Recent preclinical and clinical studies indicate that irradiation using ionizing radiation in the dose range of 15 to 30 Gy may reduce the occurrence of restenosis in patients who have undergone an angioplasty. Several delivery systems of intravascular brachytherapy have been developed to deliver radiation doses in this range with minimal normal tissue toxicity. In late 1995 the American Association of Physicists in Medicine (AAPM) formed a task group to investigate these issues and to report the current state of the art of intravascular brachytherapy physics. The report of this task group is presented here. © 1999 American Association of Physicists in Medicine.

Key words: intravascular brachytherapy, angioplasty, restenosis, dosimetry, radiation protection
Coronary artery disease is the leading cause of morbidity and mortality in the western world. Approximately 450,000 angioplasties are performed annually in the USA. Although major complications from angioplasty occur in only 1%–2% of patients, angiographically diagnosed restenosis occurs in 35%–40% of patients. Restenosis is the major limitation of angioplasty. The impact of restenosis is highlighted by studies that compared coronary angioplasty to bypass surgery as a treatment strategy for coronary artery disease. Patients treated by angioplasty had lower initial costs and fewer major complications, but at a six month to three year follow-up these patients had more angina, required more revascularization procedures, and most of the cost benefit of angioplasty was lost because of restenosis. Coronary stent placement in conjunction with angioplasty can reduce the restenosis rate to 22%–32%. The cost of restenosis has been estimated to be $4000–$7000 in direct costs for the first episode of restenosis. The societal cost of restenosis in the United States of America is estimated between 800 and 2000 million dollars per year. Recent preclinical studies indicate that irradiation using ionizing radiations in the dose range of 15–30 Gy may reduce substantially the problem of restenosis in patients who have undergone an angioplasty. Using intravascular brachytherapy, radiation doses in this range can be delivered with minimal normal tissue toxicity because of the high localization of dose to the immediate vicinity of radioactive sources in brachytherapy. It is estimated that the restenosis rate may drop from roughly 35%–40% to well below 10% if radiation is delivered to the obstruction site during or after angioplasty. Therefore, the potential of intravascular brachytherapy in reducing restenosis has aroused a tremendous interest in the cardiology community.

Dosimetry at distances of the order of a millimeter from radioactive sources is poorly known. In traditional brachytherapy the dose is typically specified at 1 cm from the source and effects of low-energy photons and secondary electrons are essentially ignored. In intravascular brachytherapy, however, the entire lesion may be 1–3 mm in thickness. To understand the results of various preclinical studies using a variety of radionuclides and delivery systems, it is essential to determine the dosimetry in the millimeter range. A better understanding of dosimetry in the millimeter range will help in the development of optimum clinical devices and their efficacious use in different institutions using different radionuclides and devices.

In late 1995 the American Association of Physicists in Medicine (AAPM) formed a task group to investigate these issues and report the current state of the art of intravascular brachytherapy physics. The specific charge to the task group included the following:

1. To review the physical, radiobiological, and clinical rationale of using intravascular brachytherapy.
2. To review the currently proposed irradiation techniques:
   a. Intravascular gamma radiation (e.g., 192Ir) brachytherapy;
   b. Intravascular beta radiation (e.g., 33P) brachytherapy.
3. To review the literature for types and applications of various interventional probes, including specifically the use of intra-arterial stents.
4. To review the interventional diagnostic imaging procedures including intravascular ultrasound used in evaluation and treatment planning for brachytherapy.
5. To recommend a dose prescription site (or region) for selected intravascular brachytherapy procedures (e.g., 1 mm depth from the arterial lumen surface or 2 mm from the center of the lumen, etc.).
6. To recommend calibration and dosimetry procedures (relative and/or absolute) for the determination of dose distributions around intravascular brachytherapy applicators, including beta-emitting stents.
7. To recommend a quality assurance procedure, including
radiation safety, for the safe and efficacious application of intravascular brachytherapy.

Here we present the recommendations of the AAPM on the physics of this novel application of radiation in the treatment of cardiovascular disease.

II. CLINICAL BACKGROUND AND RATIONALE

A. Overview of coronary anatomy

The arteries conduct blood from the heart to the capillary bed in the heart muscle. The arterial system begins in large blood vessels close to the heart. The largest, the aorta, carries the full volume of blood expelled and is approximately 2–3 cm in diameter. The division of this and subsequent major branches leads to a continuous increase in their number and spread, with a progressive decrease in their diameter.

The coronary arteries are a branching system of mildly to severely tortuous vessels lying on the outer surface of the heart. Two main coronary arteries, the left and right coronary arteries (LCA and RCA), originate from the aortic root, just outside the aortic valve. The branching of these main arteries, and the regions of the heart they serve, vary considerably among individuals, although there are some general patterns (Fig. 1). The RCA, which serves the inferior wall of the left ventricle and portions of the right ventricle, has few branches in the proximal half of its length. The LCA bifurcates within a few centimeters of its origin into the left anterior descending (LAD) and left circumflex (LCX) arteries, both of which give rise to many tertiary branches.

Normal proximal coronary arteries range from 3–5 mm diam at their origin and taper slowly throughout their length, except at major bifurcations, where the sum of the branch cross-sectional areas is approximately equal to the area proximal to the bifurcation. Angioplasty is rarely performed in arteries with a normal diameter less than about 1.5 mm, and, at present, stents are rarely placed in arteries whose normal diameter is smaller than about 3.0 mm, as measured by angiography.

Arteries consist of a tubelike structure that is lined by endothelium (Fig. 2). Next to the endothelial layer is a subendothelial connective tissue layer called the intima, which has surface cells flattened and longitudinally oriented. Intima is surrounded by an elastic layer called the internal elastic membrane. Surrounding these inner layers is a relatively thick layer of media composed of smooth muscle cells and elastic tissues in varying proportions. The outer layer of the media is called the external elastic membrane. The outermost layer of arteries is the adventitia, composed mainly of collagenous fiber. The principal difference between arteries of different sizes is found in the media. In larger vessels elastic tissue predominates, while in the smaller vessels smooth muscle cells form most of the substance.

B. Atherosclerosis and restenosis

Atherosclerosis is the formation of plaques that gradually reduce the lumen of the artery, compromising blood flow and oxygen delivery. The plaque begins in the intima by deposits of fatty debris from blood. Smooth muscle cells from the internal elastic membrane and media proliferate. Collagen and elastin are produced and accumulate in the intima, leading to focal thickening where platelets and cholesterol soon begin to adhere to the endothelium (Fig. 2). As the disease progresses, lipids accumulate in the intima to form yellow fatty streaks. A fibrous plaque then begins to form. It contains lipids, necrotic cells, and collagen. The media becomes thickened from this process. Eventually, a complex lesion develops as the core of the fibrous atherosclerotic plaque necroses, calcifies, and hemorrhages. This causes reduction in blood flow, platelet aggregation, and ultimately formation of a thrombosis with consequent myocardial ischemia and/or infarction.

Restenosis after an angioplasty follows a similar history.7 Angioplasty leads to a fracture of the atherosclerotic plaque, the intima, and sometimes extending into the media (Fig. 2). These injury sites are immediately lined by platelets and later lined by a fibrin meshwork in which platelets and red blood cells become entrapped. This thrombus usually stabilizes over the course of minutes to hours. Within several days blood borne monocytes initiate the phagocytosis of the fibrin meshwork. Simultaneously smooth muscle cells migrate from the media into the intimal subendothelial space, leading to neointimal proliferation. Over weeks to months the neointima becomes less cellular and the healing site begins to resemble a fibrous plaque. In most patients the lumienlarging effect of angioplasty outweighs the lumen-narrowing effect of neointimal hyperplasia. However, in about 40% of the patients neointimal hyperplasia is excessive and results in clinically symptomatic restenosis within three to six months.

Since the 1950s the gold standard for the diagnosis of coronary atherosclerosis has been the angiogram. The utility of the angiogram derives from its ability to determine easily the distribution of coronary arteries and the location of atherosclerotic narrowings. However, the angiogram is not able to image the atherosclerotic plaque itself. The development of intravascular ultrasound (IVUS) has led to a new tool capable of imaging the distribution of plaque, the calcium deposits in the plaque, and the placement of the stent.8–11 A typical example of IVUS images is illustrated in Fig. 3 from a recent review by Yock et al.12 Such cross-sectional views of the vessel anatomy have proven useful in treatment planning of intravascular brachytherapy.

C. Percutaneous transluminal angioplasty

The primary objective of angioplasty is to re-establish a stable lumen with a diameter similar to that of the normal artery. This goal may be achieved using a variety of interventional devices, including the angioplasty balloon, laser, rotoblator, and stent, all described briefly below. The selection of one or more interventional devices for a given stenotic lesion depends on the size, location, and characteristics of the lesion. A brief review of these devices is presented now.

Balloons: in cases where the lesion can be spanned with
an angioplasty balloon, a sufficient increase in diameter ("acute gain") can often be achieved by balloon dilatation alone. The mechanism by which balloon angioplasty increases lumen diameter is by stretching and usually rupturing the internal elastic lamina, often resulting in one or more fissures extending into the medial layer. Flaps may protrude into the lumen, and/or a dissection may extend well beyond the angioplasty site. These common post-angiographic morphologies increase the risk of thrombosis and abrupt occlusion. In addition to this source of acute failure, the most important problem is restenosis.

**Cutting and ablating devices:** while balloon angioplasty enlarges the lumen by stretching and splitting the wall, in some cases this is made impossible by lesions with a lumen too small for the balloon to cross, or by heavy calcification of the arterial wall, making it too tough and inelastic to split or stretch. In these cases it may be necessary to remove tissue by cutting (atherectomy device), abrading (rotoblator), or vaporizing (laser). Because the risk of arterial wall perforation is clearly much higher with these methods, they are usually not applied aggressively to achieve the desired final lumen size; rather, they are used to initially "debulk" the lesion, and then followed by balloon angioplasty and/or stent placement.

**Stents:** placement of one or more intra-arterial stents following angioplasty effectively repairs dissections, prevents flaps from protruding into the lumen, resists elastic recoil, and minimizes loss of lumen diameter due to remodelling, significantly improving the short term result of angioplasty. For this reason stents are being placed in an increasing fraction of angioplasty procedures. However, stents do not appear to eliminate restenosis and, in fact, may actually stimulate proliferation. For this reason there is a strong interest in finding a method, such as radiation therapy, that can be used in conjunction with stenting to produce a definitive intervention for obstructive atherosclerotic lesions.

**D. Overview of the restenosis problem**

Restenosis is a complex process comprising three separate mechanisms: early recoil, neointimal hyperplasia, and late contraction (Fig. 4). Chronologically, the first is the elastic recoil that occurs promptly after the overstretch of the artery. This has been quantitated at approximately 50% of the cross-sectional area or one-third the lumen diameter on average. In other words, an artery dilated with a 3 mm balloon will commonly have a lumen in the dilated segment of 2 mm following balloon deflation and passage of a few minutes time. This elastic recoil does not seem to progress much beyond the first few minutes after balloon deflation. Observations made the day following balloon angioplasty show little further decrease in lumen size. The second component of restenosis is intimal proliferation resulting in new tissue growth occupying the cracks and tears in the vessel wall and sometimes growing to produce very severe reobstruction of the artery. This process probably begins within days after angioplasty and continues for weeks or months. The third mechanism for restenosis that has been recently elucidated is analogous to wound contracture and is sometimes called remodeling. The entire artery may become contracted so that the external elastic lamina occupies a smaller circumference than it did following the procedure. It has been estimated by Mintz et al. that this process may account for up to 60% – 65% of the lumen loss judged by intravascular ultrasound.

Although the focus of the discussion above has been coronary arteries, similar problems of restenosis following angioplasty or stent placement have been encountered within the peripheral vascular system. Several institutions report five-year patency rates following femoropopliteal balloon angioplasty of 50% – 61%. Recent studies of stents in femoropopliteal vessels demonstrated a similarly high rate of restenosis as with balloon angioplasty. This phenomenon seems less frequent in stented iliac and renal arteries. The incidence of restenosis in peripheral vessels seems highly dependent on the anatomic location of the original lesion, the morphology of the lesion, and the distal flow with lower restenosis rates occurring in larger vessels, and focal lesions with good distal flow.

**E. Preclinical studies of vascular irradiation**

The potential role of radiation in preventing restenosis following angioplasty or stent placement was first elaborated in the literature by Dawson, although there exists clinical and preclinical studies antedating this publication. The first author to report the use of endovascular brachytherapy was Friedman and his group from the Mount Zion Hospital in San Francisco, who in the mid 1960s showed that the formation of vascular plaques could be inhibited by inserting an 192Ir wire into the aorta and delivering approximately 14.4 Gy to the vessel wall. It remained until the early 1990s when several investigators reported mixed results using external beam radiotherapy.

Interest in intravascular brachytherapy grew recently when groups led by Weinberger from Columbia, Waksman from Emory, and Raizner from Baylor reported a potential benefit of intraluminal 192Ir in the prevention of restenosis in the porcine model. In the Columbia and Emory studies the radiation was administered with a hand delivered 192Ir ribbon (Best Industries, Springfield, VA). Raizner delivered the dose in their study with a high dose rate afterloader (Omnitron, Houston, TX). Comparing their results is confounded by differences in source configuration and prescription points, and methods of analysis. Weinberger found that 15 and 20 Gy delivered at a 1.5 mm distance from the source center significantly reduced neointimal hyperplasia, but 10 Gy was worse than controls. In contrast, Waksman et al. found that doses in the range of 3.5 – 14 Gy delivered at a 2 mm distance from the source center (0.5 mm depth from a typical arterial wall) significantly reduced neointima formation compared to controls with the animals being sacrificed at two weeks following injury. Here 14 Gy was associated with the greatest reduction in neointima formation and 7 Gy when administered 48 h following balloon injury was more effective than when delivered at the time of injury. Mazur examined the potential benefit of 10, 15, and 25 Gy delivered
at 1.5 mm depth and found that 15 and 25 Gy were effective, but no benefit was seen with 10 Gy. Both Waksman and Weinberger subsequently extended these observations to six months and showed the durability of this effect. In these studies Waksman et al. showed the benefit of delivering 7 and 14 Gy at 2 mm depth and Weinberger’s group showed a durable effect with 20 Gy at 1.5 mm depth at six months.

