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REVIEW

Brachytherapy technology and physics practice since 1950: a half-century of progress

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Abstract

The 50-year tenure of *Physics in Medicine and Biology* has coincided with some of the most important developments in radiological science, including the introduction of artificial radioactivity, computers and 3D imaging into medicine. These events have profoundly influenced the development of brachytherapy. Although it is not the dominant radiotherapy modality, it continues to play an important role in cancer therapy, more than a century after its introduction. This paper reviews the impact of three broad categories of innovation introduced since 1950 from the North American perspective: the introduction of artificial radioactivity, computer- and image-based treatment planning, and basic single-source dosimetry.

1. Introduction

The distinguished 50-year tenure of *Physics in Medicine and Biology* has coincided with some of the most important radiological physics innovations, including the development of nuclear reactors, new particle accelerators, three-dimensional (3D) imaging and computer-assisted planning. These developments, along with conceptual advances in radiation transport, have had a dramatic impact on the practice of brachytherapy. By combining technological opportunity with clinical need, brachytherapy has continued to serve as an important and rapidly evolving tool in the radiotherapeutic armamentarium for cancer management. In the author's opinion, the most notable milestones during the last 50–60 years of brachytherapy are

(1) new radioisotopes and afterloading technologies that significantly expanded clinical applications of brachytherapy (1950s–1970s);
(2) the introduction of individualized anatomy-based dose evaluation;
(3) quantitative dosimetry.

Each of these developments will be reviewed in the sections below.

Historical developments from 1950 to 1970 (which predate the author's association with radiation oncology) were researched by searching the National Library of Medicine's extended 'Old MEDLINE' database for articles from selected journals (*Radiology*, *American Journal of Roentgenology*, *British Journal of Radiology*, *Acta Radiologica* and *Physics in Medicine and Biology*) having titles containing selected keywords (caesium, iridium, cobalt, interstitial, intracavitary, implant, radium, afterloading, iodine, cervix, brachytherapy). In addition, a number of contemporaneous textbooks, memoirs and other articles cited below were reviewed. This review largely, but not exclusively, emphasizes the development of brachytherapy in North America.

2. Brachytherapy in 1950

By the early 1950s, brachytherapy had become a well-established and mature modality. As is true today, intracavitary brachytherapy was used to deliver most of the central tumour dose for cervical cancer patients. Radium-226 tubes with 1 mm Pt filtration remained the dominant intracavitary source through the late 1960s (Krabbenhoft 1958). In the US, a wide variety of applicator systems were in use, including preloaded Manchester ovoids at Washington University (Perez *et al* 1991, Tod and Meredith 1953), Paris system-like 'Kaplan' applicators at the University of Minnesota (Stenstrom 1957) and Stockholm system 'Morris' applicators at Yale University (Nath *et al* 1991). The Fletcher applicator, the most widely used vaginal colpostat in the US today, was introduced in 1953 (Fletcher 1953). Interstitial brachytherapy was also widely used. The Holt Radium Institute reported performing 500 interstitial procedures per year in the early 1950s, of which half were single-plane permanent ^{222}Rn seed implants with the most frequent indication being skin cancer (Farr 1953, Meredith 1951). In the UK, well-standardized ^{226}Ra needles (Meredith 1967) were used for implanting other sites. In the US, most interstitial implants were permanent ^{222}Rn seed implants until low linear activity ^{226}Ra needles became widely available in the 1940s (Martin 1949, Quimby 1956).

However, the role of brachytherapy in the 1950s was not secure. Perhaps, the most revolutionary of all radiotherapy developments, megavoltage beam therapy, was well underway, permitting delivery of doses to deep tumours competitive with those achievable by brachytherapy. Efforts to improve the penetration of external beam therapy included teleradium, supervoltage (500–800 kVp) x-ray beams (Rose and Loughridge 1936), the 2 MV Van de Graff generator (Trump *et al* 1947) and the high-energy betatron (Adams *et al* 1949). Broad market penetration of megavoltage radiation therapy was made possible by ^{60}Co teletherapy, first introduced at the University of Saskatchewan (Johns *et al* 1951) in 1951 and MD Anderson Hospital (Grimmett *et al* 1952) in 1952. By 1956, there were more than 80 such units in operation in North America alone (Brucer 1956b).

The literature of the late 1950s makes clear that radiation oncologists were well aware of the disadvantages of brachytherapy. Classical radium needles were rigid structures with outer diameters of 1.65 mm or more. High levels of surgical skill were needed to position such needles with sufficient accuracy and regularity to achieve good clinical outcomes. Brachytherapists had to work quickly to avoid excessive personnel doses to themselves and their support staff (Quimby 1956, Simon 1965). Given these disadvantages, many medical centres opted for surgical or supervoltage beam therapy alternatives, which limited the number of adequate training opportunities for rigid needle interstitial implantation (Krabbenhoft 1958, Simon *et al* 1972). While data quantifying mid-20th century clinical practices are lacking, one receives the impression that, except for gynaecological brachytherapy, interstitial brachytherapy was in decline during the 1950s and 1960s.

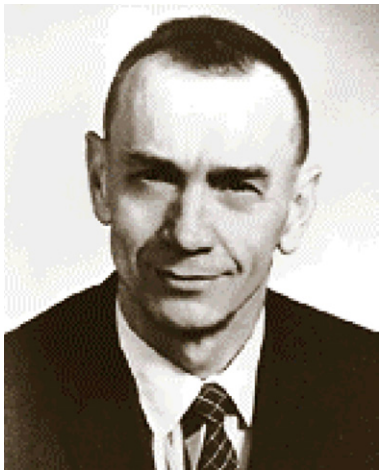


Figure 1. Marshall Brucer, MD (1913–1994), about 1960. American pioneer in the introduction of artificial radionuclides in brachytherapy. Chairman (1948–1962) of Medical Division of the Oak Ridge Institute for Nuclear Studies and founding president of the Society of Nuclear Medicine. (From Ketchum (1987) with permission.)

3. Artificial radionuclides for brachytherapy

Artificial radioactivity induced by particle accelerators was first reported by Curie and Joliot-Curie (1934). However, quantities and forms of radioactivity useful for brachytherapy were not available until 1940s (Manhattan Project 1946), when civilian applications of nuclear reactors were encouraged. In the US, reactor-produced teletherapy and brachytherapy source development was coordinated by the Medical Division of the Oak Ridge Institute for Nuclear studies, which was created by the US Atomic Energy Commission. Marshall Brucer[1] (see figure 1), an early nuclear medicine specialist, was appointed its first chair in 1948. Along with developing one of the first cobalt teletherapy devices (Grimmett *et al* 1952), his group collaborated in the design, production or dissemination of virtually all of the radium-substitute sources investigated in the US during the 1950–1965 period. In Canada and UK, the Chalk River and Harwell (Sinclair 1952) reactor sites made important contributions to medical use of artificial radionuclides.

3.1. Temporary brachytherapy radionuclides and afterloading techniques

Cobalt-60 (^{60}Co) was one of the first artificial radionuclides applied to brachytherapy in the form of interstitial needles and wires (Brucer 1952, Morton *et al* 1951, Myers 1948) and intracavitary tubes (Wilson 1951). Beyond improving upon the cost effectiveness and radiochemical safety of radium therapy, ^{60}Co seemed to do little to advance the clinical art of brachytherapy. In addition, its relatively short half-life (5.26 years) increased the complexity of low dose-rate (LDR) implant techniques, many of which emphasized the importance of fixed low dose rates (Paterson 1948). Hence, ^{60}Co-based manual LDR brachytherapy was relatively short lived. The longer lived (30-year half-life) radionuclide ^{137}Cs has enjoyed a

[1] Brucer (1956a, 1958) was an early promoter of the term 'brachytherapy' to describe what had been traditionally been referred to 'implant therapy' or 'Curie therapy.' The author could find no references using the word 'brachytherapy' published earlier than 1956.

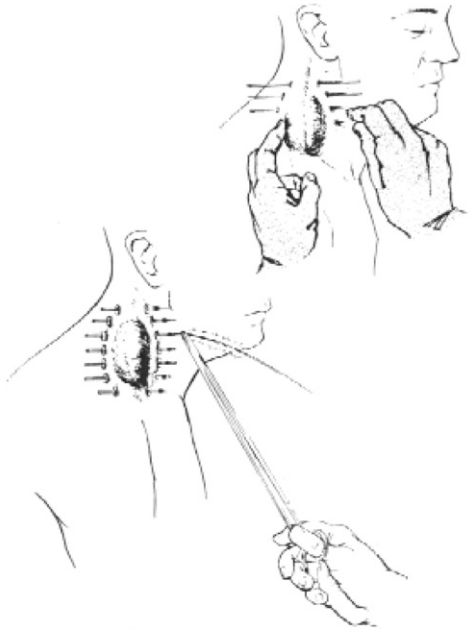


Figure 2. Illustration of flexible implanted double-ended afterloading applicators from Henschke's 1963 paper (Henschke *et al* 1963).

longer tenure in radiation oncology, first as a teletherapy source in the early 1950s (Brucer 1956c) and as a substitute for ^{226}Ra in LDR needles and intracavitary sources beginning in the 1960s. Both Amersham in the UK (Horsler *et al* 1964) and 3M in the US (Horwitz *et al* 1964) introduced intracavitary products by 1960, the former using caesium bound to a silver metallic matrix and the latter incorporating radioactive caesium chloride sintered within zirconium phosphate microspheres (Ryan 1964). Sealing the relatively toxic caesium salts in a sintered ceramic or glass core was an important technical advance and was eventually incorporated into all modern commercial ^{137}Cs sources. From the late 1970s to the present day, ^{137}Cs tubes were used almost exclusively for LDR intracavitary brachytherapy due to their lower costs of disposal and radiation safety hazards. As of 2002, the last ^{137}Cs source manufacturer ceased operations, effectively ensuring that HDR intracavitary techniques will come to dominate gynaecological brachytherapy.

