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Direct comparison of gamma, electron beam and X-ray irradiation doses on characteristics of low-density polyethylene, polypropylene homopolymer, polyolefin elastomer and chlorobutyl rubber medical device polymers

Leonard S. Fifield [a,*], Matt Pharr [b], David Staack [b], Suresh D. Pillai [b,c], Larry Nichols [d], James McCoy [e], Tony Faucette [e], Tucker T. Bisel [a], Min Huang [b], Md Kamrul Hasan [b], Lucas Perkins [e], Scott K. Cooley [a], Mark K. Murphy [a]

[a] Pacific Northwest National Laboratory, Richland, WA, 99354, United States
[b] Department of Mechanical Engineering, Texas A&M University, College Station, TX, 77843, United States
[c] National Center for Electron Beam Research, Texas A&M University, College Station, TX, 77843, United States
[d] Steri-Tek, Fremont, CA, 94538, United States
[e] Global Sterility Assurance, Becton, Dickinson and Company, Research Triangle Park, NC, 27709, United States

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ABSTRACT

There is a growing need for increased efficiency in the sterilization of single use medical devices and other products that contain polymer components. Gamma radiation is widely used for devices suited for radiation sterilization; however, safety, throughput and cobalt-60 source availability are challenging the prospect of relying on gamma radiation to meet the anticipated needs of the industry. Use of electron beam (e-beam) and X-rays as alternatives to gamma for radiation sterilization have been hampered in part by a concern that these modalities may adversely affect polymer integrity and performance relative to the gamma method, for which the industry has had much more experience. To address this concern, the effects of sterilization-relevant doses of e-beam, X-ray and gamma radiation were directly compared using common medical device polymers found in two prototypical commercial devices currently sterilized using cobalt-60 gamma irradiation. The Becton, Dickinson and Company (BD) Vacutainer™ Plus tube contains low-density polyethylene and chlorobutyl rubber components, while the BD Vacutainer™ Push Button Blood Collection Set contains polypropylene homopolymer and polyolefin elastomer components. Injection-molded samples prepared from the polymers used in these products were exposed to target doses of 15, 35, 50 and 80 kGy using gamma, e-beam and X-ray radiation. Changes in coloration, tensile properties and hardness were measured for each condition, and the effects of e-beam and X-ray irradiation compared with the effects of gamma irradiation on these properties. Both e-beam and X-ray appear as viable alternatives to gamma irradiation for sterilization of the polymers tested.

1. Introduction

Plastic polymers have seen increased use in medical devices in the last half-century. It is estimated that over 25 percent of hospital waste is plastic (Gibbens, 2019). To prevent infection, devices are sterilized to inactivate bacteria, fungi, viruses and bacterial endospores. In the United States, sterilization modalities used in the medical industry are approximately 50% ethylene oxide (EO) gas, 41% cobalt-60 gamma radiation, 4.5% electron beam (e-beam) radiation, and <5% other (including steam and X-ray radiation) (GIPA IIA, 2017). Radiation sterilization is less time consuming than EO and is well-suited for temperature-sensitive materials such as plastics. However, radiation is known to cause deleterious effects on plastics, such as discoloration and embrittlement, with degree of damage dependent on material and dose level. Therefore, the medical device industry spends a significant amount of resources to qualify each of their products for specific sterilization technologies. In order to ensure a sufficient safety factor, the performance of polymers used in these devices is rigorously tested at varying irradiation dose levels to identify the dose range at which the devices can be sterilized and yet retain their targeted functionality and

* Corresponding author.
E-mail address: leo.fifield@pnnl.gov (L.S. Fifield).

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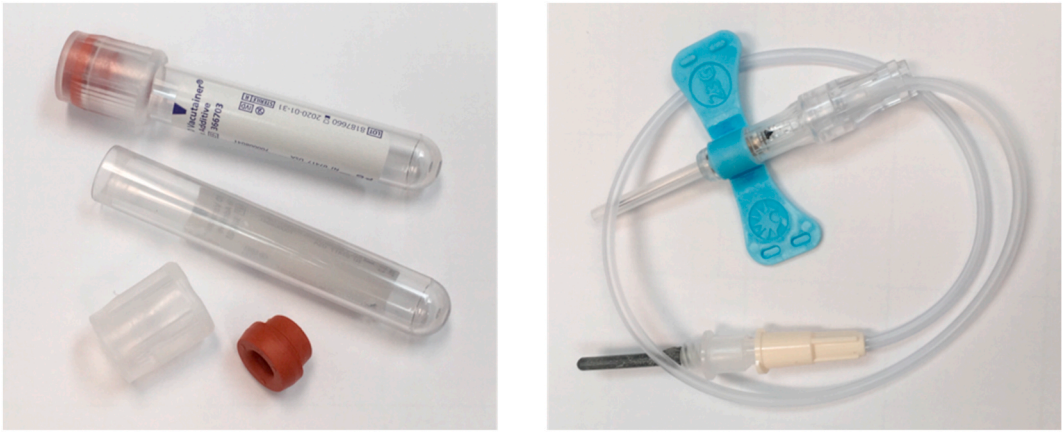

Fig. 1. *Vacutainer™ Plus* tube (VT) (Left), with low-density polyethylene (LDPE) cap and chlorobutyl rubber (CIIR) stopper components; and *Vacutainer™ Push Button Blood Collection Set* (PB) (Right), with polyolefin elastomer (POE) finger wing and polypropylene homopolymer (PPH) finger grip components.

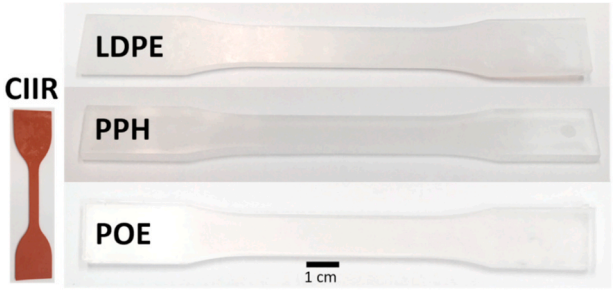

Fig. 2. Tensile specimens of the polymers investigated. CIIR-chlorobutyl rubber, LDPE-low-density polyethylene, PPH-polypropylene homopolymer, POE-polyolefin elastomer.

material characteristics.

As the medical device market continues its rapid growth (compound annual growth rate > 6%) (marketandmarkets.com, 2020), gamma sterilization of medical products is challenged by growing shortages in cobalt-60 irradiation capacity, cobalt-60 irradiation costs, and national and international pressures to switch from radioactive sources such as cobalt-60 to non-isotope based methods such as e-beam and X-ray technologies. In addition to potential cost, security and availability advantages of e-beam and X-ray methods, these technologies may also help meet the growing need for sterilization to be integrated into the medical device manufacturing, either in-line or at end-of-line. However, there is a knowledge gap in how the different radiation sources affect common medical device materials (Kroc et al., 2017). There is also the challenge that most of the test data that companies have accumulated are not available in the public domain. This gap in information hampers the switch to alternate technologies such as e-beam and X-ray. This work is part of an effort to lower adoption barriers for alternate technologies for the sterilization of medical devices.