Two groups reported on preclinical studies utilizing beta sources developed specifically for clinical use. Verin et al. showed that a regular metallic stent radiotherapy in a cyclotron could reduce restenosis when applied to rabbit iliac vessels. A stepwise reduction of neointimal hyperplasia was seen with stent activities between 3.9 and 35 μCi. Although there was evidence of delayed neoendothelialization, no increase in vascular thrombosis was seen. Laird et al. has reported that neointimal hyperplasia could be inhibited in the short term by the application of a 32P impregnated stent. These stents had activities in the range of 0.14 μCi and delivered doses to tissue of approximately 280 cGy (a more detailed analysis of dosimetry is discussed later in Sec. VII C and Table VI). When assessed at 28 days post-implantation, there was a significant reduction in neointimal proliferation and stenosis with the radioactive stents. There would seem to be some advantage to the 32P impregnated stent over the radioactive steel stent due to the long half-life of some of the decay products of the steel stent. Sources with activities described by these authors could be handled without significant radiation precautions unlike the catheter-based systems.

F. Clinical studies of vascular irradiation

1. Peripheral vessels

The first study done using radiation to prevent restenosis was carried out by Liermann, Schopohl, and Bottcher in Frankfurt. In this study they selected patients for treatment who had a clinically relevant recurrent stenosis in the superficial femoral artery greater than 4 cm in length that had occurred less than six months after the last percutaneous transluminal angioplasty (PTA). All the patients had undergone prior PTA or laser therapy and had a stent placed prior to or at the time of irradiation, and all patients were 65 years or older. The patients received 12 Gy at the luminal surface with a HDR afterloader. With 25 patients treated as of their latest follow-up report and some patients with over five years of follow-up, they have not seen any evidence of restenosis in the treated segment. Not all of the patients have undergone systematic reevaluation with angiography so there is no information published or presented at this time as to any degree of luminal narrowing following treatment. One would have generally expected at least a 30% restenosis rate in these size vessels following primary angioplasty, and this study provides strong evidence for the benefit of adjuvant
irradiation. What is more important, however, is the fact that there was no late restenosis or other evidence of complications of the adjuvant irradiation. The authors point out in their paper that the source was not centered within the peripheral vessel, and if the catheter had remained opposed to one of the coronary arteries for the duration of the treatment it is possible that the absorbed dose, based on minimum and maximum distances of the vessel wall, ranged from 8–28 Gy. This information gives us some indication that the dose range of effective treatment and safety could be quite broad.

The second clinical study of irradiation in peripheral vessels was also carried out in Germany by Steidle and his colleagues in Ravensburg. This study was a randomized study between stent placement with and without adjuvant, fractionated external radiation treatment. The patients were treated with 12.5 Gy in 2.5 Gy fractions following stent placement in superficial femoral arteries. Of the 11 patients who received radiation treatment, there were only two episodes of occlusion with minimum seven months follow-up. In the 13 control patients there were five episodes of occlusion. Furthermore, there were no complications attributable to the radiation.

The only additional study carried out in peripheral vessels in humans is a preliminary report from Waksman et al. involving adjuvant irradiation following angioplasty at the venous anastomotic stenosis in percutaneous grafts in dialysis patients. Stenosis at the venous anastomosis of the polytetrafluoroethylene (PTFE) graft with the outflow vein is the most common (±80%) underlying cause of graft failure. Patency rates after recanalization with thrombolysis and angioplasty are plagued by recurrent restenosis: six months patency rates are only 30%–45%. In the 11 patients (16 lesions) treated at Emory with radiation following angioplasty, only 36% of the grafts remained patent at 44 weeks. This pilot study was too small to determine effectiveness of radiation and did not use a centering catheter for the wire, a probable requirement for dose optimization.

A randomized multicenter trial for intravascular brachytherapy of femoral popliteal arteries has been initiated by Waksman. This protocol is approved by the USFDA. In this protocol the irradiated group will receive 14 Gy to a depth of 2 mm from the vessel wall. The intent is to deliver this dose to the adventitia using a centered catheter-based beta source. Nori et al. have initiated a phase I/II FDA approved pilot study using external beam irradiation therapy following angioplasty of venous outflow stenosis in failing grafts.

2. Coronary vessels

The first study of intracoronary brachytherapy in humans was initiated in July 1994 by Condado and his colleagues in Caracas, Venezuela. This study involved the administration of radiation from the insertion of a special small diameter 192Ir wire (1.5 Ci) into the vessel after angioplasty, rotoblator, or stent placement. In this study 22 arteries in 21 patients were treated over a five-month period of time. At the initiation of their study, the patients received 25 Gy at a standard depth of 1.5 mm from the source center. After the first ten arteries were treated, a further 12 arteries were treated with all but one of these patients receiving 20 Gy at the luminal surface of the reference diameter. With a minimum of six months follow-up in the treatment groups there have been four cases of restenosis. Angioplasty was successful in 20 of 22 lesions. The delivery of radioactive source wire was successful to all treated sites and was free of major procedural complications. Angiographic study at 24 h post-procedure
demonstrated a reduction of the mean minimal lumen diameter (MLD) from 1.9 ± 0.6 mm to 1.4 ± 0.3 mm. At 60 days, angiography demonstrated total occlusion in two arteries and a pseudoaneurysm in one artery. At late follow-up all remaining arteries (20) remained patent with a mean MLD of 1.7 ± 0.8 mm. Angiographic restenosis was demonstrated in four patients. Clinical events included myocardial infarction in one patient, a repeat of percutaneous transluminal coronary angioplasty (PTCA) in four, and persistent angina in seven patients. None of the four restenosis cases occurred in the initial group treated with 25 Gy. What is more interesting in this study is the fact that there were some vessels that got slightly larger after treatment, suggesting positive remodeling.

The second clinical trial that has been presented is the randomized trial of endovascular irradiation using a hand delivered 192Ir source train organized by Teirstein et al. at The Scripps Clinic in La Jolla, CA. In this trial patients are randomized to receive or not receive endovascular irradiation following intracoronary stent placement. In this study the prescribed dose is based on intravascular ultrasound (IVUS) assessment of the maximum distance from the catheter to the coronary stent. Here 8 Gy is delivered to this point as long as the maximum dose does not exceed 30 Gy. Fifty five patients were enrolled: 26 were assigned to the 192Ir group and 29 to the placebo group. Restenosis occurred in 17% of the patients in the 192Ir group versus 54% of those in the placebo group. What is more important about this trial is the fact that they have managed to use a hand-delivered iridium source of up to ~140 mCi without seeing any increase in badge readings of the participating physicians. Furthermore, they have left the radiation source within the coronary artery for up to one-half hour without any increase in complications from this procedure. Results of this randomized trial indicate that radiotherapy and stenting significantly reduced subsequent restenosis in patients with previous restenosis; restenosis was decreased by angiographic, ultrasonographic, and clinical measurements; and no adverse events were observed at about 12 months. The investigators conclude that radiotherapy with 192Ir reduces the proliferative response to human coronary angioplasty.

Intraluminal beta irradiation has been shown by Popowski et al. to markedly decrease fibrointimal proliferation after PTCA. Between June 21 and November 15, 1995, 15 patients (six women and nine men, age 72 ± 5 years) underwent intracoronary beta irradiation immediately after a conventional PTCA procedure. Both the PTCA and irradiation procedure were done in a conventional catheterization laboratory, using an endoluminally centered pure metallic 90Y source, a newly developed technique of intracoronary beta irradiation. Both the PTCA and the irradiation procedure were technically feasible in all attempted cases, and a dose of 18 Gy was delivered, with a local exposure time of 400 ± 200 s (the range 153–768 s). In four patients the intervention was completed by intra-arterial stent implantation because of dissection induced by the initial PTCA. These early experiences of Popowski et al. suggest that reliable and reproducible dose delivery can be achieved, and that coronary endoluminally centered beta brachytherapy is both feasible and safe on a short-term basis in the clinical setting.

King et al. initiated a feasibility trial using a catheter system based on a 90Sr/90Y beta source. At present, 23 patients have undergone balloon angioplasty followed by endovascular irradiation. The 30-day safety endpoint examination has been completed without any adverse events being noted, and the patients are being followed with angiographic examinations at six months to document the degree of neointimal formation, the late lumen loss and loss index, the restenosis rate, and any other effects that might be observed angiographically. Although there is no control group for this study, the patients were selected by the criteria of the Lovastatin™ restenosis trial and the quantitative angiographic assessment is being performed by the same core laboratory that performed that trial. Early results from this feasibility study are also highly encouraging.

Early clinical trials with 32P stent activities of 0.5–3.0 μ Ci have shown no untoward events at 1 month follow-up. Presently, clinical dose escalation safety studies using 32P Palmaz–Schatz stents are underway in the USA and Europe; additionally planned randomized clinical trials are forthcoming.

III. IRRADIATION TECHNIQUES

Intravascular brachytherapy techniques fall naturally into two categories: (1) temporary implant-balloon angioplasty (radioactive seed or wire) and (2) permanent implant-radioactive stent. For temporary implants, single fraction, acute doses of 15–20 Gy are required to a length of 2–3 cm of the vessel wall, which may be 2–5 mm in diameter. The dose distribution should be confined to the region of the angioplasty, with reduced doses to normal vessels and the myocardia. Dose rates greater than 5 Gy/min would be optimal in order to maintain treatment times within tolerable limits, although precise requirements are not yet known. Depending on catheter design, the patient will have greatly reduced arterial blood flow during irradiation, and longer treatment times will increase the risk of complications. This suggests high dose rate (HDR) afterloading, perhaps with specially designed sources suitable for insertion into standard or modified catheters.

Current angiographic techniques utilize open ended catheters flexible enough to negotiate multiple bends between the femoral and coronary arteries, yet stiff enough to be pushed through greater than 100 cm of the artery. Vessels suitable
for intravascular brachytherapy may be as small as 3 mm diam and small radii of curvature need be navigated. The radioactive source must have similar flexibility. Source integrity is of great importance as dislodgment into a coronary artery could be fatal. Seeds should have dimensions on the order of less than or equal to 1 mm diam and 1–10 mm length. Treatment with such a source would require either multiple sources on a line (such as those currently available for conventional afterloading), or programmable source placement (similar to conventional HDR units) to permit treatment of 2–3 cm of coronary artery wall, or up to 5 cm of the vessel wall in peripheral vessels. In theory, the source could be inserted directly into the coronary artery, or, more likely, into a conventional or slightly modified balloon catheter. In either case, it is desirable that the source be centered within the coronary artery to ensure uniform dose to the arterial walls. Balloon catheters designed to ensure some centering have recently been developed by some manufacturers.

The objective of intravascular brachytherapy is to irradiate a lesion with a size of millimeters in contrast to conventional brachytherapy, where the lesion may be 1–5 cm in size. This makes it possible to consider low-energy photon emitters and beta emitters as potential sources for intravascular brachytherapy. For conventional interstitial brachytherapy procedures such as those for prostate cancer photon energies as low as of 20–50 keV are considered adequate. However, for conventional intracavitary brachytherapy, such as those for gynecological cancers, it is necessary to use a minimum photon energy of about 50 keV in order to obtain adequate depth of penetration. For the same reason, i.e., the inadequate depth of penetration in tissue, the beta emitters are generally not suitable for conventional brachytherapy. Nath and Liu explored this issue of intravascular brachytherapy by calculating radial dose functions of a range of energies for photons and electrons in the range of 1–10 mm using Monte Carlo simulation. Calculated radial dose functions for photons and electrons in a point source geometry are shown in Fig. 5. The reference depth was chosen to be 2 mm. It was concluded that photons above an energy of 20 keV and electrons above an energy of 1.0 MeV are acceptable from the point of view of an adequate depth of penetration for intravascular brachytherapy.

Many different radionuclides are under investigation for intravascular brachytherapy (Table I). Most intravascular brachytherapy studies to date have used $^{103}$Ir seeds of 10–20 mCi activity. Typical seed dimensions are 0.5 mm diam, 3 mm in length. Multiple seed arrays embedded in a 1 mm diam plastic catheter are used with variable spacing but usually less than or equal to 0.5 cm. While these sources have proven useful for preliminary studies, the relatively high-energy and low dose rates are not ideal. In addition, to achieve the dose rates of 4–5 Gy/m, approximately 500–1000 mCi of gamma emitting isotopes will be required. This will present additional radiation safety problems, with either HDR or hand loaded sources. Lower-energy gamma and x-ray emitters such as $^{125}$I and $^{103}$Pd also present fewer radiation safety problems, but are not currently available at the required specific activities.

$^{32}$P, $^{90}$Sr, $^{90}$Y, and other beta emitters have been suggested. Beta emitters would require much lower total activities (20–50 mCi) and have additional, obvious radiation safety advantages. Electrons from some common beta emitters, however, may not have sufficient range for treating larger diameter peripheral vessels.

An alternative possibility for irradiation is to inject a beta-emitting liquid directly into the angioplasty balloon. This may have advantages over other proposed procedures in that accurate source positioning and uniform dose to the vessel walls is assured, and it can be used in conjunction with existing catheters. About 370 MBq (equal to 10 mCi) of $^{32}$P in a 0.2 ml balloon would be required to deliver 20 Gy at a distance of 2 mm from the center. The chemical and radiological toxicity must also be acceptable, in the event of balloon rupture (the probability of balloon rupture is less than 0.001). Several high-energy beta-minus emitters (and possibly positron emitters) appear to be possible for this application.

Beta-minus emitters, such as $^{32}$P and $^{90}$Y also appear to be most suitable for use with permanently implanted radioactive stents, although low-energy x-ray emitters such as $^{125}$I and $^{103}$Pd may also be possible. The radioactive material can be coated onto, or impregnated into, the actual stent using ion implantation techniques. Activation of the stent in a nuclear reactor is also possible. The advantages of radioactive stent implantation include conformity of dose to the lesion and very low activities ($\mu$mCi).

For any of these techniques, cost and half-life will be factors in source selection. If the amortized cost of the radioactive source is greater than $10^3–10^4$ per patient, the treatment may not be economically viable. A high demand for these treatments, however, can reduce substantially the cost per patient. The remote-controlled afterloaders may have a higher capital cost but lower operational cost compared to radioactive stents.

