The Choice of Sterilization Modality

Technical & Normative Aspects

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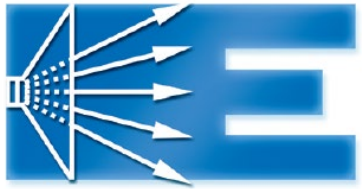
IONIZING RADIATION FOR MEDICAL DEVICE STERILIZATION

Three Technologies – Two Goals:

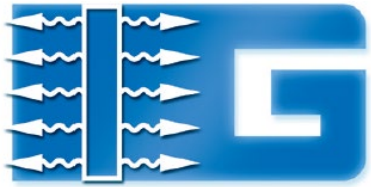
- ❑ Eliminate Biological Pathogens
- ❑ Keep Medical Device Functional

MEDI SCAN

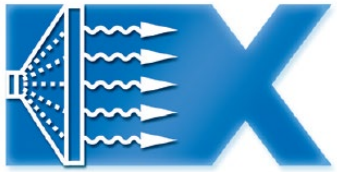
IONIZING RADIATION FOR MEDICAL DEVICE STERILIZATION



FAST & EFFICIENT ≈ 10%



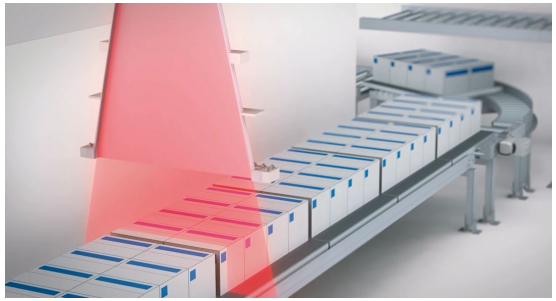
RELIABLE & PROVEN ≈ 90%

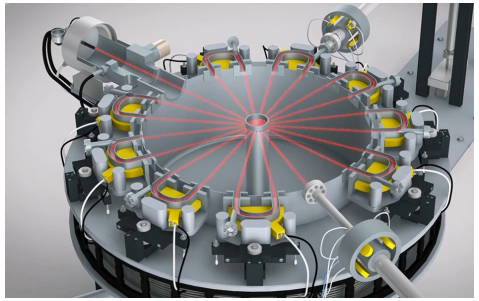


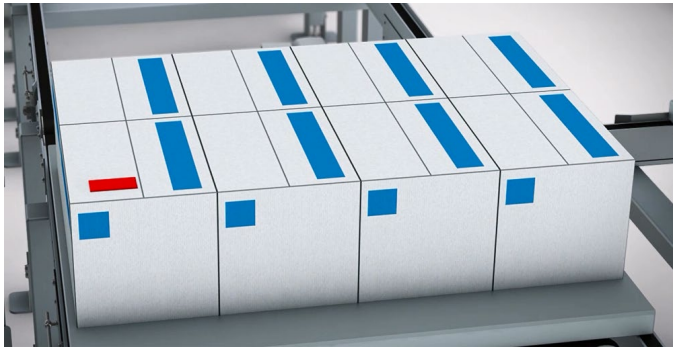
SMART & INNOVATIVE <1%

MEDI SCAN

FAST & EFFICIENT





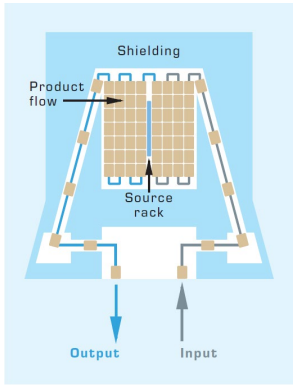


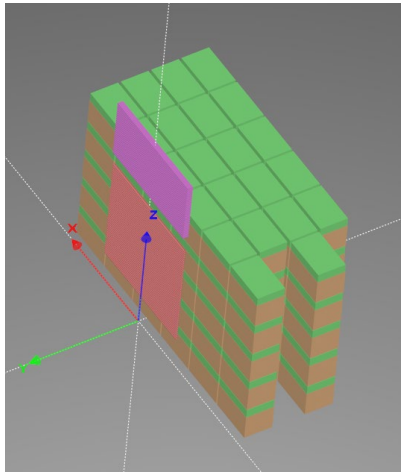
Scalable Power: 20 - 200 kW

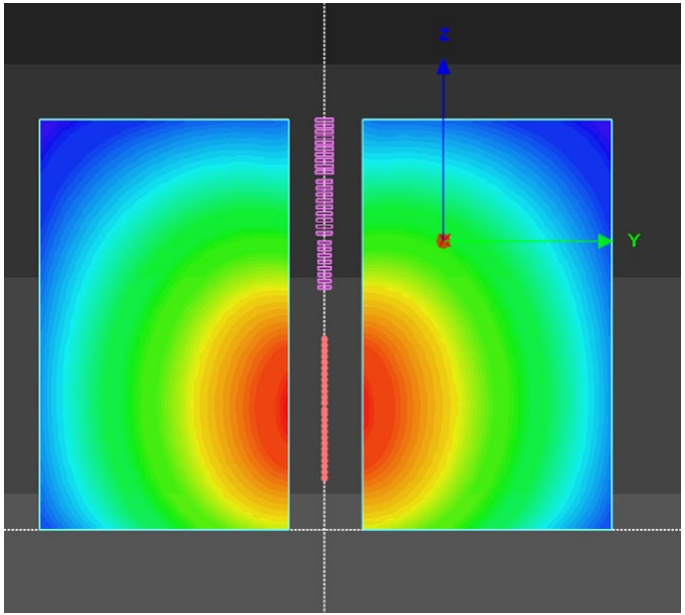
High Throughput: 1 Truckload =2h

Limited Penetration

RELIABLE & PROVEN



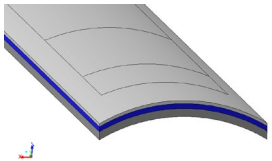


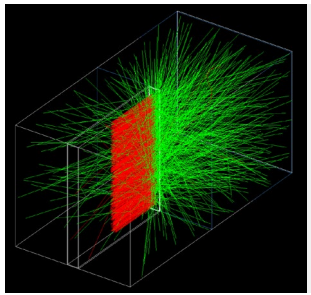


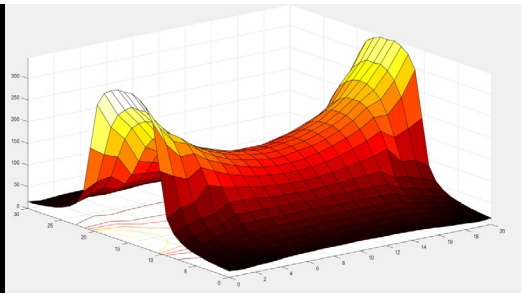
