PNNL-SA-147382

Pacific Northwest
NATIONAL LABORATORY
Proudly Operated by Battelle Since 1965

Transitioning from Cobalt-60 to E-beam or X-ray for Sterilization – a Model for Collaboration

Presented at Fermilab on September 18, 2019

[1]Mark Murphy, [1]Leo Fifield, [2]Tony Faucette, [2]James McCoy, [3]Rod Parker, [4]Suresh Pillai, [4]Matt Pharr, [4]David Staack, [5]Larry Nichols,[6]Emily Craven,[7]Christophe Malice, [7]Jeremy Brison, [8]John Logar, and [9]Kevin O'Hara

[1]Pacific Northwest National Laboratory, Richland, WA, USA
[2]Becton-Dickinson Corp., Franklin Lakes, NJ, USA
[3]Stryker Corp., Kalamazoo, MI, USA
[4]Texas A&M University, College Station, TX, USA
[5]Steri-Tek Corp., Fremont, CA, USA
[6]Mevex Corp., Stittsville, Ontario, CANADA
[7]IBA Corp., Louvain-La-Neuve, Belgium
[8]Johnson & Johnson, Raritan, NJ, USA
[9]Sterigenics Corp., Stittsville, Ontario, CANADA

U.S. DEPARTMENT OF ENERGY

Topics to Discuss

- **Drivers** pushing medical device manufacturers to transition from ethylene oxide (EO) and cobalt-60
- **Impediments/challenges** to this transition
- **NNSA mission and Team Nablo** (NAY-blo)
- **Project Goals**
- **Medical products selected** for testing
- **Functionality tests** of actual products
- AAMI/ASTM suite of **Mechanical tests** using associated polymer samples
- **Test Results**
- **Industry/Public Outreach**

Drivers for Transitioning from Cobalt-60

- **Regulatory** (transportation, use and disposal)
- **Supply and Demand** for the isotope
- **Logistics** in irradiation and manufacture➔end use pathway
- **Growth Potential** of alternative technologies
- Resulting **Political Pressures** that are now influencing risk assessments (Gamma-ray isotopes, ethylene oxide)

Impediments/Challenges in Transitioning to E-beam or X-ray

The 89% dominance of cobalt-60 over accelerator technologies reflects E-beam and X-ray challenges, namely:

- **Financial Obstacles**
- **Institutional Inertia**
- **Data/Knowledge Gaps**
- **Education Gaps**

NNSA Project

- **The Office of Radiological Security (ORS)** within the U.S. DOE's National Nuclear Security Administration (NNSA) is charged to…"*work with government, law enforcement, and businesses across the globe to protect radioactive sources used for medical, research, and commercial purposes; remove and dispose of disused radioactive sources; and reduce the global reliance on high activity radioactive sources through the promotion of viable non-radioisotopic alternative technologies.*"
- **The NNSA/ORS, along with the Office of Defense Nuclear Nonproliferation R&D**, has been working with government and private entities that utilize gamma-ray irradiators in areas that include *blood irradiation*, *radiotherapy*, *biology research*, *well logging*, and *radiation processing* to consider alternative technologies that do not depend upon radioactive materials.
- **The NNSA proposal solicited DOE laboratories** to build a team that included major players in the medical sterilization industry (medical device manufacturers, sterilization facilities, accelerator manufacturers, polymer testing labs).

Team Nablo Members

Pacific Northwest NATIONAL LABORATORY
Proudly Operated by Battelle Since 1965

- PNNL
- Becton-Dickinson
- Stryker
- Texas A&M University National Center for E-beam Research
- Texas A&M University Mechanical Engineering Department
- Steri-Tek
- Johnson and Johnson
- Sterigenics
- Mevex
- IBA

Project Goals

- **Identify specific polymers/elastomers** used in medical products that present the greatest data gaps for radiation effects, and would be of greatest industry impact if transitioned to e-beam or X-ray
- **Measure any physical effects** that these materials exhibit when they are given sterilization-level radiation doses from e-beam or X-ray
- Determine **whether these effects would preclude the use of E-beam or X-ray** for associated medical products
- **Execute an industry and public outreach** component that will identify and fill knowledge and education gaps that impede the transition to E-beam and X-ray sterilization
- **Encourage increased use of E-beam and X-ray** for sterilization of single-use medical products

Five Selected Medical Products

- **#1**: Becton-Dickinson *Vacutainer*™ tube.
  - Ultrahigh production volumes for the blood collection market at >5B products/year.
- **#2**: Becton-Dickinson *Vacutainer*™ "Push Button" blood collection set.
  - Significant production volume for the blood collection market at ~260M products/year using multiple polymer families.
- These BD products involve over 6 separate polymers.
- All test measurements recently completed for these BD products.