Two artificial radionuclides that had far-reaching impact on expanding brachytherapy clinical applications were ^{182}Ta (Sinclair 1952) (110-day half-life, 1.1 MeV mean photon energy) and ^{192}Ir (74.2-day half-life, 0.40 MeV mean photon energy). ^{182}Ta wires were inserted interstitially using hypodermic needles, thus serving as more flexible and versatile replacements for radium needles in temporary interstitial implants (Ellis 1956). ^{192}Ir appears to have been introduced by Henschke (1957, 1958) in 1956 for permanent implantation of lung and prostate tumours: earlier reviews (Brucer 1952, Mitchell 1946) do not mention ^{192}Ir, despite the fact it has a much higher neutron activation cross section and specific activity than ^{182}Ta. By the early 1960s (Chase *et al* 1961, Henschke *et al* 1963, Simon 1965), ^{192}Ir seeds, encapsulated in nylon ribbons, had been introduced as temporary implant sources in conjunction with a fully afterloadable applicator system (figure 2). In Europe, afterloading implantation of iridium wire was introduced in the context of the Paris system of brachytherapy (Chassagne *et al* 1963). Surgically implanted flexible hollow tubes, into which either

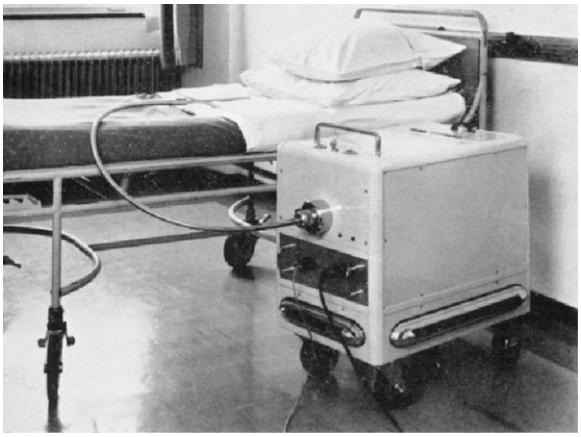


Figure 3. Illustration of early single-channel remote afterloading system (Walstam 1962). An LDR source train at the end of a flexible capable was used to move the source to and from the patient to a shielded safe under control of an automatic timer. A radiation detector was used to verify source position.

non-radioactive dummy ribbons (for imaging) or radioactive ribbons (for treatment) could be afterloaded, were used, completely eliminating operating room staff exposure. The result was a low-cost, reduced-diameter flexible radioactive source that made even single-uses cost-effective in many clinics. Compared to ^{226}Ra needles, the flexible afterloading applicators and the source active length could be much more easily and comfortably adapted to the patient's anatomy, effectively increasing domain of implantable tumours and number of qualified operators. These innovations contributed to a renaissance of interstitial brachytherapy, as evidenced by the growth of the Paris system of definitive brachytherapy for early-stage tumours and US approaches for treating large pelvic masses (Syed and Feder 1977, Syed *et al* 2001).

A related innovation in brachytherapy was remote afterloading technology, in which sources are robotically transported from a shielded safe to their treatment position in the implanted applicators. Initially, this technology (figure 3) was introduced by Walstam (1962) and Henschke *et al* (1964, 1966) in the early 1960s for the purpose of reducing personnel exposures from low and medium dose-rate intracavitary brachytherapy using ^{137}Cs or ^{226}Ra sources. Soon thereafter, high dose-rate (HDR) brachytherapy was introduced (O'Connell *et al* 1965), in which fractionated treatments lasting only a few minutes are administered. In this application, ^{60}Co pellets, which never achieved broad acceptance in manual brachytherapy, played an important role. The spherical ^{60}Co pellets had sufficient specific activity that dose rates of 2 Gy min^{-1} could be sustained in normal diameter intracavitary applicators. By varying the dwell time, radioactive decay could be compensated for. In the 1970s, the first single-stepping source remote afterloading system was introduced (Gauwerky 1977, Schulz *et al* 1984), using a miniaturized high intensity ^{192}Ir source welded onto the end of a flexible drive cable. The high specific activity of ^{192}Ir permitted development of sources with outer diameters of 1.1 mm or less (Gauwerky 1977), so that HDR brachytherapy could be applied to interstitial techniques. The ability to manipulate individual dwell times and positions offered the potential to improve implant dose distributions via formal optimization techniques (Anacak *et al* 1997, Lessard *et al* 2002). Except for permanent seed brachytherapy, the majority of temporary interstitial and intracavitary treatments in the US now appear to be delivered by HDR techniques.

3.2. Permanent brachytherapy sources and techniques

One of the first alternatives to ^{222}Rn seeds to be investigated was radioactive ^{198}Au wires (supplied by ORNL) encapsulated in gold tubing. Radiogold seeds were introduced by Henschke and colleagues at Ohio University in 1951 (Henschke 1953, Myers and Colmery 1952). To compensate for the rapid radioactive decay arising from the 2.7-day half-life of ^{198}Au and to customize source strength to the particular patient, the length of the radioactive wire was adjusted. The Ohio University group developed both permanent and temporary interstitial implant techniques, including an early form of afterloading (Morton *et al* 1951). Nylon tubes were preloaded with radioactive seeds and spacers. Dummy wires or nylon tubes loaded with dummies were inserted surgically into the tumour and localization radiographs obtained. The radioactive nylon assemblies were then pulled into place after attachment to the trailing end of the dummy applicator. To this day, a few programs (Teh *et al* 1998) continue to use ^{198}Au seeds as a permanent implant source because it supports classical low dose rates (30–100 cGy h^{-1}) in contrast to the 5–20 cGy h^{-1} dose rates characteristic of low-energy ^{125}I/^{103}Pd seeds. However, because radiogold implantation did not address logistical or radiation safety issues associated with ^{222}Rn seed implants, ^{198}Au sources never achieved wide utilization.

An important development was the introduction of interstitial seeds using electron-capture decay radionuclides, with moderately long half-lives of 10–60 days that emit a cascade of low-energy (20–40 keV) characteristic x-rays and γ-rays. The first practical K-capture source, ^{125}I (half-life: 59.6 days; mean energy: 28 keV) encapsulated in titanium seeds, was developed by Donald C Lawrence (Lawrence *et al* 1966) in the early 1960s and was investigated clinically in 1965 by Hilaris *et al* (1968) at Memorial Sloan-Kettering Hospital. While many tumour sites were implanted, including lung cancer (Hilaris *et al* 1976), prostate ^{125}I seed implantation, performed intraoperatively during pelvic lymphadectomy (Hilaris *et al* 1974), has had the most enduring impact. Other important radionuclides are ^{103}Pd (17.0-day half-life and 22 keV mean energy), introduced by John Russell in 1987, and ^{131}Cs (9.6-day half-life and 29 keV mean energy), which was initially proposed by Lawrence and Henschke (Henschke and Lawrence 1965) but has only recently become available commercially (Murphy *et al* 2004). The low-energy photons emitted by these sources dramatically reduce external exposure hazards: an 8 cm thickness of tissue reduces exposure ten-fold. Thin (0.2 mm) lead foils produce almost complete shielding. Thus, patients need not be confined to the hospital solely for radiation safety reasons. Clearly, the 1950s clinical experience with ultralow dose-rate ^{192}Ir implantation (Henschke 1958) was a critical factor in the success of this technique.

The introduction of transrectal ultrasound (TRUS)-guided transperineal implants (Holm *et al* 1983) both improved the accuracy with which permanent brachytherapy could be delivered to the prostate and eliminated the need for a highly invasive surgical procedure to expose the prostate (figure 4). The technique was further developed and investigated by the Seattle group, led by John Blasko (Blasko *et al* 1993). Ten-year survival data (Grimm *et al* 2001, Sylvester *et al* 2003) now demonstrate that brachytherapy, either as sole treatment for low-risk patients or in combination with external beam radiation for higher risk disease, results in biochemical relapse-free survival rates comparable to or superior to radical prostatectomy and definitive external beam therapy. The attraction of a one-day procedure along with a favourable profile of normal tissue complications has resulted in exponential growth of this modality. The number of procedures in the US has grown from less than 5000 in 1995 to 40 000–60 000 in 2002 (Grimm and Sylvester 2004) (30–40% of all eligible patients diagnosed annually in the US), challenging radical prostatectomy as the standard of treatment. In response to this growth, the number of commercially available low-energy interstitial seed products has increased to 24 from 3 in 1999 (Rivard *et al* 2004). As discussed below, this trend

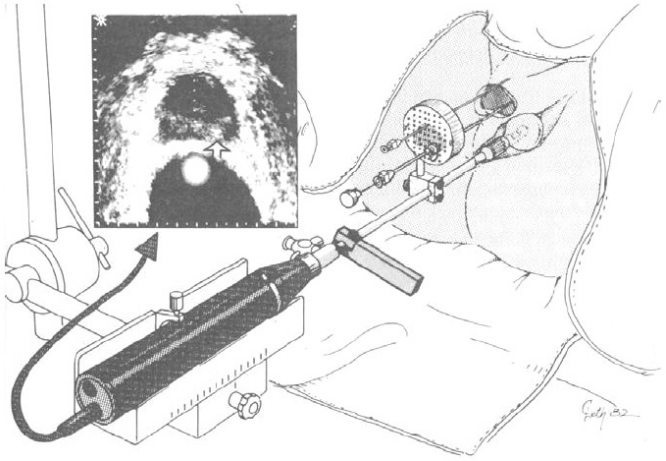


Figure 4. Illustration of transrectal ultrasound- and template-guided transperineal prostate implant from original article (Holm *et al* 1983).

has resulted in significant improvements in low-energy source dosimetry and image-guided brachytherapy.

4. Evolution of brachytherapy planning methodology

Prescription of brachytherapy in terms of exposure was commonplace in the early 1950s except for mg-h-based intracavitary brachytherapy systems. Interstitial brachytherapy applications were generally based upon the Quimby (Quimby and Castro 1953) or Manchester (Meredith 1967) implant systems. The distribution rules of these systems specified the geometric arrangement of radium needles relative to the target volume boundaries. Manual aids, such as tables giving exposure/mg-h as a function of implanted volume or area, were used to estimate the prescribed exposure to a well-defined dose-specification criterion for the idealized needle arrangements recognized by the system. The literature of the time, e.g. De Forest Smith (1958) and Farr (1953), describes many ingenious techniques for deriving effective implanted area or volume from planar radiographs. From the estimated reference dose rate, the treatment time needed to deliver the prescribed dose was estimated. It was recognized that implants frequently deviated significantly from the idealized source arrangements allowed by the system rules (Meredith 1951). Numerous approaches for more accurately controlling dose delivery were investigated, including small interstitially inserted ion chambers (Nuttall and Spiers 1946) and scale models of implants built from radiographic projections that could be used to support direct physical measurements. Meredith's excellent review of dose control (Meredith 1951) notes that dose measurements in rapidly varying radiation fields were difficult to interpret.

Dose-rate distributions around individual needles or tubes were estimated (Greenfield *et al* 1959) by integrating an isotropic point-source kernels over the extended radioactivity distribution within the source, which modelled by an encapsulated line source by the Sievert integral algorithm. Such models require tissue-buildup factors (ratio of exposure in medium to exposure in free space at same distance from a point source) and effective attenuation coefficients of the encapsulating and active core media, along with the physical and active source dimensions. The point-source kernel parameters were assumed to depend only on the radionuclide photon spectrum (Williamson 2005). Shalek and Stovall (1969) have reviewed the

application of this model to radium tubes and needles. Sievert models, more generally called 1D pathlength dose-calculation algorithms, were quickly extended to artificial radionuclides (Krishnaswamy 1972) including ^{125}I seeds (Krishnaswamy 1978) even though the validity of the model was questioned at such low energies. The evolution of dose-calculations methods has been reviewed elsewhere for ^{137}Cs (Williamson 1988a, 1998) and lower energy sources (Williamson 1996).

