiles for a specific applicator. Due to subtle variations in the manufacturing process and the steepness of the dose gradients, measured dose distributions are specific to the measured plaque and should not be generally applied to all applicators with a common model designation.

Following AAPM TG-55 recommendations,[169] Mourtada et al.[170] commissioned six different ^{106}Ru eye plaque applicators (2 of each model: CCB, COB, and CCA, manufactured by BEBIG GmbH) by using radiochromic film and a fabricated in-house hemispherical solid-water phantom. The film optical density (OD) to dose calibration used a NIST-traceable ^{90}Sr source. The reported overall measurement uncertainty was 11% (k = 2); see Table III for uncertainty budget. The absolute dose rate along the central axis for each source model was found to be within 10% of the manufacturer's reported values (see Fig. 6). All six tested plaques were found to have dose uniformity within 10% at a measured nominal depth of 2 mm from the inner surface of the plaque.

3.E. Imaging considerations for QA

Treatment simulation images are standard-of-care in most brachytherapy applications, and three-dimensional computed tomography (CT) and/or magnetic resonance imaging (MRI) datasets are used to guide both LDR and high-dose rate (HDR) brachytherapy treatments. This paradigm is generally not available in ocular plaque brachytherapy because

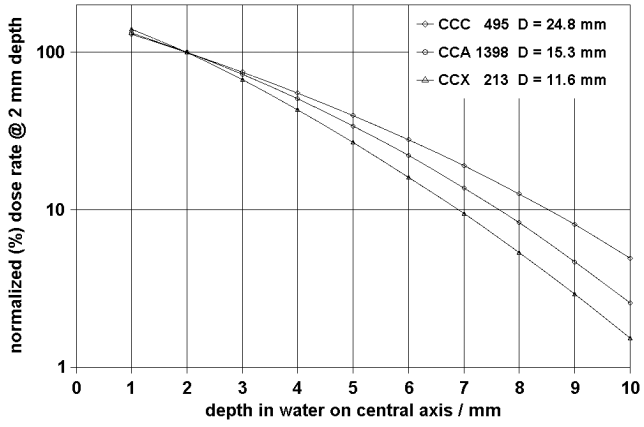

FIG. 5. Measured depth dose rate curves (normalized to 100% at 2 mm depth, P_{ref}) for three different ^{106}Ru ophthalmic applicators from acceptance testing at the University Hospital of Tübingen. Plaque type with the indicated unique serial number and plaque diameter D. The measurements were carried out in water with a small plastic scintillator (0.8 mm^3); the measurement time per measurement point was 60 s and the k = 1 uncertainty in the measurements was 5%.

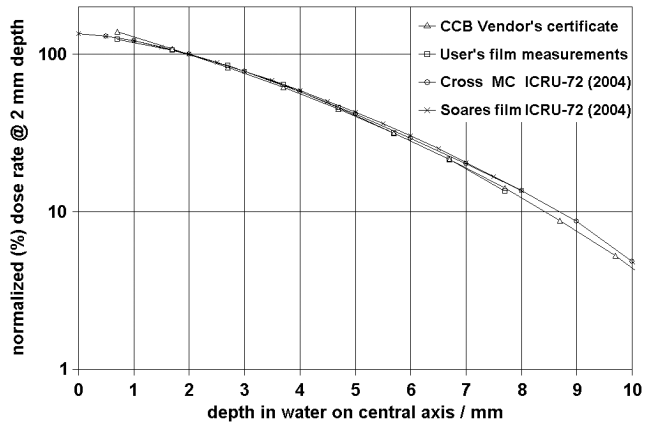

FIG. 6. Depth dose rate curves (normalized to 100% at 2 mm depth) for the CCB Plaque SN 1086 ^{106}Ru ophthalmic applicator as measured by four users. Mourtada et al.[170] compared their results with radiochromic film to the vendor-reported results on the plaque certificate, Soares et al. results[73] using radiochromic film, and Cross et al. results[95] using Monte Carlo methods as shown in fig. 5.1(c) of the ICRU 72 Report (2004).[123] The magnitude of measurement uncertainty varied widely in this figure (k = 2): the vendor's certificate stated 20% uncertainty, the film measurement uncertainty ranged from 2% to 11% (Table 3), and the MC data of Cross et al. had Type A uncertainty of 2% (with no estimate of Type B), and uncertainty for the film measurements of Soares et al. was 15%.

TABLE III. Uncertainty budget components associated with measuring concave ^{106}Ru sources with radiochromic film, including those historically provided on a National Institute of Standards and Technology (NIST) calibration certificate.[170]

Uncertainty component	Relative standard uncertainty
Calibration of the NIST ^{90}Sr/^{90}Y source	3.5%
Response of film exposed to calibration source	3.0%
Response of film exposed to ^{106}Ru source under test	3.0%
Combined standard uncertainty	5.5%
Expanded uncertainty (k = 2)	11.0%

obtaining definitive medical images of ocular melanoma are challenging and not routinely pursued. Furthermore, the plaque sutured into the treatment position often interferes with or limits the potential for obtaining images of the plaque, melanoma, and normal ocular tissues. The presence of a high-Z plaque backing can create significant imaging artefacts in CT due to photon attenuation in the plaque. Similarly, plaque and source components do not enhance under MRI imaging and appear as voids. Gold, which is diamagnetic and present in many plaque designs, can cause a significant susceptibility artefact, impairing the image near the plaque. Thus, there are limited opportunities for imaging therapeutic ocular plaques *in vivo*, however recent work reports on MRI-based treatment planning and dose verification.[171]

However, medical imaging plays a key role in treatment planning prior to plaque placement.[172] The basal dimensions of a given ocular melanoma are typically measured using ophthalmoscopy and/or fundus photography. The tumor height, which dictates the prescription depth, is assessed using ultrasound.[173] These imaging studies are generally performed by ophthalmologists, and the instruments are rarely subject to routine quality assurance testing by a clinical medical physicist. Given the potential for prescriptive errors, clinical medical physicists should make an effort to assure that these devices are surveyed through regular QA testing or receive routine preventative maintenance inspections by the manufacturer or their designate.

For the purpose of brachytherapy pre-planning, a patient may be simulated using CT or MRI. The QA of CT simulators in radiation oncology is governed by the AAPM Task Group 66 report.[174] Magnetic resonance imaging also may be used for improved spatial resolution in the orbit, although the orbit will generally need to be immobilized, for example, by using a retro-bulbar block to prevent motion artefact, during the scan. At present, there are no societal guidelines for utilization of MR-based simulation, but the clinical treatment team can assure that MRI scanners are being routinely surveyed by a diagnostic imaging-qualified medical physicist.

3.F. Treatment planning

Generalities on one-dimensional (1D) treatment planning, applicable to both photon and beta plaques, are described before separate discussions of treatment planning paradigms and commissioning for photon and beta plaques are presented in Sections 3.F.1 and 3.F.2, respectively.

In 1D treatment planning, the irradiation time is determined for delivering the prescription dose to the prescription point which is generally assumed to be a point along the plaque central axis. Dose is often calculated to other central axis points that include the center of the tumor base (inner scleral surface) and the outer scleral surface (assumed to be 1 mm from the inner sclera). Dose reporting to a depth of 5 mm is also done to allow for comparisons with other patient doses regardless of tumor height. Treatment planning may be carried out with a spreadsheet or a homemade treatment planning system. Due to clinic demands, in most cases the insertion and removal of a radioactive ophthalmic applicator is not carried out at precisely the prescribed times. Therefore, the clinical medical physicist must recalculate administered doses based on the actual insertion and removal times.

