Team Nablo – Industry Collaboration to Fill Education and Data Gaps Involving E-beam and X-ray Sterilization

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National Academies of Sciences, Engineering, Medicine

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Topics

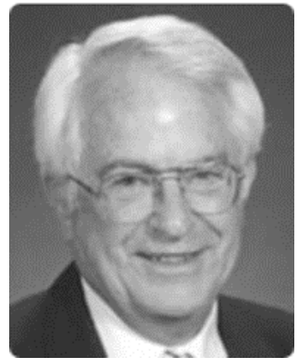
- National Nuclear Security Administration (NNSA) program and goals for Team Nablo (pronounced ‘nae-bloe’)
- Becton-Dickinson products phase
- Stryker Corporation products phase
- Sartorius products phase
- Becton-Dickinson/Aerial/IBA/PNNL dose rate study
- Roadmap for modality transition – AAMI TIR104 and webinar
- Online Library for Radiation Effects on Polymers
- Software Toolkit suite to determine best medical device design and packaging to accommodate E-beam and X-ray

NNSA Project and Goals

- A 2017 report by Fermilab, as well as a 2020 IAEA report, conclude that significant impediments remain for *medical device manufacturers* desiring to transition from cobalt-60 and ethylene-oxide sterilization modalities to electron-beam or X-ray; and that these impediments are mostly in the form of data and education gaps, not necessarily a lack in technology.
- The **Office of Radiological Security (ORS)** within the DOE's NNSA is charged to… "*reduce ... global reliance on high activity radioactive sources through … promotion of viable non-radioisotopic alternative technologies*."
- With the help of **Office of Defense Nuclear Nonproliferation R&D**, ORS began this project in late 2018.
- NNSA asked PNNL to build a team that included major players in the medical sterilization industry.
- The team was charged to focus on two of these main impediments identified by the Fermilab and IAEA reports
- Given that cobalt-60 (and ethylene-oxide) facilities are at capacity, and other market forces that are in play, this program is timely.

Team Nablo – Current Active Members

- Pacific Northwest National Laboratory
- Becton-Dickinson
- Stryker
- Sartorius
- Texas A&M University
  - National Center for E-beam Research
  - Mechanical Engineering Department
- Steri-Tek
- IBA
- Aerial CRT
- AAMI



Samuel V. Nablo
1931-2018

Project Goals

- **Identify polymers** with data gaps for radiation effects and of greatest industry impact if transitioned to E-beam or X-ray
- **Measure physical effects** materials exhibit when given sterilization-level radiation doses from E-beam or X-ray
- **Determine whether effects preclude** the use of E-beam or X-ray for associated medical products
- **Industry & public outreach** to identify & fill education and data gaps that impede transition to E-beam and X-ray sterilization

Becton Dickinson Product Testing Phase (Complete)

BD Product Selection

- #1 BD Vacutainer™ tube
  - Dominates blood collection market at ~5B units/year using multiple polymers.
- #2 BD “Push Button” blood collection set
  - Significant portion of market: ~260M units/year
  - Made using multiple polymers
- Currently sterilized using cobalt-60 gamma-rays

Vacutainer (VT) – Constituent Polymers

- 3 polymer/elastomers selected:
  - Polyethylene terephthalate (PET)
    - ASTM D638 Type 1, 3”x4” plaque
  - Low density polyethylene (LDPE)
    - ASTM D638 Type 1, 5
  - Chlorobutyl rubber (CIIR)
    - Mats → stamped ASTM D638 Type 4

Push Button (PB) – Constituent Polymers

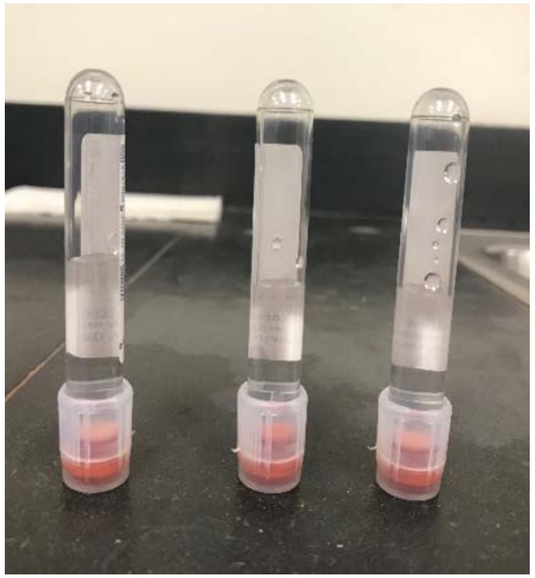
- 3 polymer/elastomers selected from device:
  - Polyvinyl chloride (PVC)
  - Polyolefin elastomer (POE)
    - ASTM D638 Type 1, 5 & 3”x4” plaque
  - Polypropylene homopolymer (PPH)
    - ASTM D638 Type 1, 5 & 3”x4” plaque