IV. OVERVIEW OF BASIC PERCUTANEOUS TRANSLUMINAL CORONARY ANGIOPLASTY (PTCA) PROCEDURES AND DEVICES

Reliable systems have evolved for establishing arterial access, controlling bleeding, and maneuvering catheters and catheter-based devices through the arterial tree to the treatment site. Systems for peripheral and coronary arteries are similar, but the smaller size and greater tortuosity of the coronaries require smaller and more flexible devices. Detailed descriptions of these systems exist in textbooks as well as in device manufacturers’ literature. Here we present an overview of typical systems for coronary angiography, balloon angioplasty, atherectomy, laser, and stent placement, with a particular emphasis on standard dimensions and other physical requirements that apply to all intraarterial devices. A list of stent types is presented in Table II.

Patients are selected for PTCA on the basis of a variety of invasive and noninvasive tests, including ECG, echocardiogram, nuclear stress test, and/or cardiac catheterization. The final decision and planning of the PTCA procedure is always
based on information from the coronary angiogram, which provides the best definition of coronary anatomy, location, and severity of lesions, and the presence of collateral vessels to regions of myocardium supplied by diseased vessels being considered for PTCA ("target lesions"). In many cases this diagnostic coronary angiogram is performed immediately prior to the angioplasty procedure, significantly reducing the cost and risk compared to two separate procedures.

Because angioplasty and/or stenting is frequently performed as an acute therapy, it is common for patients to be unstable, requiring close monitoring and possible interventions such as intravenous medications, defibrillation, or placement of an intraaortic balloon pump. Patients must be closely attended by the coronary angiography team at all times during the procedure.

**Arterial access:** patients scheduled for angiography and/or angioplasty are usually placed on medications that include aspirin, a calcium channel blocker, and antianginal medication. In the catheterization laboratory, the patient is placed on the table, covered with sterile drapes, and the potential entry sites are prepared. An intravenous line is established for the administration of fluids and drugs, and the patient is usually placed on conscious sedation. The target artery is accessed transcutaneously via a puncture of an access artery, typically the common femoral artery or the brachial artery. After administering a local anesthetic the access artery is entered percutaneously with an 18 or 19 gauge hypodermic needle or a micro puncture set, a guide wire is passed through the needle into the artery, and the needle is removed, leaving the wire in place. An introducer sheath is passed over the wire and pushed through the puncture site into the artery, forming a tight seal with the puncture opening. A guide catheter is then inserted through the introducer and into the artery, forming a tight seal with the introducer. Hemostasis is completed by a rotating hemostatic valve on the Y adaptor at the proximal end of the guide catheter.

**Introducer sheath and maximum size of interventional devices:** the use of an introducer sheath reduces arterial trauma, particularly during interventional procedures that involve multiple exchanges of catheters and guide wires. Damage to the artery and subsequent complications are directly related to introducer sheath size, which is expressed as the diameter of the largest catheter that can be passed through it, typically 7 or 8 French (1 French = 1/10 = 0.318 mm diam). This size places an upper limit on the diameter of all angioplasty catheters of less than 2 mm, since these devices must pass through the guide catheter that must itself pass through the introducer sheath. In practice, angioplasty devices must be much smaller than this limit in order to pass through target lesions with minimum lumen diameters typically less than 1 mm. Devices that are deployed following balloon dilatation, such as stent delivery systems or intravascular brachytherapy sources, can be slightly larger than 1 mm, but systems approaching the limit set by the introducer sheath/guide catheter size will fail to negotiate many coronary arteries, even after angioplasty.

**Guide catheter:** guide catheters and diagnostic angiography catheters have preformed bends at the distal end to facilitate selective entry into the left or right coronary arteries. A relatively stiff guide wire keeps the catheter straight while it is advanced up the descending aorta (femoral approach), around the aortic arch and down the ascending aorta. The wire is then withdrawn, allowing the catheter to take the proper shape for entering the ostium of the target coronary artery. Contrast material is injected to visualize the artery for diagnosis or to confirm a previous angiogram, to verify the adequate placement of the guiding catheter, and to assess the size and topography of the target lesion and arterial branches.

**Guide wire:** when angioplasty is to be performed, the angioplasty device (e.g., balloon, laser, rotoblator, or stent delivery catheter) and its flexible intracoronary guide wire are inserted into the guiding catheter via the “thru-port” of the Y adaptor and advanced to the ostium. At this point the steerable guide wire alone is advanced under fluoroscopic guidance up to, across, and as far as possible past the target lesion to provide a stable guide for repeatedly advancing the angioplasty catheter across the lesion. The guide wire is necessary because balloon and other intracoronary catheters generally lack the torquability and steerability necessary to navigate through a tortuous and/or branching arterial tree. Even if intracoronary catheters had these properties, interventional procedures frequently require that catheters be placed across the lesion and withdrawn multiple times, so that a guide wire over which these catheters can be quickly and safely advanced saves time.

A wide variety of guide wires for various situations and from various manufacturers is available. The distal 20–30 cm are typically radiopaque, and the distal tip may be formable by the operator to help negotiate a particular artery, or have a permanently bent segment ("J" tip) to facilitate steering. Standard short guide wires are at least 175 cm long. Long guide wires, or exchange wires (see below), are 300 cm long. Guide wire diameters are specified in inches, typically from 0.010 to 0.018 in. in increments of 0.002 in. Larger thickness wires are required for peripheral vessels. Wire diameter and construction determine torquability and compatibility with various balloon catheter systems. Larger wire diameter provides better torquability, but the larger wire diameter generally means the angioplasty balloon cannot be as low profile, all else being equal. Thus, low profile balloon catheters, desirable because of their superior ability to cross tight lesions, generally must be used with smaller gauge guide wires that are more difficult to maneuver into place.

**Angioplasty catheters and exchange systems:** it is often necessary to change balloon catheters, or, for example, to switch to an imaging intravascular ultrasound catheter or intravascular brachytherapy source catheter, while leaving the guide wire across the lesion. When this is done the guide wire must be held in place by the operator while simultaneously pulling back on the catheter. If the catheter is a central lumen, over-the-wire type, the wire must be long enough that the entire catheter can be removed from the guide catheter while the operator continues to hold the proximal end of the wire, or else friction with the catheter will pull the wire from its place across the lesion. Thus, guide wires designed to allow over-the-wire catheters to be ex-
changed, so-called "exchange wires," are 300 cm long, more than twice as long as the standard balloon catheter length of 135 cm. Many standard (nonexchange) guide wires, although only 175 cm long, allow an extension wire to be attached to the proximal end via a threaded or spring mechanism so that catheter exchanges may be performed. Other systems for exchanging intracoronary catheters have been developed, the most widespread of which is the "monorail" system that uses catheters in which only a short segment at the distal end slides along the wire, so that the wire and the catheter exit the guide catheter separately except for the last few centimeters at the distal end.

Catheter-based brachytherapy systems must meet the same general constraints as other angioplasty devices, i.e., they must be (1) small enough to pass through a standard 7 or 8 French guiding catheter; (2) flexible and pushable enough to track through tortuous anatomy with radii of curvature of 5 mm or less and diameter of 2–3 mm, without damaging the arterial wall; (3) small enough to be safely advanced through the target lesion; (4) compatible with standard guide wires and catheters, preferably with a monorail design for ease of exchange with the balloon or stent delivery catheter; (5) visible under fluoroscopy for precise localization of the dose relative to the treatment area; and (6) reliably constructed so that there is negligible risk of a device failure resulting in injury to the patient.

V. DOSIMETRY STUDIES OF INTRAVASCULAR BRACHYTHERAPY

To address some of the dosimetry related issues in intravascular brachytherapy, a brief summary of selected papers is presented in this section. Because of the sparse number of studies available in the literature, the task group was unable to present critical evaluation, reference dosimetry data, or recommendation of a quantitative nature. However, the de-
scription of selected papers presented below is designed to alert the medical physics community regarding some of the pertinent dosimetry issues.

A. Dosimetry studies of gamma emitting seeds and wires

Dose distributions for point or line source gamma and x-ray emitters used in interstitial brachytherapy of cancer have been well studied both theoretically and experimentally, mostly at distances of 1 cm or more. At distances smaller than 5 mm, which are of interest in intravascular brachytherapy, measurements are difficult due to the extremely large dose gradients and other technical considerations. At small distances from the source, dose perturbations caused by scatter and self-absorption of low-energy secondary radiations also make theoretical calculations difficult.

Amols et al.\textsuperscript{53} recently presented analytical calculations of dose distributions and dose rates for 192Ir, 125I, 103Pd, 32P, and 90Sr for use in intracoronary irradiation. The effects of source geometry and positioning accuracy were studied. Although some of the dosimetry parameters are not accurately known at distances of less than 1 cm, linear extrapolation of data given by the AAPM Task Group (TG) No. 43\textsuperscript{52} yielded reasonably accurate results, as demonstrated in Fig. 6, which compares calculated and measured values of dose versus radial distance from a single 192Ir source 0.5 mm diam and 3 mm length. In this study, dose was measured by sandwiching an 192Ir seed between multiple slices of GafChromic\textsuperscript{TM} film in a water equivalent plastic phantom for several hours. Using these dosimetry data isodose distribution in the axial plane around a linear array of five 192Ir seeds with 2 mm spacing between seeds was calculated (Fig. 7). This dose distribution is typical of that used for the irradiation of coronary arteries in various preclinical studies. It is also typical of the doses that would be obtained with an HDR unit programmed to treat a 2–3 cm length of artery. The dose distribution at the internal surface of the arterial wall (approximate radial distance=1.5 mm) is seen to be relatively uniform (±10%) with a rapid dose falloff radially and axially beyond the extent of the implant volume (noted schematically in Fig. 7 by the dashed seed locations). The highest dose at a radial distance of 1.5 mm was normalized to 100%, and only half of the implant zone is plotted (the graph would be symmetric about the axial center of the implant). The total length of the implant volume is approximately 22 mm.

Recently Li et al.\textsuperscript{54} used the Monte Carlo photon transport (MCPT, a code developed by Williamson at the University of Washington) simulation in the dosimetric characterization of various brachytherapy sources for intravascular brachytherapy. This study used MCPT calculations to evaluate the dose distribution of stainless steel encapsulated 192Ir seeds at the range of 1 to 20 mm from center of the source. The results were reported using the AAPM TG-43 formalism. In particular, the radial dose function and the anisotropy function are tabulated and compared with data given in the AAPM TG-43 report. Agreement to within 3% was found between the MCPT calculation results and the AAPM TG-43 reference data for most of the data points. It was found that MCPT-derived values of radial dose function agree to within 1% with the polynomial fitted radial dose function of the 192Ir seeds given in the AAPM TG-43 report at distances of 1 mm to 1 cm and 2% at distances between 1 and 4.5 cm. The largest discrepancies were observed in anisotropy functions along the source longitudinal axis.

B. Dosimetry studies of beta emitting seeds and wires

In 1995, Popowski et al.\textsuperscript{55} developed a beta emitter for intravascular brachytherapy and performed extensive dosimetry measurements using thermoluminescent dosimeters (TLDs). Nonradioactive flexible 90Y wires (diameter of 0.15 and 0.26 mm) were activated within the thermal neutron flux of an experimental reactor. Standard angioplasty balloons (2 cm long, 2.5 mm in diameter when inflated) were inserted for dosimetry into a specially manufactured tissue equivalent phantom. Four wells, drilled perpendicular to the axis of the

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<th>Table I. Some of the possible radionuclides for intravascular brachytherapy.\textsuperscript{a}</th>
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<td>Radionuclide</td>
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<td>32P</td>
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<td>40Y</td>
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<td>106Rh</td>
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<td>188Re</td>
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\textsuperscript{a}All other data from the Table of Radioactive Isotopes (Ref. 51).
\textsuperscript{b}The maximum energy of photons with a yield greater than 1%.
\textsuperscript{c}Practical sources of 90Sr always have 90Y in equilibrium.
\textsuperscript{d}Average photon energy from AAPM Task Group No. 43 (Ref. 52).
\textsuperscript{C, S, and L in the delivery system column denote the catheter-based system, radioactive stent, and radioactive liquid in a balloon, respectively.
balloon, allowed for the insertion of thin, flexible TLDs (disks of 2 mm diam) and spacers. The angioplasty balloon was inflated with air or with contrast media. Radioactive $^{90}$Y wires were left in the central lumen of the balloon for two minutes. Doses at the surface of the balloon and at 1, 2, and 3 mm were determined from TLD readings. Doses obtained at the surface of the balloon for a two-minute exposure for the 0.26 mm wire (balloon inflated with air) and the 0.15 mm wire (air or contrast) were 56.5, 17.8, and 5.4 Gy, respectively. As expected for a beta emitter, the falloff in dose as a function of depth was rapid. External irradiation from the beta source was negligible. Popowski’s experiments indicate that the dose rates attainable at the surface of the angioplasty balloon using this technique allow the doses necessary for the inhibition of intimal cell proliferation to be reached within a relatively short period of time. They conclude that the thin $^{90}$Y wires are very easy to handle and their mechanical and radioactive properties are well suited to the requirements of the catheterization procedure.

Soares$^{56}$ presented the dose evaluation of a $^{90}$Sr source developed for intravascular brachytherapy at Emory University. The dosimetry and characterization of this catheter-based beta-particle emitting brachytherapy source was accomplished in three distinct steps. The first step involved a characterization of seed sources to determine the axial and transaxial uniformity of each seed, as determined by measurements near contact and at 3 mm in a tissue-equivalent material such as A150 plastic. Since there were no axial orientation markings on these very small sources, uniformity of the dose rate perpendicular to the seed axis was crucial to obtaining reproducible results. Once a seed demonstrated suitable axial and transaxial uniformity, it was used in the second step, which involved the measurement of the absorbed-dose rate at a depth of 2 mm in a water equivalent medium. Next, this seed was used in the third step, which involved radiochromic film measurements at several depths in a water-equivalent phantom; the information resulting from these irradiations were then used to construct tables of data that were used to determine the dose rate at any arbitrary point in the tissue-equivalent phantom. Finally, guidance was given for determining the dose rate in media other than the tissue-equivalent material. Each of these topics are discussed in more detail in a later section of this report.