One-dimensional dose calculations require the following information: the largest basal diameter of the tumor (e.g., from fundoscopy), tumor height (e.g., from ophthalmic echography), and the prescribed dose to the tumor apex (or some other apical-based analog) at the time of applicator insertion. The applicator dimension and/or type are selected based upon the largest basal diameter of the tumor. Pötter and Van Limbergen suggested that a 1–2 mm expansion be included for "microscopic spread along the ocular tunicae, mainly the uvea and the sclera," and that a safety margin of 1 mm be included to account for "uncertainties in tumor

delineation ... and/or in plaque localization."[175] This total expansion of the measured maximum tumor basal dimension by 2–3 mm agrees with that recommended by the COMS.[69] Using modern parlance,[176,177] this approach describes expansions of the gross tumor volume (GTV) to the clinical target volume (CTV), and then the CTV to the planning target volume (PTV), respectively. These issues regarding treatment margins were elaborated upon by Gagne and Rivard, who examined the suitability of standardized margin expansions of the CTV based on COMS plaque diameter and lesion height.[172] Morrison et al carried out a delivered dose uncertainty analysis at the tumor apex, providing an approach for estimating an appropriate apex margin.[178]

Based on the prescription point at depth d, a 1D calculation of the implant duration T shows the following relationship

$$T = -\frac{1}{\lambda} \cdot \ln\left(1 - \lambda \cdot \frac{D(d,T)}{\dot{D}(d,t_I)}\right) \quad (1)$$

where:

λ, is the decay constant [time^{-1}], equal to ln(2) divided by the radionuclide half-life; $D(d,T)$, is the prescribed dose [e.g., Gy] at depth d [distance]for the implant duration of T [time]; and $\dot{D}(d,t_I)$,is the dose-rate [Gy time^{-1}] at depth d [distance] defined at the time of applicator insertion (t_I).

3.F.1. Photon-emitting sources

3.F.1.1. Treatment planning paradigm: The significant dosimetric effects of plaque components (reviewed in Section 2.A) help explain the potential for large differences between doses calculated with an all water environment (TG-43 approach[108]) and those which account for the effects of plaque components and other media heterogeneities. These clinically significant dose differences motivate the adoption of accurate dose calculations which account for media heterogeneities for treatment planning. However, there are currently no TPSs for heterogeneity-corrected dose calculations for ocular brachytherapy. Until such tools become available and are in widespread use, the recommendation is for a dual approach with a homogeneous water-based calculation done in parallel with a heterogeneous calculation or estimate which takes into account the dosimetric effects of the plaque, including the backing and insert (if there is one). This recommendation for dual calculations is consistent with TG-129[11] and TG-186.[68] As clinical experience (dose prescription, reporting, etc) is based on the TG-43 formalism,[108] it is important that TG-43 calculations continue to be used. Carrying out heterogeneous estimations (or calculations) in parallel to the TG-43 calculations will help clinicians prepare for the anticipated transition to MBDCAs for brachytherapy,[68] and enables the development of knowledge and the more accurate correlation of clinical outcomes with dosage. These dual calculations for multiple patients with both homogeneous and heterogeneous dosimetric data will also permit investigation that helps elucidate the relationship between prescribed doses for the two calculation methods and may lead to possible changes in prescription dose.

For the homogeneous water dose calculations, TG-221 recommends that the TG-43 line source (2D) formalism be used.[107,108] The 2D formalism is recommended over the 1D formalism as seed orientations within plaques are known and dose differences >5% exist between the 1D and 2D formalism for positions off the plaque central axis.[11] AAPM report TG-43U1 includes a discussion of the brachytherapy dosimetry formalism for short radial distances, and example dataset characteristics and resultant dosimetry calculations are presented in Rivard et al.[108,109]

In addition to the water-based calculation, a parallel dose calculation or estimation accounting for the effects of plaque media heterogeneities should be performed. This requirement limits clinical use to plaque models that have undergone dosimetric characterization (or, at least, to plaque models similar to ones having undergone such characterization). Potential heterogeneous dose calculation algorithms which may form the basis of brachytherapy TPSs were reviewed by TG-186 and include semi-analytic path-length correction, Monte Carlo, collapsed cone, discrete ordinates and others.[68,109] Once clinical TPSs based on these approaches are available clinically, they should be used to evaluate the dosimetric effect of plaque components. Until that time, TG-221 recommends that alternate approaches be used for heterogeneous dose calculations or estimates. While full 3D dose distributions are desirable for assessment of tumor dose and doses to normal critical structures, central axis doses should be calculated at a minimum. Various methods may be used to estimate heterogeneous dose distributions or central axis doses, and a few examples are given in the following.

Published literature may be used to estimate central axis dose data. For example, Lesperance et al developed five plaque models representative of plaques described in the published literature and performed MC simulations to evaluate plaque dosimetric effects for these and the COMS 16 mm plaque[102] (see Table IV describing the plaque models and Fig. 2). Table V presents central axis dose ratios (HETERO:HOMO; "HETERO" corresponds to a plaque in water; "HOMO" corresponds to sources in water with no interseed effects, approximating TG-43) for three different radionuclides (and particular source models) for a single source located at the plaque center. Table VI presents analogous central axis dose ratios for a plaque loaded with 13 sources (in three rings with angular arrangement corresponding to the COMS 16 mm plaque model). Dose ratios such as these may be applied as correction factors to doses computed using the TG-43 (2D) formalism,[108] thus providing an estimate of heterogeneous CAX doses. Data tabulated in Table VI shows that dose ratios for 16 mm diameter plaques loaded with 13 seeds vary considerably with plaque model and radionuclide. Dose ratios (HETERO:HOMO) at 5 mm from the inner sclera are 0.879 (^{125}I), 0.811 (^{103}Pd), and 0.892 (^{131}Cs) for COMS plaques, and higher (0.974 (^{125}I), 0.976 (^{103}Pd), and 0.969 (^{131}Cs)) for the "short lip — acrylic" plaques in Table IV. The analogous dose ratios for "stainless steel —

TABLE IV. Summary of representative plaque model characteristics from Lesperance et al.[102] with collimating lip height (h_{lip}) if present, plaque height (h), and radial distance from the eye center to the seed center (R_{seed}) values (see Fig. 2). All plaque models have the same diameter of 16 mm not including the lip width and the same angular arrangement of 13 seeds [consistent with the Collaborative Ocular Melanoma Study (COMS) 16 mm plaque arrangement], with the exception of the "slotted" plaque which contains 15 seeds (arranged as shown in Fig. 3 of Ref. [102]). The cited reference describes the indicated type of plaque.

Notation	Backing (thickness)	Insert	h (mm)	h_{lip} (mm)	R_{seed} (mm)	References
COMS	Modulay (0.5 mm)	Full, Silastic	2.75	2.7	13.70	[96]
COMS — thin acrylic	Modulay (0.5 mm)	Thin 0.85 mm, acrylic	–	2.7	13.70	[43]
Short lip — acrylic	Modulay (0.5 mm)	Full, acrylic	1.8	1.5	12.95	[52]
No lip — Silastic	Modulay (0.5 mm)	Full, Silastic	1.8	–	12.95	[51]
Stainless steel — acrylic	stainless steel (1 mm)	Full, acrylic	2.75	2.1	13.45	[56]
Slotted	Modulay	–	2.75	–	12.81	[48]

acrylic" plaques have values (0.945 (^{125}I), 0.970 (^{103}Pd), and 0.924 (^{131}Cs)) in between those of COMS plaques and the "short lip — acrylic" plaques. MC statistical uncertainties on these dose ratios are <0.2%. Note that the dose ratios are sensitive to many factors, including variations in backing composition (e.g., gold alloy Modulay vs pure gold or another gold alloy),[96,102] backing position and design,[46,102] source model,[98] and source position.[19,46,96,102] Of course, clinicians may carry out their own MC or other calculations, and/or use data from other publications for these sorts of calculations. Furthermore, online dosimetric databases may provide useful information, including the CLRP eye plaque database (https://physics.carleton.ca/clrp/eye_plaque, accessed October 9, 2019).