Three developments in brachytherapy planning technology during the last 50 years have dramatically altered brachytherapy clinical practice: computer isodose calculations, 3D imaging for defining target volumes and for guiding applicator insertion, and dwell-weight optimization of single-stepping source remotely afterloaded implants. While modern quantitative dosimetry methods confirm that 1950-era single-source dose calculations were quite accurate in many cases, manual source-superposition calculations about arrays of arbitrarily oriented sources were simply not feasible until the introduction of computer-assisted planning in the 1960s (Hope *et al* 1964, Nelson and Meurk 1958, Shalek and Stovall 1961). By evaluating isodose curves in selected planes for the geometric arrangements of needles, wires and intracavitary tubes actually achieved clinically, the prescribed dose could be based on delivered doses rather than intended doses derived from an abstract idealization of the implant. Subsequent innovations included fully 3D dose calculations and dose–volume histogram (DVH) indices for quantifying dose delivery and implant quality (Anderson 1986, Saw and Suntharalingam 1988).

The second development, use of x-ray computed tomography (CT) and other 3D imaging modalities in interstitial (Herskovic *et al* 1980, Pierquin and Fayos 1962) and intracavitary (Ling *et al* 1987, Schoeppel *et al* 1994) brachytherapy planning, constituted a radical departure from the purely surgical practice of brachytherapy. Localization of the clinical target volume (CTV) and dose-limiting normal tissues relative to the implanted sources allowed absorbed dose to be specified using anatomy-based coverage indices that are more likely to correlate with clinical outcome than the non-anatomic dose-specification quantities used by the classical systems. Intraoperative imaging to guide applicator insertion in principle makes the position of the implanted sources free parameters for optimizing the dose distribution with respect to CTV and normal tissue coverage. Image-guided brachytherapy techniques were first developed for stereotactically guided brain implants in the late 1980s (Weaver 1995). TRUS-guided permanent (Blasko *et al* 1993, Holm *et al* 1983) and HDR temporary (Martinez *et al* 2001) implantation have become standard of practice for prostate brachytherapy in North America.

A third cluster of innovations is related to single-stepping source remote afterloading and dwell-weight optimization as a tool for improving dose uniformity and target coverage within implants. Early geometric and dose-point optimization algorithms (Edmundson 1992) were first used to create non-uniform source loadings so that the dose uniformity and target coverage nonideal patient implants could approach the quality of idealized Manchester implants. More recent approaches extended both dwell weight (Lessard *et al* 2002) and source position optimization (Pouliot *et al* 1996) based upon target and normal tissue coverage indices derived from 3D imaging.

5. Brachytherapy dosimetry

As used here, ‘dosimetry’ refers to estimation of absorbed dose by means of experimental or fundamental theoretical techniques about single brachytherapy sources. Both experimental and computational techniques have undergone substantial development during the last 50 years, driven mainly by the utilization of newer isotopes.

5.1. ^{226}Ra dosimetry: from threshold erythema dose to semi-empirical models

Early experimental techniques for quantifying radiation fields associated with radioactive sources included the gold-leaf electroscope introduced by Becquerel in 1900 and the constant potential ionization chamber introduced by Villiard in 1908. Although absorbed dose-like quantities had been defined as early as 1914 (Christen 1914), no theory existed from which the absorbed dose or any other radiation field quantity could be inferred from the measured detector response. The first rigorously measurable field quantity, exposure, was defined in terms of specific instrument, the free-air chamber (FAC), introduced in the 1920s. FAC exposure standardization provided a sound foundation for external beam radiotherapy of the time, which was limited to x-ray spectra of 300 kVp (Wyckoff 1980). However, the FAC could not accurately measure ^{226}Ra exposure rates due to the difficulty of establishing secondary charged-particle equilibrium for high-energy (about 1.2 MeV on average) radium gamma rays. In 1941, Quimby (1941) noted that experimental estimates of the ^{226}Ra exposure-rate constant in the 1920–1940 period varied by a factor of 2. Prior to 1940, the radiological physics community struggled with problem of specifying brachytherapy treatments in a reproducible fashion. This void was filled by a number of biological and chemical dosimeters for mapping 'dose' distributions about early brachytherapy sources, including bleaching butter and tissue necrosis in rabbits (Quimby 1928, 1941). By plotting the distance to effect (e.g., butter bleaching) as a function of exposure time and source strength, 'dose' fall-off as a function of distance could be inferred. Perhaps, the most widely used biological endpoint was threshold erythema dose (TED), which is defined as the dose needed to produce a barely detectable skin erythema in 80% of the subjects so irradiated. This technique, developed by Quimby and colleagues at Memorial Hospital, apparently had a reproducibility of about 10% (Dean 1923, Quimby 1928, 1941) and was use to intercompare radium and supervoltage beams to lower energy beams calibrated in terms of exposure.

A rigorous method for measuring exposure from radium sources was made possible in the 1930s when quantum mechanical treatments of photon scattering (Gray 1929) and electron-energy loss (Bethe 1930, Bloch 1933) were published. This made possible the development of a practical cavity theory (Gray 1936, Laurence 1938), which allowed exposure to be rigorously inferred from small ion chambers with condensed matter walls thick enough to establish transient charged-particle equilibrium. By 1938, experimental estimates of $(\Gamma_\delta)_{\mathrm{Ra},0.5}$ had converged to within a few per cent of Attix's definitive 1957 measurement (Attix and Ritz 1957) of 8.25 R cm^2 mg^{-1} h^{-1} for radium needles filtered by 0.5 mm of Pt.

To compute dose distributions about implanted ^{226}Ra needles and tubes, physicists employed semi-empirical computational dosimetry models (Williamson 2005). Quimby (1922) developed a numerical technique for partitioning needles into a linear array of point sources, from which away-and-along exposure tables could be inferred. This was followed by Sievert's more elegant analytical solution, the Sievert integral method, in 1923. By the late 1930s, the exposure/mg-h tables used by the Quimby (1952) and Manchester (Parker 1938) interstitial implant systems were based upon computed single-source dose distributions.

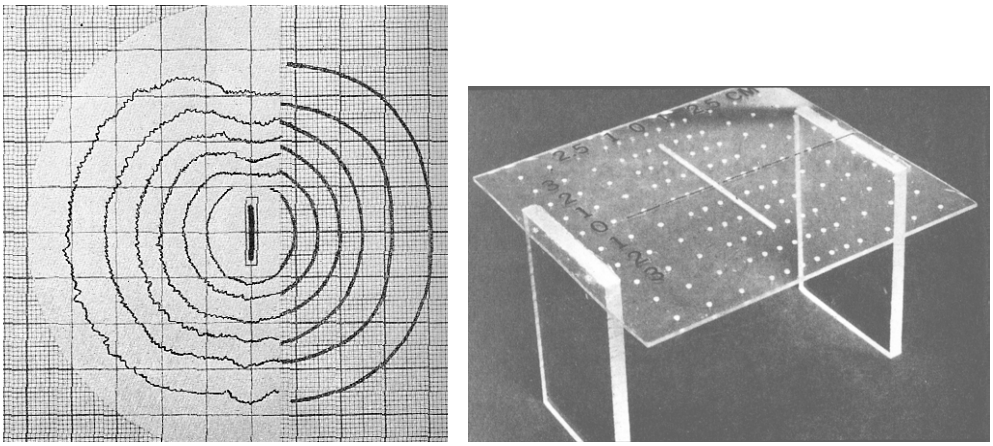
5.2. Dosimetry during the classical era of brachytherapy (1940–1980)

While brachytherapy may have been in clinical decline in the early 1950s, the clinical and dosimetric techniques, upon which classical systems brachytherapy was based, were very mature. Computed exposure rates were based upon a firm foundation of national and international standards based upon standard cavity chambers.

During this period, brachytherapy treatment planning made the transition from table-based systems to patient-specific 2D and 3D dose distributions. In addition, the underlying dosimetry methods successfully adapted to the replacement of radium and radon sources by artificial radionuclides. A major advance was the extension of exposure-based primary standards to the new radium-substitute sources. In the US, NIST (the National Institutes of Standards and Technology, known before 1988 as the National Bureau of Standards) developed reference exposure-rate primary standards based upon carbon wall spherical ionization chambers for ^{137}Cs and ^{60}Co sources in 1974 (Loftus 1970) and for ^{192}Ir brachytherapy sources in 1980 (Loftus 1980). This transition was not always free of serious mishaps. For example, 3M model 6500 ^{137}Cs intracavitary tubes were calibrated by direct intercomparison of caesium tubes with a NIST-calibrated radium needle in a nuclear medicine re-entrant ionization chamber (Kubiatowicz 1981) from 1966 until 1979. Because this procedure ignored differences in polar anisotropy, caesium tube calibrations were overestimated by 5–9%. In contrast, the early Amersham caesium tubes avoided this error by using a carbon-wall ionization chamber to intercompare caesium sources against a calibrated radium needle (Horsler *et al* 1964). In the 1980s, the quantities equivalent mass of radium and reference exposure rate were replaced by reference air-kerma rate (ICRU 1985) or, in North America, by the numerically identical quantity, air-kerma strength (S_K) (Nath *et al* 1987).

5.2.1. The role of experimental dosimetry during the classical brachytherapy era. Relatively few articles on experimental dosimetry were published during this era. The most influential studies focused on measurement of quantities needed to implement Sievert/1D pathlength models for various types of sources. For example, Keyser (1951) and Whyte (1955) used ion chambers to measure the attenuation of radium γ-rays by concentric cylindrical Pt filters. The resultant thickness-dependent effective filtration coefficients served as standard data for Sievert integral implementations through the 1970s (Shalek and Stovall 1969, Young and Batho 1964). Due to an influential theoretical analysis (Evans and Evans 1948), the spectrum-weighted mean value of μ_{en} was used to approximate the effective attenuation coefficient for radium-substitute radionuclides (Hall *et al* 1966, Krishnaswamy 1972).

As the clinical role of radium grew, a number of authors sought to more quantitatively map radium source dose distributions by experimental means. Commonly used instrumentation included brass- and aluminium-walled ion chambers (Nuttall and Spiers 1946, Sievert 1930), liquid-filled ion chambers, and organic (Ter-Pogossian *et al* 1952) and inorganic (Hine and Friedman 1950) scintillators. It was soon recognized (Wootton *et al* 1954) that air ionization chambers with air- or tissue-equivalent walls were necessary to accurately quantify the small deviations of sealed-source dose distributions from inverse-square law. Such measurements reassured the community that exposure-calibrated higher energy artificial radionuclide sources indeed had dose distributions that were equivalent to ^{226}Ra sources of similar geometry. Another important advance was introduction of 1D Monte Carlo and deterministic solutions of the Boltzmann transport equation. The radial dose distributions arising from isotropic point sources in medium by Berger (1968) and Meisberger (Meisberger *et al* 1968) further refined the radionuclide-dependent tissue-attenuation and scatter-buildup factors. The standardized tables (Shalek and Stovall 1961) of recommended tissue-attenuation and scatter factors derived from these early dosimetry investigations were used to implement Sievert integral dose-computation models that dominated brachytherapy dosimetry through the 1980s. Since 1D pathlength algorithm input parameters were assumed to depend only on the primary spectrum of the radionuclide and the encapsulating material, single-source dose distributions for sources of arbitrary design could be generated without having to perform source-specific dose measurements. Recent investigations have shown that in many cases this approximation



(a) (b)

Figure 5. Contemporary illustrations of two early dose-mapping technologies applied to radium sources. (a) Comparison of calculated isodoses curves to isodoses measured by a calcium tungstate (3 mm × 3 mm) scintillating crystal optically coupled to a photomultiplier tube (Hine and Friedman 1950). (b) Lucite holder for positioning TLD-100 crystals in a fixed matrix about a radium needle (Lin and Cameron 1967). The holder was immersed in a water phantom.

was justified, e.g., for ^{192}Ir (Wang and Sloboda 1998). However, early investigators recognized the need for caution in extending this approach to very low energy ^{125}I brachytherapy sources (Krishnaswamy 1978).