Five Selected Medical Products

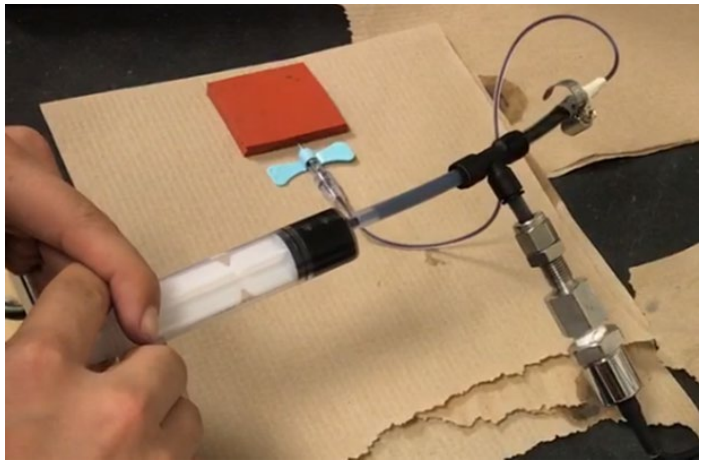
Pacific Northwest NATIONAL LABORATORY
Proudly Operated by Battelle Since 1965

- **#3** Stryker *Interpulse™ lavage system:*
  - Disposable wound/cavity flushing device.
- **#4** Stryker *MixVac-III™ bone cement mixer:*
  - Disposable cement mixer device.
- **#5** Stryker *ACM Mixer™ bone cement mixer and applicator system:*
  - Disposable cement mixer device
- Stryker products represent 11 common polymers.
- Stryker product Functionality and Coloration testing planned for October-December
- All 5 products currently sterilized using cobalt-60

Functionality and Mechanical Testing of Products and Associated Polymer Samples

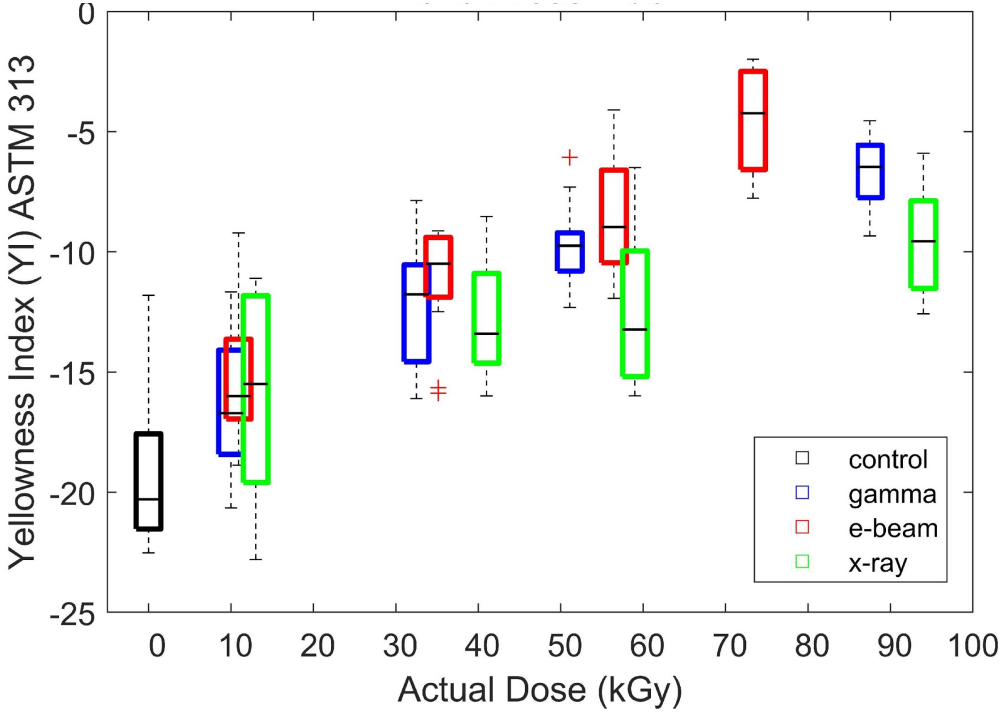
The following embrittlement and discoloration tests are considered for the irradiated samples, as per AAMI TR17 and associated ASTM standards:

- Functional and Coloration Testing of Products Measures
  - Air seal in tubes.
  - Flexibility/resistance to breakage
  - Yellowness index, Optical spectrometry
- Mechanical and Coloration Testing of Polymer Samples Measures
  - Tensile (Modulus of elasticity, Tensile strength, Ultimate elongation)
  - Flexural, Hardness
  - Yellowness index, Optical spectrometry



Data Results – BD Product Coloration

- The data indicate that Yellowness Index changed as much as 20 units for some polymers for the 0-90 kGy dose spread in the study; however, there was little to no discernible trend in the yellowness index between Cobalt-60, E-beam and X-ray samples.

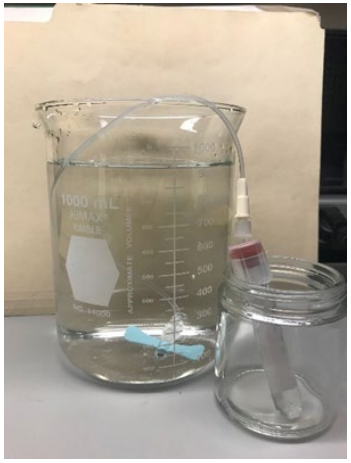


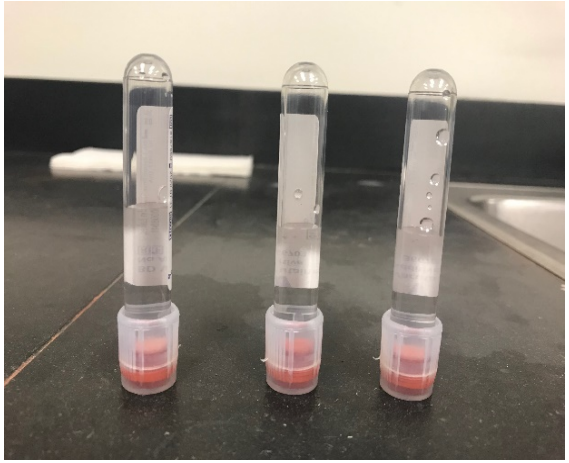
Yellowness Index vs. dose for *Push Button tubing* for all 3 irradiation modalities.

Data Results – BD Product Functionality

Pacific Northwest NATIONAL LABORATORY
Proudly Operated by Battelle Since 1965

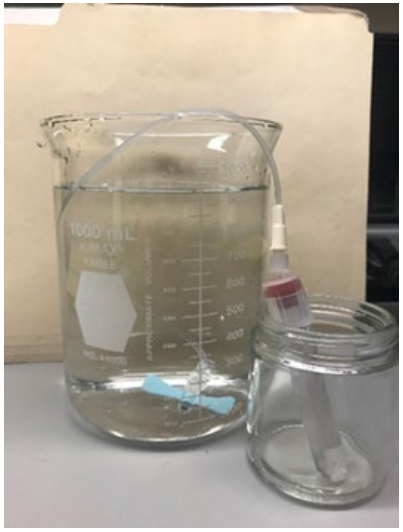
Functional Test	Control	gamma				e-Beam				X-ray			
Prescribed Dose (kGy)		10	35	50	80	10	35	50	80	10	35	50	80
F1: Vacutainer Liquid Draw	16/16 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓
F2: Vacutainer Liquid Leak	16/16 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓
F3: Push Button Pressure Test	16/16 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓
F4: Push Button Retraction Test	16/16 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓	6/6 ✓