In some brachytherapy-specific TPSs such as Plaque Simulator, doses are computed as the superposition of individual seed doses; and the clinical medical physicist may enter distance-dependent correction factors to account for the dosimetric effects (radiation scatter and attenuation) due to plaque components. Data for the Plaque Simulator correction function, $T(r)$, may be derived from the single-source dose ratios presented in Table V, noting that the correction function employs data given at distances r from the source center rather than from the inner sclera. The TG-129 report (see Table III) provides $T(r)$ data for COMS plaques containing ^{125}I (model 6711) or ^{103}Pd (model 200) seeds.[11]

An alternate approach to estimate heterogeneity-corrected doses involves TG-43 hybrid planning, such as the method proposed by Rivard et al.[93] to use conventional TPSs for treatment planning with MC-based brachytherapy dose distributions. In this approach, an eye plaque (fully loaded with brachytherapy seeds) is modeled as a virtual source with its longitudinal axis (z-axis) coincident with the plaque central axis.[93] Using data from MC dose distributions for COMS plaques fully loaded with ^{125}I, ^{103}Pd, or ^{131}Cs seeds, the 2D anisotropy function in the cylindrical coordinate system and the radial dose function for the virtual source were derived and entered into the Pinnacle^3 TPS (Philips Medical Systems, Madison, WI). Some drawbacks of this approach are volume averaging around the plaque axis of symmetry and the entry of a large number (~30,000) of dosimetric parameter values for each plaque and radionuclide (needed for accurate estimation of doses in penumbral regions). Subsequently, Deufel et al. proposed dome and annular geometry functions to more accurately describe particle streaming which resulted in a more smoothly varying and smaller correction function.[179] However, this approach requires the inclusion of other geometry functions besides those for line and point source in the TPS. Both approaches (Rivard et al.[93] and Deufel et al[179]) require full MC data for each combination of plaque, source configuration, and source model, which limits their application.

Deufel and Furutani proposed using the TG-43 formalism with revised radial dose and 2D anisotropy functions (but the usual TG-43 line source geometry function) to compute heterogeneity-corrected dose distributions accounting for the Silastic insert and Modulay backing of COMS plaques.[94] In their approach, the radial dose function is obtained from MC simulation of an eye plaque containing only a single central seed; the 2D anisotropy function is then determined by applying a Nelder-Mead simplex routine to best estimate MC results using the TG-43 formalism dose. As their approach allows clinical medical physicists to specify actual seed configurations for calculations, dose distributions for non-standard seed loadings may be estimated. With this technique, a spreadsheet or commercial TPS with TG-43 line source geometry function calculation capabilities may be used to estimate most heterogeneity-corrected doses for calculations of COMS eye plaques with 2% accuracy, excepting superficial regions near the plaque lip. This approach does not calculate heterogeneity-corrected doses outside the eye as well as the approaches of Rivard et al.,[93] Deufel et al.,[179] or Plaque Simulator.[90] However, it enables dose calculations with FDA-approved TPSs and using arbitrary seed configurations in COMS plaques.

3.F.1.2. TPS commissioning (photon sources): As TG-221 is recommending a dual approach for dose calculations involving both the homogeneous water-based TG-43 formalism as well as the heterogeneous estimates, TPS commissioning will need to address these dual aspects. The TPS commissioning process outlined by TG-129 consists of three parts: (a) verifying seed coordinates, (b) verifying single-source dosimetry, and (c) estimating the heterogeneous dose distributions, which may be limited to the central axis for

TABLE V. Dose ratios MC(HETERO)/MC(HOMO) for a single seed at the center of the plaque models for indicated depths from the inner sclera (assumed to be 1 mm thick). Seeds are GE Healthcare/Oncura model 6711 for ^{125}I, Theragenics model 200 for ^{103}Pd, and IsoRay Medical model CS-1 Rev 2 for ^{131}Cs. Statistical uncertainties on dose ratios are less than 0.2% and 0.7% at depths of 5 and 23 mm, respectively.[102]

	COMS			COMS-thin acrylic			Short lip-acrylic			No lip-Silastic			Stainless steel-acrylic			Slotted		
Depth (mm)	^{125}I	^{103}Pd	^{131}Cs	^{125}I	^{103}Pd	^{131}Cs	^{125}I	^{103}Pd	^{131}Cs	^{125}I	^{103}Pd	^{131}Cs	^{125}I	^{103}Pd	^{131}Cs	^{125}I	^{103}Pd	^{131}Cs
0	0.921	0.839	0.944	1.012	1.004	1.017	1.019	1.013	1.024	0.979	0.946	0.988	0.995	1.004	0.990	1.032	1.011	1.036
1	0.913	0.836	0.940	1.007	0.996	1.013	1.017	1.009	1.026	0.974	0.944	0.987	0.985	1.001	0.980	1.005	0.989	1.008
2	0.908	0.833	0.934	1.001	0.990	1.005	1.011	1.003	1.020	0.966	0.937	0.978	0.977	0.995	0.969	0.984	0.976	0.984
3	0.903	0.830	0.928	0.996	0.987	0.999	1.006	0.994	1.009	0.962	0.931	0.969	0.971	0.993	0.959	0.967	0.968	0.966
4	0.897	0.828	0.920	0.990	0.984	0.990	1.000	0.993	0.999	0.959	0.930	0.964	0.967	0.991	0.953	0.953	0.957	0.948
5	0.892	0.824	0.913	0.983	0.975	0.981	0.992	0.992	0.990	0.952	0.928	0.956	0.959	0.987	0.943	0.939	0.950	0.933
6	0.883	0.822	0.903	0.973	0.973	0.968	0.985	0.986	0.981	0.947	0.923	0.948	0.954	0.984	0.930	0.930	0.942	0.923
7	0.877	0.818	0.893	0.963	0.967	0.960	0.974	0.981	0.973	0.940	0.920	0.940	0.941	0.981	0.923	0.920	0.940	0.907
8	0.874	0.818	0.886	0.953	0.968	0.953	0.970	0.977	0.962	0.933	0.917	0.927	0.942	0.972	0.920	0.916	0.938	0.900
9	0.870	0.817	0.882	0.952	0.972	0.945	0.963	0.976	0.952	0.923	0.914	0.921	0.933	0.966	0.914	0.903	0.933	0.893
10	0.860	0.800	0.879	0.943	0.956	0.939	0.957	0.968	0.943	0.923	0.903	0.918	0.928	0.961	0.905	0.900	0.925	0.882
11	0.863	0.801	0.868	0.950	0.963	0.932	0.952	0.954	0.939	0.916	0.897	0.915	0.922	0.956	0.904	0.899	0.927	0.872
12	0.858	0.802	0.865	0.944	0.958	0.931	0.950	0.965	0.935	0.914	0.900	0.912	0.923	0.959	0.904	0.886	0.931	0.867
13	0.845	0.794	0.864	0.934	0.946	0.925	0.940	0.959	0.928	0.906	0.899	0.907	0.917	0.955	0.899	0.883	0.929	0.865
14	0.845	0.799	0.859	0.935	0.947	0.915	0.937	0.955	0.929	0.903	0.890	0.905	0.919	0.958	0.886	0.881	0.924	0.864
15	0.840	0.812	0.859	0.938	0.955	0.923	0.935	0.959	0.921	0.902	0.894	0.898	0.912	0.948	0.886	0.883	0.916	0.863
16	0.845	0.802	0.849	0.927	0.943	0.912	0.931	0.956	0.922	0.907	0.906	0.900	0.909	0.941	0.892	0.880	0.913	0.854
17	0.845	0.814	0.846	0.923	0.960	0.906	0.935	0.955	0.916	0.902	0.903	0.896	0.908	0.938	0.878	0.872	0.908	0.853
18	0.837	0.797	0.833	0.918	0.953	0.906	0.937	0.959	0.908	0.902	0.910	0.893	0.899	0.962	0.873	0.876	0.917	0.849
19	0.825	0.795	0.829	0.911	0.955	0.893	0.916	0.950	0.904	0.891	0.911	0.884	0.897	0.964	0.872	0.874	0.929	0.851
20	0.832	0.804	0.830	0.905	0.954	0.895	0.912	0.960	0.902	0.889	0.920	0.883	0.894	0.936	0.875	0.866	0.917	0.846
21	0.832	0.792	0.819	0.919	0.944	0.890	0.913	0.944	0.903	0.887	0.919	0.885	0.891	0.943	0.868	0.878	0.908	0.840
22	0.833	0.809	0.821	0.907	0.959	0.876	0.921	0.950	0.904	0.886	0.912	0.891	0.888	0.955	0.865	0.863	0.936	0.831
23	0.841	0.801	0.823	0.909	0.965	0.877	0.922	0.955	0.882	0.895	0.913	0.869	0.895	0.942	0.864	0.873	0.921	0.826

