Advances in Reference and Transfer Dosimetry

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Abstract

All prerequisites are now in place to create a fundamentally and radically different type of calibration service for the radiation processing industry. Advancements in dosimetry and information technology can be combined to provide industry with on-line calibrations, on demand at a low cost. The remote calibration service will serve as a basis for other areas of metrology.

Introduction

Large-scale ionizing radiation sources, particularly accelerator electron beams and radionuclide (gamma-ray) sources, are now widely used by a number of processing industries. This is an industry which operates in the tens-of-billions of dollars per year, and has a large growth potential. Industries have been established the areas of medical device and pharmaceutical sterilization, curing of materials and coatings, and the treatment of municipal and industrial wastes. An even larger market looms on the horizon; the irradiation of food. With many clearances in place and a growing public demand for a safer food supply, application of this rigorously tested technology seems inevitable.

Food can be treated quite safely with radiation to prevent *e.g.* sprouting in onions, garlic and potatoes, to extend shelf-life of mushrooms, cherries and strawberries, to eradicate insects in grain, spices and fruit, to kill pathogenic microorganisms in fish and meat, and to delay ripening of fruit and vegetables. In spite of the tremendous potential promised by food irradiation treatment, this area of radiation processing has not yet achieved widespread public acceptance in the United States. With heightened concerns over food-borne illnesses, the United States is poised for rapid expansion in this application.

A significant portion of industrial radiation applications involves the modification of properties of polymers. Radiation is used to polymerize and cure monomers into polymers, to cross-link polymers, and to graft different types of monomers onto polymer molecules to form new materials with special properties. Radiation curing of coatings is considered a "green" technology since it reduces emissions of volatile organic compounds (VOCs). One of the most successful enterprises in radiation processing is the manufacture of heat-shrink materials (wrapping films, tubes, *etc.*), which represent a large market both in volume and in commercial value.

Radiation sterilization of medical products is one of the most widespread and successful applications of radiation processing. It is based on the ability of ionizing radiation to kill pathogenic microorganisms. The relationship between absorbed radiation dose and the death of microorganisms is well characterized and predictable. Radiation sterilization developed rapidly and is currently applied to a broad range of disposable medical products (syringes, surgical sutures and utensils, implanted materials and tissues, *etc.*). Sterilization is carried out by ^{60}Co gamma irradiation and, using a variety of electron accelerators, by electron-beam irradiation. Sterilization by irradiation represents about 50% of the market share for sterilization; this represents an increase of nearly double that of 1990. The majority of the remaining product is treated by exposure to ethylene oxide gas. The mutagenic and industrial safety problems associated with ethylene oxide sterilization are the primary reasons for its declining market share.

More than 200 industrial irradiators are currently operating throughout the world and approximately one-third of these are in North America. Large-scale sterilization is performed in a commercial or semi-commercial production plant operating as part of the manufacturing system. Some multipurpose units are set up entirely for contract work, executing service irradiations for the chemical, food and medical industries. In the routine operation of a radiation processing facility, the dose measurements made in the product at regular intervals provide the facility operator and also regulatory authorities with an independent quality control of the process. In some radiation processes, especially those of concern for public health and safety, the release of irradiated product for public use depends on dosimetry measurements demonstrating that the required treatment has been achieved. Thus, it is important and often required that dosimetry in radiation processing be suitably accurate and traceable to a primary standard.

The public health authority will insist on the use of "good manufacturing practice" to reduce the pre-irradiation bacterial contamination of the medical products to a minimum. At the same time, the public health authority (and/or the manufacturer) may insist that the product is not adversely affected by the radiation treatment, and therefore a maximum dose limit may have to be imposed. The operator of a irradiation facility sterilizing medical products will be required to demonstrate that all the products are irradiated to the dose defined by the public health authority. This means that the dosimetry used by the operator has to meet certain requirements with respect to accuracy, precision and calibration, and the traceability of the calibration to national or international standards. It is important to realize that accurate dosimetry provides a completely independent measure of the correctness of the irradiation process and forms the basis for the regulation of the radiation process.

Alanine dosimetry

Alanine dosimetry is the most accurate system available to industry for routine (daily, in-house) use and transfer calibrations (documented traceability to national standard). The dosimeters are composed of microcrystalline alanine (an amino acid) which is usually held in a polymeric binder. The mixture is made into a rod, pellet, film, or cable. The chemical reaction involves radiation-induced fragmentation of the molecule to form stable free radicals (molecules containing unpaired electrons, also known as paramagnetic).