Recently, Xu et al.$^{57}$ presented dose measurements for a $^{32}$P source developed for intravascular brachytherapy. They used TLDs for distances up to 1–5 mm and scintillation detectors. A calibration jig was developed for determining the total source activity and its nonuniform activity distribution along a $^{32}$P source designed for endovascular irradiation. The $^{32}$P source was 27 mm in length and 0.3 mm in diameter and was embedded in the end of a NiTi wire. The distribution of the source activity was obtained and a total activity of 12.25 mCi was determined, which was in agreement with the value measured using a well-type chamber. The radial dose rate distributions were measured using GafChromic film and calculated assuming a both nonuniform and uniform source. The results showed that the best agreement was achieved between the measured and calculated data if the nonuniform source activity was taken into account. These results have been further verified by Monte Carlo dosimetry.$^{58}$

### C. Dose inhomogeneity due to noncentering of source

Amols et al.$^{55}$ calculated dose asymmetry resulting from inaccurate source centering of a catheter-based system. In Fig. 8 the magnitude of the dose asymmetry resulting from centering errors of 30 mm long $^{90}$Sr/Y and $^{192}$Ir wires is shown. Plotted are the ratios of the maximum dose to the vessel wall divided by the minimum dose in a cylindrical vessel 5 mm in diameter as a function of centering offset. As seen, centering errors as small as 0.5 mm in a 5 mm diam vessel result in dose asymmetries of 1.6 for $^{192}$Ir, and 2.1 for $^{90}$Sr/Y. For catheter-based delivery systems, dose uniformity to the arterial wall depends critically on centering the source within the artery and the cylindrical symmetry of the artery itself. Amols et al. concluded that centering is more critical for beta emitters than gammas.

Dose uniformity can be improved if the design of the balloon catheter incorporates some method of centering the source. Popowski et al.$^{59,60}$ presented a dosimetric evaluation of such a new device dedicated to intravascular irradiation, associating a beta source and a centering device prior to initiation of a clinical pilot study. A 29 mm long $^{90}$Y coil, coated with titanium and fixed to the end of a thrust wire, was introduced into the inner lumen of centering balloons of different diameters (2.5, 3, 3.5, and 4 mm). Dose homogeneity was evaluated by studying both axial and circumferential dose variations, based on readings from TLDs placed on the
balloon surface. Axial homogeneity was determined by comparing the readout values of dosimeters located on peripheral balloon segments compared to those located on segments adjacent to the midpoint of the source. The centering ability of the device was studied by comparing measurements on opposing surfaces of the balloon. The dose attenuation by water and contrast medium was evaluated and compared with that in air. The total $^{90}$Y coil activity was measured by liquid scintillation in order to relate activity to surface dose. The activity–surface dose correlation showed that for a linear coil activity of 1 mCi/mm the mean dose rate at the surface of a 2.5 mm balloon filled with contrast medium was 8.29 Gy/min. The doses at the surface of larger balloons (3, 3.5, and 4 mm) filled with contrast were 78%, 59%, and 47%, respectively, of the dose measured at the surface of the 2.5 mm balloon (Fig. 9). The coefficient of variation (CV) in the surface dose for 2.5, 3, 3.5, and 4 mm centering devices filled with contrast medium were 9%, 8%, 9%, and 12%, respectively. There was no statistically significant difference between readouts from central and peripheral balloon segments or among rows of dosimeters facing each other. For a 2.5 mm balloon compared with air, the dose attenuation by water and contrast medium was similar (0.70 and 0.69, respectively), but a significant difference was seen between the readouts of water- and contrast-filled balloons when the diameter was larger than 3 mm ($p<0.001$). No contamination was found in the balloon shaft after source retrieval. The dosimetric tests showed very good surface dose homogeneity, demonstrating satisfactory centering of the source within the centering balloons. From this study Popowski et al. concluded that the achievable dose rates will permit intravascular irradiation with a beta emitter within a short time interval.

D. Comparison of depth dose from gamma and beta rays

Calculations of dose from internally deposited beta-minus emitters is also a well-studied problem, with rigorous reports presented by Loevinger. Recently, a version of this method was used by Amols et al. to estimate dose distributions produced by point sources of beta emitters. Radial dose distributions for either $^{32}$P or $^{90}$Sr/Y beta sources were compared with similar data for $^{192}$Ir (Fig. 10). All doses were normalized to unity at a radial distance of 2 mm. The short range of the betaparticles results in a more rapid dose falloff versus distance than the $^{192}$Ir gamma source. $^{32}$P with the lowest transition energy has the shortest radial dose penetration. From this study, Amols et al. concluded that beta emitters have radiation safety advantages, but may not have suitable ranges for treating large diameter vessels. Gamma emitters deliver larger doses to normal tissues and to staff. Low-energy x-ray emitters such as $^{125}$I and $^{103}$Pd reduce these risks but are not available at high enough activities. They found that accurate source centering is of great importance. If this can be accomplished, then high-energy beta emitters such as $^{90}$Y or $^{90}$Sr/$^{90}$Y would be ideal sources. Otherwise gamma emitters such as $^{192}$Ir may be optimal.

Nath et al. determined the radial dose function for gamma emitters $^{103}$Pd, $^{125}$I, and $^{192}$Ir; and beta emitters $^{90}$Sr, $^{32}$P, and $^{90}$Y using the rts Monte Carlo code for the simulation of electron–photon transport. They used unencapsulated point sources of these radionuclides in these calculations, which included the entire spectra of beta and gamma emissions from each radionuclide and charged particle transport of secondary radiations (Fig. 11). They concluded that for depths up to 10 mm, even low-energy gamma emitters of $^{103}$Pd and $^{125}$I provide as good dose penetration in depth as $^{192}$Ir. However, the specific activity of $^{125}$I or $^{103}$Pd is too low for a catheter-based system.

E. Dosimetry studies of permanent radioactive stents

Fischell et al. have used stents into which $^{32}$P was permanently implanted just below the stent outer surface. Typical dimensions of the stent are 20 mm in length with diameters of 3, 4, and 5 mm. Most of the work in coronary arteries involves the 3 mm diam stent. Activities as low as 5 kBq (0.13 μCi) have been considered. In 1995, Prestwich et al. presented the results of a calculation of the dose distribution surrounding uniform cylinders of $^{32}$P in order to obtain information relevant to the utilization of radioactive stents. The dose distribution surrounding a cylindrical source of $^{32}$P was estimated by the dose-point-kernel method employing numerical integration. Cylinders 20 mm in length with diameters of 3, 4, and 5 mm were considered. The radial distribution is cusp shaped for planes within the length of the cylinder, becoming monotonic for planes beyond the ends of the cylinder. The dose variation from the cylinder wall was roughly exponential and the dose at a specific distance from the wall decreases with cylinder diameter.

In a later study, Prestwich et al. represented the dose along the radial direction located at the midplane of a radioactive stent, simulated by a uniform cylinder of $^{32}$P by an analytical function consisting of the sum of two modified
exponentials. This procedure reproduces values obtained from numerical integration, for which no closed form exists, to within 5% for distances up to 6 mm from the wall and for stent diameters from 2–6 mm.

Coffey and Duggan calculated the dose to tissue from a 1 μCi 32P stent using the dose-point-kernel method, assuming the tissue outside the stent is homogeneous and uniform with properties close to that of water. The cylindrical geometry for a Palmaz–Schatz coronary stent was introduced into the model calculation since this device is the most widely used coronary stent. Dose maps were calculated for distances ranging from 0.1 to 3 mm radially out from the stent surface. The results were compared to actual measurements made using radiochromic film dosimetry from a 32P impregnated Palmaz–Schatz stent produced by an ion implantation process. In this study, verification of the Prestwich model for 32P stents (modified Strecker and Palmaz–Schatz) was provided by measuring a dose for the radial distance from 0.5 to 5 mm from the stent surface using radiochromic film dosimetry (Fig. 12).

Duggan et al. described a model similar to the point dose kernel models of Berger, Brookeman, and Prestwich for the estimation of the dose distribution surrounding a pure beta-emitting 32P coronary stent. In addition, radiochromic dosimetry methods were utilized to experimentally determine the absolute dose and relative dose distributions parallel to the short axis of a 32P Strecker stent (0.22 cm diam and 2.0 cm length, 2.15 μCi) and parallel to the short axis of half a 32P Palmaz–Schatz stent (0.35 cm diam and 0.70 cm length, 8.4 μCi). Correlation of theoretical dose calculation methods and experimental dose distribution results were reported as encouraging. This study provides verification of a theoretical model by measuring a dose with radiochromic film for radial distances from 0.25 to 3 mm from the stent surface and axial distances of up to 4 mm from the center of the stent (Fig. 13). The peaks at 0.2 mm distance represent the extremely high dose areas in the immediate vicinity of the wire mesh of the stent.

Janicki et al. calculated the near-field dose distribution of a realistic 32P impregnated vascular stent employing the dose-point-kernel method in a homogeneous medium. The cylindrical wire mesh geometry for the Palmaz–Schatz stent was numerically introduced in the model calculation, and the dose distribution of the 32P beta emitting isotope was computed at distances ranging from 0.1 to 3 mm from the outside of the stent surface. Measurements made using radiochromic film dosimetry of the dose from Palmaz–Schatz stents impregnated with 32P produced by shallow ion implantation were used to validate the model at radial distances from 0.11 to 4 mm from the stent surface and axial distances of up to 4 mm from the center of the stent (Fig. 14). The close agreement between the model and the film dosimetry results confirmed the validity of this geometry-specific model. As reported recently by Janicki et al., this calculational dose-point-kernel methodology can be adapted to any stent design to yield dose distribution results. Finally, Whiting et al. reported computed dose distributions surrounding a Palmaz–Schatz stent using the Monte Carlo N-particle (MCNP) transport code, which agreed well with the results from Janicki’s model.

In 1995, Ly et al. (aka Li) reported a feasibility study and preliminary dosimetry for a brachytherapy source based on proton-beam activation of a removable intracoronary stent made of shape-memory nickel–titanium alloy (Nitinol™). The stent was activated by 8.5 MeV proton bombardment to produce Vanadium-48: 48Ti(p,n)48V. Due to the high attenuation of the protons by Nitinol, the stent was rotated axially during proton bombardment to achieve uniform activation. A 16.0 day half-life and gamma emissions of 0.511, 0.945, 0.983, 1.312, and 2.241 MeV were measured by spectral analysis to confirm the production of 48V. All other activation products were decayed to the background by three days. Despite the presence of penetrating gamma emissions, over 96% of the dose within 1.0 mm of a 48V stent was from positron absorption, and the dose at 10 cm from the stent was less than 0.02% of the treatment dose. GAF Chromic™ film (23 μm thick active polymer emulsion) was calibrated with a 60Co radiation treatment beam and was used to measure dose distributions for five planes parallel to the stent long axis, spaced 126 μm apart. The complete three-dimensional dose distribution surrounding the stent was estimated by computing the dose distribution for a single “strut” segment by Monte Carlo calculation (MCNP version 4a), then using this as a “strut dose kernel” to perform a summation over all 48 struts making up the stent. The absolute dose based on this calculation and measured total 48V activity agreed with the direct radiochromic film measurements to better than 10%. Full three-dimensional dose distributions can be computed for stents expanded to any diameter, and even for irregularly deployed stems, allowing detailed dose descriptions throughout the treatment volume (an example is shown in Fig. 15).
the balloon was approximately 0.14 cGy/s per mCi/ml solution were also presented. The dose rate at the surface of balloon rupture with present catheter design is described above. Agreement between measurements and calculations is ±3%. While this technique clearly yields desirable dose distributions, the chemical and radiological toxicity of the radioactive liquid must be considered, as there is a risk of balloon rupture with present catheter design (approximately 0.1%). Since most commonly available beta emitters (and all of those listed in Table I, except for 188Re, which in the form of 188Re perchenate as eluted from a 188W/188Re generator is not a bone seeker and is eliminated via the urine with a biological half-life of about 10 h) are bone seeking compounds, the whole body and bone marrow doses that would ensue after a balloon rupture are unacceptably high (100–1000 cGy). New data on 90Y and 188Re chelates, which have short biological half-lives, indicate that those risks may be reduced to a tolerable level.

VI. RECOMMENDATIONS FOR INTRAVASCULAR BRACHYTHERAPY PHYSICS

A. Dose specification and renormalization for catheter-based intravascular brachytherapy systems

The irradiation techniques and specification of radiation doses in various studies using catheter-based intravascular brachytherapy differ from each other significantly, making a direct comparison of the techniques difficult. This AAPM task group reviewed the dosimetry of these catheter-based intravascular brachytherapy techniques. An initial review indicated that different investigators have employed different methods of dose specification. Some were using the dose to the adventitia, some to the wall of the lumen, and some at varying radial distances from the source center. This created a great deal of confusion regarding the efficacy reported in different studies at different dose levels. Therefore, the task group decided to undertake a major scientific effort to renormalize the dosimetry to a common framework. This original analysis was divided into three groups: (1) catheter-based systems using gamma emitters for peripheral vessels; (2) catheter-based systems using gamma emitters for coronary vessels; and (3) catheter-based systems using beta emitters for coronary vessels.

In order to use a common frame for comparing the dosimetry, it was assumed that in the peripheral vessel studies the inner diameter of the vessel is 6 mm and in the coronary arteries it is 3 mm. Assuming these common dimensions, the doses to the luminal wall and at depths of 1, 2, and 3 mm from the walls were calculated.

1. Catheter-based intravascular brachytherapy for peripheral vessels using gamma emitter

Liermann et al. reported the use of a remote afterloading unit (Nucletron MicroSelectron HDR) delivering an 192Ir source of 10 Ci activity to the restenosis site in human femoropopliteal arteries. The delivery technique used a 5 French close-ended catheter inserted into a non-self-centering 9 French catheter (diameter 3 mm). The prescription is specified as delivering 12 Gy to a distance of 3 mm from the center of the source. The vessel segment has a diameter of 6 mm by use of an expanded 6 mm stent. It is therefore assumed that the vessel lumen surface is given 12 Gy. Depth dose calculations were performed to obtain doses of 8.77, 5.51, 3.96, and 3.03 Gy at 4, 6, 8, and 10 mm from center of the source, respectively. Actual minimum and maximum doses delivered to the vessel wall were reported to be 8 and 28 Gy, due to the deviation of the catheter from the center of the vessel.