The overall goal of the research reported here was to compare the material characteristics of two representative medical devices when exposed to similar cobalt-60, e-beam, and X-ray irradiation doses. The two devices chosen were the Becton, Dickinson, and Company (BD) *Vacutainer™ Plus* tube and the BD *Vacutainer™ Push Button Blood Collection Set*. The BD *Vacutainer™ Plus* tube (VT) device consists of a main polyethylene terephthalate (PET) tube, a chlorobutyl rubber (CIIR) stopper, and a low-density polyethylene (LDPE) cap. The VT device, currently sterilized solely by cobalt-60, represents over 90% of the world market of blood collection tubes, with more than 5 billion units produced each year. The BD *Vacutainer™ Push Button Blood Collection Set* (PB) device consists of flexible polyvinyl chloride (PVC) tubing, a polypropylene homopolymer (PPH) finger grip and polyolefin elastomer (POE) control wings. Over 260 million PB devices are produced each year and are sterilized solely by cobalt-60 technology. We chose these devices for this study since replacing the current gamma irradiation sterilization modality with either e-beam or X-ray would result in a significant reduction of cobalt-60 use in the United States. The underlying hypothesis was that e-beam and X-ray irradiation would have the same effects on polymer properties as gamma irradiation at similar doses. The effects of radiation modality and dose level on the functionality, coloration and mechanical performance of the two BD devices themselves are described in our previous manuscript (Fifield, 2020).

The Materials and Methods section below describes the BD devices and constituent polymers investigated, as well as the irradiation details. Test results versus dose level and modality, along with a summary of the statistical analyses are given in the Results and Analysis section. Remarks on the suitability of e-beam and X-ray radiation modalities as alternatives for sterilization of products containing the CIIR, LDPE, PPH and POE polymers investigated are provided in the Conclusion section. Additional analysis details and test results are provided in the Supplemental Information.

2. Materials and methods

2.1. Medical devices and polymers

Fig. 1 shows the VT and PB devices that were used in these studies.

Non-sterile samples were obtained from Becton Dickinson for these studies. The polymer test samples used were like the polymers used in the actual BD *Vacutainer*™ products, and were generously provided for this work by BD. The CIIR (chlorobutyl rubber, also known as chloro isobutylene isoprene rubber) used is of proprietary BD formulation. It was provided in pressed, 15 cm × 15 cm x 0.32 cm mats (Fig. 2). Subsized ASTM D638 Type 4 specimens with 16 mm gauge length were stamped from the mats with a NAEF Punch Press (NAEF Press & Dies, Inc.). The LDPE, PPH and POE samples (Fig. 2) were provided as ASTM D638 Type 1 injection-molded tensile specimens (Fig. 2) of 165 mm overall length, 50 mm gauge length, 13 mm gauge section width, and 3.2 mm thickness. The LDPE is Purell PE 1840H (LyondellBasell), the PPH is product 3620WZ (Total Polymers), and the POE is ENGAGE™ 8440G Polyolefin Elastomer, an ethylene-octene copolymer (The DOW Chemical Company).

2.2. Choice of radiation doses and radiation processing

Bioburden-based ionizing radiation dose for sterilization is determined by standard methods and is typically in the range of 15–50 kGy

Table 1
Target doses, average measured doses, and approximate dose rates for each modality.

Modality	10 kGy	35 kGy	50 kGy	80 kGy	Dose Rate (kGy/s)[a]
Gamma	10.1	36.2	51.3	85.2	~0.003
E-beam	12.4	40.8	51.4	86.2	3.0
X-ray	11.0	36.0	51.5	83.5	~0.03

[a] Approximate values provided for order-of-magnitude comparison.

Table 2
Results of dosimetry comparison between E-beam and X-Ray irradiation facilities.

Dosimeter #	TAMU Alanine Readings (kGy)	Steri-Tek B3 Readings (kGy)
1	13.9	12.5
2	13.7	12.2
3	13.4	12.2
Mean:	*13.6*	*12.3*

(ANSI/AAMI/ISO 11137-2: 2013 R2019). To directly compare the effects of dose from different modalities on CIIR, LDPE, PPH and POE medical device polymers, batches of the polymer specimens were processed to common target doses of 10, 35, 50, 80 kGy using gamma, e-beam and X-ray fields. Preliminary dose uniformity studies were conducted to ensure that the dose uniformity ratio (DUR) of these polymer samples was approximately 1.0. Discoloration, hardness and tensile performance of the processed polymer samples were analyzed as a function of dose level and modality. *Gamma* processing was performed by BD in the research loop of a nominal 3.5 MCi cobalt-60 irradiation cell in Broken Bow, Nebraska. Polymer samples were irradiated in boxes at approximately 35 °C to the doses indicated in Table 1. The applied dose rate is on the order of a few Gy per second (~0.003 kGy/s). *E-beam* processing was performed using a 10 MeV, 15 kW s-band Varian linear accelerator at the University National Center for Electron Beam Research (ebeam-tamu.org), part of Texas A&M University (TAMU) in College Station. Polymer samples were assembled flat on a surface in a single layer. They were irradiated at 22–24 °C to the doses indicated in Table 1. Associated beam current/scan settings were 1.6 mA/61 cm. Dose rate was empirically calculated to be approximately 3.0 thousand Gy/second (3.0 kGy/s). Conveyor speed was adjusted to achieve desired minimum target dose. Samples were routed through the cell multiple times, without flipping, to achieve the desired dose levels, with a unilateral geometry. The average dose per pass was 15 ± 3 kGy. The average conveyor speed was 3 m per minute. Dose distribution in the samples was determined through preliminary trials. *X-ray* processing of the polymer samples was performed using a 7.5 MeV, 30 kW X-ray machine at Steri-Tek (steri-tek.com) in Fremont, California. Samples were irradiated in boxes at 21 °C to the doses indicated in Table 1. Polymer samples were loaded into boxes and boxes into totes on the conveyor. Associated beam scan settings were 30.5 cm from target and the conveyor speed was 0.025 m per minute. A dose of 11 kGy was applied per pass at this conveyor speed. The resulting dose rate is on the order of a few tens of Gy per second (~0.03 kGy/s). Conveyor speed was increased to deliver the final doses to the polymers to achieve desired total doses.