TABLE VI. Dose ratios MC(HETERO)/MC(HOMO) for indicated plaque models loaded with 13 seeds (except for the slotted plaque which is loaded with 15 seeds) for indicated depths from the inner sclera (assumed to be 1 mm thick). Seeds are GE Healthcare/Oncura model 6711 ^{125}I seeds, Theragenics model 200 ^{103}Pd seeds, and IsoRay Medical model CS-1 Rev 2 ^{131}Cs seeds. Statistical uncertainties on dose ratios are less than 0.2% and 0.7% at depths of 5 and 23 mm, respectively.[102]

	COMS			COMS-thin acrylic			Short lip-acrylic			No lip-Silastic			Stainless steel-acrylic			Slotted		
Depth (mm)	^{125}I	^{103}Pd	^{131}Cs	^{125}I	^{103}Pd	^{131}Cs	^{125}I	^{103}Pd	^{131}Cs	^{125}I	^{103}Pd	^{131}Cs	^{125}I	^{103}Pd	^{131}Cs	^{125}I	^{103}Pd	^{131}Cs
0	0.851	0.733	0.886	0.998	0.986	0.997	1.017	1.004	1.011	0.925	0.857	0.938	0.973	0.991	0.956	0.409	0.396	0.422
1	0.870	0.771	0.898	0.991	0.981	0.986	1.004	0.993	1.002	0.936	0.886	0.947	0.966	0.988	0.948	0.739	0.749	0.706
2	0.875	0.789	0.897	0.982	0.979	0.977	0.995	0.987	0.992	0.941	0.902	0.948	0.962	0.985	0.946	0.883	0.890	0.855
3	0.878	0.795	0.901	0.979	0.967	0.977	0.987	0.987	0.984	0.940	0.909	0.947	0.955	0.975	0.938	0.926	0.944	0.922
4	0.877	0.803	0.895	0.970	0.975	0.967	0.980	0.975	0.975	0.941	0.909	0.945	0.951	0.977	0.930	0.931	0.939	0.918
5	0.879	0.811	0.892	0.965	0.965	0.957	0.974	0.976	0.969	0.938	0.913	0.942	0.945	0.970	0.924	0.930	0.944	0.921
6	0.876	0.813	0.887	0.959	0.965	0.954	0.975	0.974	0.957	0.935	0.910	0.933	0.943	0.968	0.922	0.919	0.943	0.909
7	0.872	0.807	0.883	0.950	0.960	0.945	0.967	0.971	0.960	0.937	0.920	0.933	0.938	0.971	0.917	0.916	0.937	0.913
8	0.866	0.814	0.873	0.952	0.965	0.939	0.963	0.969	0.953	0.926	0.911	0.927	0.932	0.968	0.913	0.921	0.944	0.901
9	0.865	0.809	0.863	0.951	0.957	0.926	0.949	0.968	0.940	0.932	0.906	0.924	0.929	0.967	0.907	0.905	0.934	0.886
10	0.853	0.802	0.864	0.940	0.944	0.929	0.955	0.959	0.939	0.928	0.909	0.922	0.924	0.961	0.895	0.902	0.925	0.885
11	0.853	0.798	0.859	0.930	0.946	0.915	0.942	0.964	0.929	0.920	0.901	0.913	0.916	0.946	0.892	0.891	0.923	0.882
12	0.843	0.810	0.853	0.926	0.950	0.912	0.939	0.957	0.924	0.919	0.910	0.910	0.901	0.964	0.888	0.899	0.939	0.879
13	0.855	0.794	0.846	0.926	0.940	0.897	0.944	0.947	0.922	0.914	0.902	0.908	0.913	0.953	0.882	0.898	0.927	0.864
14	0.852	0.789	0.846	0.921	0.932	0.892	0.926	0.942	0.916	0.916	0.908	0.905	0.910	0.950	0.880	0.891	0.925	0.858
15	0.839	0.798	0.838	0.914	0.935	0.891	0.922	0.955	0.909	0.905	0.909	0.905	0.903	0.947	0.887	0.888	0.910	0.867
16	0.834	0.793	0.836	0.917	0.961	0.893	0.925	0.965	0.908	0.907	0.909	0.897	0.901	0.954	0.868	0.881	0.918	0.855
17	0.832	0.791	0.837	0.914	0.932	0.890	0.911	0.953	0.893	0.905	0.905	0.892	0.909	0.944	0.872	0.872	0.922	0.855
18	0.825	0.786	0.831	0.905	0.913	0.875	0.917	0.943	0.903	0.892	0.931	0.902	0.908	0.938	0.873	0.869	0.912	0.838
19	0.828	0.793	0.819	0.891	0.942	0.878	0.922	0.956	0.897	0.901	0.903	0.887	0.903	0.938	0.872	0.859	0.933	0.840
20	0.828	0.778	0.806	0.899	0.932	0.866	0.920	0.969	0.886	0.896	0.911	0.889	0.891	0.963	0.861	0.869	0.916	0.827
21	0.828	0.779	0.796	0.898	0.940	0.866	0.921	0.959	0.888	0.906	0.906	0.890	0.888	0.941	0.856	0.854	0.898	0.825
22	0.828	0.789	0.824	0.889	0.958	0.875	0.915	0.936	0.878	0.898	0.904	0.880	0.884	0.954	0.853	0.848	0.901	0.830
23	0.810	0.776	0.820	0.866	0.936	0.868	0.900	0.942	0.893	0.881	0.882	0.885	0.883	0.933	0.851	0.854	0.887	0.828

some institutions. This report affirms the recommendations of the TG-129 report[11] with regards to the verification of seed coordinates and single-source dosimetry. For the part related to the heterogeneous calculation (c),[11] there are two distinct scenarios to be considered: (A) the TPS does not calculate a heterogeneous dose distribution taking into account the effect of the plaque backing and insert (i.e., the TPS does not incorporate a MBDCA) and (B) the TPS performs a heterogeneous calculation. These scenarios are discussed separately, in turn, in the following two paragraphs.

For scenario (A), a TPS without heterogeneous calculations/estimates, medical physicists may use one of several methodologies to estimate heterogeneous dose for known plaques, such as those reviewed in Section 3.F.1.1 (Treatment planning paradigm). If the published work has verified the heterogeneous dose calculation to a MBDCA and/or measurement, then the clinical medical physicist is not required to repeat that verification prior to clinical use of the heterogeneous dose calculation. However, if the published work does not exist, then TG-221 recommends that (at a minimum) the central axis heterogeneous dose calculation must be verified by either a MBDCA or measurements prior to clinical use. Ideally, a measurement would be done to confirm the heterogeneous dose calculation, but there are known challenges (Section 3.D). If a measurement can be performed that verifies the heterogeneous dose calculation, then verification with a MBDCA is not required. Alternatively, a clinical medical physicist may reference published central axis homogeneous and heterogeneous dose distributions for specific ocular plaques and source types. These publications could, for example, be used to determine a 1D scalar correction for the central axis calculation points.