PPH

POE

VT Functional Testing*

- Liquid draw (mass of water in)
- Leak test (upon needle withdrawal)



Test results (pass-fail):

Target dose	Gamma	E-beam	X-ray
0 kGy	16/16		
10 kGy	6/6	6/6	6/6
35 kGy	6/6	6/6	6/6
50 kGy	6/6	6/6	6/6
80 kGy	6/6	6/6	6/6

* TAMU's functionality tests used, not BD's

PB Functional Testing*

- Pressure test (30 psig for 20 sec)
- Retraction test (needle retracts)

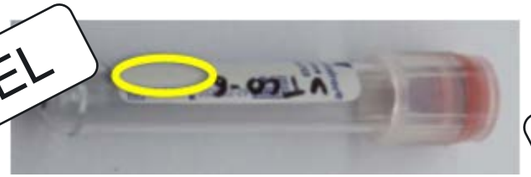
Test results (pass-fail):

Target dose	Gamma	E-beam	X-ray
0 kGy	16/16		
10 kGy	6/6	6/6	6/6
35 kGy	6/6	6/6	6/6
50 kGy	6/6	6/6	6/6
80 kGy	6/6	6/6	6/6

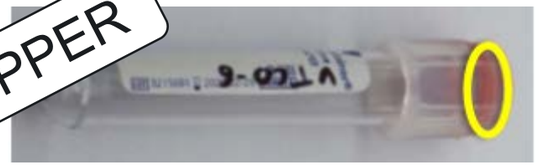
* TAMU's functionality tests used, not BD's

