The Fundamentals of Ionizing Radiation as Applied to Radiation Processing

Kevin O’Hara, Director of Radiation Physics

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Outline

- Introduction to Radiation Processing
  - Brief Market Overview
  - Applications
  - Typical Energies, Radiation Types
  - Irradiator Designs
- Complexities of the radiation-processing world
  - New processes and Improved Performance of Materials
  - More stringent dose requirements
  - Dose rate and temperature constraints
- Discussion

Processing Categories

- Terminal sterilization processing
  - 10 - 25 kGy minimum dose
  - Typically 6 log reduction in bioburden
- Microbial reduction
  - 500 Gy - 10 kGy minimum dose
  - Surface dose certification
  - Salvage product
  - Viral reduction
- Viral non-proliferation and leukocyte inactivation
  - 70 - 150 Gy minimum dose for viruses
  - Blood irradiation (15 – 50 Gy)

Capabilities and Technologies

- ▶ Radiation
  - ▶ Gamma Radiation
  - ▶ Electron Beam Radiation
  - ▶ X-Radiation
- ▶ Ethylene Oxide (EO)
- ▶ Moist Heat

Market Overview

- Medical Device Sterilization
- Pharmaceutical and Biotechnology
- Advanced Applications, Materials Modification, Radiation Crosslinking, Radiation Hardness Testing
- Food Safety, Cosmetics, Pet Treats and Commercial Products

Introduction to Radiation Processing

Modality	Type of Particle	Energy Range and Dose Rates	Application
E-Beam	Electrons	<1 MeV – 12 MeV 10^3 Gy s^{-1} 20 MeV	Healthcare Product Material Modification Food Treatment Gemstones
Gamma	Photons	1.17, 1.33 MeV (^{60}Co) 1 Gy s^{-1} 0.667 MeV (^{137}Cs) 1 – 10 Gy min^{-1} 150 kV X-Rays 14 Gy min^{-1}	Healthcare Product Medical Research Blood Irradiation
X-ray	Photons	3 MeV – 7.5 MeV 10 Gy s^{-1}	Healthcare Product Food Treatment

Comparison of Dose Rates

- Electron Beam Highest Dose Rate (10^3 Gy s^{-1})
  - Instantaneous Energy Deposition
- X-Ray Intermediate Dose Rate (10 Gy s^{-1})
- Gamma Lowest Dose Rate (1 Gy s^{-1})

- What is the practical implication of dose rate?
  - Product Throughput
  - Material Changes
  - Pathogen Reduction