For scenario (B), the TPS includes a heterogeneous calculation, and the clinical medical physicist should follow the TG-186 report, which provides commissioning guidance to early adopters of MBDCAs.[68] Furthermore, a joint AAPM/GEC-ESTRO/ABG Working Group on MBDCAs in brachytherapy (ABG: Australasian Brachytherapy Group) is working on issues related to TPS commissioning, including the development of test case plans. The TG-186 report[68] notes that the implementation of MBDCAs for treatment planning generally involves compromises between computational speed and accuracy; thus, these TPSs must be benchmarked against analogous Monte Carlo calculations or experimental results to ensure accurate dose estimations. To this end, TG-186 developed two levels of commissioning tests to be performed in addition to the various TPS QC/QA already in place based on AAPM guidelines (e.g., TG-53).[180] While these commissioning tests are summarized briefly below, full descriptions are presented in the TG-186 report.[68] The commissioning Level 1 tests involve direct comparison of doses calculated using the model-based dose calculation in a reference-sized homogeneous water phantom (with full scatter conditions) to AAPM consensus TG-43 data to provide a check of the dose distribution due to the physical source model without consideration of the surrounding environment. The pass criteria for this Level is 2% agreement with the AAPM consensus TG-43 dosimetry parameters; any deviations >2% should be thoroughly examined, their potential cause(s) discussed, and clinical impact understood and documented prior to patient use. Commissioning Level 2 involves checking the ability of the algorithm to accurately account for media heterogeneities surrounding sources which consist of the plaque backing and insert in the present context. Three-dimensional (3D) dose distributions calculated using TPSs with MBDCAs for specific virtual phantoms mimicking clinical scenarios should be compared with benchmark dose distributions for the same phantom geometries. These benchmark dose distributions may be obtained by using a well-documented Monte Carlo code, from the published literature, or from the database of test cases being prepared by the joint AAPM/GEC-ESTRO/ABG Working Group. TG-186 provides a commissioning workflow for heterogeneous dose distributions (see Fig. 4 of Ref. 68).

The AAPM TG-53 report remains a useful tool for commissioning brachytherapy TPSs.[180] Non-dosimetric tests include determining processes for entering source locations, verifying the accuracy of source position display, testing of data input, and validating tools such as the dose-volume-histogram (DVH).[181] For dosimetric tests, TG-53 notes that commissioning within the TG-43 paradigm can be relatively straightforward compared to external beam, due to the simplistic calculation algorithm, standardized sources, use of dosimetric parameters from the literature, and assumption of a homogeneous medium. Still, the clinical medical physicist should validate the source library, examine methods for source strength entry, record dose in the allowed units, and provide test source decay calculations, among others. These considerations are relevant for TG-43 calculations as well as for heterogeneous calculations within a TPS, that is, scenario (B) described above. Use of 3D imaging modalities should be evaluated, and the process for setting and adjusting the tumor:plaque or source geometry should be assessed. Finally, the gamut of data output from a brachytherapy TPS should be evaluated, including dose to organs-at-risk, isodose line display options, and plan printing capabilities.

3.F.2. Beta-emitting sources

Because the dosimetry formalism for planar beta sources is not compatible with the AAPM TG-43 report formalism,[107,108] the approach to treatment planning differs from that for photon-emitting sources. Calculations may be carried out using a 1D, 2D, or 3D geometry. The treatment planning paradigm and related commissioning depends on the chosen calculation geometry. Generally, a 1D dose calculation must be carried out to determine the therapeutic treatment time. While TG-221 strongly encourages 2D and/or 3D dose calculations, these calculation geometries are not required because there is no TPS with FDA approval or CE-mark for ^{106}Ru sources. Furthermore, published dose distributions, such as those by Hermida-López,[58] cannot be generalized to all applicators due to variations in source plating and encapsulation and their resultant impact on dose distributions. In addition,

few publications explore the role of plaque and/or tissue heterogeneities for ^{106}Ru sources, which limit the reporting of heterogeneity-corrected doses as required by the TG-129 report for photon sources.[11]

3.F.2.1. Treatment planning paradigm: Treatment planning for ^{106}Ru eye plaques is typically based on fundus photographs and 2D ultrasound, similar to approaches for COMS plaques treatment planning.[11] Treatment planning in 1D is based only on the depth-dose curve (i.e., the dose distribution along the plaque central axis). The plaque center is assumed to be at the center of the tumor base, where the tumor is assumed to have maximal thickness. Thus, a 1D calculation allows for a calculation of the time required to deliver the desired dose to a fixed distance along the plaque central axis, without correction for tumor eccentricity or asymmetry. The sclera is the only organ-at-risk that can be evaluated using a 1D calculation.

Using the example prescription worksheet in Fig. 7, Eq. (1) may be used as follows for derivation of the implant duration for a tumor with a height of 4.2 mm and maximum basal diameter of 14 mm. The calculation assumes a prescription depth of 5.2 mm with a CCB plaque and a scleral thickness of 1 mm and a basal expansion of 2 mm in all directions. After accounting for radionuclide disintegration and diminishment of the source strength since the calibration, the calculation indicates an implant duration of 126.9 h is needed in this example. This example spreadsheet is not exhaustive in the information that might be pertinent in planning treatments; for example, considerations might include a maximum dose on the sclera and a maximum treatment time.

Treatment planning in 2D allows the clinician to correct the treatment time based on off-axis treatment considerations, which is necessary for notched or asymmetric ^{106}Ru eye applicators (e.g., the BEBIG model COB). While the overall treatment time is determined by the 1D approach, the 2D method allows evaluation of the minimum prescribed dose and the dose to organs-at-risk in planes perpendicular to the plaque central axis as a function of applicator geometry and prescribed dose. The minimum and maximum dose is calculated in each plane as a function of the radial distance from the central axis of the plaque, and these data can be transcribed to display approximate minimum and maximum isodose lines. Finally, those isodose lines can be transferred onto 2D ultrasound images of the tumor and allow verification of tumor coverage and evaluation of regions of interest (i.e., organs-at-risk) across the profile of the tumor as a function of applicator design.

Complete 3D planning can be performed when anatomic data from CT or MRI can be integrated with a 3D calculation of brachytherapy dose from the applicator and a PTV for the target can be evaluated using volumetric tools (e.g., a DVH). Plaque Simulator can be used to provide visualization of dose to the tumor and organs-at-risk with ^{106}Ru applicators and 3D calculations using the patch source dose model.[126] Each applicator model requires a unique combination of patch sources, and the total volumetric dose distribution is calculated using superposition. Dose distributions for a specific BEBIG applicator are replicated by scaling dose calculations to match measurements made with a plastic scintillator 1 mm from the plaque surface at 33 positions (i.e., the source uniformity) and along the central axis of the plaque (i.e., the depth dose profile). The clinical medical physicist can also input measurements for specific or custom applicators into Plaque Simulator; however, the measurements must have the same spatial distribution as the measurements used to characterize a particular BEBIG applicator distribution. Since Plaque Simulator software is not FDA-approved or CE-marked, the clinical physicist must appropriately commission and validate dose calculations.

3.F.2.2. TPS commissioning (beta sources): The goals for commissioning a treatment planning system for beta-emitting ophthalmic brachytherapy applicators are three-fold: to establish a system for calculation of treatment doses; to identify and obtain input parameters needed for these calculations; and to create a system that ensures the consistency of treatment planning system output. As noted above, the three primary methods for performing dose calculations are the 1D, 2D, and 3D methods. The 1D method of treatment planning is based on a central axis calculation and is concerned only with depth. The algorithm can be tested against published dose values for both apex and scleral dose points. Currently, the 2D and 3D approaches are supported by only one commercially available TPS (i.e., Plaque Simulator). Hand calculated or independently published data obtained using Monte Carlo simulation can be useful to verify beta particle TPS calculated results. For example, Cross et al.[95] and more recently Hermida-López[58] tabulated 2D dose distribution values in water for several commercially available ^{106}Ru eye plaques. Both depth-dose and lateral dose profiles were presented by Hermida-López in tabular form for ease of interpretation by the clinical medical physicist, although dose distributions for a specific plaque may vary considerably due to manufacturing variations. In addition, the dose to organs-at-risk may be compared to values in the published literature.[100]

As discussed in Section 3.F.1.2 [TPS commissioning (photon sources)], the AAPM TG-53 report also provides useful general guidance for commissioning TPSs.[180] Although the brachytherapy source dosimetric parameters cannot be entered, there are brachytherapy-specific tests that may be useful for beta-emitting ophthalmic brachytherapy applicators. Among others, these dosimetric parameters include source strength entry, dose distribution data, source decay calculations, display options, and input/output capabilities.