VT Color Change via Yellowness Index

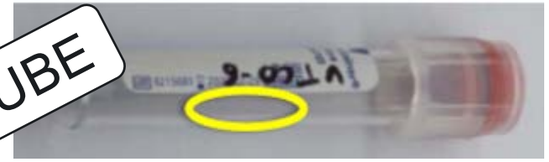
LABEL



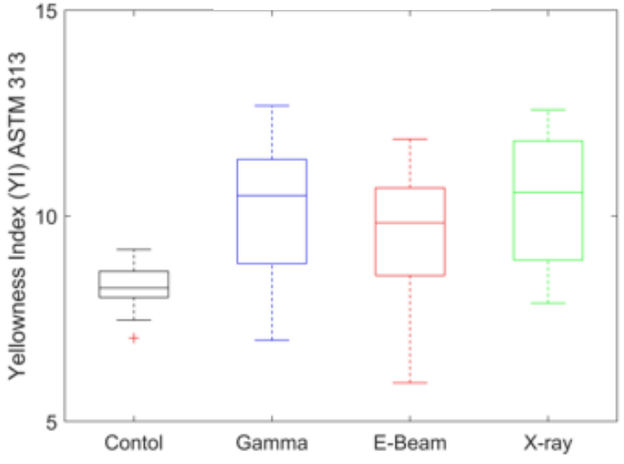
STOPPER

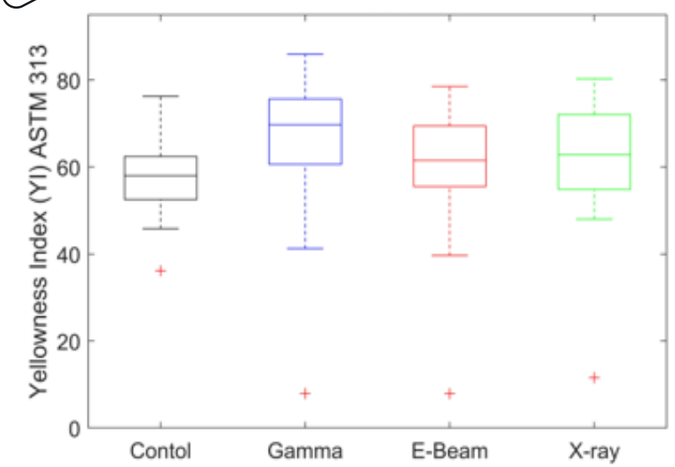


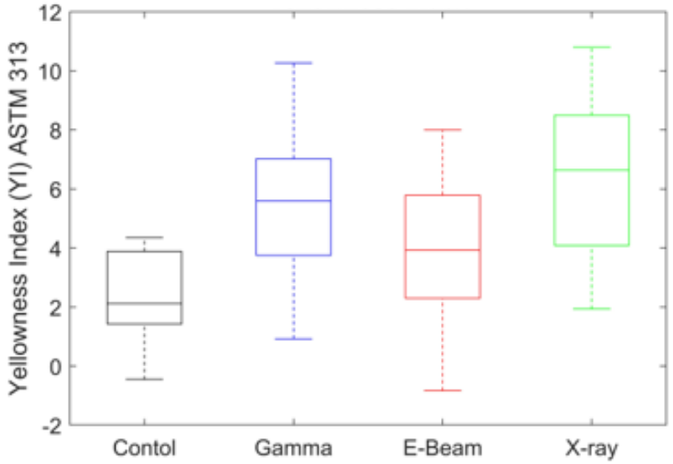
TUBE



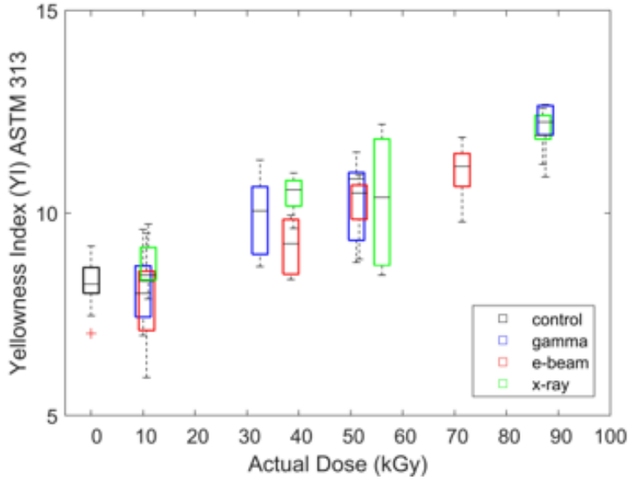
vs. MODALITY

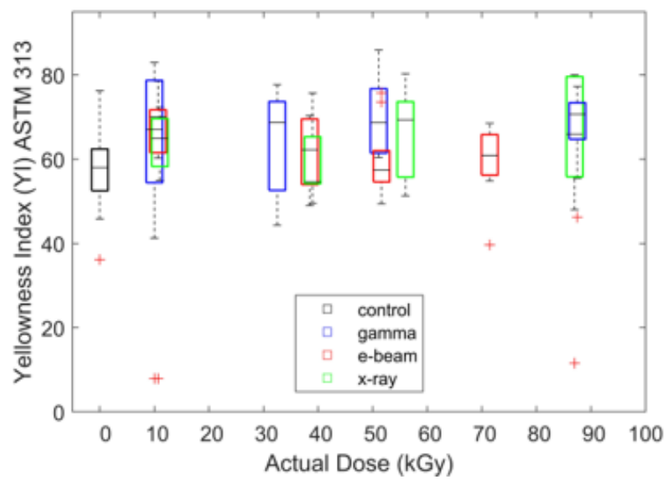


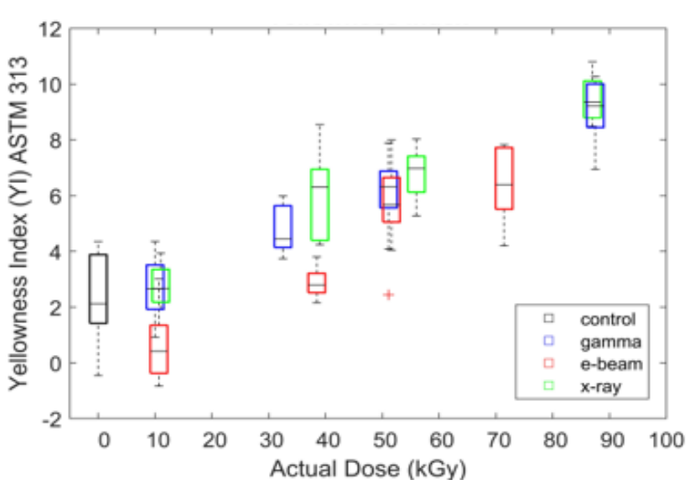




vs. DOSE



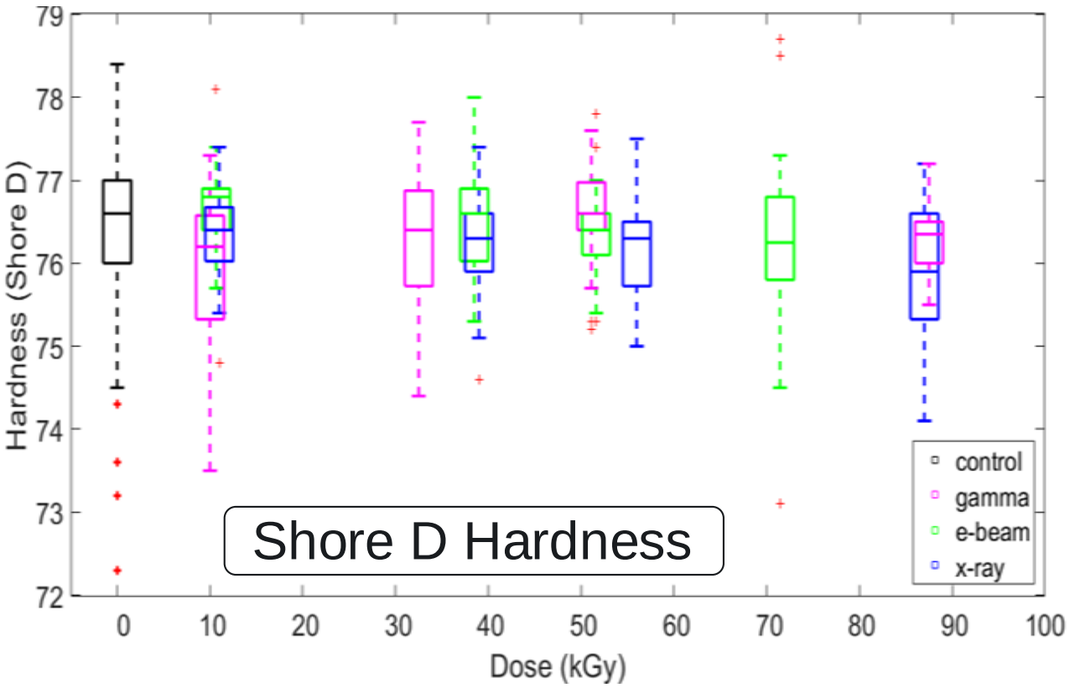


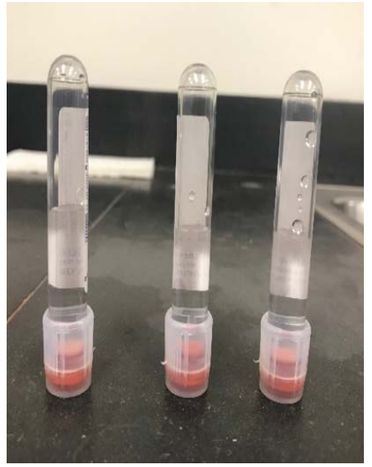


ASTM E313

VT Polymer Test Results – PET

- Tensile
- Hardness





Summary of BD Test Results

- **Six constituent materials** from 2 products, irradiated at 4 doses relevant to sterilization using Gamma, E-beam and X-ray
- **Products** were tested for function and color change
- **Polymer constituents** were tested for color, tensile, and hardness
- **Dose-dependent effects** were observed as expected, especially for color change
- **Modality-dependent effects** were observed, but were few and small
- Statistical differences were clear in a few cases:
  - Improved functional performance of the Vacutainer Tube (for X-ray)
  - Yellowing of PET and POE (all modalities).
  - Tensile performance of POE was statistically different for E-beam compared to Gamma.

Stryker Corporation Product Testing Phase

(Will complete by January)

Stryker Product Selection

- #1 Stryker *Interpulse*™ lavage system:
  - Disposable wound/cavity flushing device.
- #2 Stryker *MixVac-III*™ bone cement mixer:
  - Disposable cement mixer device.
- #3 Stryker *ACM Mixer*™ bone cement mixer and applicator system:
  - Disposable cement mixer device.
- Represents 11 common polymers. Currently sterilized using cobalt-60 gamma-rays.