2.3. Dosimetry

Dosimetry between irradiation facilities was compared to verify measured levels of absorbed dose that the samples received. Dosimetry protocols utilized were reported by each of the associated irradiation facilities. Each facility was required to provide documentation that their dosimetry system had a valid calibration traceable to the primary standard (National Institute of Standards and Technology), as well as documentation on the calculated measurement uncertainty (at the 95% confidence level) associated with their quoted product doses. The alanine dosimetry systems used at the gamma and e-beam facilities provide a measurement uncertainty of approximately 5% at the 95% confidence level, and the B3 dosimetry system used at the X-ray facility provided a measurement uncertainty of approximately 7% at the 95% confidence level. In order to provide extra assurance that the reported delivered doses at each of the three irradiation facilities were within the stated uncertainties, a dosimetry comparison study was performed that involved the TAMU e-beam facility and the Steri-Tek X-ray facility. The protocol involved Steri-Tek providing three B3 film dosimeters to TAMU, which TAMU co-located with their alanine dosimeters within an Ethafoam (closed cell polyethylene) block, then exposed the assembly to their e-beam for a targeted 12 kGy. The irradiated B3 film dosimeters were then shipped back to Steri-Tek for readout, and the alanine dosimeters were read out at TAMU. The resulting data is tabulated in Table 2 and indicate a difference less than 10% in measurement accuracy between TAMU and Steri-Tek.

2.4. Randomization and blind testing of sample characteristics

The samples for irradiation were shipped out from a central location and received back at this central location. The samples for material characteristic testing were assembled into six test batches (bags), each containing one sample from each exposure condition (modality and dose) and two unirradiated (control) specimens. The batches were tested one after the other with samples randomly drawn one at a time from the bag under test. In this way, a sample from every condition was tested before the next set of replicates and test order bias was eliminated.

2.5. Material characteristic testing

2.5.1. Device discoloration

A common effect of ionizing radiation in polymers is a dose-dependent yellowing. Color change in medical device polymers due to sterilization processing may be undesirable for aesthetic reasons, even if it does not affect mechanical properties or device function. Yellowness Index (YI) (ASTM E313, 2015) of the polymer samples was measured and correlated with each dose and modality. A Color Assessment Cabinet and a Nikon D5600 camera with 100 mm f/2.8 Series E AIS manual focus lens were used to photograph each set of samples next to an X-Rite ColorChecker Classica White Board (X-Rite, Inc.). Nikon Electronic Format (NEF) raw files were converted to Digital Negative (DNG) format using Adobe Digital Negative Converter software. ColorChecker Passport software was used to create a profile specific to the camera used, and Adobe Photoshop software was used to apply the created camera profile to the photos. MATLAB® software was used to calculate the YI and RGB value at the 95% confidence interval. Color measurement and analysis were performed at TAMU in College Station.

2.5.2. Mechanical testing

Hardness (ASTM D2240) and tensile properties (ASTM D638, ASTMD412) were used to compare the effects of radiation dose and modality on the medical device plastics. Standard geometries and methods were used except where noted. Displacement rates for tensile testing were chosen according to ASTM D638 and D412 as appropriate for each material. For the Type I specimen geometry, ASTM D638 Section 8.2 recommends using the slowest displacement rate among 5, 50, and 500 mm/min that gives specimen breakage within a 0.5–5 min test time. 50 mm/min met this requirement for the LDPE and PPH specimens used here. ASTM D412 recommends a 500 mm/min displacement rate for elastomeric materials such as POE and CIIR. This rate also satisfied the guidelines for ASTM D638.

2.5.2.1. Sample conditioning prior to test. The polymer samples were pre-conditioned prior to mechanical testing according to ASTM

Table 3
Experimental parameters used in tensile testing.

Material	Specimen Geometry	Specimen Length (mm)	Gauge Length (mm)	Distance between grips (mm)	Displacement rate (mm/min)
CIIR	Type IV	115	25	65	500
LDPE	Type I	159	50	115	50
POE	Type I	162	50	96.5	500
PPH	Type I	162	50	115	50

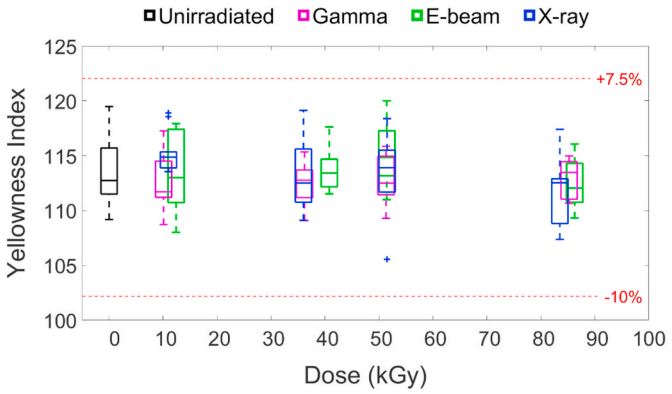

Fig. 3. Box plot representation of CIIR YI versus dose and modality.

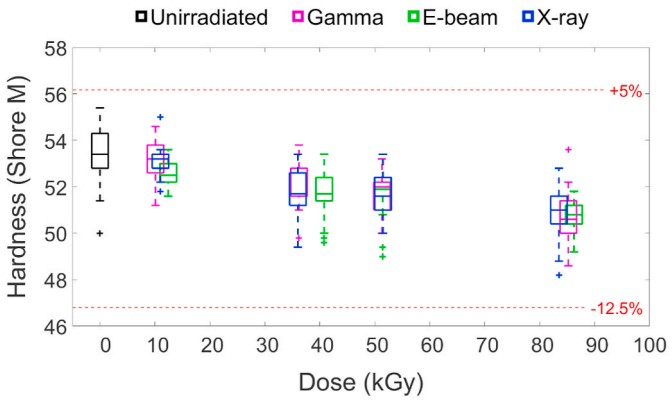

Fig. 4. Box plot representation of CIIR Shore M hardness versus dose and modality.

D618-13. The samples were stored in a sealed chamber at 22 °C for at least 48 h until just before testing. Relative humidity in the chamber was maintained at 43% with the use of saturated potassium carbonate solution (ASTM E104-02).

2.5.2.2. Hardness testing. The CIIR was tested on the Shore Type M scale (ASTM D2240-15, 2015) using the stamped tensile specimens. A Rex Model DD-4 Type M Digital Durometer with pneumatically damped Model OS-1 Operating Stand (Rex Gauge Company, Inc.) was used to obtain hardness values. The 3.2 mm thickness of the rubber was greater than the minimum 1.25 mm required by ASTM D2240. Measurements were performed at locations at least 2.5 mm from specimen edges. Tests were conducted at 23 °C. At least five measurements were performed per specimen, five specimens per dose and modality, and ten unirradiated specimens for a total of 70 samples and 350 measurements per material. Shore M measurements were performed at the Pacific Northwest National Laboratory (PNNL) in Richland, WA.