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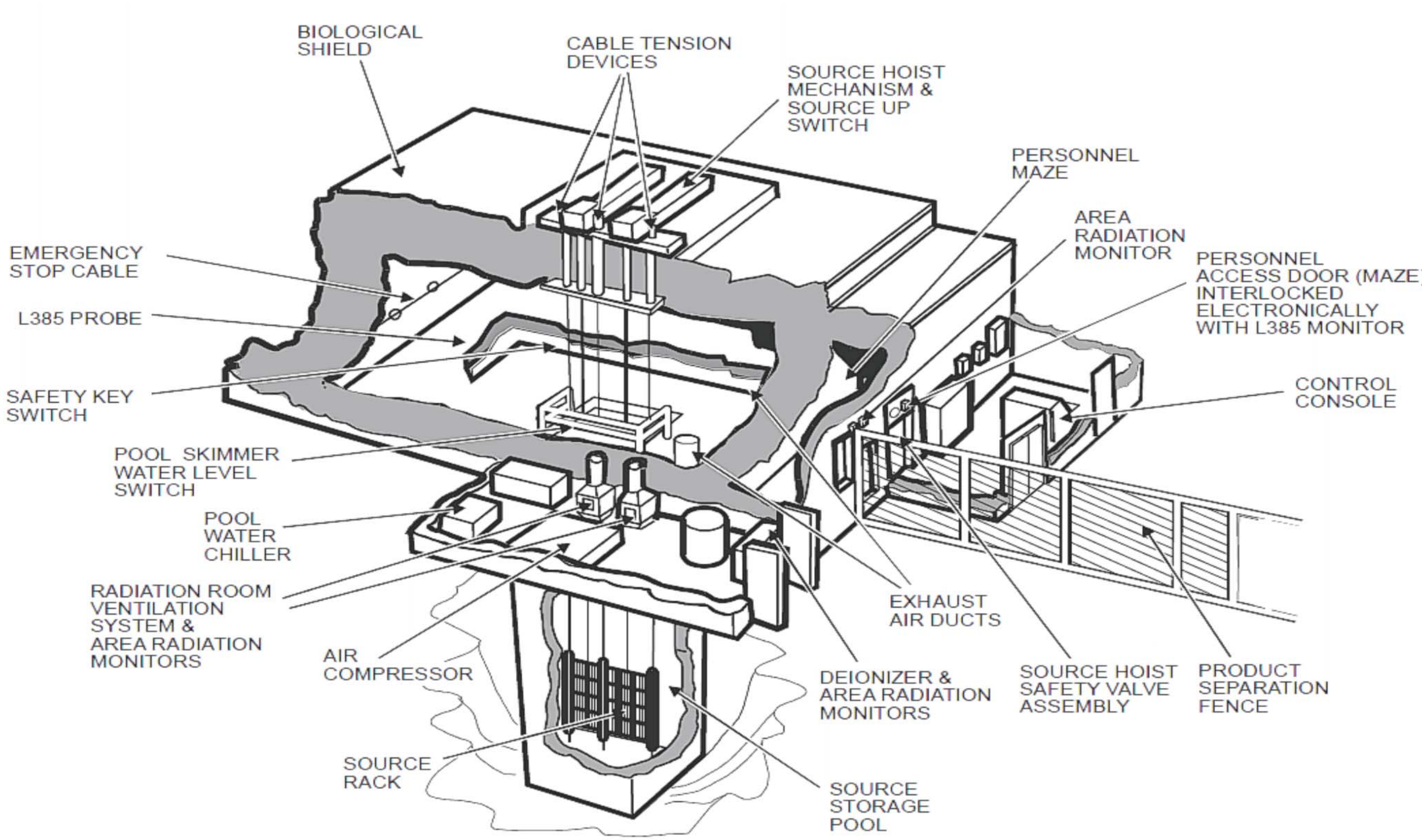
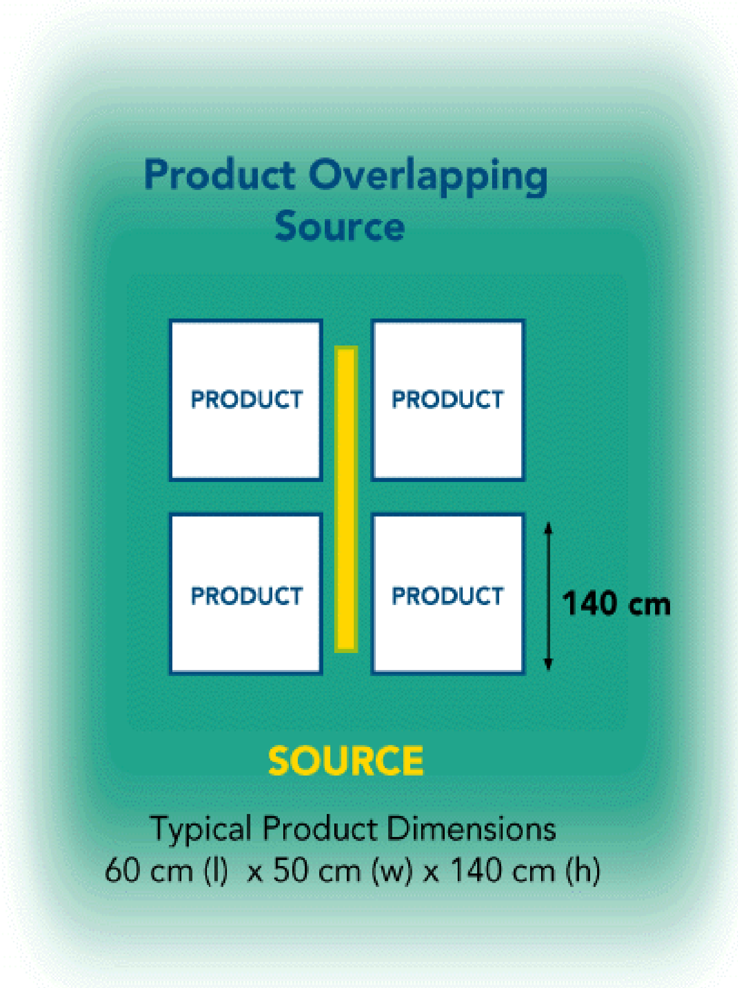
- Implication of Dose Rate?
  - Product Throughput
  - Material Changes
  - Pathogen Reduction