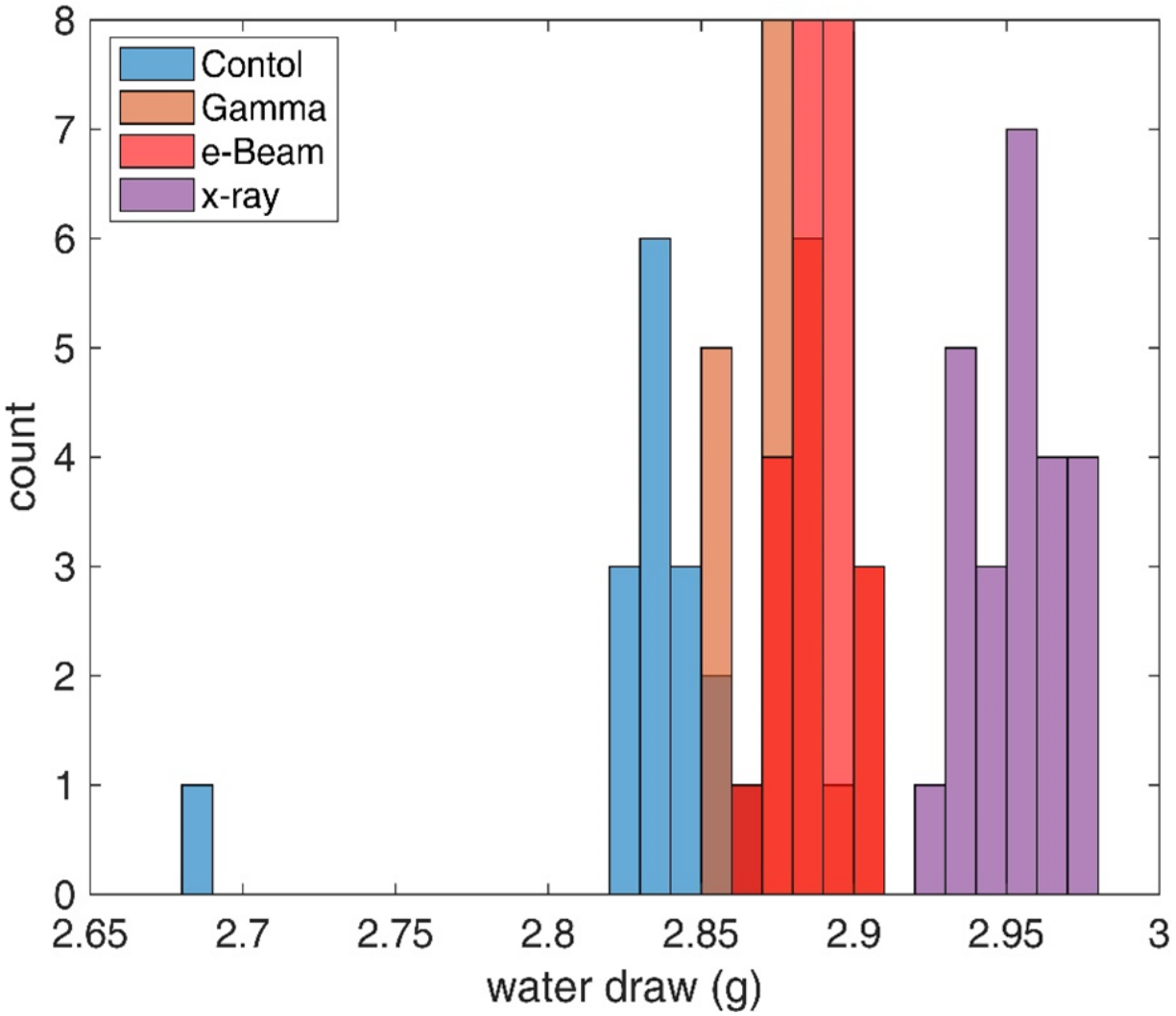




Data Results – Liquid Draw Leakage Test

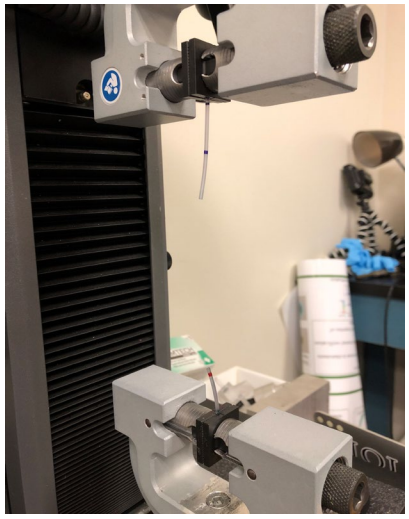
- Liquid Draw Leakage test for the PET-based BD *Vacutainer™ Tube* shows slight improvement after irradiation, and a slight dependence on irradiation modality.