Electron Paramagnetic Resonance (EPR) is a non-destructive method sensitive to free radicals. An EPR spectrometer possesses an electromagnet equipped with a sample chamber that is usually operated in the microwave X-band with an external linearly-swept magnetic field that is modulated at radio frequencies. The EPR absorption is measured by sweeping the external magnetic field strength over prescribed limits. When materials containing free radicals are placed in a strong magnetic field, a splitting of their energies occurs and microwaves induce electron spin-flip transitions between the energy levels. The resultant measurable microwave energy loss is proportional to the number of free radicals in the material. The EPR analysis is generally carried out with a small (~5 mm x ~5 mm cylinder) dosimeter sample inserted into a fixed, repetitive position in the magnetic field. Following the magnetic field sweep, the spectrometer computer displays and stores the absorption intensity. Standardizing the EPR absorption intensities can be accomplished by measurement of a standard sample having a stable and relatively simple EPR signal. Recent advances in spectrometer technology and design has led to production of a small, table-top EPR spectrometer (EMS104, Bruker Instruments) dedicated to radiation dosimetry. The key features of EMS104 spectrometer is the inclusion of a small permanent magnet and a low-noise Gunn-diode microwave source system. Although controlled via its own internal computer, the EMS104 can interface with external PC's through an ethernet interface.

Alanine-EPR dosimetry represents a tremendous advance for industrial dosimetry in that it is a reference class dosimeter that can be mailed for conducting transfer calibrations and can be used for routine dosimetry as well. Some of its important attributes are listed below:

- large dynamic range (from high-dose material processing down to medical therapy applications — six orders of magnitude)
- high accuracy and precision (< 1%)
- pre- and post-irradiation stability (years)
- relatively insensitive to environmental parameters (temperature and humidity)
- inexpensive in large quantities, rugged, reproducible
- different dosimeter designs can be fabricated
- easily calibrated
- non-destructive analysis

In order to provide its customers with the best possible alanine service NIST researchers studied two critical issues faced by industrial users: the effect of humidity and temperature.

Changes in the radiation-induced electron paramagnetic resonance (EPR) signal between the irradiation and subsequent EPR measurements are an important factor directly affecting the accuracy of alanine-EPR dosimetry. It is well known that radiation-induced radicals in alanine are far more stable than the free radical species produced by ionizing radiation in most other organic substances; this is the primary reason for alanine being the most commonly used material for high-dose EPR dosimetry. However, the stability of the alanine radicals is not absolute, and they are known to decay at elevated temperatures and higher humidity. Over the past two decades, many sources of inaccuracies in alanine dosimetry have been successfully eliminated such that errors even below even 1% are significant. Therefore, EPR dosimetrists now need very precise information on the stability of alanine radicals under normal environmental conditions of dosimetry.

A one-year study of the EPR signal of -irradiated (^{60}Co) L α--alanine with simultaneous monitoring of the cavity Q-factor was undertaken. The widespread opinion that the EPR signal remains absolutely stable under normal laboratory storage conditions is inaccurate. At 0% humidity, the signal can be regarded as stable within ±1% of its initial value for 6 months for 1 and 10 kGy doses, but for only 3 months for 100 kGy. When stored at the same relative humidity values up to 60%, the fading rates for dosimeters irradiated to 1 and 10 kGy are similar, whereas signals of dosimeters irradiated to 100 kGy fade considerably faster for all humidities. The rates of fading increase with the relative humidity, especially above 60% R. H. Environmental humidity also deteriorates the accuracy of alanine dosimetry by changing the resonant cavity Q-factor. This is particularly important when irradiated alanine dosimeters are used as instrument calibration standards. Short-term changes in alanine EPR signal amplitudes were recorded upon removal of the irradiated dosimeters from their storage environments. The importance of an in situ standard to correct for measurement errors due to environmental effects will be demonstrated.

Appreciable heating of dosimeters during irradiation is an inevitable effect of any high-dose irradiation at moderate and high dose rates. Ideally a dosimetric system would be insensitive to temperature; in practice, however, application of an appropriate temperature correction is necessary. The alanine-EPR system, currently in wide use as a reference class dosimeter in the industrial and, to a lesser extent, therapeutic dose ranges, is radiation temperature dependent. The effect of irradiation temperature on the EPR signal is not large, but quite noticeable. Irradiation temperature increases of 10 °C, which are very common in practice, result in EPR signal differences and potential dose errors of more than 1%, which are significant at the precision level presently achieved by this method. To make an accurate correction for differences in the irradiation temperatures for test and calibration dosimeters, one needs to know (i) the precise temperature dependence of alanine response and (ii) the precise temperatures of the test and reference dosimeters during irradiation.