Pallet/Tote Treatment

Co-Supply/Reload “No Turn Off“

SMART & INNOVATIVE







“Turn Off“ Pallet/Tote/Box Treatment

“Costly“ Photon Generation – Lost Heat Recovery

ISO 11137-Standard Family

1 Requirements

2 Dose Setting

3 Process Setting

4 Process Control

Process Definition:

- **Sterilization Modality**
- D_{ster} Sterilization Dose
- $D_{max,acc}$ Maximum acceptible dose

Due 2020 ?

Requirements on Radiation Source – Sterilizing Agent

Electron beam /X-ray: Electron Energy shall be specified

E-Beam E > 10 MeV

X-ray E > 5 MeV

Assessment of Potential of Induced Radioactivity necessary

Literature: e.g. Gregoire et. al.

Activation Experiments

PERGAMON

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Radiation Physics and Chemistry 67 (2003) 149–167

Radiation Physics and Chemistry

www.elsevier.com/locate/radphyschem

Radiological safety of medical devices sterilized with X-rays at 7.5 MeV

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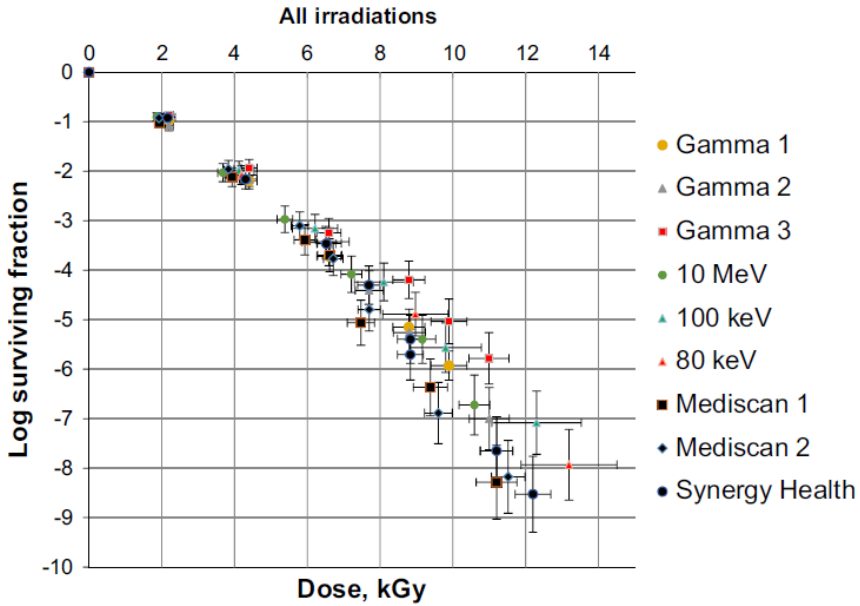
Received 28 December 2001; accepted 18 September 2002