Individual Stryker Product Parts Tested

Black O Ring

Black Runner

Mixing Paddle

Mixing Shaft

Coloration of Stryker's *MixVac-III™*

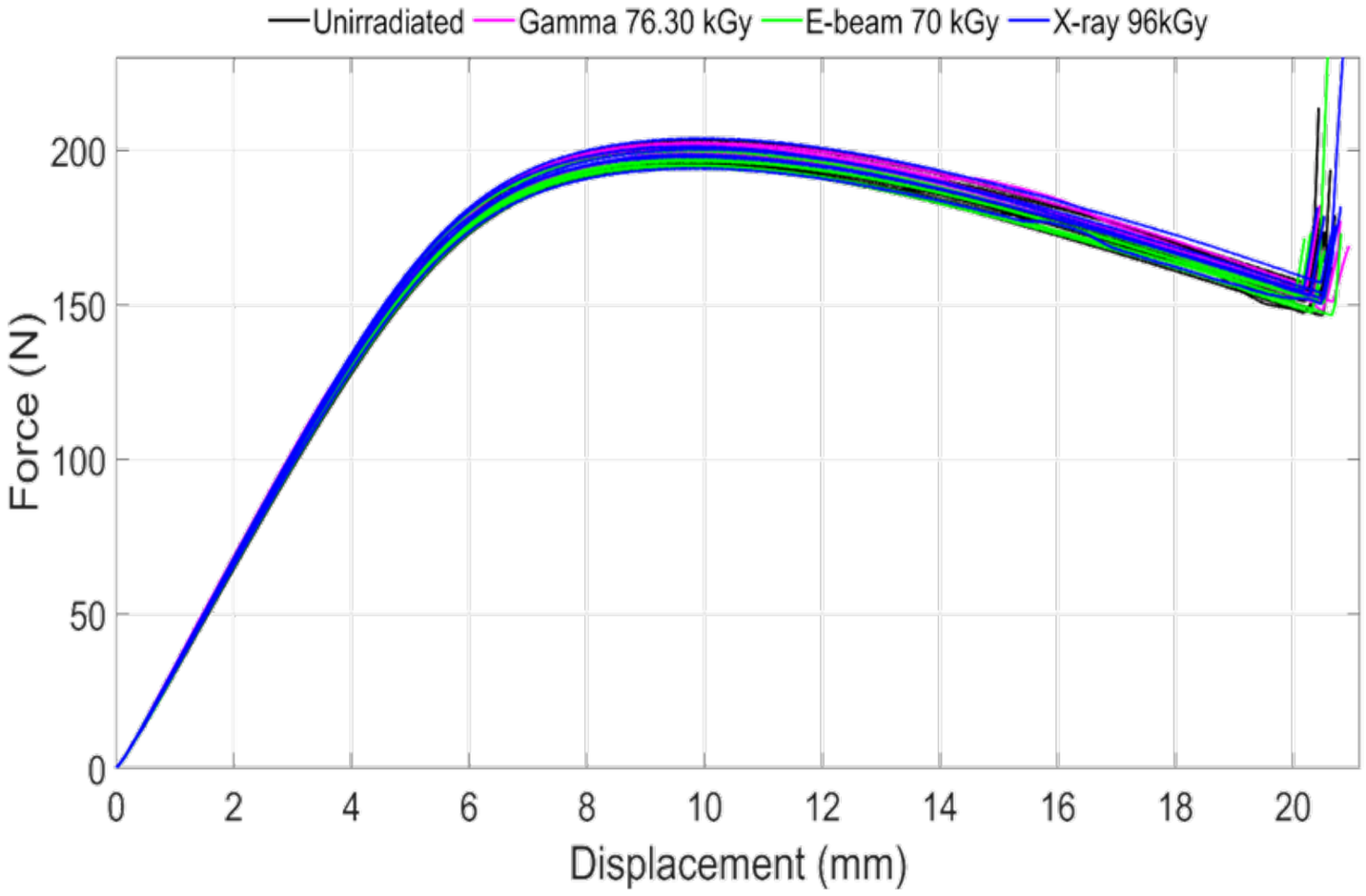
Control, 0 kGy

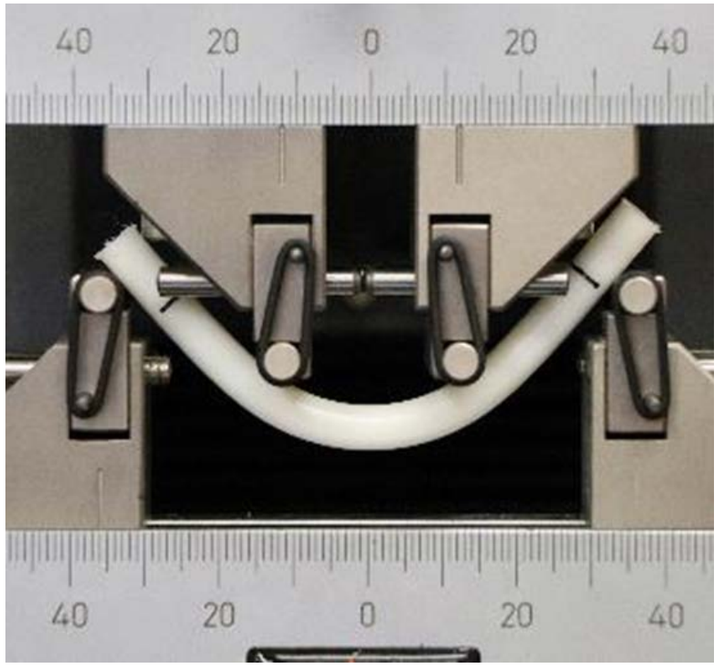
E-beam, 89 kGy tubing

X-ray, 89 kGy Ave

Gamma, 82 kGy Ave

Bending Test of Mixing Shaft – PBT





- Exact e-beam dose needs to be verified

Stryker Products – Preliminary Results

- In terms of **aesthetic properties/color,** for most materials there was no-modality dependence. For the PC copolymer, xray was most yellowing; for the polyvinyl chloride parts, ebeam was most yellowing.
- In terms of **mechanical property effects,** for 7/8 of the Stryker materials tested thus far (ABS, HIPS, butyrate, PBT, glass-filled PBT, PVC, silicon, and Buna-N), there was no measurable differences among the 3 irradiation modalities.
  - The only potential exception is that the strength slightly increased in highly irradiated X-ray samples of ABS, relative to other modalities.