Beyond standardization of Sievert integral input parameters, the rather elegant scintillation (figure 5(a)) and thermoluminescent dosimetry (TLD) (figure 5(b)) detector methods for dose mapping were used only infrequently and had little impact on clinical practice. The classical era was clearly dominated by semi-empirical computational models. This dosimetry paradigm was perhaps most succinctly summarized by Quimby (Quimby 1956): "Once the output of a milligram of radium under specified conditions is known, it is not necessary to calibrate the output of every tube or needle: this can be calculated on a basis of the actual radium content, the geometrical size and shape of the source, and the filtration. Therefore the study of distribution of radiation within the tissues for a particular distribution of sources is much simpler than if large series of measurements had to be made in suitable phantoms with adequate ionization chambers. In fact, the latter would be an almost impossible procedure."

6. The rise of modern experimental and computational dosimetry methods

The development of modern quantitative approaches to brachytherapy dosimetry is intimately linked with clinical utilization of low-energy ^{125}I and ^{103}Pd seeds. Interest in basic experimental and computational dosimetry methods began to grow in the mid-1960s because of concerns that semi-empirical computational dose-calculation models, applied so successfully to radium-equivalent radionuclides, might not be valid for the 28 keV x-rays of ^{125}I. Table 1 shows the nearly two-fold historical evolution of absolute dose-rate estimates for the 3M (later Amersham and now GE Healthcare) family of sources. Dosimetry and calibration techniques used in the first decade of clinical ^{125}I practice are undocumented, although the original TG-43 report (appendix C in Nath *et al* (1995)) hints that a very large dose-rate constant,

Table 1. Historical evolution of dose-rate constant for 3M/Amersham ^{125}I interstitial source.

Investigator	Method	Source model	Dose-rate constant Λ (cGy h^{-1}/(μGy m^2 h^{-1}))
Hilaris/Holt 1965	Unknown	6701	1.7
Hilaris/Hot 1975	TLD	6701	1.38
Krishnaswamy 1975	Analytic	6701	1.04
Williamson 1988b	Monte Carlo	6711	0.909
Ling 1983	Analytic	6711	1.04
ICWG 1990	Analytic	6711	0.85
TG-43 1995	Monte Carlo	6711	0.88
AAPM 1999	Monte Carlo	6711	0.98
TG-43 2004	TLD, Monte Carlo	6711	0.96

$\Lambda = 1.7$ cGy h^{-1} U^{-1} (where 1 U = 1 μGy m^2 h^{-1}),[2] was used. The first published ^{125}I dosimetry studies were those of Hilaris *et al* (1975) and Krishnaswamy (1978). The 1975 Memorial study calibrated model 6702 seeds using a carbon-wall extrapolation chamber at 30 cm distance and measured transverse-axis dose rates by means of TLD rods in a Mix-D phantom. Krishnaswamy, on the other hand, derived his estimated Λ from Berger's (1968) theoretical point-source buildup factor data. His paper included confirmatory TLD dose measurements. As shown by table 1, the two methods differed by more than 30%. In 1982, Ling (Ling *et al* 1983) published a somewhat updated theoretical Λ estimate for the model 6711 seed (which was recognized to have a some different photon spectrum than the 6701 seed) along with a radial dose function table derived from silicon diode measurements. These data continued to be used by most practitioners until acceptance of the first TG-43 report in the late 1990s.

6.1. Modern experimental dosimetry and calibration methods

Development of primary air-kerma strength standard for ^{125}I seeds by NIST (Loftus 1984) was a major advance for low-energy seed brachytherapy. This standard was based upon the Ritz FAC (Ritz 1960), which to this day serves as the US air-kerma standard for low-energy x-ray beams. These standardization measurements were performed in 1983 and transferred to a re-entrant ionization chamber for the ^{125}I seed models then available. When vendor-assigned seed strengths are consistently traceable to a stable primary standard based upon accurate realization of a well-defined physical quantity, theoretical as well as experimental estimates of absolute dose rates can be made. In addition, doses delivered to groups of clinically evaluated patients treated at different times can be reconstructed consistently. One of the lessons of the quantitative dosimetry era is that calibration errors and shifts, as well as dose-measurement uncertainties, can undermine clinical dose specification and prescription uncertainty (Williamson *et al* 2005, 1999). At least for the small sample seeds used to develop the 1985 standard (denoted by $S_{K,N85}$ in the recent literature), it appears that the exposure rate derived from the vendor's 'apparent activity' assay agrees closely with Loftus' measurements (Loftus 1984).

In 1986, the US National Cancer Institute funded a 3-year multi-institutional contract to perform a definitive review of low-energy seed dosimetry. The three institutions, collectively

[2] The dose-rate constant is defined as the dose rate in water 1 cm from the seed centre on its transverse axis per unit air-kerma strength or reference-air kerma rate (Rivard *et al* 2004).

called the Interstitial Collaborative Working Group (ICWG), consisted of Memorial Sloan-Kettering Institute, Yale University and University of California-San Francisco led by principle investigators Lowell Anderson, Ravinder Nath and Keith Weaver, respectively (Anderson *et al* 1990). Using TLD-100 chips and powder capsules embedded in machined solid-water phantoms, the ICWG developed procedures, for calibrating TLD detectors and correcting for higher TLD response to low-energy photons, for quantitatively estimating absolute dose rates in water. Each of the three ICWG investigator groups independently measured (Chiu-Tsao *et al* 1990, Nath *et al* 1990, Weaver *et al* 1989) transverse-axis dose distributions for the ^{125}I and ^{192}Ir then available to validate their TLD measurement methodology. This was followed by more complete 2D dose distributions about the extant ^{125}I, ^{192}Ir and ^{103}Pd brachytherapy sources (Chiu-Tsao and Anderson 1991, Meigooni *et al* 1990, Nath *et al* 1993). The results showed good agreement among the different measurements and overall, but large (up to 18% as per table 1) differences between measured and classically computed dose rates for ^{125}I seeds, but good agreement between the classical and experimental approaches for ^{192}Ir. As a result of the ICWG efforts and subsequent contributions from later investigators, TLD dosimetry came to be accepted as the most reliable and best validated experimental approach in brachytherapy and its results are widely used as the basis for clinical dose computation.

6.2. The rise of modern computational dosimetry techniques

Independently of the ICWG initiative, other investigators were investigating Monte Carlo photon-transport techniques for quantitatively evaluating single-source dose distributions. Based on an accurate and detailed mathematical model of the internal structure of the source, photon histories can be generated and then evaluated to assess absorbed dose. 1D Monte Carlo simulations and other transport equation solutions have been used since the 1960s to calculate radial dose distributions arising from isotropic point sources in medium, e.g., the widely used point-source buildup factors of Berger (Berger 1968) and the tissue-attenuation and scatter-buildup factors of Meisberger (Meisberger *et al* 1968). 1D Monte Carlo techniques were first applied to ^{125}I by Dale (1983). However, Monte Carlo techniques were applied to more geometrically complex problems in brachytherapy only relatively recently. One of the earliest 3D studies (Williamson *et al* 1983) (see figure 6) used Monte Carlo simulation to assess the accuracy of the Sievert model for platinum-encapsulated ^{226}Ra and ^{192}Ir sources suspended in free space and was later extended to ^{137}Cs sources embedded in medium (Williamson and Seminoff 1987). Burns and Raeside (1988) published one of the first Monte Carlo dosimetry studies based upon a geometrically realistic ^{125}I seed model.

The author's 1988 Monte Carlo study (Williamson 1988b) demonstrated theoretically that semi-empirical dose-calculation models indeed overestimate ^{125}I absolute dose rates by 10–14% and that the primary cause of this discrepancy is non-penetrating 4.5 keV titanium characteristic x-rays detected by the Ritz FAC, which artificially inflated NIST's $S_{K,N85}$ estimate (figure 7). Comparisons of ICWG TLD measurements and Monte Carlo based dose distributions (Anderson *et al* 1990, Williamson 1991) showed excellent agreement. Williamson and his colleagues published a series of studies comparing Monte Carlo dose-rate predictions to silicon diode (Perera *et al* 1994, Williamson *et al* 1993) and TLD (Das *et al* 1997, 1996, Kirov *et al* 1995, Valicenti *et al* 1995) experimental benchmarks which established the reliability and accuracy of Monte Carlo based dose predictions across the energy spectrum of brachytherapy in both heterogeneous and homogeneous geometries. Currently, Monte Carlo simulation is a widely used and accepted dosimetry tool.

For higher energy sources (mostly ^{192}Ir and ^{137}Cs sources), relatively good (<5%) agreement (at least on transverse axis) between classical dose-calculation algorithms and

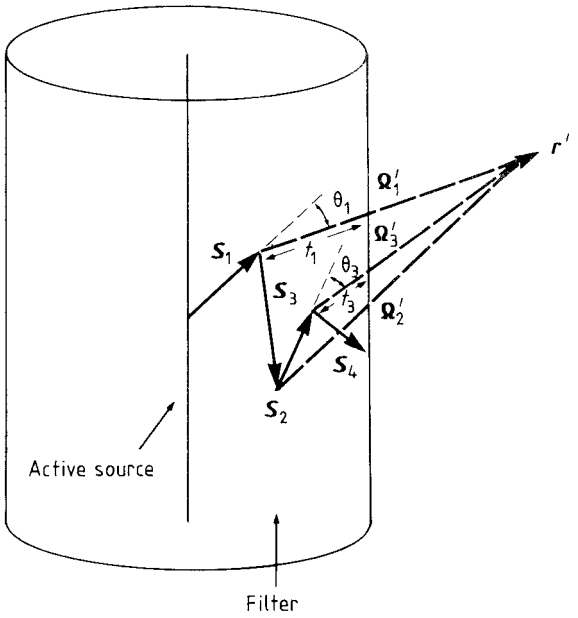


Figure 6. Illustration of the geometry used to make Monte Carlo estimates of dose to a geometric point (Williamson 1987) from filtered line sources. (From Williamson *et al* (1983) with permission.)