4. RECOMMENDATIONS

As stated in Section 1, TG-221 was charged with assisting the clinical medical physicist to implement an ocular

PRESCRIPTION DOSE WORKSHEET

Patient Name:	Patient #:

Diagnosis: _____

CCB 1294	$^{106}Ru/^{106}Rh$ ophthalmic applicator, 20.2 mm diameter

Insertion time	20171228T1535Z	
Activity @ insertion time	9.52 0.26	MBq mCi
Prescription dose	100	Gy
Tumor apex	4.2	mm
Prescription depth (from applicator interior)	5.2	mm
Prescription depth dose rate	13.2	mGy/min
Implant duration	126.9	hours
Removal time	**20180102T2230Z**	

Central-axis positions	depth, mm	dose, Gy
Outer sclera	0	441
Inner sclera	1	358
Prescription depth	5.2	100
COMS 5 mm point	6	75

Radionuclide	$^{106}Ru/^{106}Rh$
Half-life	371.5 days
BEBIG calibration date	20160815T1100Z
Calibration activity	24.2 MBq 0.65 mCi

Measured depth-dose rate data on calibration date

depth, mm	dose rate, mGy/min
0.6	131
1	121
2	93
3	69.9
4	50.6
5	36.3
6	25.2
7	16.7
8	10.8
9	6.5
10	3.8

5th order polynomial fit parameters for the depth-dose calculation

a0	147.83
a1	-26.605
a2	-1.7798
a3	0.91498
a4	-0.09424
a5	0.003275

Physics Check: Signature/Date **Physician Approval: Signature/Date**

FIG. 7. An example prescription dose worksheet for beta-emitting plaques. Insertion and removal times are indicated using the ISO 8601 time format to avoid ambiguity,[182] for example, the insertion is December 28, 2017 at 15:35 UTC.

brachytherapy program using either photon- or beta-emitting sources. Section 2 of this report provides a general overview of the variety of ocular applicators and their related dosimetric studies. Section 3 offers a general discussion of the various core facets of an ocular brachytherapy program. In the current section, the Task Group seeks to distil these discussions into concise recommendations for the clinical treatment team. While these recommendations provide a high-level summary of the aforementioned discussions, the clinical medical physicist is advised to refer back to the prior discussions and read the appropriate references to assure understanding of these recommendations. Finally in Section 4.C, recommendations are made to the broader community (e.g., manufacturers, standards laboratories, dosimetry investigators, etc.) regarding the specific needs of the field of ocular brachytherapy.

4.A. Commissioning an ocular brachytherapy program

While formulating a commissioning plan, the clinical medical physicist is advised to consult not only with medical physics colleagues (if applicable), but also with key stakeholders, including the radiation oncologist(s), ophthalmic surgeon(s), and representatives of health physics (i.e., radiation safety), the operating room, nursing, sterilization

department (e.g., central sterile processing), shipping and receiving, and security. This clinical treatment team should advise the clinical medical physicist on the planned treatment process in their departments and assist in implementing the planned clinical practice. The clinical treatment team should meet annually to review the treatment process and implement changes required due to changes in policy, equipment, staffing, learned experiences, or other processes. For institutions that provide existing brachytherapy services, conversations with some parties, for example, shipping and receiving, may only concern the integration of new sources/suppliers into existing workflows.

TG-221 summarizes its general commissioning recommendations in the following list. Its purpose is not to circumscribe all possible commissioning steps, but to provide general guidance on the core principles and concepts that warrant consideration for a new ocular brachytherapy program. Physicists with an established clinical practice may also benefit from reviewing these recommendations, as some institutions have been active for decades, and in some cases, the physicists who established the clinical practice may no longer be at the institution. Personnel groups can vary significantly based upon the clinical resources and organizational structure of specific institutions. The roles and responsibilities outlined below will depend on the composition of the clinical treatment team.

1. Identify and assemble the clinical treatment team

2. Draft the expected clinical process tree (Section 3.A) and determine accountabilities and responsibilities (Section 3.B), including making plans for team communications and patient coordination
   a. Establish the required treatment data and processes of dissemination with radiation oncologists and ophthalmic surgeons
   b. Establish source logistics (i.e., shipping and receiving) with health physics, institution shipping and receiving personnel, and security
   c. Establish source storage and transport within the institution with health physics and security
   d. Establish plaque preparation processes with vendor, operating room, sterilization department, health physics, and security
   e. Establish sterilization and storage stewardship with sterilization department, health physics, and security, including the related impact on source preparation time (see f, *below*)
   f. Establish the amount of time required to procure and prepare sources prior to treatment (e.g., sterilization, cooling, loading), consider physician and operating room scheduling as well as methods of source acquisition, plaque preparation, sterilization, and transport to operating room
   g. Establish the implant procedure with the clinical treatment team
   h. Determine and review inpatient/outpatient considerations with radiation oncologist, ophthalmologist, nursing, health physics, and security
   i. Establish the plaque removal procedure with the clinical treatment team, including consideration of emergency transportation procedures in the event of unexpected conditions (e.g., weather emergency)
   j. Establish the applicator cleaning and post-treatment source handling with sterilization department, health physics, and security

3. Establish a process for treatment planning
   a. Homogeneous dose calculations using TG-43 (photon sources) or 1D approach (beta plaques), or equivalent (Sections 2.A and 3.F)
   b. Heterogeneous dose estimations or calculations using model-based dose calculation algorithms (MBDCA) or appropriate correction factors (Sections 2.B and 3.F)
   c. Establish image guided aspects
   d. Standardize specification of the target volume, including planning margins
   e. Establish dosimetric constraints for organs at risk[67,173]

4. Establish local source calibration standard
   a. For photon sources, comply with established guidelines (Section 3.C.1)
   b. For beta sources, absolute calibration is preferred but relative measurements may be more achievable due to limitations in available primary standards, detectors, and phantoms (Section 3.C.2)

5. Assemble and test all mechanical components, including supporting devices (Section 3.D)
   a. Commission applicators and disposable inserts
      i. Mechanical commissioning and evaluation
      ii. Cleaning and sterilization of reusable components and process for handling disposable components (consult with sterilization department, as needed)
   b. For beta plaques the clinical treatment team should additionally evaluate/ consider
      i. Wipe testing system to test for loose contamination
      ii. Relative depth-dose and off-axis dose profiles (verify manufacturer certificate)
      iii. Cleaning and sterilization of the plaques (consult with sterilization department, as needed)

6. For image guided brachytherapy, review the imaging QA processes in place (note that these may not fully meet the requirements of the clinical treatment team, e.g., for MRI) (Section 3.E.)