Systematic measurements of the temperature coefficient for alanine electron paramagnetic resonance (EPR) response have been performed for irradiation in the temperature range (10 to 50) °C and in the absorbed dose range (1 to 100) kGy at the dose rate 9.5 kGy/h. During the 60Co γ-ray irradiation, L α--alanine dosimeters were kept in a sealed aluminum holder that provided an effective heat exchange with the temperature-controlled environment. The time between the irradiation and signal measurements was standardized, and a reference sample fixed in the resonant cavity was used to correct the signals for small variations in the spectrometer sensitivity. The temperature coefficient for each dose was determined from approximately 30 experimental points processed by the weighted least-squares technique after the necessary statistical tests were done. The temperature coefficients thus determined were considerably lower than previously reported. The dose dependence of the temperature coefficient features a minimum at (20 to 30) kGy (about 0.135%/K) with higher values at 1 kGy (0.17 %/K) and at 100 kGy ((0.175 to 0.19) %/K). With the exception of very high doses, no significant distinction was found between the temperature coefficients of Bruker and NIST dosimeters, which differ in shape and binder content.

The problem

Despite these new improvements to dosimetry practices, a major issue remains — turnaround time for transfer calibrations. The radiation processing industry operates its facilities 24 hours per day, 365 days per year, in a just-in-time manufacturing mode. When problems arise which require resolution through transfer dosimetry, the turnaround time can be critical. Processing stoppages on the order of days can be crippling (*e.g.*, slowdown in shipments of medical devices, food shipments with short a shelf-life held in waiting). The NIST Ionizing Radiation Division has been attempting to respond to the call by industry to address this pressing need. Over the past few years, NIST and industry has hosted several workshops, from which a few non-technical solutions were attempted, but eventually failed. Recent discussions with industry representatives regarding the technical solution proposed here were enthusiastic, optimistic and encouraging.

The solution: A remote calibration service

The objective is to create a system for fast remote calibration of high-dose radiation sources against the U.S. national standard gamma-radiation source using the Internet. The Internet-based system will deliver immediate calibration results to the industry customer on-demand at a lower cost. The calibration results can be rapidly incorporated into the product dose-map model to ensure the highest quality manufacturing.

At present, the procedure of calibrating a source for a customer comprises sending unirradiated alanine pellets from NIST to the customer, who irradiates them with the industrial radiation source to be calibrated. The irradiated pellets are returned to NIST, the EPR signals are measured at NIST, compared with the signals from pellets irradiated with the NIST standard calibration source, and the dose values are calculated. Finally, a NIST Certificate of Calibration containing the NIST-interpolated dose values is sent to the customer. This process takes several days and considerable labor at NIST, which makes the cost of the calibration relatively high and prevents customers from frequent use of this NIST service

All prerequisites are now present for automating this operation on the basis of modern technologies and commercially available products. Bruker Instruments manufactures (relatively) small EPR spectrometers designed specifically for dosimetry purposes, which exhibit the necessary high accuracy of measurements in combination with a significantly reduced cost. These spectrometers can be used in parallel at a customer's laboratory and at NIST for concerted measurements. Bruker also manufactures high-quality alanine pellets, which can be used for the calibrations in question and are available both for the interested customers and NIST directly from that company. Finally, there is the Internet, which provides an easy link between the EPR spectrometer and computers at NIST and the identical computer-controlled EPR spectrometer at the customer's laboratory. Combination of these means holds promise for entirely redesigning the source calibration process to make it faster, less laborious, much cheaper and, consequently, much more accessible for present and potential customers.

Once built, the Internet-based transfer calibration process will be the most modern calibration service. The system can be described as follows. The industrial site will first be connected to the NIST calibration facility via Internet and fiber optic link. The industrial facility will access the Internet program, request a calibration, and begin by irradiating pre-supplied dosimeters. The Internet calibration program will control their EPR spectrometer and instruct the industry technician to perform the required measurements in a step-wise manner. The raw data will be transferred and evaluated by the program and a provisional certificate of calibration will be generated for the customer; the clear advantage is that these calibration data could be used immediately in the industrial process. After appropriate quality checks are made at NIST, an official certificate will be issued (this step is to fulfill the regulatory requirement of a signed calibration certificate, and would not slow the application of the calibration data by the customer). The Internet calibration program would provide industry with on-demand calibrations, immediate turnaround times, lower cost, and improve the quality of the manufacturing process. NIST would be able to increase its customer base and use less staff time to service it.

The Internet-based calibration service will be established in a series of progressive stages. The first stage will be to establish a testbed system within NIST. This system will be built in consultation with industrial partners so that, when it is transferred, it can be immediately implemented. Radiation processing facilities operate non-stop and do not have the luxury to test and develop dosimetry systems. A fully-functioning testbed system can be used to demonstrate and train industry partners. The system will be transferred to companies representing each of the three major high-dose radiation applications: food irradiation, medical device sterilization, and materials processing. Many U.S. companies have foreign irradiation plants. This service would provide the foreign facilities with the same real-time calibration service as their U.S. counterparts. NIST currently has customers as distant as Taiwan; these customers would enjoy the same high-quality service.