Waksman et al. used another remote afterloading (Omnitron) unit for treatment of narrowed arteriovenous grafts,
giving a higher dose of 14 Gy at a depth of 0.5 mm from the arterial wall. They have since then decommissioned the remote afterloading unit and switched to the same unit that Liermann et al. used. A non-self-centering catheter is used.

Since the same remote afterloading unit and treatment planning system is used, it is relatively easy to compare the dose specifications used in these studies. The Nucletron MicroSelectron NPS/PLATO treatment planning system used for this remote afterloading unit has optimization algorithms that, in this treatment geometry, in effect increase the source dwell times for dwell positions at the ends of the treated length, so as to maintain dose homogeneity along the treated vessel. The dose calculation algorithm models the source 3.5 mm active length, 5 mm physical length as a point source, but is able to perform calculations based on dose distribution anisotropy data at one given distance from the source center. Tissue attenuation and scattering are corrected for using the formula given by Van Kleffens and Star. For the renormalization of dose specifications presented here, optimized dwell times are calculated using the same treatment planning system, with optimization on dose points placed at prescription distances from the source center for a treated length of 4.5 cm with nine dwell positions, with a dwell position step size of 5 mm. These dwell times are used to calculate the renormalized dose distribution, corrected for dose distribution anisotropy using the data from Williamson.
and Li.\textsuperscript{75} The diameter of the treated vessel is assumed to be 6 mm.

Results of the renormalization process are given in Table III. Average as well as the minimum and maximum doses along the inner 4 cm of the treated length, calculated with a 1 mm grid size, are also given. It can be seen that the failure to account for the dose distribution anisotropy, especially the oblique filtration by source encapsulation, results in a 6%--10% deviation in the actual delivered dose from the nominal prescription dose. In addition, the dose distribution inhomogeneity is underestimated by the computer treatment planning system calculations, though to a smaller extent.

2. Catheter-based intravascular brachytherapy for coronary vessels using gamma emitters

\textsuperscript{192}Ir seeds of the same design as those used in conventional low dose rate brachytherapy, but with higher activity per seed, are also used for the treatment of coronary vessel restenosis. Teirstein \textit{et al.}\textsuperscript{45} uses ribbons of stainless steel encapsulated \textsuperscript{192}Ir seeds, at activities up to 150 mCi per ribbon, to deliver a nominal prescription dose of 8 Gy to the plaque and media region of human coronary vessels. The interseed center spacing between \textsuperscript{192}Ir seeds is 4 mm, and two lengths of ribbons, one using five seeds to obtain 1.9 cm active length and the other using nine seeds to obtain 3.5 cm active length, are used. The ribbon is manually inserted into a non-self-centering 4 French catheter. Ultrasound scans are obtained during the implant procedure to ensure that the minimum and maximum doses to the media remain within the range of 7 to 30 Gy. Dosimetric data for the ribbons at the treated distance (average 3.2 mm from the center of the sources) is based on those by Kline \textit{et al.}\textsuperscript{76}

Weinberger’s group\textsuperscript{30} used ribbons of stainless steel encapsulated \textsuperscript{192}Ir seeds to deliver 20 Gy at a 1.5 mm distance from the center of sources in an animal model. A non-self-centering 4 French catheter within an 8 French guide catheter is used. The ribbons contained five \textsuperscript{192}Ir seeds with 5 mm interseed center spacing. Waksman \textit{et al.}\textsuperscript{32,33} used ribbons of stainless steel encapsulated \textsuperscript{192}Ir seeds in an animal coronary vessel study. The 3 mm long seeds were contained in the plastic ribbon, with no spacing between the seeds (3 mm interseed center spacing). The study prescribes a dose of 3.5,
7, or 14 at a distance of 2 mm from center of the source, along the transverse axis of the $^{192}$Ir ribbon. A non-self-centering 4 French catheter within an 8 French guide catheter is used.

Condado et al.\textsuperscript{44} reported the clinical experience of using an $^{192}$Ir wire of 1.5 Ci activity delivered manually into coronary vessels. The dose is specified as delivering 20 or 25 Gy at a distance of 1.5 mm from the center of the source. A non-self-centering 4 French catheter is used in the study.

It should be noted that while both the Teirstein group and the Condado group used non-self-centering 4 French catheters only for the delivery of treatment, the former group adjusted treatment time using ultrasound measured media thickness, to ensure that no part of the vessel wall received more than 30 Gy dose, while the latter group exercised no adjustment of the treatment time based on individual patient measurement. The resulting hot spot in the latter case therefore can be more than 50 Gy, based on a prescription of 25 Gy to 1.5 mm distance from the center of $^{192}$Ir wire, using the Sievert integral approximation.

Renormalization of prescribed doses as well as the dose distribution at other points within the treated volume is performed in the same manner as the case for peripheral vessel intravascular brachytherapy. For $^{192}$Ir ribbon-based techniques, the source activities and treatment times are first determined from the nominal prescription doses, using the Kline et al.\textsuperscript{76} data for the Teirstein et al.\textsuperscript{45} technique and the Condado et al.\textsuperscript{44} technique, and the point source approximation for the Waksman et al.\textsuperscript{32,33} technique and the Weinberger\textsuperscript{30} technique. These activities and treatment times are then used to recalculate dose distributions, using radial dose function and anisotropy function data calculated by Monte Carlo photon transport simulations\textsuperscript{54} for distances smaller than 1 cm, in combination with the AAPM TG-43 report\textsuperscript{52} data for distances larger than 1 cm, while the dose rate constant data are from the same AAPM task group report. The average, minimum, and maximum doses are calculated using the 1 mm calculation grid size along the treated length, delimited by the centers of the $^{192}$Ir seeds at ends of the ribbons. Coronary vessels are assumed to have a diameter of 3 mm. The treated lengths are as specified by the respective studies. Results of the renormalization are given in Table IV below. It can be seen that, due to the close distance at which prescribed doses are specified, there can be significant uncertainty in the dose actually delivered.

### 3. Catheter-based intravascular brachytherapy using beta emitter

Two groups have reported use of a beta-emitting source in catheter-based intravascular brachytherapy. The Popowski group\textsuperscript{59,60} in Berne, Switzerland, developed a balloon-fitted catheter that is capable of self-centering within a coronary vessel when the balloon is inflated. A $^{90}$Y wire was then used in this catheter for treatment. Dosimetry data were obtained using a TLD measurement technique. Waksman et al.\textsuperscript{37} experimented with a 2.5 cm long source train of five $^{90}$Sr/$^{90}$Y seeds, each of 5 mm length, with no spacing between the seeds. Dosimetry data were calculated using the Monte Carlo method.
Dose distribution data from these reports are used directly to obtain the values given in Table V.

4. Recommendations on dose prescription for a catheter-based system

Results of the above analysis indicate a wide variation in dose specification for catheter-based intravascular brachytherapy, in the extreme case by as much as 56%. When these results were first presented to the cardiology community it became apparent to them that a careful analysis of dosimetry by a qualified medical physicist has great merit in making a meaningful evaluation of the results of preclinical and clinical studies using ionizing radiation. These data (Tables III–V) have, in fact, resolved a puzzling lack of efficacy in some of the studies by showing that the reported doses were, in fact, too low compared to those in other studies showing efficacy because of the choice of a different point for dose specification.

Based upon the above analysis of dose specification and its renormalization in preclinical and clinical studies on catheter-based studies, the task group recognizes that a uniform practice of dose reporting is needed. To this end, the task group recommends that prescription for a catheter-based system should be in terms of a dose delivered at a reference...
distance in water. For intracoronary application, a reference
distance of 2 mm from the source center is recommended.
For a larger, peripheral vessel the reference distance should
be 2 mm larger than the average lumen radius of the vessels
under study.

For the coronary arteries, the choice of 2 mm as a refer-
dence distance provides a dose specification relative to the
source location, which can be easily reproduced and verified
by a data review committee in a multi-institutional study.
However, it suffers from the fact that it does not express dose
delivered to an anatomical structure, e.g., the lumen wall,
adventitia, etc. In fact, for any given patient the lesion is
likely to be eccentric and vary in thickness and eccentricity
along its length; therefore doses to any given anatomical struc-
ture such as the lumen wall are going to vary widely. The
recommendation regarding dose specification for peripheral
vessels is dose at a depth of 2 mm from the average lumen
radius because peripheral vessels can be much larger than
coronary vessels. In a larger vessel the centering of the
batheter-based source becomes more important because of
the larger potential for eccentricity and consequently hot and
cold spots.

Ideally a three-dimensional dose distribution over the en-
tire irradiated volume should be generated for each specific
patient. If detailed three-dimensional quantitative measure-
ments such as those from an IVUS study are available, the
average, minimum, and maximum doses delivered should be
estimated for each clinical case. These dosimetry parameters
should be determined in at least three planes perpendicular to
the catheter and along its length over the lesion.

Because of the potential of a significant market, a large
number of commercial vendors are developing various deliv-
ery systems for intravascular brachytherapy. In order to
evaluate different systems it is important to compare them
using a common specification. Even though it is too early to
develop a rigid standard for intravascular brachytherapy sys-

Fig. 14. Measured dose profiles (dots) and the dose point kernel (DPK) model predictions (solid lines) taken at $\theta=30^\circ$ and along the long axis of the 3.5 mm diam one-half Palmaz–Schatz stent impregnated with $^{32}$P, at radial distance $d$ of (a) 0.112 mm, (b) 0.328 mm, (c) 0.436 mm, (d) 0.784 mm, (e) 1.039 mm,
(f) 1.294 mm, (g) 1.549 mm, and (h) 1.804 mm exterior to the stent surface. All dose values are normalized to a 14.3 days exposure with an initial activity $A_0=37$ kBq (1 $\mu$Ci). The agreement between the experimental dose profiles and the dose-point-kernel model predictions is very satisfactory, despite some
large discrepancies over limited regions for some scans, which can be explained by scanning artifacts. (Reprinted with permission from Janicki, Duggan,
1997, American Association of Physicists in Medicine.)
The AAPM recommends the use of the TG-43 dose calculation formalism for catheter-based intravascular brachytherapy systems using photon-emitting sources. The TG-43 formalism recommends that the dose at a point \((r, \theta)\), as shown in Fig. 17, be calculated using

\[
D(r, \theta) = S_K \Lambda [G(r, \theta) / G(r_0, \theta_0)] g(r) F(r, \theta),
\]

where \(S_K\) = air kerma strength, \(\Lambda\) = dose rate constant, \(r\) = radial distance from the source, \(\theta\) = angle between the line segment from point of interest to center of source, as measured from a line containing the source’s long axis, \(F(r, \theta)\) = anisotropy factor describing the dose variation versus angle. This function is normalized to unity at \(\theta = 90^\circ\), \(G(r, \theta)\) = geometry factor resulting from spatial distribution of the radioactivity within the source, \(g(r)\) = radial dose function, and \((r_0, \theta_0)\) = the polar coordinates of the reference point.

The reference point recommended by TG-43 is the point on the transverse axis at a distance of 1 cm, i.e., \(r_0 = 1\) cm and \(\theta_0 = \pi/2\). Under the point source approximation, the geometry factor and radial dose function are

\[
G(r, \theta) = \frac{1}{r^2},
\]

\[
g(r, r_0) \approx \frac{D(r)}{D(r_0)} \frac{r^2}{r_0^2}.
\]
Using the TG-43 notation, the dose at a distance \( r \) from a source under the point source approximation can be expressed as

\[
D(r) = S_K \Lambda \frac{r^2}{r^2} g(r) \phi_{\text{avg}},
\]

where \( \phi_{\text{avg}} \) is the average anisotropy factor. For a line source, the geometry factor is

\[
G(r, \theta) = \frac{\beta}{L r \sin \theta},
\]

where \( \beta \) is the angle subtended by the active length \( L \) at the point of interest.

The strength of the gamma-emitter source should be determined in terms of its air kerma strength, as described in the AAPM TG-43 report. The air kerma strength of the intravascular brachytherapy source should be traceable to a NIST standard or to an ADCL standard. For gamma-emitting sources these procedures for the specification and determination of source strength are identical to those described in the TG-43 report.

Because distances of interest in intravascular brachytherapy are much smaller than the conventional brachytherapy reference distance of 1 cm, it is recommended that the reference distance for intravascular brachytherapy dosimetry be \( r_0 = 2 \text{ mm} \). In order to avoid confusion with TG-43 terminology, the following modified notation is recommended to generalize Eq. (1):

\[
D(r, \theta) = S_K \Lambda r_0 [G(r, \theta)/G(r_0, \theta_0)] g_{r_0}(r) F(r, \theta),
\]

where \( \Lambda r_0 \) is the dose rate constant at a reference distance of \( r_0 = 2 \text{ mm} \), and \( g_{r_0}(r) \) is the radial dose function normalized to a radial distance of \( r_0 \) and given by Eq. (2) for a point source.

The radial dose function for intravascular brachytherapy should be expressed with a reference point at 2 mm. Similarly, the dose rate constant \( \Lambda r_0 \) should also use the reference distance of \( 2 \text{ mm} \) i.e., it should be the dose rate at a reference distance of \( 2 \text{ mm} \) in water from a source of unit air kerma strength. All relative dosimetric parameters such as \( g_{r_0}(r) \); \( G(r, \theta) \); and \( F(r, \theta) \) should be measured for each specific type and model of a delivery system. However, all users do not have to measure these parameters as long as they have verified the validity of the parameters used.