Log Survival Fraction B. Pumilus

Radiation Physics and Chemistry 107 (2015) 128–130



Transfer of an Established Sterilization Dose…

… to a radiation modality different from the that on which the dose was originally established shall not be permitted unless data are available to demonstrate the differences in operation conditions have no impact on the microbial effectiveness

Guidance:

A successful dose verification experiment is considered necessary

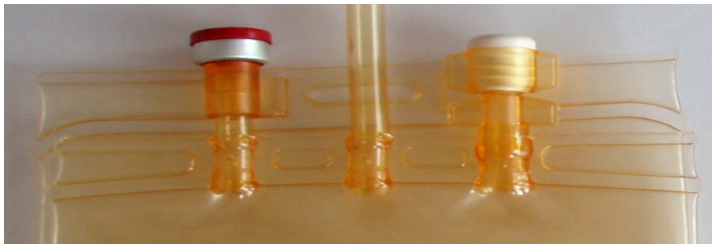
Transfer of an Established $D_{max,acc}$ …

… to a radiation modality different from the that on which the dose was originally established requires a recorded assessment that the differences in irradiation conditions do not affect the validity of the established dose

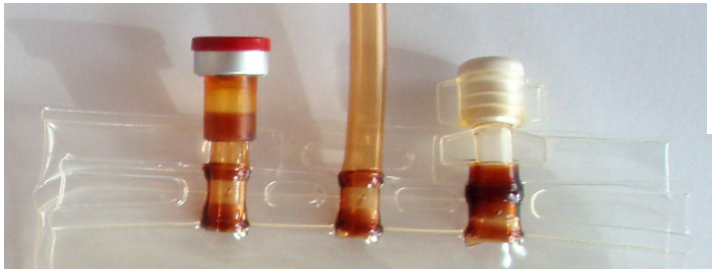
Guidance:
…higher dose rate may lower the unwanted effects upon product…

Need for more studies.
Today re-establishing on the new modality is required.

Material Qualification Experiment: 125 kGy



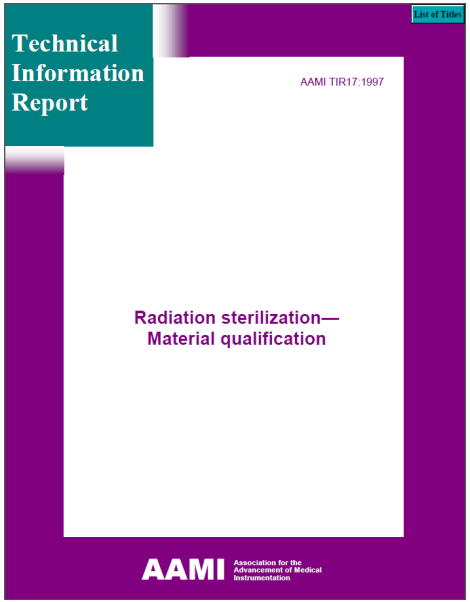
E-Beam



Gamma

Guide on the establishment of the maximum acceptable dose ($D_{max,acc}$) for a product

PANEL ON GAMMA & ELECTRON IRRADIATION



Change of Modality: Gamma → X-ray (7 MeV)

- Same or better penetration – No need to change process load
- Experience/Acquaintance with technology
- Availability of X-ray source
- Easier for new products
- Low dose products
- Flexibility in dose setting/product Presentation
- Higher dose rate can mitigate adverse material effects
- Cost considerations/effective photon utilization