The LDPE, PPH, and POE were tested on the Shore Type D scale (ASTM D2240, 2015) using the injection-molded specimens prior to tensile testing. A Rex Model DD-5-D Type D Digital Durometer with pneumatically damped Rex Model OS-1 Operating Stand was used for hardness measurements. ASTM D2240 specifies that test samples be at least 6.0 mm thick unless it is known that equivalent results are obtained from thinner specimens, and specimens may be stacked to reach the required thickness. The Type I samples with 3.2 mm thickness were found to exhibit similar hardness values to those obtained for stacked, 6.4 mm specimens. Therefore, results were taken from single thickness specimens. Additionally, according to ASTM D2240, test locations must at least 12 mm from the edge of a specimen unless it can be verified that edge proximity does not change the results. The location farthest the edge, 9.5 mm, was confirmed to be acceptable. Six measurements were made per specimen (3 on each grip section) on five specimens per dose and modality. Counting ten unirradiated specimens, there were 70 samples and 420 measurements for each polymer, or 210 samples and 1260 hardness measurements total for the injection-molded specimens. Shore D measurements were performed both at PNNL and at TAMU. Hardness data in the Results section was recorded at TAMU. PNNL Shore D results are included in the Supplemental Information.

2.5.2.3. Tensile testing. Tensile testing of the polymer samples followed ASTM D638 and utilized an Instron 5943 tensile tester with a 1 kN load cell (at TAMU), an Instron 5984 tensile tester with a 5 kN load cell (at TAMU), and an Instron 3367 extended travel instrument with 30 kN load cell (at PNNL). Testing parameters for the four materials, including specimen geometry, specimen overall length, gauge length, distance between grips during test, and strain rate are indicated in Table 3. Video extensometry was performed using a digital camera and a custom-written video analysis method (details provided in the Supplemental Information). Two sets of 16 unirradiated control specimens and 24 irradiated specimens (6 replicate samples from each of the 4 doses) from each method (gamma, e-beam, and X-ray) were prepared, giving a total of 176 test specimens for each material. Specimens were randomized by dose and modality prior to testing to avoid test-order bias. All tensile tests were performed at 22 °C. Tensile testing of all materials was performed at both PNNL and TAMU. Tensile data in the Results section was recorded at TAMU. PNNL tensile data is included in the Supplemental Information.

2.6. Data compilation and statistical analyses

Statistical analysis was performed to identify differences between results of samples processed using the standard gamma radiation and samples processed using either e-beam or X-ray. Numerical results were extrapolated from actual dose to target dose for each modality prior to comparison between methods to account for differences between modalities in actual measured doses. Most radiation sterilization byproducts and residuals decay or dissipate within 48 h, according to AAMI TIR17:2017 (AAMI TIR17:2017, 2018). A minimum time of at least 1 week before testing was implemented, rather than controlling time between irradiation and testing for each of the modalities. Samples were stored out of direct light and at ambient temperature following radiation processing and prior to testing. This work sought to understand how sterilization effects from e-beam or X-ray might differ from the effects of gamma sterilization on specific polymers from single-use medical devices. Statistical analysis was used to determine whether differences in effects were statistically significant and focused on 1) e-beam versus gamma radiation and 2) X-ray versus gamma radiation, at the dosage levels investigated. Analysis was performed using R software (R Core Team, 2019) and based on a significance level of 0.05 using a strategy detailed in the Supplemental Information. Differences for a given test result from a device irradiated with e-beam or X-ray at a given target dose from the test result of the device gamma irradiated at the same target dose with 95% confidence are defined as Significant (S), Not Significant (NS), or of Inconclusive (I) significance. Statistical analyses

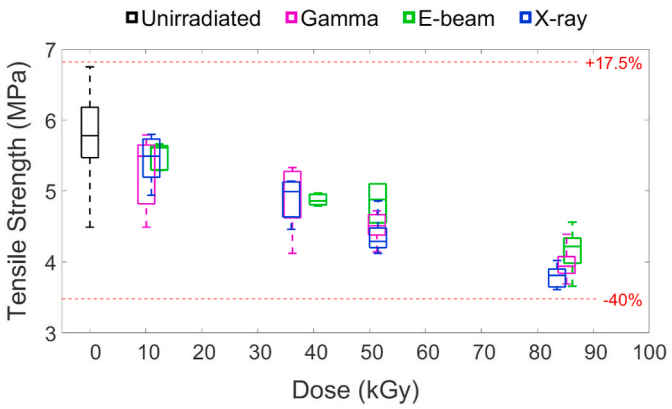

Fig. 5. Box plot representation of CIIR tensile strength versus dose and modality.

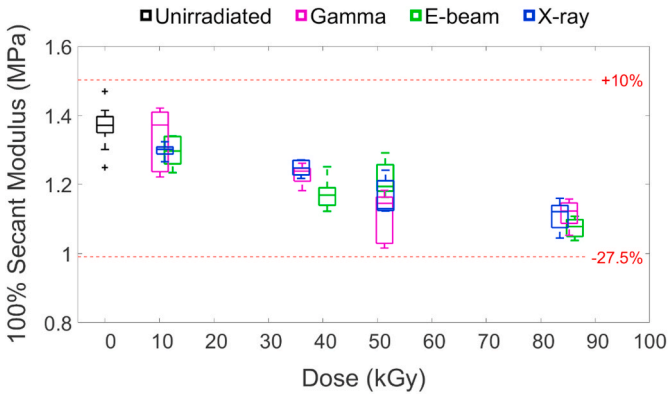

Fig. 6. Box plot representation of CIIR 100% secant modulus versus dose and modality.

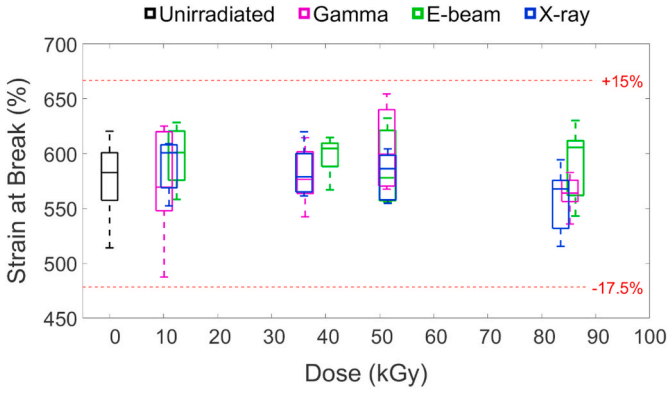

Fig. 7. Box plot representation of CIIR elongation at break versus dose and modality.

were performed at PNNL.

3. Results and discussion

The polymers studied here were selected as representative for single-use medical devices prevalent in the industry, as demonstrated by the high volume of VT and PB devices produced each year. The irradiation doses chosen for this study represent the range of sterilization doses generally used in the industry. The minimum sterilization dose for medical devices is generally on the order of 10–25 kGy (AAMI TIR17:2017, 2018), but plastic device components may receive doses as high as 70 kGy or more due to packaging and processing conditions. Included in each of the results plots below are bounding levels labeled with percent fraction of average unirradiated sample results to indicate the relative magnitude of variation in tested values following irradiation.