7. Create a written directive program to assure that all written directives comply with governing regulations and institution policies

8. Establish items for periodic follow-up and review

9. Draft and finalize a report summarizing the commissioning steps that were performed
   i. The report and clinical decisions should be distilled into a set of policies and procedures that are accessible to the entire treatment team
   ii. The policies and procedures should be reviewed periodically for accuracy with current practice

4.B. Clinical practice standards for ocular brachytherapy

The clinical practice standards for ocular brachytherapy at a particular institution are largely dictated by the program that was commissioned at that institution. Any routine aspect of the clinical treatment process should be rooted in processes developed during commissioning, or in programmatic changes that were made since commissioning that have been thoroughly reviewed step by step and accepted by the clinical treatment team. The items in the following list represent characteristics that should be addressed and/or documented for each patient, assuming the commissioning steps in Section 4.A were followed. The physicists at some institutions may need to include additional steps depending on their institution's clinical process tree (Section 3.A). The clinical medical physicist and radiation oncologist, both with brachytherapy experience, should review the process tree and identify the clinical practice standards applicable to their institution. For this task, societal guidance reports such as the 2003 and 2014 ABS reports may be useful references.[67,173]

1. Patient provided education is commensurate with their needs as an inpatient or outpatient during ocular brachytherapy

2. A complete and accurate written directive is prepared in accordance with governing regulations that specifies the applicator, radionuclide, intended dose, and duration of treatment, among other applicable components

3. Dimensions of the tumor are documented, along with requested applicator size, depth of treatment, treatment margin and/or radiation margin
   a. The combination of plaque size and prescription depth may affect the radiation margin
   b. The presence of the optic nerve may affect plaque selection and placement

4. The source(s) and/or applicator to be used for treatment have been appropriately commissioned and accepted for use, including any review of disposable components (e.g., Silastic inserts). Please see Section 3.D.1 for detailed recommendations.

5. Sources have been assayed to independently determine the air kerma strength for photon sources or the reference dose rate and depth-dose curve for beta sources. Significant challenges are presented to the clinical medical physicist in measuring the reference dose rate for a beta-emitting source, such that TG-167[146] may be consulted towards establishing a local constancy standard. The clinical medical physicist should make every effort to establish a wipe test system and a constancy test and/or relative dose measurement to evaluate the reference dose rate and depth-dose curve.

6. Treatment plan is in accordance with the written directive, and includes both a homogenous dose plan and a heterogeneous dose plan (or estimate) for comparison

7. Work spaces are surveyed for contamination before and after work with results documented, including the plaque assembly/handling areas and the operating/procedure room environment

8. Patient is surveyed for radioactivity before the implant and also after the implant to assure compliance with patient release requirements and for the purposes of managing patient care. Following plaque removal, the patient should be surveyed again with results documented.

9. Assure that sources are transported to their final destination and prepared for disposal or re-assayed for compliance with internal practices, if applicable. Note that all sources (photon or beta) need a wipe test if there is suspicion of mechanical damage to the encapsulation.

4.C. Additional recommendations

Safe and continued utilization of beta-emitting sources requires a traceable calibration for ^{106}Ru eye plaques from the pertinent NMI. This calibration is essential for both plaque manufacturers and clinical medical physicists. As discussed in Section 3.C.3, an erroneous source calibration practice led to systematic errors in patient dose calculations that had the potential to exceed a factor of two. Even the most recent calibration that was previously available at NIST had a stated uncertainty of 20%, a significant increase over the uncertainties typically observed in brachytherapy.[141,183] It is not only the responsibility of the vendor to seek calibration services from the NMIs, but also the responsibility of clinicians and their professional societies, who seek the most accurate and reproducible medical therapies. The lack of a widely accessible calibration service is currently a critical shortcoming.

In addition to the need for a traceable calibration, there is a need for detectors and phantoms designed to support ocular

brachytherapy. In particular, commercialization of an eye phantom, such as that used for some previous studies,[164] would support reproducible irradiation of radiochromic film and/or other dosimeters (e.g., TLDs, scintillators, diodes, or ionization chambers) for ocular brachytherapy, and would be valuable to the medical physics community. Radiochromic film could provide relative and/or absolute dose characterizations of plaque dose distributions using a suitable eye phantom. In addition, development of a phantom and dosimeter (film, TLD, or other) combination may enable end-to-end testing and/or establish a tool for third-party verification. Similarly, a scintillation detector of appropriate size to measure plaque depth-dose characteristics would also be valuable. With growing interest in beta-emitting plaques in North America and an established user base in Europe, TG-221 encourages vendors to make the following equipment commercially available to clinicians to improve the standard-of-care: an eye phantom, development of a phantom and dosimeter (film, TLD, or other) combination, and a scintillation detector.

Regarding the development of TPSs, TG-221 further recommends that vendors provide a library of plaque models ready for loading, just as modern brachytherapy TPSs have a library of accurate applicator models (with detailed composition descriptions for advanced dose calculation algorithms). ^{106}Ru applicator models should be able to convolve the basic source geometry with source-specific characteristics of a given source. The development of novel dose calculation algorithms for beta applicators may allow for the development of new TPSs for those source-types. Furthermore, TG-221 recommends that the AAPM commission a Task Group to evaluate recommendations of TG-53 to assure that specific and unique characteristics of brachytherapy dose calculations are adequately assessed.

TG-221 endorses the recommendations of TG-129[11] and supports the estimation of heterogeneous dose distributions in tandem with the "traditional" TG-43 calculations that are based on a homogeneous water medium. However, there are few tools available for estimation of the heterogeneous dose for low-energy brachytherapy sources. TG-221 encourages vendors to develop FDA-approved and CE-marked software that can more accurately estimate dose in an environment with material heterogeneities for a variety of plaque designs, for example, using a hybrid TG-43 method.[93] Similarly, TG-221 encourages dosimetry investigators to examine generalizable treatment configurations that allow construction of nomograms or 1D correction functions for use by clinicians.

Finally, in addition to seeking heterogeneity corrections in ocular brachytherapy, TG-221 recommends that clinicians should move to 3D image-guided dose calculations. Patient-specific and, in some cases, applicator-specific calculations allow for improved evaluations of tumor coverage and dose to critical organs/structures at risk. Advancements in ocular brachytherapy are needed in patient imaging and treatment planning to achieve this goal; however, 3D is the standard-of-care for alternate radiotherapy modalities and is necessary for a more accurate evaluation of efficacy.

5. DISCUSSION

The recommendations of TG-221 extend the prior relevant guidance documents for ocular brachytherapy, including TG-129,[11] ISO 21439 standard,[70] and ABS recommendations.[67,173] In particular, TG-221 reaffirms the TG-129 recommendation[11] that a heterogeneous dose estimate or calculation should be done in parallel with a water-based TG-43 dose calculation for photon-emitting plaques. This issue may present a challenge to the clinical physicist whose center employs a plaque model not previously evaluated dosimetrically for ocular brachytherapy. In support, Section 3.F.1.1 (Treatment planning paradigm) provides published estimates of the dosimetric effects of plaque backing and insert combinations, and reviews other approaches to account for these effects to aid the clinical physicist in implementing the dual calculation until such time as advanced model-based dose calculation algorithms are incorporated into clinical TPSs.

TG-221 also recognizes that clinical physicists undertaking dose calculations and measurements for beta plaques face challenges related to the lack of approved TPS, calibration standards, and appropriate measurement equipment. However, we have provided possible avenues for addressing challenges and encourage the community and vendors to work together to collaboratively develop the needed equipment and software. Given the challenges for the practice of ocular brachytherapy outlined in the current report, the following paragraphs describe and reflect on areas for future research and development.

In the future, considerable advances in ocular brachytherapy treatment planning are expected with the clinical adoption of model-based dose calculation algorithms for brachytherapy.[68] These algorithms will enable more accurate dosimetric characterization of all plaque types (photon and beta-emitting), in addition to more accurate routine treatment planning and evaluation than currently possible. Development and use of these advanced model-based dose calculation algorithms require the release of detailed plaque model and material information to TPS vendors for accurate modeling. Development and updating of online dosimetric databases (e.g., the CLRP eye plaque database https://physics.carleton.ca/clrp/eye_plaque, accessed October 9, 2019), and open-source release of advanced dose calculation algorithms will enable accurate dose evaluations.[184,185]

Radiation response is dependent on dose, and hence accurate dose calculations should enable meaningful comparisons between treatments with different plaque types as well as different radiotherapy treatment modalities. Retrospective and prospective studies employing model-based dose calculations should enable investigation of potential changes to prescription dose, such as the possibility of dose de-escalation studies. For example, Perez et al. have demonstrated equivalent control rates with decreased treatment toxicity using TG-43

based treatment doses of 69 Gy in lieu of 85 Gy to the tumor apex when using ^{125}I.[186]

Future work will involve investigation of relevant dose-volume metrics for dose reporting and 3D image-based treatment planning,[114] for example, rather than reporting dose to a point in the lens, it may consider average, minimum, and maximum lens doses.[60] Accurate dose calculations may require realistic models of the non-water patient anatomy, in addition to plaque modeling; these models require accurate average ocular tissue compositions and knowledge of their expected variation within the population.[60,68,102,114] Further, development of realistic 3D patient models may require high-resolution (sub-millimeter) imaging and integration of multiple image datasets.