### 2. Dosimetry of catheter-based beta emitters

Because national standards for the air kerma strength of beta-emitting sources do not exist, the AAPM recommends that the dose at a point \( (r, \theta) \) be determined using

\[
D(r, \theta) = D(r_0, \theta_0) [G(r, \theta)/G(r_0, \theta_0)] g_{r_0}(r) F(r, \theta),
\]

where \( D(r_0, \theta_0) \) is the dose rate in water at the reference point \( (r_0, \theta_0) \). The reference point for intravascular brachytherapy calibration for beta sources should be \( r_0 = 2 \text{ mm} \) and \( \theta_0 = \pi/2 \). All other quantities have the same meaning as in the case of gamma emitters. For the calibration of beta-emitting sources, i.e., the determination of \( D(r_0, \theta_0) \), the method used by Soares et al. is an equivalent method, should be used. Soares et al. measured dose rate averaged over a 1 mm diam area from current measurements with an

### Table III. Dose distribution of gamma emitter intravascular brachytherapy in peripheral vessels.

<table>
<thead>
<tr>
<th>Author</th>
<th>Liemann et al. 1994 (Ref. 40)</th>
<th>Waksman et al. 1996 (Ref. 43)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of study</td>
<td>Clinical trial, peripheral vessel stenosis</td>
<td>Clinical trial, occluded arteriovenous graft</td>
</tr>
<tr>
<td>Type of catheter</td>
<td>Non-self-centering, 5 French catheter in a 9 French catheter</td>
<td>Non-self-centering, 5 French catheter</td>
</tr>
<tr>
<td>Nominal prescription dose</td>
<td>12 Gy to 3 mm from the source center</td>
<td>14 Gy to 0.5 mm from the vessel wall</td>
</tr>
<tr>
<td>Normalized prescription dose</td>
<td>10.9 Gy</td>
<td>12.9 Gy</td>
</tr>
<tr>
<td>Average, minimum, and maximum dose at vessel surface b</td>
<td>10.7 Gy, 14.8 Gy</td>
<td>11.1 Gy, 16.5 Gy</td>
</tr>
<tr>
<td>Average, minimum, and maximum dose at mm depth b</td>
<td>7.7 Gy, 10.7 Gy</td>
<td>7.1 Gy, 11.3 Gy</td>
</tr>
<tr>
<td>Average, minimum, and maximum dose at mm depth</td>
<td>5.9 Gy, 8.6 Gy</td>
<td>5.2 Gy, 7.8 Gy</td>
</tr>
<tr>
<td>Average, minimum, and maximum dose at mm depth</td>
<td>5.2 Gy, 7.8 Gy</td>
<td>4.8 Gy, 6.9 Gy</td>
</tr>
<tr>
<td>Average, minimum, and maximum dose at mm depth</td>
<td>4.1 Gy, 6.0 Gy</td>
<td>4.1 Gy, 7.1 Gy</td>
</tr>
<tr>
<td>Average, minimum, and maximum dose at mm depth</td>
<td>4.1 Gy, 6.0 Gy</td>
<td>4.1 Gy, 7.1 Gy</td>
</tr>
</tbody>
</table>

b Indicates the dose prescription point position.

Assuming a lumen diameter of 6 mm and exact source centering.
extrapolation ionization chamber with a graphite electrode. In this case, the absorbed-dose rate to A150 plastic in Gy/s at the surface of the plastic was given by

\[ D_{\text{\~}} r, u \]

\[ = 33.97 \times 1.13 \times B \times U \times \left( \frac{\Delta I}{\Delta d} \right)_{0}, \]

where \( (\Delta I/\Delta d)_{0} \) = the rate of change of current (normalized to a reference temperature and pressure) with extrapolation chamber air-gap thickness as the thickness approaches zero, in units of nA/mm,

33.97 = the average energy in Joules needed to produce one Coulomb of ions of either sign in air,

1.13 = the ratio of the mean mass stopping power of A150 plastic to that of air,

1.197 = the density of air at the reference temperature and pressure (22 °C and 1 standard atmosphere) in kg/m³,

\( B \) = a correction for reduced backscatter from the collecting electrode, taken as 1.000,

\( U \) = a correction for attenuation by the high-voltage electrode, taken as 1.003, and

\( A \) = the area of the collecting electrode, measured with a traveling microscope as 0.648 mm².

The overall uncertainty in the calibration is estimated by Soares to be ±15%.

Finally, some guidance is given for converting from the dose in A150 plastic to the dose in water or some other medium. While A150 might not be the ideal choice for a water- or tissue-equivalent material for beta particles, it does have the advantage of being a conductor, and thus avoiding the charge buildup problems characteristic of the high dose rates possible from these sources. For point sources in infinite media, the dose at a distance \( r_m \) corresponding to an aerial density of \( r_m \rho_m \) (in g/cm²) in the medium, \( D_m(\rho_m \rho_w) \), is related to the dose in water, at the same aerial density, \( r_w \rho_w \), but scaled by 78

\[ D_m(\rho_m \rho_w) = \eta^3(\rho_m / \rho_w)^2 D_w(\eta r_w \rho_w), \]

where \( \eta \) is the scaling factor of the medium relative to water.
and $\rho_w$ and $\rho_m$ are the densities of water and the medium, respectively. For A150 plastic, Soares et al. recommend $\eta = 0.968$ and $\rho_m = 1.127 \text{ g cm}^{-3}$.

### 3. Recommendations on dose calibration of catheter-based system

The AAPM recommends that the dose rate from a catheter-based system using photon emitters be determined using the dosimetry protocol described by AAPM TG-43, with the modification that the reference distance be 2 mm instead of the conventional reference distance of 1 cm. For photon sources, the source strength should be measured in terms of air kerma strength. The penetrating ability of the radiation should be described by the radial dose function normalized at 2 mm and its angular dependence by the anisotropy function.

For beta emitters in a catheter-based system, the AAPM recommends the same protocol, except that the source strength cannot be expressed in terms of air kerma strength. Instead, the source strength in this case should be specified in terms of the dose rate in water at a reference distance of 2 mm.

In order to develop a consistent set of specifications of their equipment, manufacturers of catheter-based systems should express the output in terms of a dose rate in water at a distance of 2 mm, and use radial dose function and anisotropy functions over a distance of 10 mm to describe the dose distribution around their products.

### C. Dosimetric characterization of radioactive stents

Analogous to the previous case of catheter-based brachytherapy, analysis by the task group revealed a confusing variety of different dose specifications in radioactive stent implantation. Again, the task group undertook a major effort to analyze all existing clinical studies of radioactive stents using a common framework. We chose a depth of 0.5 mm from the surface of the stent as the reference depth and a total treatment time of 28 days as a common framework for this purpose. The 28 day period has also been the most commonly used time to sacrifice in the animal studies in this area.

Dosimetry of the following four radioactive stent studies were reviewed by the task group using a common approach that was selected to be the numerical integration model of Prestwich. The results of this evaluation are shown in Table VI. The dose at 0.5 mm depth given in 28 days varies widely from 0.6 to 414 Gy in these studies, which is not surprising because different activities were chosen deliberately by the investigators. The more interesting observation is that the dose delivered per unit activity for the same radionuclide varied by almost a factor of 4. The dose normalized per $\mu$Ci of $^{32}$P varied from 4.5 to 19.6 Gy/$\mu$Ci, indicating the effects of stent type, diameter, and length. In most cases, the dose to 28 days was reported because that was also the time to sacrifice. Direct comparison of dose delivery by stent versus an acute catheter-based irradiation is complicated because the dose rate effects are different. There is some evidence that the dose delivered acutely more than three days after angioplasty is not effective in reducing neointimal proliferation. But it is not known whether this applies to a continuous low dose rate delivered by stents. We have arbitrarily chosen to tabulate the dose delivered in 28 days, recognizing that biological effects may correlate better with other dose descriptors. Again, it is necessary to evaluate dosimetry consistently from study to study so that meaningful conclusions can be made from clinical and preclinical studies.

### Table V. The dose distribution of beta-emitter intravascular brachytherapy in coronary vessels.

<table>
<thead>
<tr>
<th>Author–→</th>
<th>1995 (Ref. 59), 1996 (Ref. 60)</th>
<th>Waksman et al. 1995 (Ref. 37)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of study</td>
<td>Animal model</td>
<td>Animal model</td>
</tr>
<tr>
<td>Type of catheter</td>
<td>Self-centering $^a$</td>
<td>Non-self-centering, 4.5 French in an 8 French</td>
</tr>
<tr>
<td>Isotope/form</td>
<td>$^{90}$Y wire</td>
<td>$^{90}$Sr/$^{99}$Y seeds to 5 mm length, five seeds with 5 mm interseed center spacing</td>
</tr>
<tr>
<td>Nominal prescription dose</td>
<td>18 Gy to 1.25 mm from the wire center</td>
<td>14 Gy to 2 mm from the seed center</td>
</tr>
<tr>
<td>Dose at 2 mm from the center $^b$</td>
<td>14.6 Gy</td>
<td>14 Gy</td>
</tr>
<tr>
<td>Dose at the vessel surface $^b$</td>
<td>18 Gy</td>
<td>24.5 Gy</td>
</tr>
<tr>
<td>Dose at 1 mm depth $^b$</td>
<td>7.2 Gy</td>
<td>10 Gy</td>
</tr>
<tr>
<td>Dose at 2 mm depth $^b$</td>
<td>2.7 Gy</td>
<td>4.9 Gy</td>
</tr>
<tr>
<td>Dose at 3 mm depth $^b$</td>
<td>1.4 Gy</td>
<td>2.3 Gy</td>
</tr>
</tbody>
</table>

$^a$Catheter with a 2.5 mm diameter self-centering balloon.
$^b$Assuming a lumen diameter of 3 mm and exact source centering.
surface of the stent. If the vessel diameter is 3 mm, for example, the dose calculation point for a catheter-based source would typically be specified as 2 mm from the center of the source. This same point would be 0.5 mm from the surface of a radioactive stent, and should be specified as such.

Another question peculiar to a permanently implanted radioactive stent is that of treatment time. Since neointimal hyperplasia in a stented artery occurs in the first few weeks to two months after stent placement, only the dose delivered during this period is effective. Hence, an effective treatment time should be specified; 28 days is reasonable.

For the specification of the strength of radioactive stents, the AAPM recommends that the activity, nominal diameter, deployed diameter, length, type, and model be specified for each individual case. It is also recommended that doses radial to a stent can be calculated using beta point dose kernels. The axial dependence of the dose at a fixed radial distance can be calculated by the cylindrical shell method of Prestwich et al. and Duggan et al. for a uniform distribution of $^{32}$P on the outside of the stent, and Janicki et al. for the Palmaz–Schatz geometry (Figs. 13–14) or the advanced stent design model. All of these dose models, except for the latter, have been verified by radiochromic film dosimetry.

A difficulty with determining the activity and consequently calculating the dose of a $^{32}$P stent is the necessity that the stent remain sterile for patient use. The stents are shipped in a Plexiglas safety cylinder with sufficient wall thickness to absorb all the beta particles. Although the beta particles are absorbed within the Plexiglas walls of the shipping container, bremsstrahlung x rays are produced. Larsen and Mohrbacher have reported a technique to determine $^{32}$P activity by bremsstrahlung counting methods. The bremsstrahlung x rays detected are directly proportional to the number of betas emitted. Also, it is assumed that no other contaminating radionuclides are present in the sample.

In preliminary experiments, Coffey and Duggan have demonstrated that a NaI(Tl) scintillation crystal and a multi-channel analyzer (MCA) can be used to count bremsstrahlung x rays from low activity $^{32}$P stents. Early experiments indicate that individual determinations of the activity of each stent can be achieved to an accuracy of $\pm 10\%$ while maintaining sterility.

The source activity of mixed beta-gamma emitters may be conveniently measured by counting the gamma photo peak in standard geometry, with a possible correction for the bremsstrahlung continuum if necessary. In the case of a positron emitter such as $^{48}$V, the 511 keV annihilation photons provide another simple solution. Because the maximum beta energy for $^{48}$V is only 696 keV, bremsstrahlung makes no significant contribution at 511 keV, and absolutely none at the strongest gamma energy of 1.15 MeV (100%) of $^{48}$V, so activity can easily be determined with a calibrated detector with a lower-energy threshold, just including the 511 keV photo peak, or even in a calibrated ionization well chamber in a beta-absorbing plastic shield. The small gamma contribution to the dose distribution may be calculated using a point dose kernel integration, but the beta dose distribution is best calculated using a Monte Carlo technique that can properly account for absorption of the emitted betas within the metallic stent material. This is more important for the proton activated $^{48}$V stent because its activity is distributed throughout the stent metal and has a relatively low energy compared to the higher-energy betas from $^{32}$P distributed only on the stent outer surface.

NIST does offer a reference standard $^{32}$P source for activity analysis. The user can use a number of relative calibration procedures including a well-type ionization chamber, an NaI(Tl) scintillation counter, or a liquid scintillation counter. For the particular counting method chosen, a calibration factor traceable to NIST must be available. The NIST standardization process utilizes a high efficiency liquid scintillation counting method. Solutions standardized by this technique may then be used to establish the counting efficiencies for various practical sample geometries for reentrant ionization chamber dose calibrations and NaI(Tl) photon counters. These very practical transfer techniques are exceedingly useful for relative measurements, but standards are needed to first calibrate the instrument. An unacceptably large error may be encountered if one compares sources of different geometries in these "secondary instruments."

D. Recommendation of clinical prescription and dose reporting of radioactive stents

The measurement of dose distributions in close proximity to a radioactive stent is a monumental task, which need not be repeated for each clinical case. Instead, reasonably consistent treatments can be achieved by specifying the activity implanted in a given stent model provided the geometry is carefully reported. Therefore, the AAPM recommends that for each type of radioactive stent the three-dimensional dose distributions around stents of various lengths, diameters, and activities should be carefully determined by benchmark dosimetry studies before clinical implementation. Also, it is recommended that for each radioactive stent procedure the
activity of the stent, its nominal diameter, deployed diameter, length, type, and model be used for a clinical prescription, and doses delivered at a depth of 0.5 mm from the surface of the stent in the midplane and over a time period of 28 days should be reported for treatment and evaluation. Although the dose to full decay and the dose over several time periods is important for a full evaluation of biological and clinical results, the task group recommends a dose accumulated over 28 days as a common reference time. Even for different radionuclides of varying half-lives, most animal studies in this field use 28 days as the time to sacrifice for endpoint evaluation.