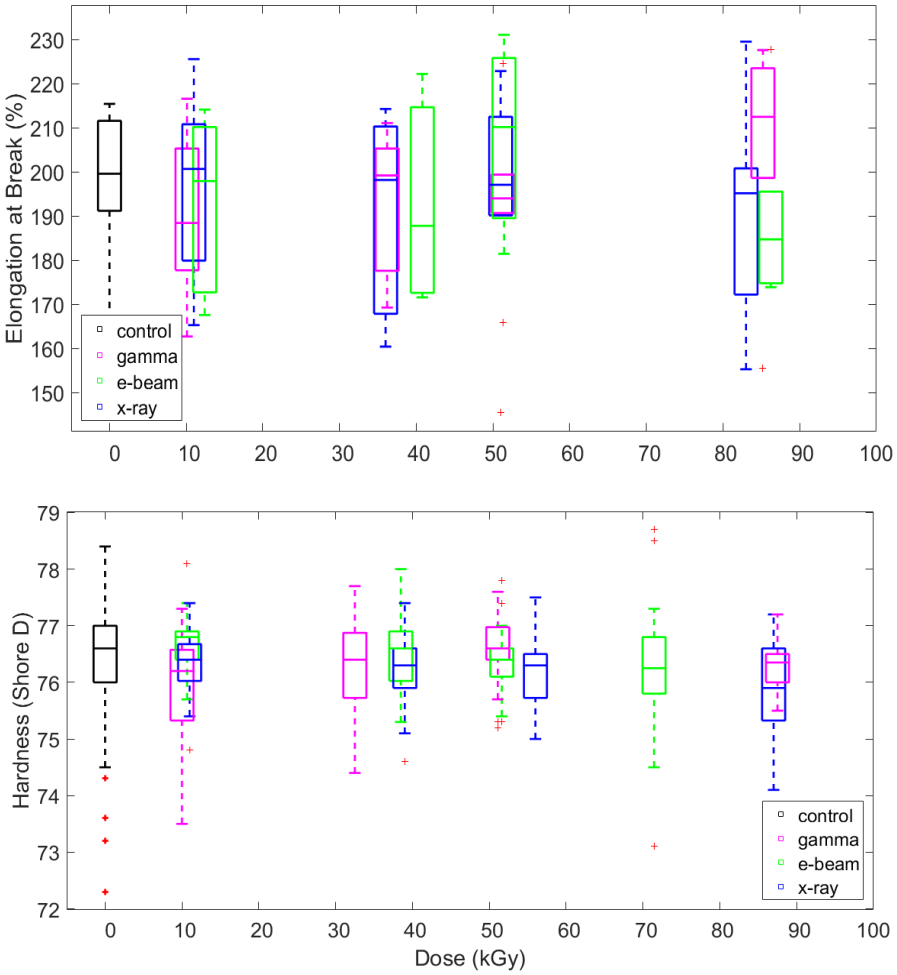




Data Results – BD Elongation & Hardness

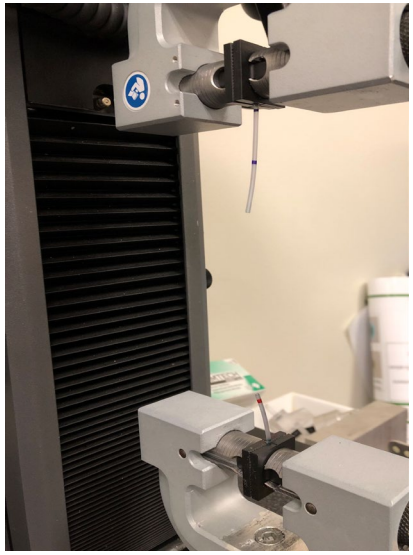
- Both *Elongation at break* and *hardness* results for polyvinyl chloride (PVC) tubing from the BD *Vacutainer™ Push Button* show little discernable variation, either over the range of doses used or over the 3 irradiation modalities.