- In terms of a **surface or handling effects**, one can observe some "stickiness" to the touch in the highly-irradiated X-ray specimens of ABS. Perhaps due to the significantly longer durations within the oxidative irradiation environment.

Sartorius
Product Testing Phase
(Began August 2020)

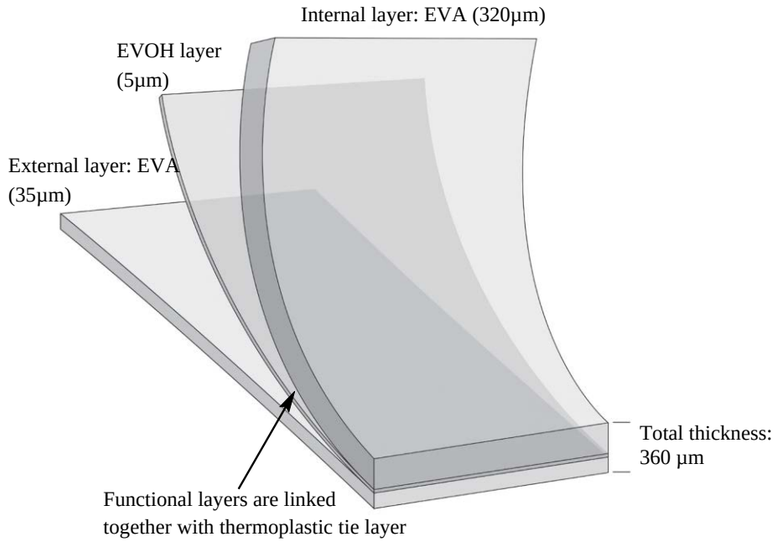
Sartorius Product Selection – S71 Film

Buffer and Drug Substance Storage Bags

Flexboy Bags for
fluid handling and storage

Celsius Bags for
freeze & thaw applications

S71 film structure



Test Plan – Sartorius Products

- The following test materials and irradiation conditions are planned for the Sartorius study:
  - S71 film, consisting of layers of EVA/EVOH/EVA
  - Individual samples are approximately 3 by 30 cm, with a thickness of 0.36 mm.
  - 3 irradiation modalities (cobalt-60 gamma-ray, e-beam and X-Ray)
  - 0, 30, 45, and 60 kGy dose levels for each irradiation modality (~60 samples each)
  - Test categories: Tensile (modulus, strength, elongation at break), Permeation, DSC, DMA, FTIR, Color