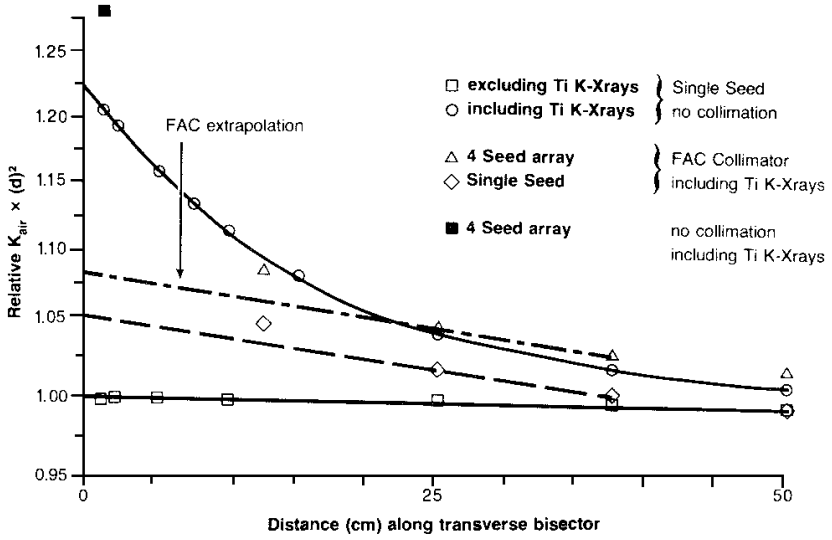


Figure 7. Product of transverse-axis air-kerma rate and distance squared for a model 6711 seed plaque modelled by Monte Carlo techniques, showing how low-energy contaminant x-rays inflate $S_{K,N85}$ by overestimating the air-attenuation correction. (From Williamson (1988b) with permission.)

more contemporary computational or experimental approaches is observed (Williamson 1996, 1998). For lower energy sources, single-seed dose distributions are much more sensitive to model-specific variations in source internal geometry, limiting the accuracy of semi-empirical models in this energy range (Williamson 2005).

6.3. Recent developments in low-energy seed brachytherapy

A major advance in low-energy photon brachytherapy was the 1999 implementation of a new NIST primary standard of air-kerma strength, denoted in the recent literature by $S_{K,N99}$. The new standard used the wide-angle free-air chamber (WAFAC) (Seltzer *et al* 2003) to realize air-kerma strength. This cylindrical FAC was designed to filter out contaminant low-energy x-rays and had a larger collection volume so that that single seeds, compared to plaques of seeds for the 1985 Loftus standard, could be accurately measured. This dedicated brachytherapy WAFAC-based calibration service allows new brachytherapy sources to be added to the system of national standards as they are introduced to market and also provides the infrastructure for vendors to periodically intercompare their calibration processes with NIST so as to maintain traceability to the primary standard. On the negative side, the new $S_{K,N99}$ resulted in a lowering of dose-rate constants (see table 1) relative to $S_{K,N85}$. In addition, NIST-traceable ^{103}Pd seed calibrations turned out to differ by more than 20% from vendor calibrations requiring a realignment (Williamson *et al* 2000) of both dose-rate constants and recommended prescribed doses. In addition, the field was swamped by multiple dosimetry publications (as many as 20 different datasets for 6711 seed) and a rapidly growing array of commercially available seed models (from 3 in 1999 to over 20 in 2004). Taken together, these developments had the potential to cause significant confusion and dose-delivery errors.

6.4. The role of the AAPM in standardizing low-energy brachytherapy dosimetry

During era of rapid growth in low-energy seed permanent implantation and shifting dosimetry standards, the AAPM has had substantial impact on the clinical practice of brachytherapy dose calculation, successfully promoting uniformity of dose-calculation practice that has benefited literally hundreds of thousands of patients. The AAPM's role in brachytherapy dose computation began with the publication of the original TG-43 report (Nath *et al* 1995). Its proposed dose-calculation formalism, derived from the ICWG recommendations (Anderson *et al* 1990), used measured or Monte Carlo based single-source dose distributions rather than semi-empirical models. In addition, TG-43 reviewed the published TLD and Monte Carlo data available for the models 6711 and 6702 ^{125}I sources, the model 200 ^{103}Pd source and the stainless-steel-clad ^{192}Ir seed. For each of these sources, a consensus dataset was recommended, including dose-rate constants, anisotropy constants and factors, anisotropy functions and radial dose functions.

The 1995 TG-43 recommendations implied that ^{125}I dose rates were 10–15% lower than those predicted by then current dose-calculation practices. Implementation of the new $S_{K,N99}$ standard (Seltzer *et al* 2003) necessitated another 10% change, but in the opposite direction. Because the potential for error in simultaneously modifying the source strength and absorbed dose scales by more than 10% was high, the AAPM created an Ad Hoc Working Group under the leadership of Dale Kubo to assist the community in adapting to these changes. The Working Group report (Kubo *et al* 1998) developed a step-by-step procedure for implementing the new WAFAC standard and the TG-43 formalism and recommended that the ^{125}I monotherapy prescribed dose be revised from 160 Gy to 145 Gy. In the author's opinion, the complexity of these changes motivated the community and planning software vendors to rapidly adopt the TG-43 dose-calculation formalism.

Given the rapid shift from radical prostatectomy to permanent seed implantation as the dominant modality for treatment of low-risk prostate cancer, in 1997 the AAPM created a permanent Radiation Therapy Committee (now Therapy Physics Committee Working Group (later subcommittee) on Low Energy Interstitial Brachytherapy Dosimetry or LIBD, under the leadership of Jeffrey Williamson. As LIBD's activities grew in scope, it became a permanent

subcommittee (currently named 'Brachytherapy Subcommittee (BTSC)' with six Working Groups under the chairmanship of Mark Rivard). BTSC took an active role in the introduction of new source strength standards and revised dosimetry practices, coordinating efforts by NIST, source vendors, the clinical community and ADCL secondary dosimetry laboratories often on a source model-by-model basis. BTSC devised a set of dosimetry guidelines (Williamson *et al* 1998), recommending that every routinely used low-energy interstitial source product has a NIST-traceable S_K vendor calibration process and independent experimental and Monte Carlo dose-rate evaluations as documented by peer-reviewed publications. These guidelines have become *de facto* industry standards, accepted by nearly all vendors involved in the market. BTSC also took leadership in implementing the NIST WAFAC standard for the model 200 ^{103}Pd source in a coordinated fashion with the vendor including a historical assessment of 'administered-to-prescribed' dose ratios that enabled users to duplicate dose delivery practices of the past in the face of multiple revisions to the ^{103}Pd dosimetry parameters and calibration changes (Williamson *et al* 2000, 2005). In collaboration with the Radiological Physics Center, BTSC maintains an online registry[3] of brachytherapy source models and vendors that voluntarily comply with AAPM dosimetric prerequisites (Williamson *et al* 1998).

Another BTSC contribution was a major revision of the TG-43 dose-calculation formalism, the preparation of consensus dosimetry parameters for eight source models, and guidelines for the practice of TLD and Monte Carlo dosimetry (Rivard *et al* 2004). A supplement to this report, including consensus dosimetry parameters for an additional 10–12 source models, is expected to be published in late 2006.

6.5. Current status of brachytherapy dosimetry and future directions

Detailed reviews of state-of-the-art brachytherapy dosimetry about 2005 are given in the updated TG-43 Report (Rivard *et al* 2004) and as a recent review chapter (Williamson and Rivard 2005). The total combined uncertainties for TLD transverse-axis ^{125}I seed dosimetry are estimated to be 7.9% (1 cm) to 9.5% (5 cm). The dominant uncertainties are poor reproducibility of repeated TLD readings, uncertainties in the relative energy response correction and uncertainties in the solid-to-liquid water conversion. This last source of uncertainty can be eliminated by use of phantom materials with better-documented compositions. Using state-of-the-art photon cross sections (Cullen *et al* 1997), the corresponding uncertainties of Monte Carlo based absolute dose rates are 2.5% and 5% (Williamson and Rivard 2005). These uncertainties are likely to be much smaller for higher energy sources. An example of the agreement observed between measured and Monte Carlo dose-rate estimates is shown in figure 8 for ^{125}I seeds.

Because Monte Carlo dosimetry is subject to potentially large and unpredictable systematic errors (S_K standard implementation errors, presence of contaminant radionuclides, etc), both experimental and Monte Carlo dose-rate characterization continue to be indicated, at least for low-energy sources. The current BTSC practice for forming consensus datasets is to accept Monte Carlo estimates of relative dose ratios (anisotropy and radial dose functions) if they agree within experimental uncertainty with measured datasets and while forming consensus dose-rate constants by averaging candidate Monte Carlo and measured values (Rivard *et al* 2004).

Ongoing research developments in brachytherapy dosimetry include the search for experimental dosimetry methods that have lower uncertainty and higher spatial resolution than TLD dosimetry. Relatively well established systems for relative dosimetry include single-element silicon diode detectors (Williamson *et al* 1993) and plastic scintillator probes

[3] http://rpc.mdanderson.org/rpc/htm/Home_htm/Low-energy.htm.

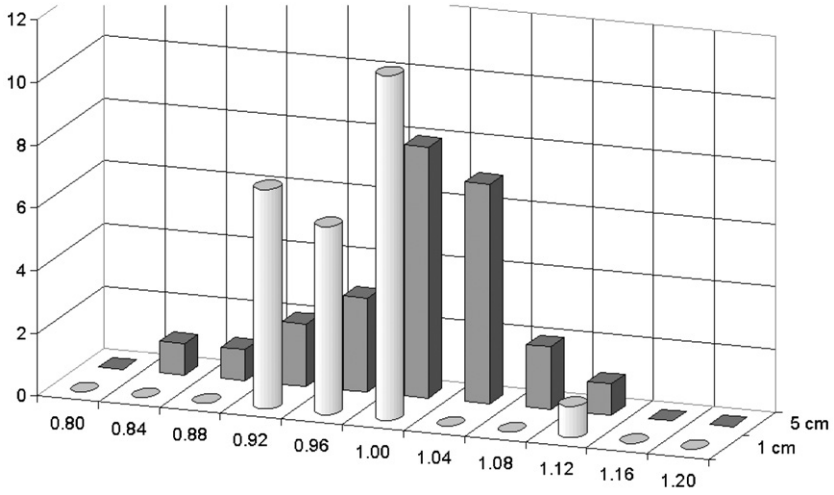


Figure 8. Distribution of calculated (Monte Carlo)-to-measured (TLD-100) absolute transverse-axis dose rates for 1 cm and 5 cm distances. The ordinate gives the frequency of dose ratio plotted on abscissa from 25 sets of TLD measurements for 14 different ^{125}I seed models compared to TG-43 consensus Monte Carlo data. (From Williamson and Rivard (2005) with permission.)

(Bambynek *et al* 2000). Polymer gel dosimetry (De Deene *et al* 2001) shows promise at least for relative dosimetry, as it is capable of high-resolution 3D dose mapping. Radiochromic film dosimetry is currently the best validated (Dempsey *et al* 2000) for both relative and absolute dose measurement of the emerging multidimensional detector systems.

Another emerging development is extension of Monte Carlo dose-computation methods from single-source dosimetry to treatment planning, i.e. calculation of patient-specific dose distributions based upon the actual locations of the implanted sources in the patient. In contrast to conventional single-source dose superposition calculations, Monte Carlo dose calculations can account for tissue-composition heterogeneities, applicator shielding and interseed attenuation. While occasional Monte Carlo studies have been published that address these issues (Chibani and Williamson 2005, DeMarco *et al* 1999, Markman *et al* 2001), clinical use of Monte Carlo simulation has been limited by the long computing times required. Recently, accelerated Monte Carlo codes have been developed (Chibani and Williamson 2005, Hedtjarn *et al* 2002), with single-processor running times as short as 2 min for clinically realistic implant geometries. For low-energy sources, a major problem is characterizing tissue heterogeneities, requires estimation of the photoelectric cross section as well as tissue density (Devic *et al* 2000).