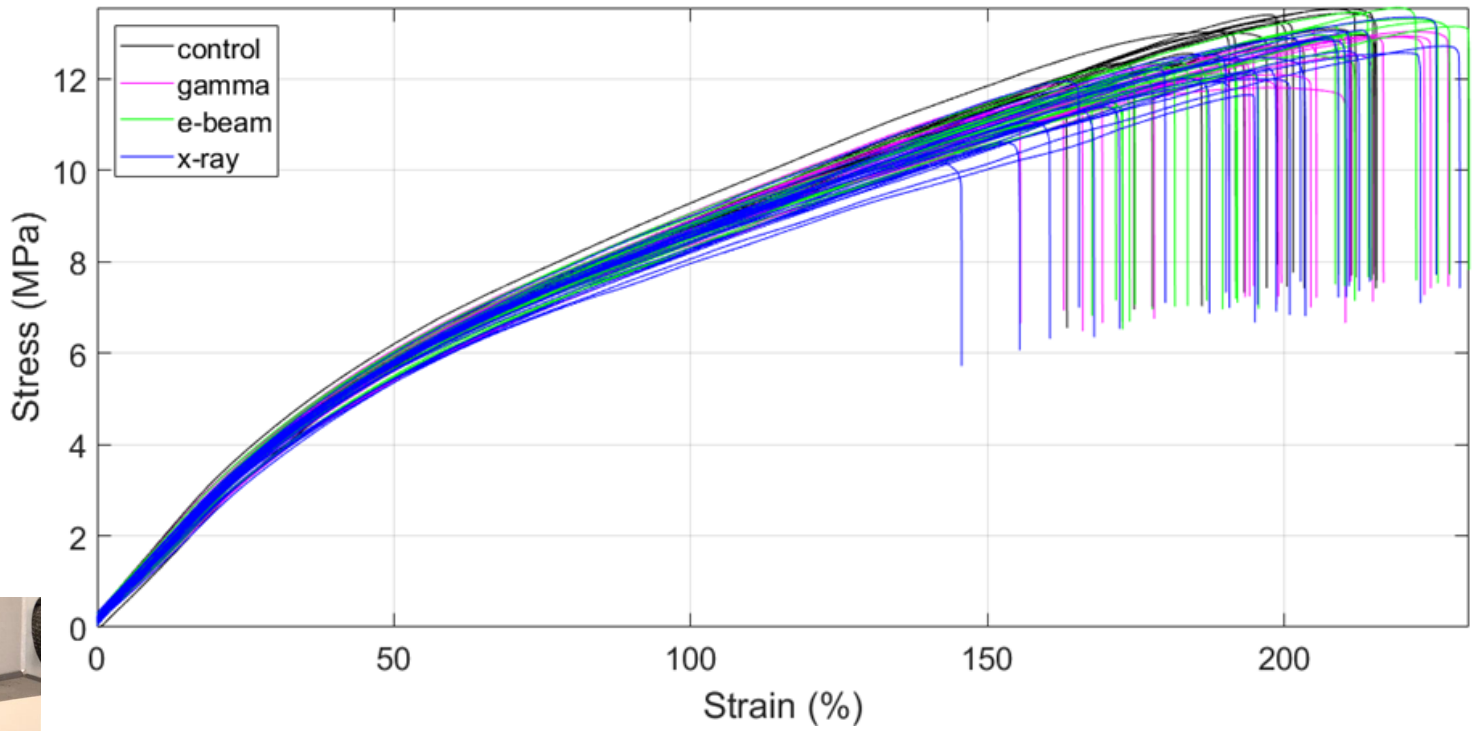




Tensile Elongation at Break and Shore M hardness of BD *Vacutainer™ Push Button* PVC tubing vs. dose for all 3 irradiation modalities.

Data Results – BD Sample Elongation





- Tensile elongation at break results for polyvinyl chloride (PVC) tubing from the BD *Vacutainer™ Push Button* show little discernable variation, either over the range of doses used or over the 3 irradiation modalities.

Industry and Public Outreach

- **Presentations** at industry conferences (IMRP, Kilmer, Fermilab, Q1 Productions, American Nuclear Society)
- **White Papers** led by Team Nablo members, and to be communicated via industry Trade Magazines, etc.
- **Engaging FDA/CDRH** office for proposed development of a "Guide" for medical product manufacturers who are considering transitioning to E-beam or X-ray
- **Engaging relevant AAMI and ASTM subcommittees** to ensure conformance to standards, as well as assistance with updating standards
- **Major peer-reviewed journal** targeted for publication of results
- Create **publicly-available website data repository** to begin building sets of test results/data

Lessons Learned/Conclusions

- We are confident the **challenges identified can be overcome,** and that this **collaboration team can be utilized** to support additional progress.
- Team members are working with AAMI and ASTM to **update important polymer testing standards.**
- Team members expect to work with FDA/CDRH **to develop a "guide" for medical device manufacturers** considering transition.
- Knowledge gained can be used **to refine future research projects**.
- The data results are being used for scientific comparison of effects between irradiation modalities, but are **not part of the official FDA approval process at this time**.
- The data results presented indicate that, for the associated BD medical products, **transitioning from cobalt-60 to E-beam or X-ray for sterilization may be a future option for the manufacturer.**
- **The medical sterilization industry can work successfully with academia and government** to explore accelerator-based solutions and advance public health services.

Questions?

Samuel V. Nablo

Scientist, Inventor, Entrepreneur, Friend

1931-2018