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Dose Rate Effects Study
BD/IBA/Aerial/PNNL

(Began September 2020)

Dose Rate Effects Study – BD Products

Dose Rate Effects Study – BD Products

- The following test materials and irradiation conditions are planned for the study:
  - 4 materials (LPDE, PPH, CIIR and POE)
  - 2 irradiation modalities (e-beam and X-Ray)
  - 3 dose rates for each irradiation modality
    - (e.g. 0.12, 6, 12 kGy/s for e-beam), and
    - (e.g. 0.003, 0.12, ≥ 0.23 kGy/s for X-ray)
  - 3 dose levels (in range of 15-85 kGy)
  - 3 irradiation temperatures

Summary of Industry/Public Outreach

- Nine conference presentations
- Two articles in *Radiation Physics & Chemistry* journal
- Engagement with relevant AAMI task groups
  - Includes collaboration with Radiation Sterilization working group on development of a roadmap for device manufacturers in TIR104.
  - Planning TIR104 webinar for early 2021
- Engagement with ASTM subcommittees involving polymer testing – presented data, and helping update standards
- Developing online Library for Radiation Effects on Polymers
- Proposed teaming with Aix-Marseille University in southern France to educate young professionals on polymer effects and benefits of e-beam and X-ray sterilization.

The Tony Faucette Library for Radiation Effects on Polymers – Demo

DATAHUB

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PROJECT

Polymer Effects

Datasets

Tensile Testing measurements for LDPE dog bone specimens

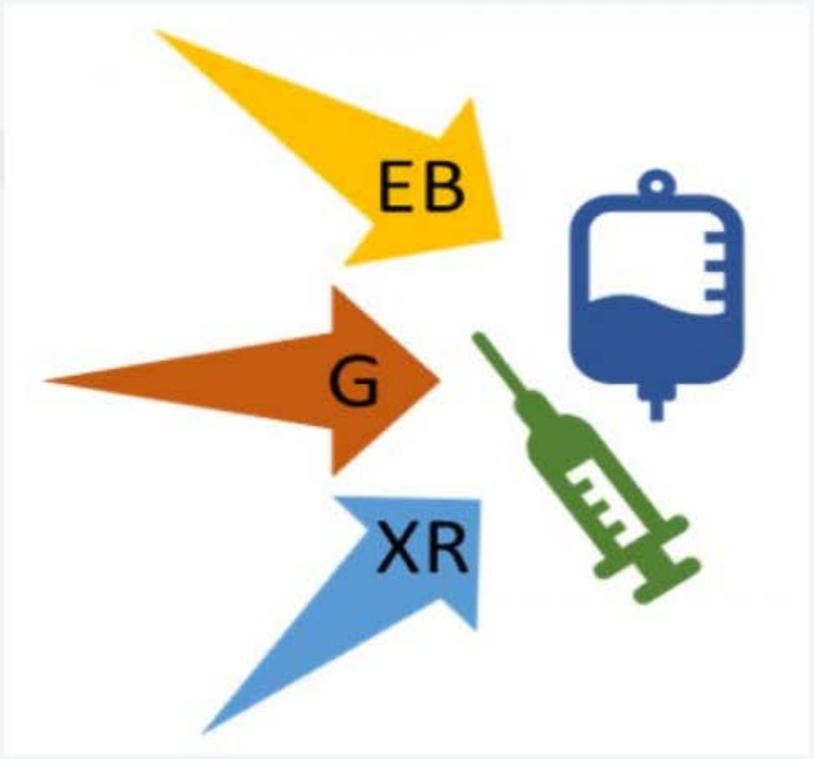
People (4)

Dr. Thomas Kroc

Dr. Thomas Kroc is an Applications physicist for Technology Development with the Illinois Accelerator Research Center

Suresh Pillai

Professor Suresh D. Pillai is the Director of the National Center for Electron Beam Research (NCEBR). He brings together



Thank you

Dedicated to:

Tony G. Faucette
1971 - 2019