7. Conclusion

This highly selective review demonstrates that brachytherapy has been profoundly affected by mainstream advances in experimental, theoretical and computational physics as well as technological and clinical innovations specific to radiation therapy and medical physics. The broad areas of development include replacement of radium and radon sources with artificial radionuclides, the rise of quantitative dosimetry and treatment planning, and increased utilization of imaging in brachytherapy planning and delivery. Probably, the most influential of these developments was artificial radionuclides. Brachytherapy is essentially an invasive surgical procedure. The clinical need driving this development was not dose-delivery limitations: doses delivered by 1950s era brachytherapy procedures were often as high as or

higher than those delivered today. Rather, the concerns were minimizing radiation exposure hazards (primarily to operator and staff), maximizing the flexibility of the implantation system and minimizing the required level of surgical skill, i.e., steepness and difficulty of the learning curve. The latter two issues impact the quality of implants (and hence local control) achievable and the accessibility of the technique to the population of eligible patients. Image guidance has been shown to significantly improve clinical outcomes, at least for prostate brachytherapy, compared to direct surgical exposure of the tumour. Another important achievement of the last 50 years is the remarkable evolution of brachytherapy dose computation from a semi-qualitative estimate of delivered dose based upon an idealized source arrangement to a physically realistic estimate with uncertainties of less than 5% for even the lowest energy photon-emitting sources. Progress in brachytherapy has resulted from an intersection of clinical need, technological capability and conceptual sophistication.

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References

Adams G *et al* 1949 Techniques for application of the betatron to medical therapy: with report of one case *Am. J. Roentgenol.* **61** 591–625

Anacak Y, Esassolak M, Aydin A, Olacak I and Haydarolu A 1997 Effect of geometrical optimization on the treatment volumes and the dose homogeneity of biplane interstitial brachytherapy implants *Radiother. Oncol.* **45** 71–6

Anderson L L 1986 A natural volume–dose histogram for brachytherapy *Med. Phys.* **13** 898–903

Anderson L L, Nath R, Weaver K A, Nori D, Philips T L, Son Y H, Chiu-Tsao S T, Meigooni A S, Meli J A and Smith V 1990 *Interstitial Brachytherapy: Physical, Biological, and Clinical Considerations* (New York: Raven)

Attix F H and Ritz V H 1957 A determination of the gamma-ray emission of radium *J. Res. Natl Bur. Stand.* **59** 293–305

Bambynek M, Fluhs D, Quast U, Wegener D and Soares C G 2000 A high-precision, high-resolution and fast dosimetry system for beta sources applied in cardiovascular brachytherapy *Med. Phys.* **27** 662–7

Berger M J 1968 MIRD Pamphlet 2: Energy deposition in water by photons from point isotropic sources *J. Nucl. Med.* **9** (Suppl. 1) 17–25

Bethe H A 1930 Zur Theorie des Durchgangs schneller Korpuskularstrahlen durch Materie *Ann. Phys.* **5** 325–400

Blasko J, Grimm P and Ragde H 1993 Brachytherapy and organ preservation in the management of carcinoma of the prostate *Semin. Radiat. Oncol.* **3** 240–249

Bloch F 1933 Bremsvermögen von Atomen mit mehreren Elektronen *Z. Phys.* **81** 363

Brucer M 1952 Therapeutic potentialities of radioisotopes *Merck Rep.* **61** 9–15

Brucer M 1956a A survey of brachytherapy *Roentgens, Rads and Riddles: A Symposium on Supervoltage Radiation Therapy* ed M Friedman, M Brucer and E Anderson (Oak Ridge, TN: US Atomic Energy Commission) pp 449–56

Brucer M 1956b World production estimates: cobalt-60 teletherapy *Roentgens, Rads and Riddles: A Symposium on Supervoltage Radiation Therapy* ed M Friedman, M Brucer and E Anderson (Oak Ridge, TN: US Atomic Energy Commission) pp 155–62

Brucer M 1956c An automatic controlled pattern cesium-137 teletherapy machine *Am. J. Roentgenol. Radium Ther. Nucl. Med.* **75** 49–55

Brucer M 1958 Brachytherapy *Am. J. Roentgenol. Radium. Ther. Nucl. Med.* **79** 1080–90

Burns G S and Raeside D E 1988 Two-dimensional dose distribution around a commercial ^{125}I seed *Med. Phys.* **15** 56–60

Chase N E, Atkins H L and Correll J W 1961 Interstitial irradiation of brain tumors with iridium-192 *Radiology* **77** 842–3

Chassagne D, Janvier L, Pierquin B and Flaisler A 1963 Curie-like therapy of cancers of the cavum with plastic tubing and iridium-192 *Ann. Radiol. (Paris)* **17** 719–26

Chibani O and Williamson J F 2005 MCPI: a sub-minute Monte Carlo dose calculation engine for prostate implants *Med. Phys.* **32** 3688–98

Chibani O, Williamson J F and Todor D 2005 Dosimetric effects of seed anisotropy and interseed attenuation for ^{103}Pd and ^{125}I prostate implants *Med. Phys.* **32** 2557–66

Chiu-Tsao S-T and Anderson L L 1991 Thermoluminescent dosimetry for ^{103}Pd seeds (model 200) in solid water phantom *Med. Phys.* **18** 449–52

Chiu-Tsao S T, Anderson L L, O'Brien K and Sanna R 1990 Dose rate determination for ^{125}I seeds *Med. Phys.* **17** 815–25

Christen T 1914 Radiometry *Arch. Roentgenol. Ray* **29** 210

Cullen D E, Hubbell J H and Kissel L 1997 EPDL97: the Evaluated Photon Data Library, '97 version *Report No* UCRL-50400, vol 6, rev 5 (Lawrence Livermore National Laboratory, University of California)

Curie I and Joliot-Curie F 1934 Artificial production of a new kind of radio-element *Nature* **133** 201

Dale R G 1983 Some theoretical derivations relating to the tissue dosimetry of brachytherapy nuclides with particular reference to iodine-125 *Med. Phys.* **10** 176–83

Das R K, Keleti D, Zhu Y, Kirov A S, Meigooni A S and Williamson J F 1997 Validation of Monte Carlo dose calculations near ^{125}I sources in the presence of bounded heterogeneities *Int. J. Radiat. Oncol. Biol. Phys.* **38** 843–53

Das R K, Li Z, Perera H and Williamson J F 1996 Accuracy of Monte Carlo photon transport simulation in characterizing brachytherapy dosimeter energy response artifacts *Phys. Med. Biol.* **41** 995–1006

Dean A L 1923 Results of skin tests made to determine an objective dose for radium radiations *Am. J. Roentgenol.* **10** 654–61

De Deene Y, Reynaert N and De Wagter C 2001 On the accuracy of monomer/polymer gel dosimetry in the proximity of a high-dose-rate ^{192}Ir source *Phys. Med. Biol.* **46** 2801–25

De Forest S M 1958 A graphic method of reconstructing radium needle implants for calculation purposes *Am. J. Roentgenol. Radium Ther. Nucl. Med.* **79** 42–8

DeMarco J J, Smathers J B, Burnison C M, Ncube Q K and Solberg T D 1999 CT-based dosimetry calculations for ^{125}I prostate implants *Int. J. Radiat. Oncol. Biol. Phys.* **45** 1347–53

Dempsey J F, Low D A, Mutic S, Markman J, Kirov A S, Nussbaum G H and Williamson J F 2000 Validation of a precision radiochromic film dosimetry system for quantitative two-dimensional imaging of acute exposure dose distributions *Med. Phys.* **27** 2462–75

Devic S, Monroe J I, Mutic S, Whiting B and Williamson J F 2000 *Dual Energy CT Tissue Quantitation for Monte-Carlo Based Treatment Planning for Brachytherapy* 1-MO E309-01 (Chicago, IL: IEEE Engineering Medicine and Biology Society)

Edmundson G K 1992 Geometry-based optimization for stepping source implants *Brachytherapy: HDR and LDR* ed A A Martinez, C G Orton and R F Mould (Columbia, MD: Nucletron Corporation)

Ellis F 1956 Use of tantalum wires *Roentgens, Rads and Riddles: A Symposium on Supervoltage Radiation Therapy* ed M Friedman, M Brucer and E Anderson (Oak Ridge, TN: US Atomic Energy Commission) pp 459–64

Evans R D and Evans R O 1948 Studies of self-absorption in gamma-ray sources *Rev. Mod. Phys.* **20** 305–24

Farr R F 1953 Dosage control through radiographs of radon seed implants *Br. J. Radiol.* **26** 429–34

Fletcher G H 1953 Cervical radium applicators with screening in the direction of bladder and rectum *Radiology* **60** 77

Gauwerky F 1977 Short time afterloading curietherapy of gynecological carcinomas: technique and problems *Strahlentherapie* **153** 793–801 (author's transl)

Gray L H 1929 The absorption of penetrating radiation *Proc. R. Soc.* A **122** 647–68

Gray L H 1936 An ionization method for the absolute measurement of γ-ray energy *Proc. R. Soc.* A **156** 578–96

Greenfield M A, Fichman M and Norman A 1959 Dosage tables for linear radium sources filtered by 0.5 and 1.0 mm of platinum *Radiology* **73** 418–23

Grimm P D, Blasko J C, Sylvester J E, Meier R M and Cavanagh W 2001 10-year biochemical (prostate-specific antigen) control of prostate cancer with (125)I brachytherapy *Int. J. Radiat. Oncol. Biol. Phys.* **51** 31–40

Grimm P and Sylvester J E 2004 Advances in brachytherapy *Rev. Urol.* **6** (Suppl. 4) 37–48

Grimmett L G, Kerman H D, Brucer M, Fletcher G H and Richardson J E 1952 Design and construction of a multicurie cobalt teletherapy unit: a preliminary report *Radiology* **59** 19–31

Hall E J, Oliver R and Shepstone B J 1966 Routine dosimetry with tantalum-182 and iridium-192 wires *Acta Radiol.* **4** 155

Hedtjarn H, Carlsson G A and Williamson J F 2002 Accelerated Monte Carlo based dose calculations for brachytherapy planning using correlated sampling *Phys. Med. Biol.* **47** 351–76

Henschke U K 1953 Radiogold seeds for cancer therapy *Nucleonics* **11** 46–8

Henschke U K 1957 A technique for permanent implantation of radioisotopes *Radiology* **68** 256

Henschke U K 1958 Interstitial implantation in the treatment of primary bronchogenic carcinoma *Am. J. Roentgenol.* **79** 981–7

Henschke U K, Hilaris B S and Mahan G D 1963 Afterloading in interstitial and intracavitary radiation therapy *Am. J. Roentgenol.* **90** 386–95