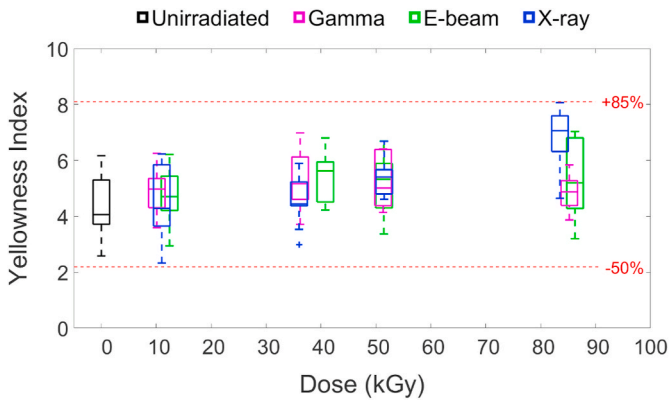

Fig. 8. Box plot representation of LDPE YI versus dose and modality.

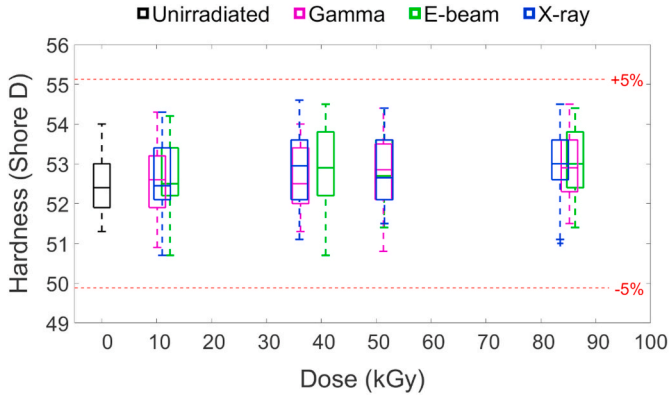

Fig. 9. Box plot representation of LDPE Shore D hardness versus dose and modality.

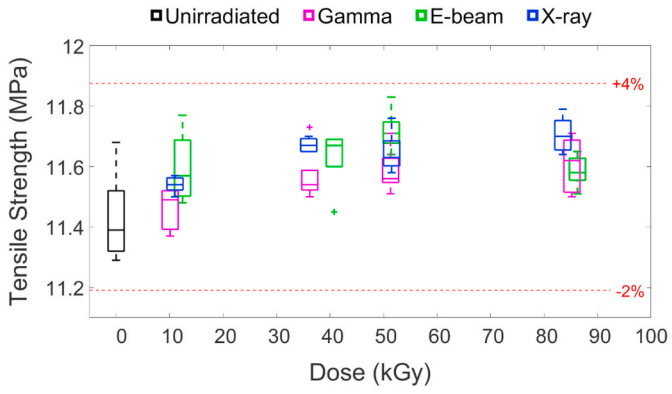

Fig. 10. Box plot representation of LDPE tensile strength versus dose and modality.

CIIR. The YI of CIIR, plotted in Fig. 3, was not found to be sensitive to either irradiation dose or modality over the ranges of doses explored. The Shore M hardness of CIIR, plotted in Fig. 4, decreased with dose level in a similar fashion for each of the modalities. Tensile strength (Fig. 5) and 100% secant modulus (Fig. 6) of CIIR also decreased with dose for all modalities, while elongation at break (Fig. 7) changed little

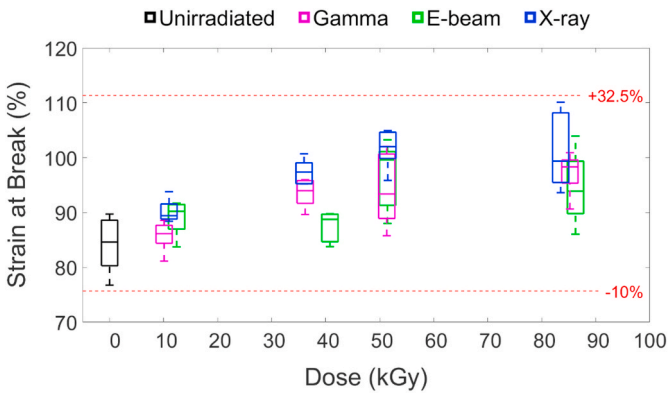

Fig. 11. Box plot representation of LDPE elongation at break versus dose and modality.

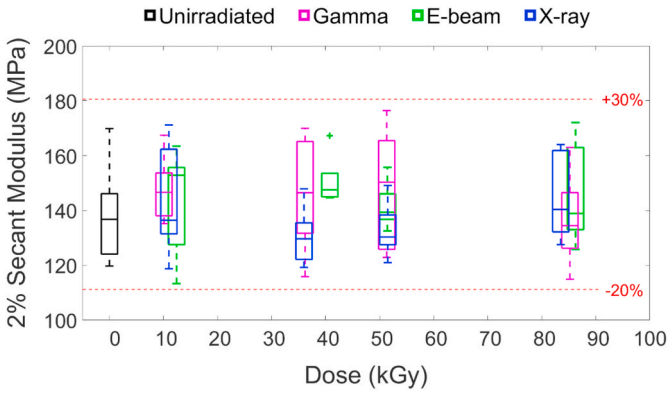

Fig. 12. Box plot representation of LDPE 2% secant modulus versus dose and modality.

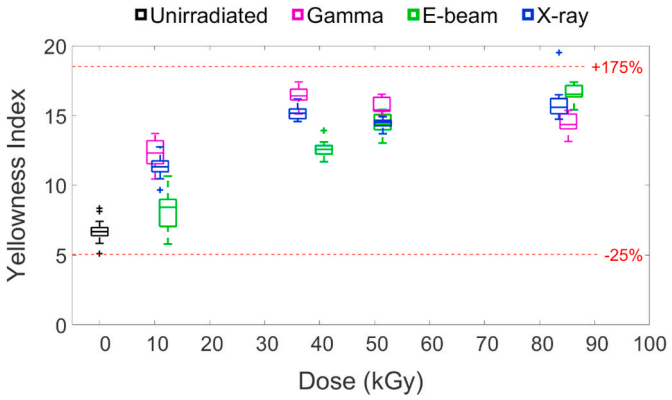

Fig. 13. Box plot representation of POE YI versus dose and modality.

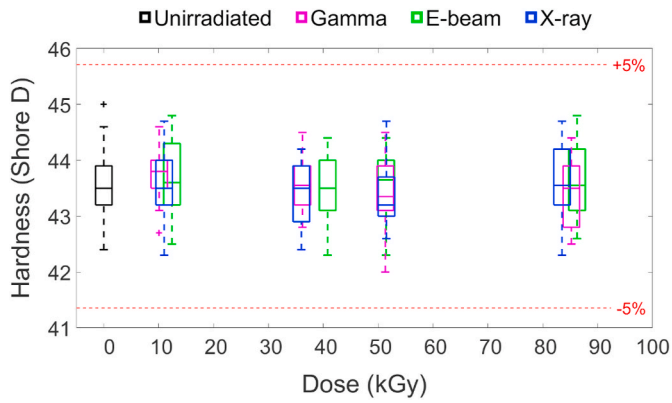

Fig. 14. Box plot representation of POE Shore D hardness versus dose and modality.