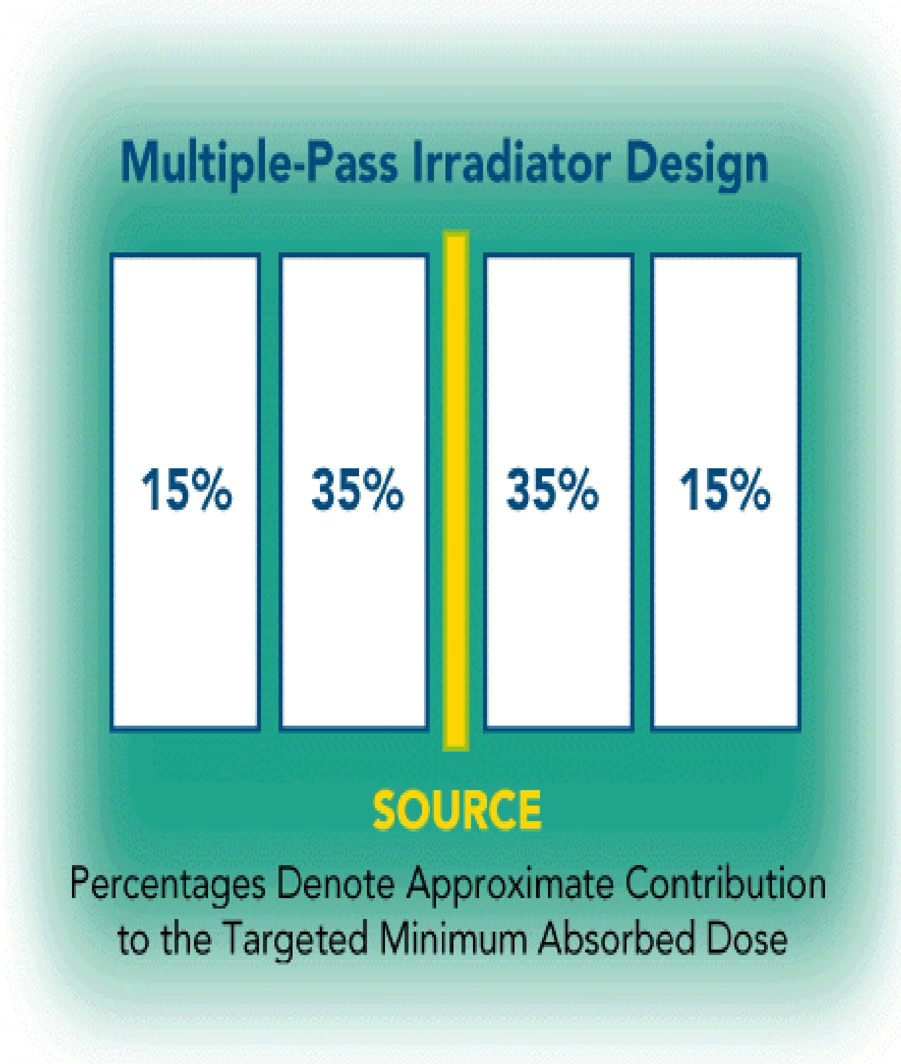
These are not generally considered to be differentiating factors – more academic than practical.