Henschke U K, Hilaris B S and Mahan G D 1964 Remote afterloading with intracavitary applicators *Radiology* **83** 344–5

Henschke U K, Hilaris B S and Mahan G D 1966 Intracavitary radiation therapy of cancer of the uterine cervix by remote afterloading with cycling sources *Am. J. Roentgenol. Radium Ther. Nucl. Med.* **96** 45–51

Henschke U K and Lawrence D C 1965 Cesium-131 seeds for permanent implants *Radiology* **85** 1117–9

Herskovic A, Lee S and Padikal T 1980 Utilization of the computed tomography scanner in interstitial dosimetry *Radiology* **135** 781–2

Hilaris B S, Henschke U K and Holt J G 1968 Clinical experience with long half-life and low-energy encapsulated radioactive sources in cancer radiation therapy *Radiology* **91** 1163–7

Hilaris B S, Holt G J and St Germain J 1975 The use of iodine-125 for interstitial implants *DHEW Publication* (FDA) 76-8022 (US Department of Health, Education and Welfare)

Hilaris B S, Kim J H and Tokita N 1976 Low energy radionuclides for permanent interstitial implantation *Am. J. Roentgenol.* **126** 171–8

Hilaris B S, Whitmore W F Jr, Batata M A and Grabstald H 1974 Radiation therapy and pelvic node dissection in the management of cancer of the prostate *Am. J. Roentgenol. Radium Ther. Nucl. Med.* **121** 832–8

Hine G J and Friedman M 1950 Isodose measurements of linear radium sources in air and water by means of an automatic isodose plotter *Am. J. Roentgenol.* **64** 989

Holm H H *et al* 1983 Transperineal iodine-125 seed implantation in prostatic cancer guided by transrectal ultrasonography *J. Urol.* **130** 273–86

Hope C S, Laurie J, Orr J S and Walters J H 1964 The computation of dose distribution in cervix radium treatment *Phys. Med. Biol.* **9** 345–57

Horsler A F C, Jones J C and Stacey A J 1964 Cesium-137 sources for use in intracavitary and interstitial radiotherapy *Br. J. Radiol.* **37** 385

Horwitz H, Kereiakes J G, Bahr G K, Cuxton S E and Barrett C M 1964 An after-loading system utilizing cesium-137 for the treatment of carcinoma of the cervix *Am. J. Roentgenol. Radium Ther. Nucl. Med.* **91** 176–91

ICRU 1985 Dose and Volume Specification for Reporting Intracavitary Therapy in Gynecology *ICRU Report No* 38 (Bethesda, MD: ICRU)

Johns H E, Bates L M, Epp E R, Cormack D V, Fedorux S O, Morrison A, Dixon W R and Garrett C 1951 1000-curie cobalt-60 units for radiation therapy *Nature* **168** 1035–6

Ketchum L E 1987 Marshall Brucer: still full of acerb wit 30 years after serving as SNM president *J. Nucl. Med.* **28** 1645–50

Keyser G M 1951 Absorption corrections for radium standardization *Can. J. Phys.* **29** 301

Kirov A, Williamson J F, Meigooni A S and Zhu Y 1995 TLD, diode and Monte Carlo dosimetry of an ^{192}Ir source for high dose-rate brachytherapy *Phys. Med. Biol.* **40** 2015–36

Krabbenhoft K L 1958 Present status of radium in radiation therapy *Am. J. Roentgenol. Radium Ther. Nucl. Med.* **79** 538–40

Krishnaswamy V 1972 Dose distribution about ^{137}Cs sources in tissue *Radiology* **105** 181

Krishnaswamy V 1978 Dose distribution around an ^{125}I seed source in tissue *Radiology* **126** 489–91

Kubiatowicz D 1981 Calibration of cesium-137 sources *Recent Advances in Brachytherapy Physics* ed D R Shearer (New York: AIP)

Kubo H D, Coursey B M, Hanson W F, Kline R W, Seltzer S M, Shuping R E and Williamson J F 1998 Report of the Ad Hoc Committee of the AAPM Radiation Therapy Committee on ^{125}I sealed source dosimetry *Int. J. Radiat. Oncol. Biol. Phys.* **40** 697–702

Laurence G C 1938 Some problems of gamma-ray measurement in radiology *Am. J. Roentgenol.* **40** 92–103

Lawrence D, Sondhaus C, Feder B and Scallon J 1966 Soft x-ray "seeds" for cancer therapy *Radiology* **86** 143

Lessard E, Hsu I C and Pouliot J 2002 Inverse planning for interstitial gynecologic template brachytherapy: truly anatomy-based planning *Int. J. Radiat. Oncol. Biol. Phys.* **54** 1243–51

Lin F M and Cameron J R 1967 The radiation distributions around linear radium sources as measured with thermoluminescence dosimetry (TLD) *Am. J. Roentgenol. Radium Ther. Nucl. Med.* **100** 863–9

Ling C C, Schell M C, Working K R, Jentzsch K, Harisiadis L, Carabell S and Rogers C C 1987 CT-assisted assessment of bladder and rectum dose in gynecological implants *Int. J. Radiat. Oncol. Biol. Phys.* **13** 1577–82

Ling C C, Yorke E D, Spiro I J, Kubiatowicz D and Bennett D 1983 Physical dosimetry of ^{125}I seeds of a new design for interstitial implant *Int. J. Radiat. Oncol. Biol. Phys.* **9** 1747–52

Loftus T P 1970 Standardization of cesium-137 gamma-ray sources in terms of exposure units (roentgens) *J. Res. Natl Bur. Stand.* **74** 1–6

Loftus T P 1980 Standardization of iridium-192 gamma-ray sources in terms of exposure *J. Res. Natl Bur. Stand.* **85** 19–25

Loftus T P 1984 Exposure standardization of iodine-125 seeds used for brachytherapy *J. Res. Natl Bur. Stand.* **89** 295–303

Manhattan Project 1946 Manhattan Project Headquarters announcement: availability of radioactive isotopes *Science* **103** 697–705

Markman J, Williamson J F, Dempsey J F and Low D A 2001 On the validity of the superposition principle in dose calculations for intracavitary implants with shielded vaginal colpostats *Med. Phys.* **28** 147–55

Martin C 1949 Low intensity radium element needles: Janeway lecture *Am. J. Roentgenol.* **62** 467–92

Martinez A A, Pataki I, Edmundson G K, Sebastian E, Brabbins D and Gustafson G 2001 Phase II prospective study of the use of conformal high-dose-rate brachytherapy as monotherapy for the treatment of favorable stage prostate cancer: a feasibility report *Int. J. Radiat. Oncol. Biol. Phys.* **49** 61–9

Meigooni A S, Sabnis S and Nath R 1990 Dosimetry of palladium-103 brachytherapy sources for permanent implants *Endocurietherapy/Hyperthermia Oncol.* **6** 107–17

Meisberger L L, Keller R J and Shalek R J 1968 The effective attenuation in water of the gamma rays of gold-198, iridium-192, cesium-137, radium-226, and cobalt-60 *Radiology* **90** 953–7

Meredith W J 1951 Radiotherapeutic physics: V. Dosage control in interstitial gamma-ray therapy *Br. J. Radiol.* **24** 380–4

Meredith W J (ed) 1967 *Radium Dosage: The Manchester System* 2nd edn (Edinburgh: Livingston)

Mitchell J 1946 Applications of recent advance in nuclear physics to medicine *Br. J. Radiol.* **19** 481–7

Morton J L, Callendine W G Jr and Myers W G 1951 Radioactive cobalt in plastic tubing for interstitial radiation therapy *Radiology* **56** 553–60

Murphy M K, Piper R K, Greenwood L R, Mitch M G, Lamperti P J, Seltzer S M, Bales M J and Phillips M H 2004 Evaluation of the new cesium-131 seed for use in low-energy x-ray brachytherapy *Med. Phys.* **31** 1529–38

Myers W G 1948 Applications of artificially radioactive isotopes in therapy: I. Cobalt-60 *Am. J. Roentgenol.* **60** 816–23

Myers W G and Colmery B H 1952 Radioactive Au-198 in gold seeds for cancer therapy *Cancer Res.* **12** 285

Nath R, Anderson L, Jones D, Ling C, Loevinger R, Williamson J F and Hanson W 1987 *Specification of Brachytherapy Source Strength: A Report by Task Group 32 of the American Association of Physicists in Medicine* (New York: AIP)

Nath R, Anderson L L, Luxton G, Weaver K A, Williamson J F and Meigooni A S 1995 Dosimetry of interstitial brachytherapy sources: recommendations of the AAPM Radiation Therapy Committee Task Group No. 43. American Association of Physicists in Medicine *Med. Phys.* **22** 209–34

Nath R *et al* 1991 A dosimetric analysis of Morris, Fletcher and Henschke systems for treatment of uterine cervix carcinoma *Int. J. Radiat. Oncol. Biol. Phys.* **21** 995–1003

Nath R, Meigooni A S and Meli J A 1990 Dosimetry on transverse axes of ^{125}I and ^{192}Ir interstitial brachytherapy sources *Med. Phys.* **17** 1032–40

Nath R, Meigooni A S, Muench P and Melillo A 1993 Anisotropy functions for ^{103}Pd, ^{125}I, and ^{192}Ir interstitial brachytherapy sources *Med. Phys.* **20** 1465–73

Nelson R F and Meurk M L 1958 The use of automatic computing machines for implant dosimetry *Radiology* **70** 90

Nuttall J R and Spiers F W 1946 Dosage control in interstitial radium therapy *Br. J. Radiol.* **19** 135–42

O'Connell D, Howard N, Joslin C A, Ramsey N W and Liversage W E 1965 A new remotely controlled unit for the treatment of uterine carcinoma *Lancet* **2** 570–1

Parker H M 1938 A dosage system for interstitial radium therapy: II. Physical aspects *Br. J. Radiol.* **11** 252–66

Paterson J R 1948 *The Treatment of Malignant Disease by Radium X-Rays, Being a Practice of Radiotherapy* (London: Edward Arnold)

Perera H, Williamson J F, Li Z, Mishra V and Meigooni A S 1994 Dosimetric characteristics, air-kerma strength calibration and verification of Monte Carlo simulation for a new ytterbium-169 brachytherapy source *Int. J. Radiat. Oncol. Biol. Phys.* **28** 953–71

Perez C A *et al* 1991 Impact of dose in outcome of radiation alone in carcinoma of uterine cervix: analysis of two different methods *Int. J. Radiat. Oncol. Biol. Phys.* **21** 885–98

Pierquin B and Fayos J V 1962 Dosimetry by tomography in interstitial curietherapy: point technique *Am. J. Roentgenol. Radium Ther. Nucl. Med.* **87** 585–92

Pouliot J, Tremblay D, Roy J and Filice S 1996 Optimization of permanent ^{125}I prostate implants using fast simulated annealing *Int. J. Radiat. Oncol. Biol. Phys.* **36** 711–20

Quimby E H 1922 The effect of the size of radium applicators on skin doses *Am. J. Roentgenol.* **9** 671–83

Quimby E H 1928 The intensity of radiation in the vicinity of filtered radon implants *Radiology* **10** 365–76