PANEL ON GAMMA & ELECTRON IRRADIATION

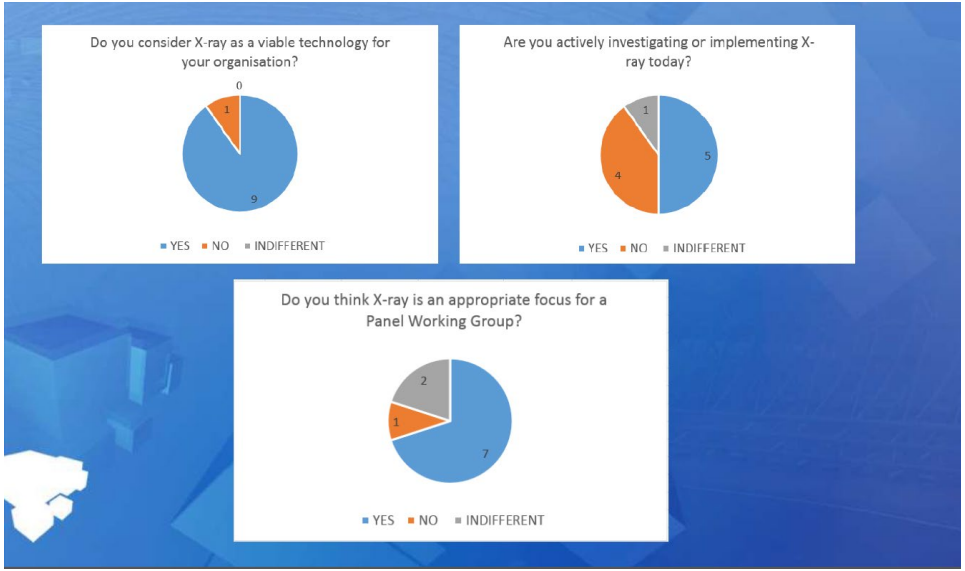
2019 X-ray WG survey results

MEDISCAN

QUESTIONNAIRE SENT TO PANEL MEMBERSHIP REPRESENTING ALL THOSE IN THE FOLLOWING CATEGORIES :

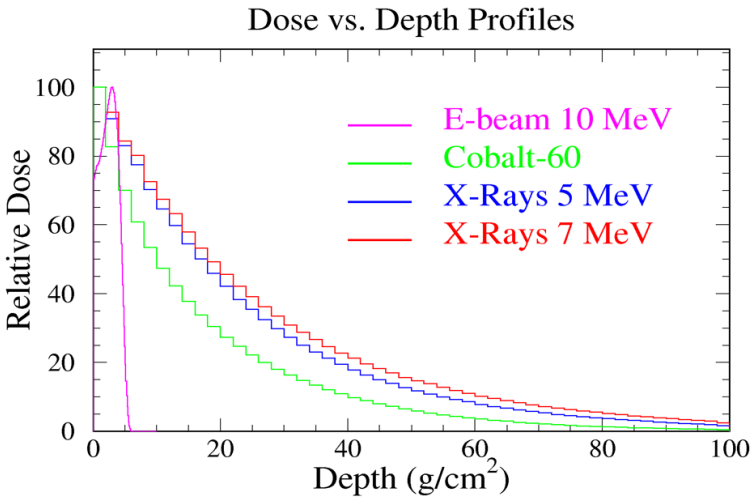
E-beam accelerator manufacturers (2)	Multi-site contract sterilization companies (5)
Cobalt-60 manufacturers (2)	Multinational medical device Manufacturers (4)

RESPONSES OBTAINED FROM 10 of 13 ORGANISATIONS



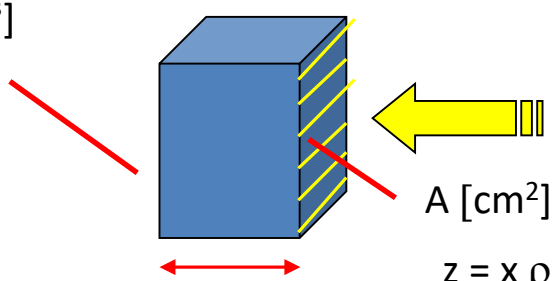
Change of Modality: Gamma → E-Beam (10 MeV)

Penetration



Product Thickness

V [cm³]
m [g]



A [cm²]