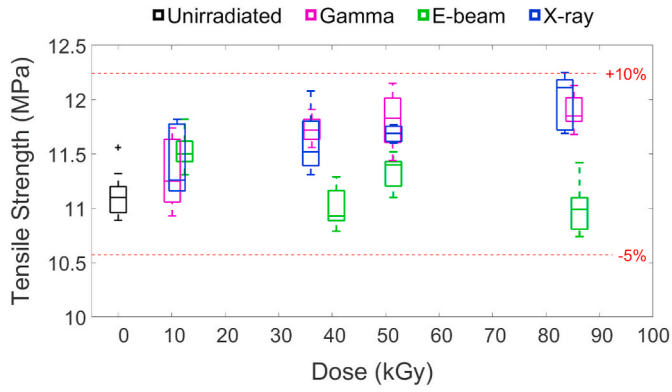

Fig. 15. Box plot representation of POE tensile strength versus dose and modality.

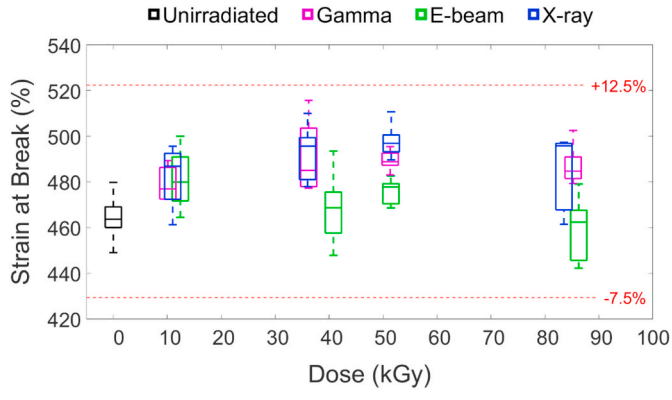

Fig. 16. Box plot representation of POE elongation at break versus dose and modality.

with dose. CIIR test results were found to be statistically equivalent for all modalities at the 10 kGy and 35 kGy dose levels. Statistical differences were detected between e-beam irradiated CIIR and gamma irradiated CIIR for 100% secant modulus at 50 kGy for TAMU results and tensile strength, elongation at break, and 100% secant modulus at 80 kGy for PNNL results. Statistical differences were detected between X-ray irradiated CIIR and gamma irradiated CIIR for 100% secant modulus at 50 kGy tensile strength at 80 kGy for PNNL results.

LDPE. Fig. 8 shows that the YI changes with dose of LDPE were negligible for all doses and modalities except for X-ray irradiation at the highest dose of 80 kGy. The variation in the Shore D hardness measurement itself was greater than the effect of dose or modality as seen in Fig. 9. Strength and elongation at break for LDPE, plotted in Figs. 10 and 11, respectively, increased with dose for all modalities, while 2% secant modulus, shown in Fig. 12, remained unchanged with dose. Statistical differences were detected between the effects on LDPE of e-beam and gamma radiation for elongation at break at 35 kGy and tensile strength at 50 kGy for TAMU results, and Shore D hardness at 80 kGy for PNNL results. Differences were detected between the effects of X-ray and gamma radiation on elongation at break of LDPE at 10 kGy and YI of LDPE at 80 kGy for PNNL results.

POE. The YI of irradiated POE increases with dose, as seen in Fig. 13.

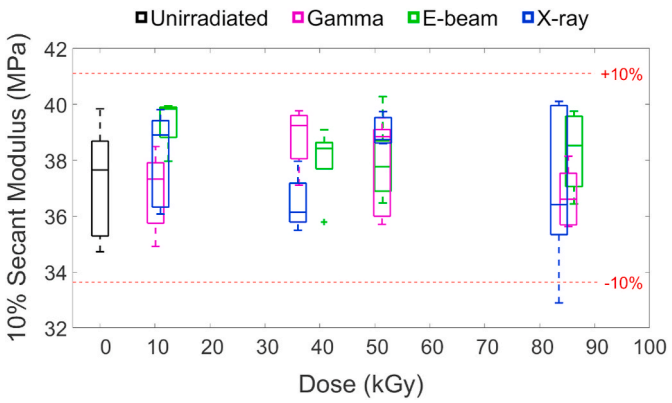

Fig. 17. Box plot representation of POE 10% secant modulus versus dose and modality.

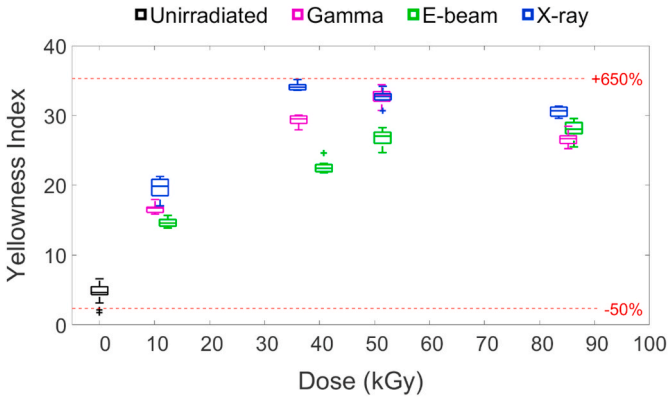

Fig. 18. Box plot representation of PPH YI versus dose and modality.

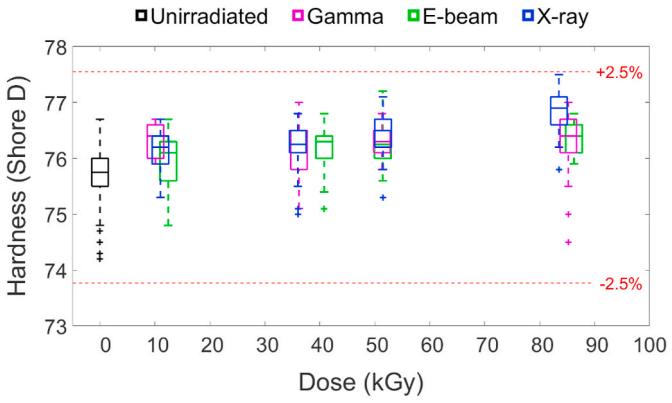

Fig. 19. Box plot representation of PPH Shore D hardness versus dose and modality.

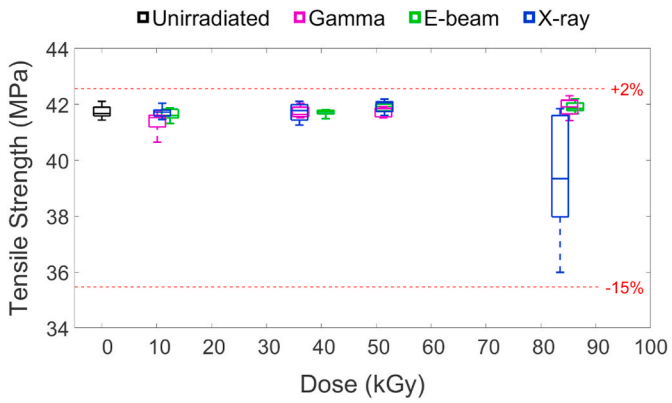

Fig. 20. Box plot representation of PPH tensile strength versus dose and modality.