Quimby E H 1941 The specification of dosage in radium therapy: 1940 Janeway lecture *Am. J. Roentgenol.* **45** 1–17

Quimby E H 1952 Dosage calculations in radium therapy *Physical Foundations of Radiology* ed O Glasser *et al* (New York: Hoeker) pp 339–72

Quimby E H 1956 The background of radium therapy in the United States, 1906–1956 *Am. J. Roentgenol. Radium Ther. Nucl. Med.* **75** 443–50

Quimby E H and Castro V 1953 The calculation of dosage in interstitial radium therapy *Am. J. Roentgenol.* **70** 739–49

Ritz V H 1960 Standard free-air chamber for the measurement of low energy x rays (20 to 100 k-constant-potential) *J. Res. Natl Bur. Stand.* **64** 49–53

Rivard M J, Coursey B M, DeWerd L A, Hanson W F, Huq M S, Ibbott G S, Mitch M G, Nath R and Williamson J F 2004 Update of AAPM Task Group No. 43 Report: a revised AAPM protocol for brachytherapy dose calculations *Med. Phys.* **31** 633–74

Rose J E and Loughridge D H 1936 Cathode bias for a supervoltage tube *Radiology* **27** 656–62

Ryan J 1964 Radioactive sources and method for making *US Patent* 3147225 (United States Patent Office)

Saw C B and Suntharalingam N 1988 Reference dose rates for single and double plane ^{192}Ir implants *Med. Phys.* **15** 391

Schoeppel S L, LaVigne M L, Martel M K, McShan D L, Fraass B A and Roberts J A 1994 Three-dimensional treatment planning of intracavitary gynecologic implants: analysis of ten cases and implications for dose specification *Int. J. Radiat. Oncol. Biol. Phys.* **28** 277–83

Schulz U, Busch M and Bormann U 1984 Interstitial high dose-rate brachytherapy: principle, practice and first clinical experiences with a new remote-controlled afterloading system using Ir-192 *Int. J. Radiat. Oncol. Biol. Phys.* **10** 915–20

Seltzer S M, Lamperti P J, Loevinger R, Mitch M G, Weaver J T and Coursey B M 2003 New national air-kerma-strength standards for ^{125}I and ^{103}Pd brachytherapy seeds *J. Res. Natl Inst. Stand. Technol.* **108** 337–58

Shalek R J and Stovall M A 1961 The calculation of isodose distributions in interstitial implantations by a computer *Radiology* **76** 119–20

Shalek R J and Stovall M A 1969 Dosimetry in implant therapy *Radiation Dosimetry* vol 3 ed F H Attix and E Tochlin (New York: Academic) pp 776–98

Sievert R M 1930 Die γ-Strahlungsintensitat an der Oberflache und in der nachsten Umgebug von Radiumnadeln *Acta Radiol.* **11** 249–301

Simon N 1965 Iridium-192 as a radium substitute *Am. J. Roentgenol. Radium Ther. Nucl. Med.* **93** 170–8

Simon N, Silverstone S M and Roach L C 1972 An overview of afterloading in radiotherapy *Am. J. Roentgenol. Radium Ther. Nucl. Med.* **114** 646–51

Sinclair W K 1952 Artificial radioactive sources for interstitial therapy *Br. J. Radiol.* **35** 417

Stenstrom K W 1957 *Manual of Radiation Therapy* (Springfield, IL: Thomas)

Syed A M and Feder B H 1977 Technique of afterloading interstitial implants *Radiol. Clin.* **46** 458

Syed A M, Puthawala A, Sharma A, Gamie S, Londrc A, Cherlow J M, Damore S J, Nazmy N, Sheikh K M and Ko S J 2001 High-dose-rate brachytherapy in the treatment of carcinoma of the prostate *Cancer Control* **8** 511–21

Sylvester J E, Blasko J C, Grimm P D, Meier R and Malmgren J A 2003 Ten-year biochemical relapse-free survival after external beam radiation and brachytherapy for localized prostate cancer: the Seattle experience *Int. J. Radiat. Oncol. Biol. Phys.* **57** 944–52

Teh B S, Berner B M, Carpenter L S, Chiu J K, Dennis S, Lu H H, Woo S Y and Butler E B 1998 Permanent gold-198 implant for locally recurrent adenocarcinoma of the prostate after failing initial radiotherapy *J. Brachytherapy Int.* **14** 233–40

Ter-Pogossian M, Ittner W B and Aly S M 1952 Comparison of air and tissue doses for radium gamma rays *Nucleonics* **10** 50–2

Tod M and Meredith W J 1953 Treatment of cancer of the cervix uteri: a revised Manchester method *Br. J. Radiol.* **26** 252–7

Trump J, Moster C and Cloud R 1947 Efficient tumor irradiation with roentgen rays of several million electron volts *Am. J. Roentgenol.* **57** 703–10

Valicenti R K, Kirov A S, Meigooni A S, Mishra V, Das R K and Williamson J F 1995 Experimental validation of Monte Carlo dose calculations about a high-intensity Ir-192 source for pulsed dose-rate brachytherapy *Med. Phys.* **22** 821–9

Walstam R 1962 Remotely-controlled afterloading radiotherapy apparatus (a preliminary report) *Phys. Med. Biol.* **7** 225–8

Wang R and Sloboda R S 1998 Influence of source geometry and materials on the transverse axis dosimetry of ^{192}Ir brachytherapy sources *Phys. Med. Biol.* **43** 37–48

Weaver K 1995 Stereotactically guided brain implants *Brachytherapy Physics: American Association of Physicists in Medicine, 1994 Summer School* ed J F Williamson, B R Thomadsen and N R (Madison, WI: Medical Physics Publishing) pp 441–51

Weaver K A, Smith V, Huang D, Barnett C, Schell M C and Ling C 1989 Dose parameters of ^{125}I and ^{192}Ir seed sources *Med. Phys.* **16** 636–43

Whyte G H 1955 Attenuation of γ radiation in cylindrical geometry *Br. J. Radiol.* **28** 635

Williamson J F 1987 Monte Carlo evaluation of kerma at a point for photon transport problems *Med. Phys.* **14** 567–76

Williamson J F 1988a Monte Carlo and analytic calculation of absorbed dose near ^{137}Cs intracavitary sources *Int. J. Radiat. Oncol. Biol. Phys.* **15** 227–37

Williamson J F 1988b Monte Carlo evaluation of specific dose constants in water for ^{125}I seeds *Med. Phys.* **15** 686–94

Williamson J F 1991 Comparison of measured and calculated dose rates in water near I-125 and Ir-192 seeds *Med. Phys.* **18** 776–86

Williamson J F 1996 The Sievert integral revisited: evaluation and extension to ^{125}I, ^{169}Yb, and ^{192}Ir brachytherapy sources *Int. J. Radiat. Oncol. Biol. Phys.* **36** 1239–50

Williamson J F 1998 Monte Carlo-based dose-rate tables for the Amersham CDCS.J and 3M model 6500 ^{137}Cs tubes *Int. J. Radiat. Oncol. Biol. Phys.* **41** 959–70

Williamson J F 2005 Semi-empirical dose-calculation models in brachytherapy *Brachytherapy Physics* 2nd edn ed B R Thomadsen, M J Rivard and W M Butler (Madison, WI: Medical Physics Publishing) pp 201–32

Williamson J F, Butler W, Dewerd L A, Huq M S, Ibbott G S, Mitch M G, Nath R, Rivard M J and Todor D 2005 Recommendations of the American Association of Physicists in Medicine regarding the impact of implementing the 2004 Task Group 43 Report on dose specification for ^{103}Pd and ^{125}I interstitial brachytherapy *Med. Phys.* **32** 1424–39

Williamson J, Coursey B M, DeWerd L A, Hanson W F and Nath R 1998 Dosimetric prerequisites for routine clinical use of new low energy photon interstitial brachytherapy sources: recommendations of the American Association of Physicists in Medicine Radiation Therapy Committee Ad Hoc Subcommittee on Low Energy Interstitial Brachytherapy Dosimetry *Med. Phys.* **25** 2269–70

Williamson J F, Coursey B M, DeWerd L A, Hanson W F, Nath R and Ibbott G 1999 Guidance to users of Nycomed Amersham and North American Scientific, Inc., I-125 interstitial sources: dosimetry and calibration changes: recommendations of the American Association of Physicists in Medicine Radiation Therapy Committee Ad Hoc Subcommittee on Low-Energy Seed Dosimetry *Med. Phys.* **26** 570–3

Williamson J F, Coursey B M, DeWerd L A, Hanson W F, Nath R, Rivard M J and Ibbott G 2000 Recommendations of the American Association of Physicists in Medicine on ^{103}Pd interstitial source calibration and dosimetry: implications for dose specification and prescription *Med. Phys.* **27** 634–42

Williamson J F, Morin R L and Khan F M 1983 Monte Carlo evaluation of the Sievert integral for brachytherapy dosimetry *Phys. Med. Biol.* **28** 1021–32

Williamson J F, Perera H and Li Z 1993 Comparison of calculated and measured heterogeneity correction factors for ^{125}I, ^{137}Cs, and ^{192}Ir brachytherapy sources near localized heterogeneities *Med. Phys.* **20** 209–22

Williamson J F and Rivard M J 2005 Quantitative dosimetry methods for brachytherapy *Brachytherapy Physics* 2nd edn ed B R Thomadsen, M J Rivard and W M Butler (Madison, WI: Medical Physics Publishing) pp 233–94

Williamson J F and Seminoff T 1987 Template-guided interstitial implants: Cs-137 reusable sources as a substitute for Ir-192 *Radiology* **165** 265–9

Wilson C W 1951 Radiocobalt (Co-60) as a therapeutic alternative to radium *Am. J. Roentgenol. Radium Ther. Nucl. Med.* **65** 726–36

Wootton P, Shalek R J and Fletcher G H 1954 Investigation of the effective absorption of radium and cobalt-60 gamma radiation in water and its clinical significance *Am. J. Roentgenol. Radium Ther. Nucl. Med.* **71** 683–90

Wyckoff H O 1980 From "quantity of radiation" and "dose" to "exposure" and "absorbed dose"—an historical review *Lauriston S Taylor Lecture No* 4 (National Council on Radiation Protection and Measurements)

Young M E J and Batho H F 1964 Dose tables for linear radium sources calculated by an electronic computer *Br. J. Radiol.* **37** 38

Biography

Jeffrey F Williamson, PhD, received his MS and PhD degrees in medical physics from the University of Minnesota's Biophysical Sciences Program. He is currently chairman of the Medical Physics Division and Professor of Radiation Oncology at Virginia Commonwealth University. Dr Williamson has made many contributions to brachytherapy, including Monte Carlo applications to dosimetry and treatment planning, experimental dosimetry techniques, quality assurance and image-guided therapies. As past Chair of the AAPM's Photon-Emitting Brachytherapy-Dosimetry Subcommittee, he played a key role in standardizing low-energy interstitial seed dosimetry in the US. Dr Williamson has authored or co-authored approximately 175 papers, book chapters and proceedings papers.