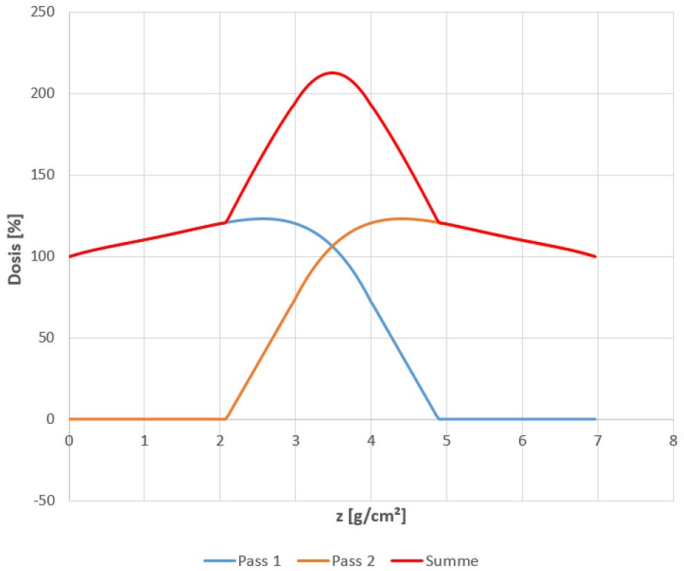
z = x ρ Surface Weight

$$z = x.\rho = x.\frac{m}{V} = x.\frac{m}{A.x} = \frac{m}{A}$$

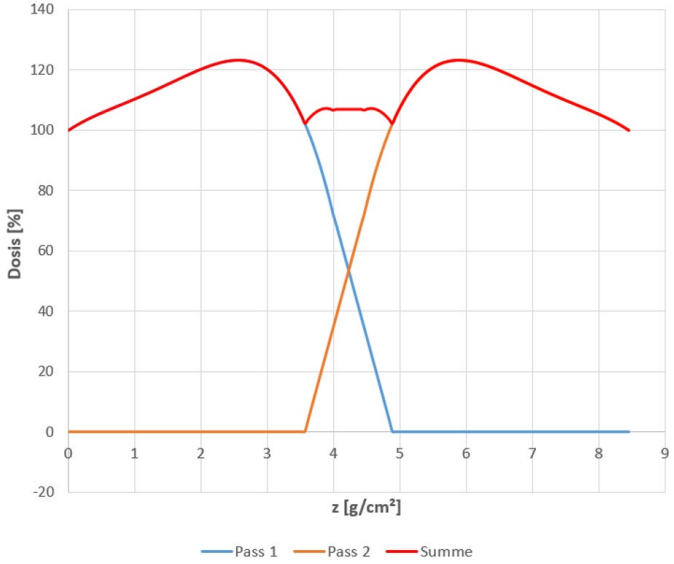
z < 9 g/cm² 2-sided E-beam Irradiation possible

Product Dimensions/Beam Energy Matters:

z=7 g/cm² DUR ≈ 2.3



z=8.5 g/cm² DUR ≈ 1.2



Product/Packaging Considerations

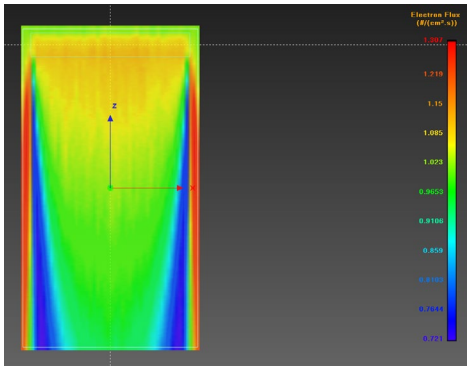
- Dose Uniformity:
  DUR < 1.5 X-ray (E-Beam needs very special treatment scheme)
- Low Density ($z<9$ g/cm²) → E-Beam High Density → X-ray
- Regular Load → E-Beam Bulk Load (Metal, Fluids) → X-ray
- Temperature Rise: $\Delta T\,[K] = D\,[kGy]/c\,[J/g.K]$ → X-ray ok!

E-Beam can do several passes

- Charge trapping in bulky polymer slabs → X-ray

Product Considerations

Intrinsic Dose Characteristics (Dose Gradients) in E-Beam to be assessed (e.g. by Mathematical Modelling)



Shielding of Biologics and Electronic Components → E-Beam

Product Considerations

Electron Beam requires fine grain PQ Dose Mapping

- ❑ Thoughtful dosimeter placement
- ❑ More dosimeter locations than Gamma/X-ray
- ❑ Probabably higher variability than Gamma/X-ray
- ❑ Backup by Mathematical Model beneficial