E. Quality assurance and safety aspects

A comprehensive quality assurance (QA) program is required for intravascular brachytherapy to assure consistency, accuracy, and safety of the personnel involved. Several reports on QA for conventional brachytherapy exist in the literature. In this section we describe QA aspects as they relate to intravascular brachytherapy procedures. Specifics of a QA program depend to an extent on the technique utilized in intravascular irradiation. Four major techniques being explored at present are (1) manually loaded sealed sources; (2) remotely loaded sealed sources; (3) radioactive stent placement; and (4) radioactive liquid balloons. Essential elements of a comprehensive QA program for each of the above techniques, except for radioactive liquid balloons, are described below. For radioactive liquid balloons, there is insufficient information in the literature to recommend a quality assurance program. For the first three techniques the following items should be part of a QA program.

1. Document in detail the essential properties (radiation and physical) of the radioactive source.

2. Develop protocols to be followed for the purchase and receipt of sources in collaboration with the institution’s radiation safety officer (RSO). For remotely loaded sources, develop acceptance testing and commissioning procedures.

3. Develop guidelines to safely store the radioactive sources and control their access and perform periodic inventory of the sources and enter the results in log books.

4. Check the physical integrity of the sealed sources prior to use and perform leak tests. Remotely loaded sources require an extensive routine QA procedure, which includes (1) room safety interlocks; (2) lights and alarm functions; (3) console functions (including audio/visual); (4) switches and batteries; (5) visual inspection of source guides; (6) accuracy of the source preparation using an autoradiograph; (7) source positioning accuracy (dummy loading and real source loading); (8) the timer function; (9) calibration of source activity; (10) mechanical integrity of the applicators; and (11) emergency response. Details of these procedures have already been described.

5. Develop a methodology to verify source activity using in-house equipment such as dose calibrators, reentrant chambers, etc.

6. Develop methods to properly sterilize sources when required. Open-ended afterloading catheters employed in intravascular irradiation come in contact with patient’s body fluid and hence require sterility.

7. Develop protocols to safely transport radioactive material from a room to a sterilization department and then onto a catheterization room.

8. Develop the protocol to safely dispose of the sources after the procedure or to store the unused sources on site.

9. Assure all the needed ancillary equipment (e.g., long forceps, stopwatch, scissors, etc.) are readily available on a tray at the time of the irradiation procedure.

10. Develop protocols to be followed in case of unexpected emergencies. Some urgent instances are (1) source breakage and contamination; (2) loss of a source within vasculature of the patient; (3) loss of a source in the catheterization room; (4) cardiac or respiratory arrest (related or unrelated to the irradiation procedure); and (5) emergency surgery. All emergency procedures should be coordinated with the RSO. For example, an emergency lead container must be present in the room during the entire procedure for use by physicists/RSO.

11. Develop a protocol that describes the role of each individual in this interdisciplinary procedure. A working team for intravascular irradiation protocol must include (1) an interventional cardiologist or radiologist; (2) a radiation oncologist; (3) a radiotherapy physicist; (4) a health physicist; and (5) a nurse/coordinator. Each individual should know the role he/she is expected to fulfill during this procedure. The duties of the health physicist in this procedure may be assigned to the radiotherapy physicist.

12. Develop a form for the dose prescription (written directive) to be filled by the authorized user prior to the initiation of irradiation.

13. Develop and document the dosimetric methods employed in computing the irradiation time. The calculation should be independently verified and signed prior to initiation of the procedure.

14. Verify that the correct sources chosen for irradiation and that all treatment planning parameters used correspond to that patient.

15. Monitor radiation levels around the patient/room during the procedure.

16. Prepare and document radiation protection surveys at the end of the procedure as mandated by state/federal regulations.

17. For permanent implants of a radioactive stent, the patient needs to be given a complete instruction on safety and follow-up aspects. This is normally accomplished at the time of patient discharge.

18. Develop a program to routinely provide education and training on radiation protection to all the staff members.
VII. SUMMARY OF RECOMMENDATIONS

1. The source strength of a catheter-based system should be expressed in terms of the air kerma rate in air for gamma sources (air kerma strength) and the dose rate in water at a reference distance of 2 mm for beta emitters.

2. Dose distributions around a catheter-based brachytherapy source should be determined using the AAPM Task Group No. 43 protocol for photon sources and a modified version of the AAPM Task Group No. 43 protocol for beta sources.

3. The source strength of a catheter-based system should be traceable to a national standard at NIST or at an ADCL.

4. The radial dose function, geometry function, and anisotropy function should be determined for each specific source design of a commercial catheter-based system.

5. The clinical prescription for a catheter-based system should be expressed in terms of the dose delivered at a reference depth in water.

6. For a catheter-based system, the depth of dose prescription for intracoronary applications should be at a radial distance of 2 mm from the center of the source and for peripheral vessels 2 mm larger than the average lumen radius. An average lumen radius should also be reported.

7. For optimal assessment of each clinical case, average, minimum, and maximum doses delivered should be estimated in at least three planes perpendicular to the catheter and along its length.

8. The output of all commercial intravascular brachytherapy catheter-based systems should be specified in terms of the dose rate in water at a radial distance of 2 mm from the center of the catheter.

9. The penetrating ability of all commercial intravascular

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### Table VI. Dose evaluation of stent experiments in animals.

<table>
<thead>
<tr>
<th>Investigator</th>
<th>Stent type</th>
<th>Length</th>
<th>Diameter</th>
<th>Isotope</th>
<th>Activity</th>
<th>Biological endpoint</th>
<th>Time to Sacrifice (days)</th>
<th>Dose in 28 days at the distance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hehrlein et al. 1995 (Ref. 38)</td>
<td>Palmaz–Schatz half-stent</td>
<td>7.5 mm</td>
<td>3.0 mm</td>
<td>Mixed 50</td>
<td>17.5 µCi</td>
<td>Neointimal thickening in rabbit iliac artery</td>
<td>28, 84</td>
<td>10 Gy from 0 to 1 mm</td>
</tr>
<tr>
<td>Hehrlein et al. 1995 (Ref. 38)</td>
<td>Palmaz–Schatz half-stent</td>
<td>7.5 mm</td>
<td>3.0 mm</td>
<td>Mixed 50</td>
<td>35 µCi</td>
<td>Neointimal thickening in rabbit iliac artery</td>
<td>28, 84</td>
<td>20 Gy from 0 to 1 mm</td>
</tr>
<tr>
<td>Carter et al. 1996 (Ref. 80)</td>
<td>Palmaz–Schatz half-stent</td>
<td>7 mm</td>
<td>3.5 mm (assumed)</td>
<td>32P</td>
<td>0.15 µCi</td>
<td>Neointimal thickening in pig coronary artery</td>
<td>28</td>
<td>2.7 Gy at 0.5 mm; 1.5 Gy at 1 mm; 0.49 Gy at 2 mm</td>
</tr>
<tr>
<td>Carter et al. 1996 (Ref. 80)</td>
<td>Palmaz–Schatz half-stent</td>
<td>7 mm</td>
<td>3.5 mm (assumed)</td>
<td>32P</td>
<td>0.5 µCi</td>
<td>Neointimal thickening in pig coronary artery</td>
<td>28</td>
<td>9.0 Gy at 0.5 mm; 4.9 Gy at 1 mm; 1.6 Gy at 2 mm</td>
</tr>
<tr>
<td>Carter et al. 1996 (Ref. 80)</td>
<td>Palmaz–Schatz half-stent</td>
<td>7 mm</td>
<td>3.5 mm (assumed)</td>
<td>32P</td>
<td>1.0 µCi</td>
<td>Neointimal thickening in pig coronary artery</td>
<td>28</td>
<td>18.0 Gy at 0.5 mm; 9.7 Gy at 1 mm; 3.3 Gy at 2 mm</td>
</tr>
<tr>
<td>Carter et al. 1996 (Ref. 80)</td>
<td>Palmaz–Schatz half-stent</td>
<td>7 mm</td>
<td>3.5 mm (assumed)</td>
<td>32P</td>
<td>3.0 µCi</td>
<td>Neointimal thickening in pig coronary artery</td>
<td>28</td>
<td>54.0 Gy at 0.5 mm; 29.2 Gy at 1 mm; 9.9 Gy at 2 mm</td>
</tr>
<tr>
<td>Carter et al. 1996 (Ref. 80)</td>
<td>Palmaz–Schatz half-stent</td>
<td>7 mm</td>
<td>3.5 mm (assumed)</td>
<td>32P</td>
<td>6.0 µCi</td>
<td>Neointimal thickening in pig coronary artery</td>
<td>28</td>
<td>107.9 Gy at 0.5 mm; 58.4 Gy at 1 mm; 19.7 Gy at 2 mm</td>
</tr>
<tr>
<td>Carter et al. 1996 (Ref. 80)</td>
<td>Palmaz–Schatz half-stent</td>
<td>7 mm</td>
<td>3.5 mm (assumed)</td>
<td>32P</td>
<td>14 µCi</td>
<td>Neointimal thickening in pig coronary artery</td>
<td>28</td>
<td>251.9 Gy at 0.5 mm; 136.4 Gy at 1 mm; 46.1 Gy at 2 mm</td>
</tr>
<tr>
<td>Carter et al. 1996 (Ref. 80)</td>
<td>Palmaz–Schatz half-stent</td>
<td>7 mm</td>
<td>3.5 mm (assumed)</td>
<td>32P</td>
<td>23 µCi</td>
<td>Neointimal thickening in pig coronary artery</td>
<td>28</td>
<td>413.8 Gy at 0.5 mm; 224 Gy at 1 mm; 75.7 Gy at 2 mm</td>
</tr>
<tr>
<td>Hehrlein et al. 1996 (Ref. 81)</td>
<td>Palmaz–Schatz half-stent</td>
<td>7.5 mm</td>
<td>3.0 mm</td>
<td>Mixed 50</td>
<td>4 µCi</td>
<td>Neointimal thickening in rabbit iliac artery</td>
<td>28, 84</td>
<td>78.4 Gy at 0.5 mm; 42.2 Gy at 1 mm; 14.2 Gy at 2 mm</td>
</tr>
<tr>
<td>Hehrlein et al. 1996 (Ref. 81)</td>
<td>Palmaz–Schatz half-stent</td>
<td>7.5 mm</td>
<td>3.0 mm</td>
<td>Mixed 50</td>
<td>13 µCi</td>
<td>Neointimal thickening in rabbit iliac artery</td>
<td>28</td>
<td>254.7 Gy at 0.5 mm; 137.3 Gy at 1 mm; 46.2 Gy at 2 mm</td>
</tr>
<tr>
<td>Laird et al. 1996 (Ref. 39)</td>
<td>Modified Strecker</td>
<td>20 mm</td>
<td>5.0 mm</td>
<td>32P</td>
<td>0.14 µCi</td>
<td>Neointimal area in pig iliac artery</td>
<td>28</td>
<td>0.63 Gy at 0.5 mm; 0.35 Gy at 1 mm; 0.12 Gy at 2 mm</td>
</tr>
<tr>
<td>Rivard et al. 1996 (Ref. 79)</td>
<td>Palmaz–Schatz half-stent</td>
<td>7.5 mm</td>
<td>3.5 mm (assumed)</td>
<td>32P</td>
<td>0.6 µCi</td>
<td>Mean area stenosis index in pig RCA</td>
<td>21</td>
<td>10.1 Gy at 0.5 mm; 5.5 Gy at 1 mm; 1.9 Gy at 2 mm</td>
</tr>
</tbody>
</table>
brachytherapy catheter-based systems should be specified in terms of the radial dose function normalized at a distance of 2 mm and at radial distances from 0.5 to 10 mm (or $R_{90}$, 90% of the electron range for beta emitters), at 0.5 mm intervals, with a reference depth of 2 mm.

(10) Uniformity of the dose delivered by catheter-based systems at points both along the source axis, at $r = 2$ mm, and around the circumference of a 2 mm radius circle centered on the source axis in a plane perpendicular to it should be better than $\pm 10\%$ (the range of values from minimum to maximum in the centered two-thirds of the treated length of at least 3 cm along the catheter axis).

(11) For each catheter-based system, an atlas of three-dimensional dose distributions should be generated to estimate the dose variation in the target.

(12) The clinical prescription of radioactive stents should be in terms of (1) stent diameter, nominal and deployed; (2) stent length; (3) stent type, brand, model; (4) radioisotope; and (5) activity.

(13) The measured activity of a radioactive stent should be traceable to a national standard at NIST.

(14) Activity for each radioactive stent to be used should be determined using an appropriate transfer technique.

(15) For radioactive stents, doses at 0.5 mm radial distance from the surface of the stent in the midplane and over time periods of 28 days should be reported.

(16) The quality assurance program presented in this AAPM task group report should be followed under the direction of a qualified medical physicist.

VIII. FUTURE CONSIDERATIONS

One of the controversies in the current literature is regarding the optimal choice of a radionuclide for a catheter-based system. The ideal catheter-based source would have high activity in a small volume, long half-life (to reduce the cost), uniform dose over treatment distances of 2–3 mm from the source center, and a low cost. No available isotope is ideal. Beta emitters such as $^{32}$P and $^{90}$Sr/$^{90}$Y have advantages in terms of high activity and dose rate, radiation safety, and half-life; while gamma emitters such as $^{192}$Ir have advantages in terms of radial dose uniformity, high dose rate, and reasonably long half-lives. Each isotope could be fabricated at the required activities and size using the current technology. There is a tradeoff between the increased radial range of gamma emitters and the safety advantages of beta emitters.

Because of the large amount of shielding required and the high activity for gamma emitters, it is possible that safety considerations may require that gamma emitters be used only with specially shielded remote controlled units. Beta emitters, on the other hand, may be usable via hand loaded techniques, thus reducing the cost. The choice of beta versus gamma should ultimately depend upon the results of clinical studies and the task group was unable to come to a consensus regarding the optimum radionuclide.

Another controversial question was regarding the need for centering in a catheter-based system. The answer to this question would depend upon the choice of radionuclide and on the biological window of therapeutic efficacy without normal tissue toxicity. It appears, for example, that a minimum dose on the order of 8–16 Gy to a depth of 0.5 mm into the vessel wall is required to prevent restenosis. The maximum vessel tolerance dose is not well known but can be speculated to be on the order of 32 Gy to the surface of the vessel wall. These limits imply that dose uniformity within the target region must be within a factor of 2–4. The normal vessel wall thickness is on the order of 0.5 mm, and it is possible that all sections of the vessel wall need to be treated in order to prevent restenosis. Also, the diseased vessels could have thicker walls. Assuming a treatment wall thickness of 0.5 mm, even for a perfectly centered source, the dose variation to the various sections of the vessel wall (say, from radial distances of 1.5–2.0 mm) will be on the order of 50%–70%. Again, the answer to the question regarding the need for centering will have to wait for the completion of clinical investigations.