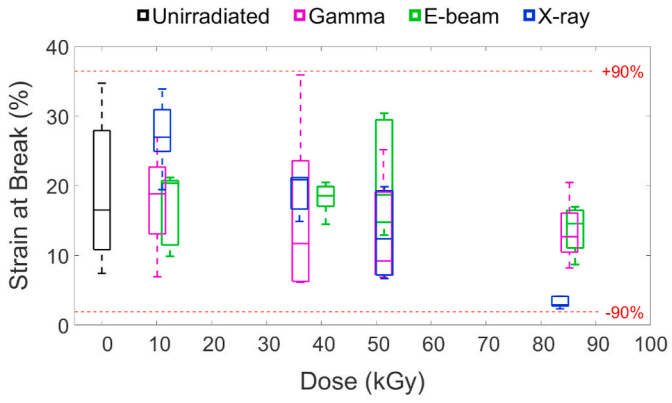

Fig. 21. Box plot representation of PPH elongation at break versus dose and modality.

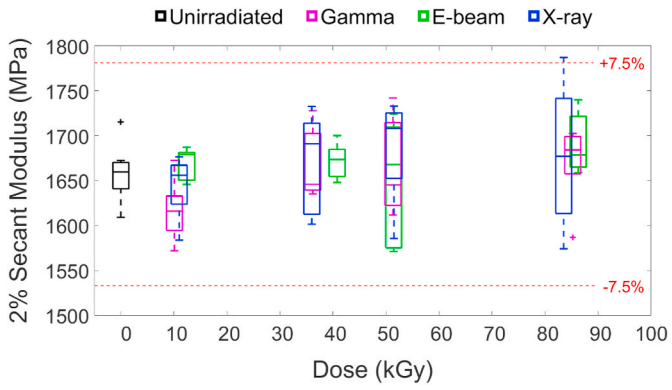

Fig. 22. Box plot representation of PPH 2% secant modulus versus dose and modality.

Statistical differences in YI were observed between gamma irradiated POE and the POE irradiated by the other modalities for nearly all doses investigated. YI values for gamma and X-ray irradiated samples were similar for all doses investigated. YI values for e-beam irradiated samples were lower than for samples irradiated using the other modalities at lower doses, but similar at doses above 50 kGy. Shore D hardness of POE in Fig. 14 shows no effective change with dose for any modality. Tensile strength of POE in Fig. 15 appears to increase with dose for gamma and X-ray irradiation but remain largely unchanged for e-beam irradiation. A similar trend is observed for the elongation at break of irradiated POE in Fig. 16, except that 80 kGy values for all three modalities appear not to follow the upward trend with dose of the values of lower doses. Fig. 17 indicates that the 10% secant modulus is not sensitive to either dose or modality, although statistical differences are detectable between the results of e-beam irradiation at 10 kGy and X-ray irradiation at 35 kGy versus gamma irradiation, respectively, for the TAMU results. Differences were detected between the effects of e-beam and gamma radiation on tensile strength of POE at 35, 50 and 80 kGy and on Shore D hardness at 25 kGy for PNNL results. Differences were noted between e-beam and gamma effects on elongation at break of POE at 50 and 80 kGy for TAMU results.

PPH. The YI of irradiated PPH appears to show an asymptotic

Table 4
Statistical analysis. Green signifies no significant statistical difference (NS), orange signifies statistical difference (S) detected, and no fill color signifies that the statistical difference check was inconclusive (I).

Equivalency to Gamma	10 kGy		35 kGy		50 kGy		80 kGy	
	E-beam	X-ray	E-beam	X-ray	E-beam	X-ray	E-beam	X-ray
CIIR								
Tensile Strength, TAMU	NS	NS	NS	NS	NS	NS	NS	NS
Tensile Strength, PNNL	NS	NS	NS	NS	NS	NS	S	S
Elongation at Break, TAMU	NS	NS	NS	NS	NS	NS	NS	NS
Elongation at Break, PNNL	NS	NS	NS	NS	NS	NS	S	NS
100% Secant Modulus, TAMU	NS	NS	NS	NS	S	NS	NS	NS
100% Secant Modulus, PNNL	NS	NS	NS	NS	NS	S	S	NS
Shore M Hardness, PNNL	NS	NS	NS	NS	NS	NS	NS	NS
Yellowness Index, TAMU	NS	NS	NS	NS	NS	NS	NS	NS
LDPE								
Tensile Strength, TAMU	NS	NS	NS	NS	S	NS	NS	NS
Tensile Strength, PNNL	NS	NS	NS	NS	NS	NS	NS	NS
Elongation at Break, TAMU	NS	S	S	NS	NS	NS	NS	NS
Elongation at Break, PNNL	NS	NS	NS	NS	NS	NS	I	NS
2% Secant Modulus, TAMU	NS	NS	NS	NS	NS	NS	NS	NS
2% Secant Modulus, PNNL	NS	NS	NS	NS	NS	NS	NS	NS
Shore D Hardness, TAMU	NS	NS	NS	NS	NS	NS	NS	NS
Shore D Hardness, PNNL	NS	NS	NS	NS	NS	NS	S	NS
Yellowness Index, TAMU	NS	NS	NS	NS	NS	NS	NS	S
POE								
Tensile Strength, TAMU	NS	NS	S	NS	S	NS	S	NS
Tensile Strength, PNNL	NS	NS	NS	NS	NS	NS	I	NS
Elongation at Break, TAMU	NS	NS	NS	NS	S	NS	S	NS
Elongation at Break, PNNL	NS	NS	NS	NS	NS	NS	NS	NS
10% Secant Modulus, TAMU	S	NS	NS	S	NS	NS	NS	NS
10% Secant Modulus, PNNL	NS	NS	NS	I	NS	NS	NS	NS
Shore D Hardness, TAMU	NS	NS	NS	NS	NS	NS	NS	NS
Shore D Hardness, PNNL	NS	NS	S	NS	NS	NS	NS	NS
Yellowness Index, TAMU	S	NS	S	S	S	S	S	S
PPH								
Tensile Strength, TAMU	NS	NS	NS	NS	NS	NS	NS	NS
Tensile Strength, PNNL	NS	NS	NS	NS	NS	NS	NS	NS
Elongation at Break, TAMU	NS	NS	NS	NS	NS	NS	NS	S
Elongation at Break, PNNL	NS	NS	NS	NS	NS	NS	NS	S
2% Secant Modulus, TAMU	S	NS	NS	NS	NS	NS	NS	NS
2% Secant Modulus, PNNL	NS	NS	NS	NS	NS	NS	NS	NS
Shore D Hardness, TAMU	S	NS	NS	NS	NS	NS	NS	S
Shore D Hardness, PNNL	NS	NS	NS	NS	NS	NS	NS	NS
Yellowness Index, TAMU	S	S	S	S	S	NS	NS	S
NS– Differences *Not Significant*, S–Differences *Significant*, I–Inconclusive								