Ocular brachytherapy is a radiotherapy modality utilizing temporary implants of radionuclides. Consequently, the biological response is influenced by the radiation quality, dose distribution, and dose rate (related to the treatment duration). The dose distribution is dependent on the choice of radionuclide, and globally on the choice of prescription dose. It has been shown that implant durations exceeding seven days result in diminished local control when using ^{125}I.[187] This criterion for ^{125}I may not be applicable to ocular brachytherapy implants using other radionuclides,[29] as they deliver a different dose distribution.[188] While some institutions have reported different clinical outcomes when comparing two or more radionuclides,[22,189] a multi-institution, prospective, randomized clinical trial would help elucidate the importance of these dose distribution differences and determine the most appropriate radionuclide(s) for a given circumstance.

Meanwhile, some guiding information may be gleaned from Refs. [[22,188,189]] and references therein, and studies focused on radiobiology for ocular brachytherapy. For example, Gagne and colleagues established a means of evaluating MC-based 3D dose distributions (accounting for plaque material heterogeneities) and subsequent 3D biologically effective dose distributions for plaques containing photon-emitting seeds.[190] There currently is no comparable study for beta-emitting plaques. The influence of radionuclide choice and implant duration was evaluated.[191] The ^{103}Pd sourced plaques appeared to produce more favourable outcomes in comparison to ^{125}I or ^{131}Cs sources, even for a large lesion (basal diameter of 17 mm and apical height of 8 mm). Regarding implant duration, the radiobiological advantage of reduced treatment times was more pronounced for smaller lesions and with ^{103}Pd sources although uncertainties in the values for the radiobiological parameters overshadowed the magnitude of the observed differences. Additional radiobiological studies are needed to clarify these effects.

TG-221 recognizes that there are considerable variations in clinical practice for ocular brachytherapy worldwide for both photon and beta sources. These differences are due in part, but not limited to, substantial variations in plaque models employed in clinical practice, availability of FDA-approved/CE-marked TPSs specific to ocular brachytherapy, and the lack of advanced calculation algorithms (e.g., accounting for the plaque backing and insert for photon plaques and the variability in spatial activity distribution for beta plaques). In addition, clinicians face challenges in dosimetric measurements of applicators and sources with limited commercially available equipment for such measurements, and the lack of primary calibration standards for ^{106}Ru plaques. Within the scope of its charge (see Section 1), TG-221 provides guidelines for physics-focused aspects of ocular brachytherapy practice using photon- and beta-emitting plaques. These guidelines range from discussions pertinent to commissioning an ocular brachytherapy program to providing clinical practice standards for such a program. Where possible, a unified framework for clinical physics practice has been presented for photon and beta-emitting plaques, in spite of different considerations and challenges for each radiation modality.

While these recommendations have a noted emphasis on medical physics practices, TG-221 encourages further developments of inter-society and inter-medical specialty reports to combine the knowledge and experience of ophthalmologists, radiation oncologists, physicists, and other allied health professionals within the multi-disciplinary clinical treatment team.

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APPENDIX

CLINICAL PRACTICE SURVEY

TG-221 created a survey to gain insights on clinical practices in ocular brachytherapy. The survey was announced by the AAPM, ESTRO, and the ABS in conjunction with regular electronic correspondence with members. It was available online from 15 May 2015 to 15 August 2015. A copy of the questions asked in the survey is included in the additional materials. Over 500 individual users visited the survey website, with approximately 10% initiating the process. Nearly

half of the survey respondents were in the U.S., with the remainder distributed approximately equally around the world. The survey had three sections for photon-emitting, beta-emitting, and mixed-radionuclide sources. Survey respondents were asked to complete those sections that were pertinent to their practice. Most participants completed one of the three sections, with an average time to completion of approximately 25 min. While an insufficient number of respondents participated in the mixed-radionuclide section, results for photon-emitting and beta-emitting plaques are summarized.

Users of photon-emitting sources

Respondents from 28 sites reported performing an average of 50 plaque treatments annually, with a standard deviation of 90 treatments, and a range of 1 to 400. Nearly 50% of plaque treatments utilized COMS or notched COMS plaques (32/57), with the remainder equally divided between commercially available, custom, and custom notched plaques. A majority of respondents (81%; 22/27) performed independent verification of brachytherapy source strength by using a well chamber and following the recommendations of AAPM Report 98.[134] More than half of the respondents verified all of the sources, with the remainder measuring a specified number (e.g., 10 or 5 sources). Approximately half of the respondents performed assessment of the mechanical integrity of the plaque, with the majority of these tests being described as a visual inspection. Few respondents (14%, 3/21) performed dosimetric measurements of the plaque after loading with radioactive sources. Clinical guidelines for treatment were obtained from a variety of sources, including the AAPM TG-129 report,[11] the ABS 2003 report,[173] the COMS protocol,[27,69] and internal/institutional protocols.

Most respondents (78%, 14/18) had guidelines that stipulated the maximum basal dimension of the tumor and the treatment margin for plaque selection. The average margin was 2 mm with a standard deviation of 0.6 mm. However, there was not a consensus regarding the maximum apical height of the tumor, maximum dose to the sclera, or the maximum/minimum dose rates. Approximately half of the respondents performed QA on the imaging devices that supported ocular brachytherapy, with an emphasis on CT and US devices.

Most respondents (81%, 13/16) did not perform heterogeneous dose calculations during treatment planning. A variety of commercially available TG-43-based TPSs were used, and most respondents (63%, 10/16) verified calculations by using a library of previous plans, comparison to MC simulations, or utilization of a "second" dose calculation, or others. Notably, a majority of the ocular brachytherapy programs were commissioned by persons other than those taking the survey. Finally, the aspects of plaque brachytherapy that were most often considered during commissioning were sterilization, plaque handling and security, dose prescription and guidance, and radiation protection.

Users of beta-emitting sources

Approximately ten completed survey responses (fewer than for photon-emitting sources) were compiled, which led to greater variation in survey results. Generally, beta-emitting applicators were used in clinics performing an average of roughly ten plaque treatments annually, with one survey taker reporting 100 treatments annually. Few responders (11%, 1/9) reported independently measuring source strength prior to treatment, which highlights some of the challenges discussed in Section 3.C.2. Similarly, a minority of respondents (33%, 2/6) reported assessing the mechanical integrity of the plaque, which generally included performing a visual inspection and wipe test.

There was not a consensus on clinical guidelines. Sites generally had limits on the maximum basal dimension of the tumor, which likely correlated with the limitations of applicator size. However, there were insufficient results to infer consensus regarding the maximum apical height, maximum dose to the sclera, maximum/minimum dose rates, or the treatment margin used for plaque selection. The QA for imaging studies was similar to that reported for photon-emitting sources.

Treatment planning for plaque brachytherapy was generally performed using Plaque Simulator or hand calculations, with a few respondents validating treatment planning calculations with MC simulations and radiochromic film measurements. Finally, the aspects of plaque brachytherapy that were most often considered during commissioning of a beta-emitting plaque brachytherapy program were sterilization, plaque handling and security, and radiation protection.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Process map of an ocular plaque brachytherapy clinical workflow (courtesy of Cliniques Universitaires St Luc).