There are a number of other important questions that the task group could not resolve at this time. Some of them are (1) recommendations about the accuracy desired of the source calibration under standard conditions, (2) the accuracies of various calibration methods, (3) the expected accuracy of the dose delivered under clinical conditions, (4) a comparison of the clinical efficacy of catheter-based brachytherapy, radioactive stent implantation, and radioactive liquid balloons, (5) the consideration of the dose rate effects in the use of various modalities for intravascular brachytherapy, (6) consideration of the effects of contrast media, metallic stents, and plaque composition on the dose distribution produced by various forms of intravascular radiotherapy, and (7) recommended values for dosimetry parameters for each of the commercial systems. All of these issues should be addressed by scientific and clinical investigators in this field. The AAPM will continue to monitor scientific progress in this area and make further recommendations at an appropriate time in the near future.

ACKNOWLEDGMENTS

The authors thank Deanna Jacobs for preparing and editing this manuscript. Marc Miner at Emory University helped clarify the dosimetric calculations used in the Emory University studies. Dr. Prestwich provided the details of his numerical model, which allowed us to compare the dosimetry of stents. Some of the work reported here was supported in part by a USPHS Grant No. R01-HL58022-01 (R. Nath, principal investigator) from the National Heart, Blood and Lung Institute.

APPENDIX: CORONARY AND PERIPHERAL VASCULAR INTERVENTIONS GLOSSARY

| Acute gain | Change in minimum lumen diameter (MLD) following stent insertion, usually expressed in millimeters. |
Adventitia: The outermost layer of the coronary artery.

Angiogram: An image of a blood vessel. Specifically, an x-ray image of blood vessels filled with contrast media; a cine angiogram is a 35 mm movie consisting of angiograms of the coronary arteries, typically obtained at a rate of 30 frames per second.

Angiography: The procedure used to obtain an angiogram.

Arteriosclerosis: Thickening, hardening, and loss of elasticity of the arterial wall.

Atherectomy device: A catheter equipped with a cutting tip for removing atherosclerotic plaque, often as a precursor to balloon angioplasty and/or stent placement.

Atheroma: A thickening and fatty accumulation within the arterial wall.

Atherosclerosis: A form of arteriosclerosis characterized by focal atheromas.

Balloon catheter: A catheter with a balloon at the distal tip for performing angioplasty or delivering intracoronary stents. Separate lumens provided for a guide wire and for injecting fluid to inflate the balloon are typically accessed via an integral manifold, although in some cases separate ports are provided. Standard balloon catheters are 135 cm in length from the tip to the manifold strain relief. One or more radiopaque markers is provided for visualization of the balloon for placement across the lesion.

Balloon expandable: A type of stent that is delivered on a balloon catheter.

Balloon profile: The diameter of the deflated balloon on a balloon catheter.

Calcification: Calcium deposition within the arterial wall.

Cannulation: Insertion of a tube into an orifice.

Catheter: A hollow tube designed to be passed through various canals/orifices.

Catheter lumen design: Refers to the method for providing separate lumens for balloon inflat-ion and a guide wire, e.g., coaxial (tube within a tube), dual lumen, or triple lumen. Balloon catheters of-ten have a ‘‘monorial’’ design for the guide wire lumen, which is coaxial in the distal portion, but exits through the side of the catheter within the guide catheter to facilitate balloon catheter exchange without the need for an exchange or extension wire.

Catheter shaft: The main body of a catheter. Shaft material affects conformability, tractability, and pushability.

Cine: Denoting movement related to film.

Collateral: A vessel connecting two arteries, providing alternate routes for blood flow.

Compliance: The ability of a balloon material to stretch in relation to applied pressure.

Conformability: The ability of a balloon to take the shape of the artery.

Coumadin: Oral anticoagulant medication.

Crossability: Ease with which a balloon or other device can be placed through a stenosis. Related to profile, pushability, sliding mechanics, and conformability.

Deflation time: Time required to deflate an angioplasty balloon. Influenced by inflation lumen size and balloon capacity. Short deflation times reduced ischemic time.

Diastole: The part of the cardiac cycle in which the ventricles are dilating, filling with blood.

Diffuse: Spreading, scattered.

Distal: Farthest from the center of the point of reference. When referring to catheters, the reference point is the angiographer, so the distal end of the catheter is inserted into the patient. When referring to coronary arteries, the reference point is the coronary ostium, so the normal direction of blood flow is from proximal to distal.

Eccentric: Situated or occurring away from the center. Off center. Noncircular.

ECG: The abbreviation of an electrocardiogram; a graphic record of the heart’s electrical activity.

Embolism: The sudden blocking of an artery by a clot or foreign material that has been brought to its site of lodgment by the blood current.

Embolus: A clot or other plug brought by the blood from another vessel and forced into a smaller one, thus obstructing the circulation.

Endarterectomy: Surgical excision of the thick-
<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endothelium</td>
<td>A single layer of flat cells that line any vascular lumen.</td>
</tr>
<tr>
<td>Exchange wire</td>
<td>A guide wire long enough (300 cm) to allow an entire balloon catheter to be withdrawn from the patient onto the wire external to the patient without withdrawing the wire.</td>
</tr>
<tr>
<td>Extension wire</td>
<td>A length of wire that can be attached to the proximal (external) end of a standard 175 cm guide wire so that it can be used as an exchange wire.</td>
</tr>
<tr>
<td>External elastic lamina</td>
<td>The structural membrane separating the media from the adventitia of an artery.</td>
</tr>
<tr>
<td>Femoral</td>
<td>Relating to the femur or the thigh, e.g., the femoral artery, a common arterial access site for performing angiography and angioplasty procedures.</td>
</tr>
<tr>
<td>Flexibility</td>
<td>The ease with which a guide wire or catheter can bend to negotiate tortuous anatomy.</td>
</tr>
<tr>
<td>Formability</td>
<td>The provision of a short segment at the distal tip of a guide wire that may be shaped by the operator to facilitate maneuvering through specific anatomy.</td>
</tr>
<tr>
<td>French (scale)</td>
<td>A unit for the diameter of a catheter or introducer. 1 French is 1/3 mm.</td>
</tr>
<tr>
<td>Free wire movement</td>
<td>The desirable ability of the guide wire to slide easily within a balloon catheter.</td>
</tr>
<tr>
<td>Gradient</td>
<td>The change of various functions, i.e., pressure, temperature, etc.</td>
</tr>
</tbody>
</table>
| Guide wire                                | A flexible, steerable wire placed through the guide catheter into the coronary artery and across the lesion to serve as a guide over which the balloon catheter is pushed. The distal 20–30 cm are typically radiopaque, and the distal tip may be formable or have a permanently bent segment (‘‘J’’ tip) to facilitate steering. Standard short guide wires are at least 175 cm long. Long guide wires, or exchange wires, are 300 cm long. Guide wire diameters are specified in inches, typically from 0.010 in. to 0.018 in. 0.002 in. increments. The wire diameter and construction determine torquability and compatibility with various balloon catheter systems. A large inner diameter single lumen angiography catheter through which a guide wire and balloon catheters are passed, and through which contrast injections are made for visualizing the artery. The guiding catheter is advanced only as far as the coronary ostium. Standard guiding catheters are 100 cm long with outer diameters of 6–10 F. Hemodynamic Pertaining to the movements involved in the circulation of blood. Hemostasis The control of blood flow or bleeding. Hemostatic valve A valve at the proximal end of the guide catheter to prevent arterial pressure from ejecting blood back through the lumen. The valve is designed to allow a guide wire and/or balloon catheter to be passed through it. Heparin Injectable anticoagulant medication, typically used to reduce clotting in catheters, introducers, etc., during angioplasty procedures. Hypotube A stainless steel hollow tube. Hypotube is often used for the proximal segments of guide wires and catheter shafts. Infract, infarction An area of tissue death and scarring due to ischemia. Internal elastic lamina The structural membrane separating the intima from the media. Intima The layer of a blood vessel wall inside the internal elastic lamina, composed of a single layer of endothelial cells in normal coronary arteries. Introducer (sheath) A short tubular device placed through the skin into the artery to provide arterial access. The guide catheter must make a tight seal against the lumen of the introducer to maintain hemostasis. Ischemia A deficiency of blood to the myocardium. Prolonged severe ischemia can lead to myocardial infarction. Ischemia can be caused by constriction or actual obstruction of a coronary artery due to coronary artery disease or due to the presence of a PTCA balloon or other intracoronary device. IVUS Intravascular ultrasound. LAD Left Anterior Descending coro-
nary artery. One of the two main branches of the LCA. Usually serves the anterior \( \frac{1}{3} \) of the left ventricle, including the apex, and part of the interventricular septum.

**LCA**
Left Coronary Artery. Bifurcates within 1–2 cm of its ostium into the LAD and LCX.

**LCX or CFX**
Left Circumflex coronary artery. One of the two main branches of the LCA. Usually serves the lateral wall and one-half of the posterior wall of the left ventricle, and the left atrium.

**Laser catheter**
A catheter containing a fiber-optic channel for delivering high-intensity laser energy to increase MLD by vaporizing atherosclerotic plaque, usually followed by balloon angioplasty and/or stent placement.

**Lesion**
A pathological change in tissue; wound or injury.

**Lumen**
The space in the interior of a tubular structure, such as an artery or the intestine.

**Manifold**
A connector at the proximal end of a catheter with one or more ports communicating with each of the catheter’s lumens. The simplest manifold is a ‘‘Y adapter’’ that provides two ports into a single lumen: a straight through lumen for passing a guide wire or other catheter, and a second, angled, port for injecting or withdrawing fluids such as contrast material or heparinized saline.

**Media**
Muscular layer of the arterial wall.

**MLD**
Minimum lumen diameter at the site of a stenosis, usually expressed in millimeters.

**Myocardium**
The muscular tissue of the heart.

**Myocardial infarction (MI)**
Prolonged severe ischemia that results in necrosis (death) of myocardium. The result of coronary occlusion from thrombus formation or spasm at the site of an atheroma.

**Net gain**
The change in MLD at long term angiographic follow-up.

**Nominal balloon size**
The manufacturer’s specified balloon diameter, in millimeters, reached at the nominal inflation pressure, specified in atmospheres.

**Occlusion**
A total blockage of an artery to blood flow.

**Opacification**
Making an artery or balloon opaque to radiation by the introduction of a contrast medium

**Ostium**
A general term to designate an opening into a tabular organ. The origin of a coronary artery in the aortic root.

**Patent**
Open to blood flow, unobstructed, not closed.

**Plaque**
A patch or small differentiated area on a body surface. Arteries can become obstructed with atherosclerotic plaque.

**Proximal**
Closest to the point of reference. When referring to catheters, the reference point is the angiographer, who holds the proximal end of the catheter while the distal end is inserted into the patient. When referring to arteries, the reference point is the ostium, so a balloon catheter approaches a lesion from the proximal side.

**PTCA**
Percutaneous—through the skin, transluminal—through the lumen of a vessel, coronary pertaining to the heart, angioplasty repair of a blood vessel. Usually synonymous with balloon angioplasty.

**Pushability**
The ability of the catheter shaft to transfer the force from the proximal end of the shaft to the distal tip so that the balloon or other device can be advanced through the vessel and across the stenosis.

**Radiopaque**
Impenetrable to an x-ray or other forms of radiation.

**Rated burst pressure**
The maximum pressure the manufacturer recommends for inflation of a balloon catheter, typically specified in atmospheres. The label recommends that the RBP should not be exceeded.

**RCA**
Right Coronary Artery. Serves the inferior wall of the left ventricle, parts of the right ventricle and interventricular septum, the right atrium, and may serve the left ventricular apex in some people.

**Restenosis**
Recurrence of a stenosis after a corrective procedure.
Rotoblator: rotating atherectomy device
A form of endarterectomy device consisting of a catheter equipped with a high-speed rotating abrasive burr at the tip for removal (ablation) of tissue to increase arterial MLD often followed by balloon angioplasty and/or stent placement.

Self-expanding
A type of stent that expands in the artery without use of a balloon catheter.

Sliding mechanics
The extent to which a balloon catheter slides smoothly within the guide catheter or through the coronary artery. Good sliding mechanics are enhanced by a low profile balloon and small diameter shaft used in a large lumen, kink resistant guide catheter, and the use of lubricating coatings.

Steerability
The ease with which a guide wire can be maneuvered through desired arterial branches. Related to the torque response and flexibility.

Stenosis
Narrowing or stricture of an artery, such as that caused by atherosclerotic plaque and/or an intracoronary thrombus.

Stent recoil
The fractional reduction of a stent diameter when the delivery balloon is deflated, defined as the diameter of the expansion balloon minus MLD after stent placement, divided by the diameter of expansion balloon.

Systole
The part of the cardiac cycle when the ventricles are contracting, expelling blood.

Thrombolysis
The phenomenon by which preformed thrombi are dissolved.

Thrombolytic
Dissolving or splitting up a thrombus.

Thrombus
Blood clot.

Torque response
The response at the distal tip of a guide wire or other device to the angiographer’s twisting the proximal end.

Tortuous
Referring to a vessel with many short radius bends, like a winding road.

Trackability
The ease with which the balloon catheter or other device can be advanced over a guide wire through tortuous coronary anatomy. Trackability is generally best for catheters with a small, flexible, coaxial distal shaft and good sliding mechanics.

Trans-stenotic gradient
Pressure difference across a stenosis.

Y adapter
A connector for the proximal end of a catheter providing two ports into the catheter’s central lumen: a coaxial “thru’” port for a guide wire or other device; and an angled port for fluids. Y adapters often also include a rotating hemostatic valve.

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1. Electronic mail: i: nath@nath1.med.yale.edu


32. Z. Li, C. Liu, and J. R. Palla, “Dose distribution of stainless steel 192Ir

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