increase with dose in Fig. 18 that begins to level off after 35 kGy. Significant differences between e-beam and X-ray radiation effects versus those of gamma radiation on YI of PPH were manifest at almost every dose, with e-beam radiation generally resulting in lesser changes to YI with dose than the other modalities. Shore D hardness values of PPH in Fig. 19 may exhibit a slight upward trend with dose but are largely within the sensitivity limits of the measurement. Statistical differences were detected between Shore D hardness values of PPH irradiated by e-beam at 10 kGy and PPH irradiated by X-ray at 80 kGy versus the corresponding gamma-irradiated PPH at those respective doses for TAMU results. Tensile strength of PPH in Fig. 20 appears to change very little with irradiation for all modalities except for X-ray irradiation at the targeted 80 kGy dose, in which a decrease in tensile strength with large scatter in the data was observed. This effect may have been related to the observation that most 80 kGy X-ray specimens broke in a brittle fashion prior to reaching peak stress at the material yield point. Changes in elongation at break values for irradiated PPH are largely within the scatter of the data for all doses and modalities in Fig. 21 except, again, for the highest dose X-ray irradiated samples. Statistical differences in elongation at break between X-ray and gamma irradiated PPH samples were identified for both TAMU and PNNL results. The 2% secant modulus of irradiated PPH did appear to trend upward slightly with dose for all modalities in Fig. 22, with a statistical difference from gamma irradiated PPH only detected for e-beam irradiated PPH at 10 kGy in TAMU results.

A summary of statistically significant differences between gamma irradiation effects and the effects of e-beam and X-ray irradiation with a 95% confidence level on measured polymer properties is provided in Table 4.

4. Conclusion

It is well known that ionizing radiation at high doses can induce significant chain scission and crosslinking in polymers. Chain scission can reduce tensile strength and elongation before break. Crosslinking can increase tensile strength but can also reduce elongation at break. Radiation-induced oxidation can discolor polymers at lower doses than required for significant changes in mechanical properties. Manufacturers must be aware of the impacts of sterilization radiation on the polymers in their devices due to the potential of sterilization dose levels to affect the molecular structures of polymers. Previous work has directly compared the effects of X-ray versus gamma irradiation on several medical device polymers including polyethylene, polypropylene, polystyrene, plasticized polyvinyl chloride, and acrylonitrile-butadiene-styrene copolymer at similar dose rates and at common doses of 30, 60 and 120 kGy (Croonenorghset al., 2007). In that research, the two modalities were found to have similar effects on tensile and impact strength, flexural modulus, and coloration of the polymers studied. A comparison of X-ray to e-beam radiation effects on polymers also found little difference between the two in terms of tensile strength and color change (Smith et al., 2005). In comparing the mechanical, thermal and color properties of polypropylene syringes processed at 30, 60, and 120 kGy using e-beam and gamma radiation, Fintzou and coworkers found that the effects of e-beam radiation were much lower than those of gamma radiation (Fintzou, 2007).

Most single-use medical devices contain at least one plastic component. New devices that require sterility and legacy devices that the manufacturer desires to switch to another sterilization method are required by the U.S. Food and Drug Administration to be tested to ensure device safety in terms of functionality, biocompatibility, and ability to sterilize. Guidance for such testing, provided in AAMI Technical Information Report (TIR) 17 "*Compatibility of Materials Subject to Sterilization*" (AAMI TIR17:2017, 2018), includes tests for plastic embrittlement and discoloration. In this work, the effects of e-beam and X-ray alternative sterilization modalities on four representative medical device polymers were directly compared to the effects of the standard cobalt-60 gamma modality to identify any differences. ASTM tensile, hardness and discoloration tests, as recommended in AAMI TIR17, were followed in the study. For some test categories and polymers, statistically significant differences in effects between gamma irradiated and e-beam or X-ray irradiated polymer were measured. The device manufacturer and notifying bodies determine whether the magnitude of these effect differences preclude the use of X-ray or e-beam for sterilization.

The hypothesis that e-beam and X-ray radiation modalities would produce no significant difference in polymer characteristics (coloration, hardness and tensile strength) as compared to the currently employed cobalt-60 based gamma irradiation was largely correct. Out of a total of 280 independent tests, only 13% of these tests (37 tests) showed statistically significant differences. A statistically significant difference in an irradiated plastic property between an alternative modality and gamma radiation may reflect either a more severe or a less severe effect and does not necessarily indicate that the irradiated plastic does not meet performance specifications for use. Out of these 37 tests that were significantly different, 14 of these tests were related to yellowness index. Differences were particularly notable in the effects of both e-beam and X-ray relative to gamma radiation of YI for POE and PPH. Discoloration will not affect the sterility of the device in question. However, visual appearance is important to the end-user. It must be noted that even though YI differences were detectable analytically, in the majority of cases these differences were not identifiable by the unaided eye. Moreover, color changes can be prevented by the addition of specific additives in polymers (Gugumus, 2002). Other than YI differences observed for POE and PPH, all the instances of statistical differences between measured properties of e-beam or X-ray irradiated plastics were observed at only a subset of the four doses explored for each material. Considering the whole dose ranges of the three modalities, it may be concluded from our observations that both e-beam and X-ray can effectively substitute for gamma as sterilization options.

The results of this work support e-beam and X-ray methods as viable alternatives to cobalt-60 gamma radiation sterilization for the more than 5.3 billion devices produced by BD each year represented by the four polymers investigated here. These data on CIIR, LDPE, POE, and PPH can encourage other medical device manufacturers to consider e-beam and X-ray as potential sterilization alternatives to gamma radiation for devices fabricated from similar polymers. The effects of modality and dose level on the functional, mechanical and visual properties of the two BD devices themselves are described in a previous manuscript (Fifield, 2020).

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

The National Center for Electron Beam Research (NCEBR) is a unit of Texas A&M AgriLife Research, a part of the Texas A&M University System. NCEBR is committed to expand the commercial applications of electron beam technology. To this end, NCEBR partners with private industry to employ electron beam processing for commercial purposes. NCEBR currently works with the food, food ingredients, spices, pet food, fresh produce and the biotechnology industries (https://ebeam-tamu.org/new-page-3).

Steri-Tek offers electron beam and X-ray irradiation sterilization services to the Medtech, Biotech and food/drug industries, academic institutions and technology businesses, for a variety of materials and combination devices including medical device, biologic, pharmaceutical, cross-linking/materials modification, and food/agricultural products (https://www.steri-tek.com/about-us/).

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.radphyschem.2021.109505.

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