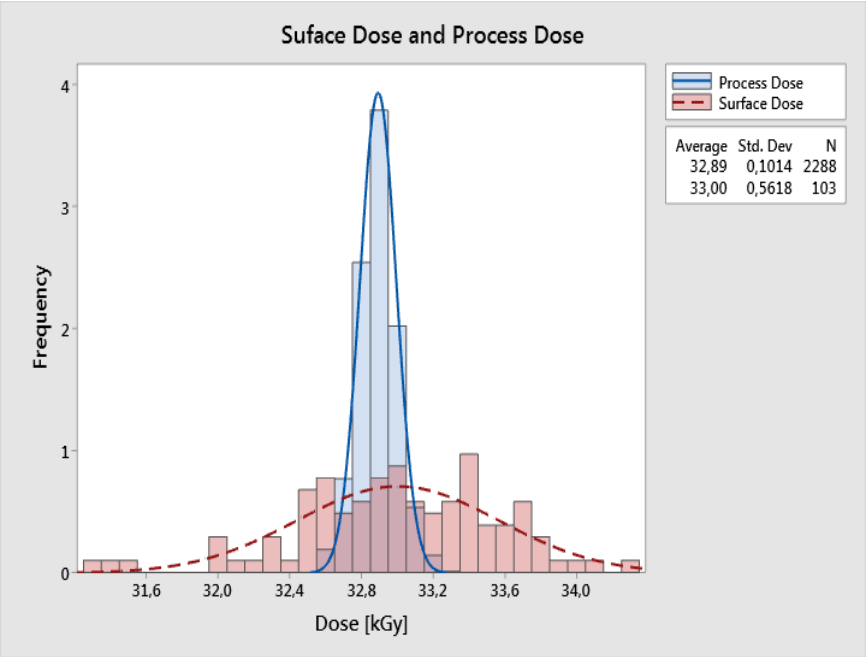
Thoughtful Definition of Processing Categories

Beam Based Process Considerations

Flexible Dose Setting: $D = k\frac{I}{Vs}$

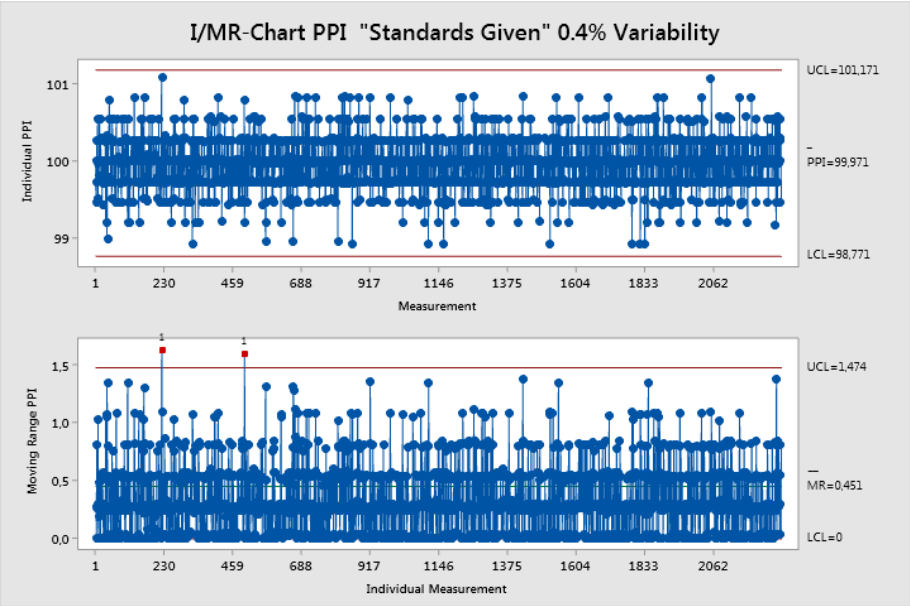
Very accurate & precise dosing:

Variability:
Dosimeter ≈ 1.5%
Process Parameter ≈ 0.4%



Beam Based Process Considerations

Process Control via Process Parameter for each process load possible !



Facility Considerations:

- ❑ Accelerator Energy & Power
- ❑ Irradiation Topology (top-down, side)
- ❑ Irradiation Container/ Process Load
- ❑ Conveyor System

Delivery: System + Shielding/Building Specification

Maintenance/Training

Conclusion

- ❑ Widening of Modality Spectrum is Essential
- ❑ Beam Based Technologies are Capable and Mature
- ❑ Consider Sterilization Modality already in Product Development
- ❑ Validate Alternative Modalities
- ❑ Beam Based: Consider E-Beam first, X-ray as Alternative