Safety - First and Foremost

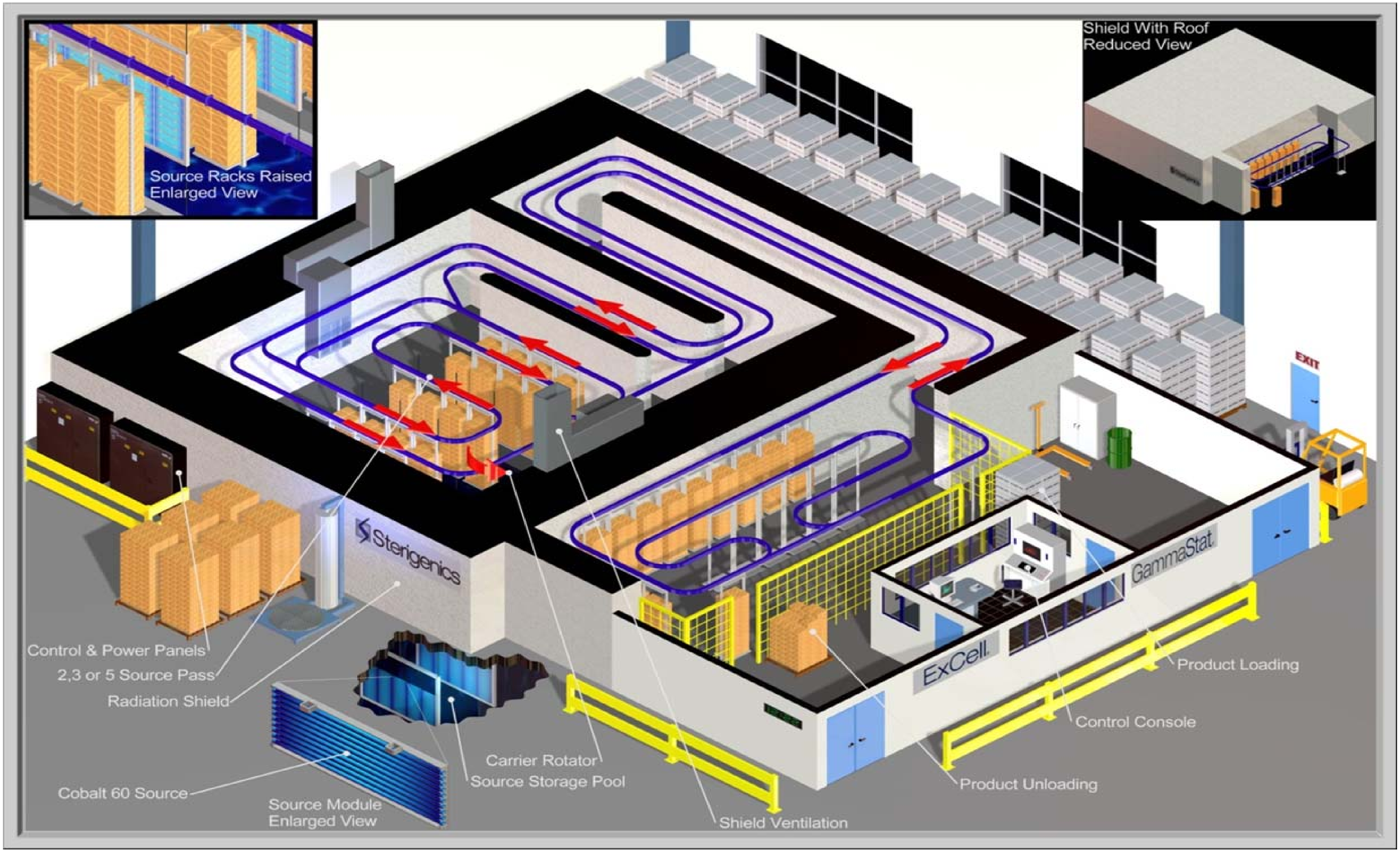


Basic Irradiator Designs

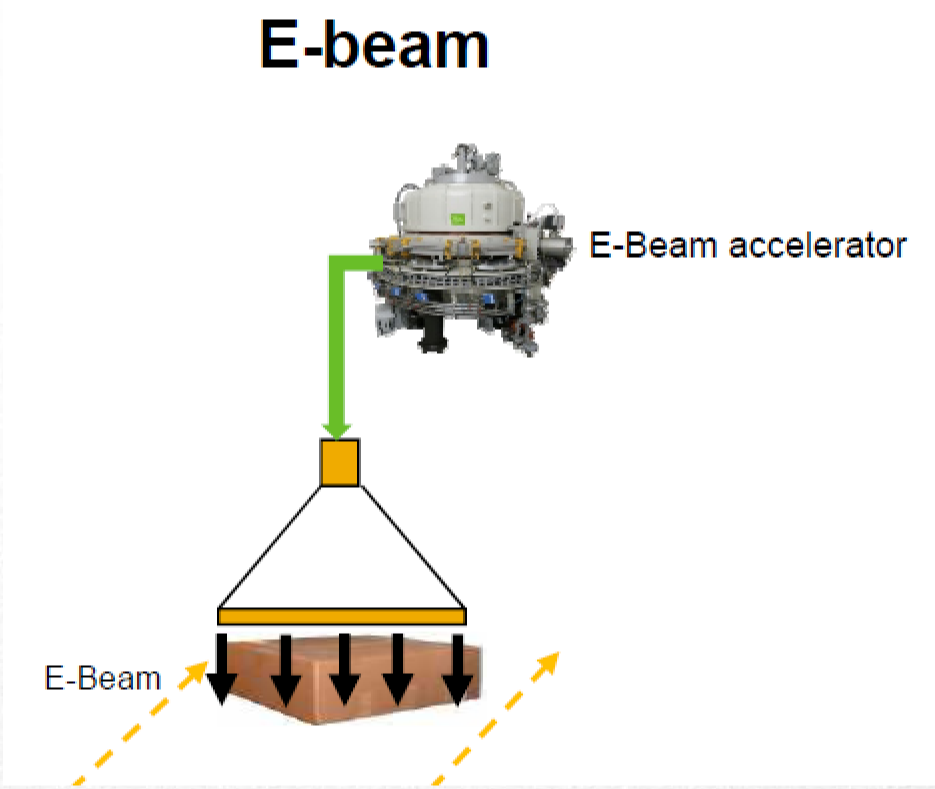


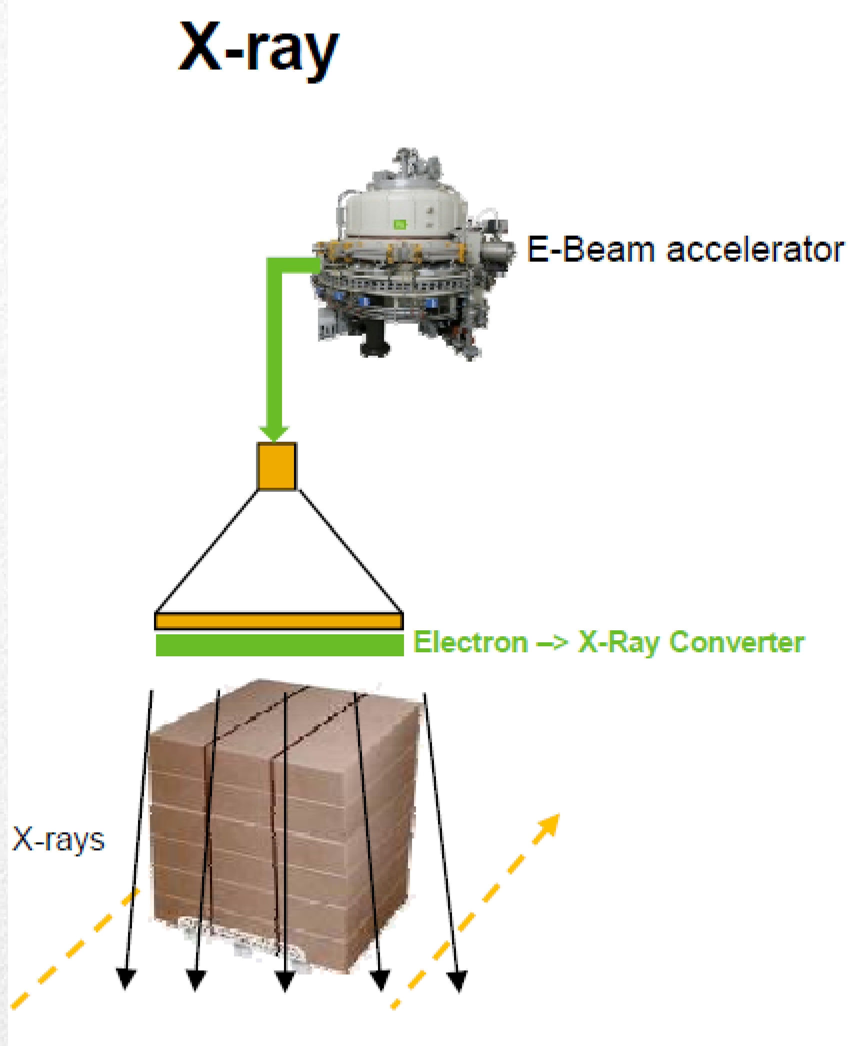


Precision Dose Delivery



E-beam and X-Ray





Food Irradiation Applications

Dose Range (Low, Medium or High)	Irradiation Application	Typical Dose or Dose Range (Gy)
LOW	Sprout inhibition (for example, potatoes, onions, garlic, yams)	20 to 150
LOW	Delay in ripening (for example, strawberries, potatoes)	10 to 1,000
LOW	Insect disinfestation (for example, insects in grains, cereals, coffee beans, spices, dried fruits, dried nuts, dried fish products, mangoes and papayas)	20 to 1,000
LOW	Quarantine security (against, for example, tephretid fruit flies in fruits and vegetables)	150
LOW	Inactivation of pathogenic parasites (for example, tape worm and trichina in meat)	300 to 1,000
MEDIUM	Reduction in food spoilage causing micro-organisms	1,000 to 10,000
MEDIUM	Improve the hygienic quality of food by inactivating food-borne pathogenic bacteria and parasites	2,000 to 8,000
HIGH	Pathogenic organism reduction in dried spices, herbs and other dried vegetable seasonings	10,000 to 30,000
HIGH	Sterilization to extend the shelf-life of pre-cooked food products in hermetically sealed containers	25,000 to 75,000
LOW, MEDIUM AND HIGH	Radiation Research	Unlimited

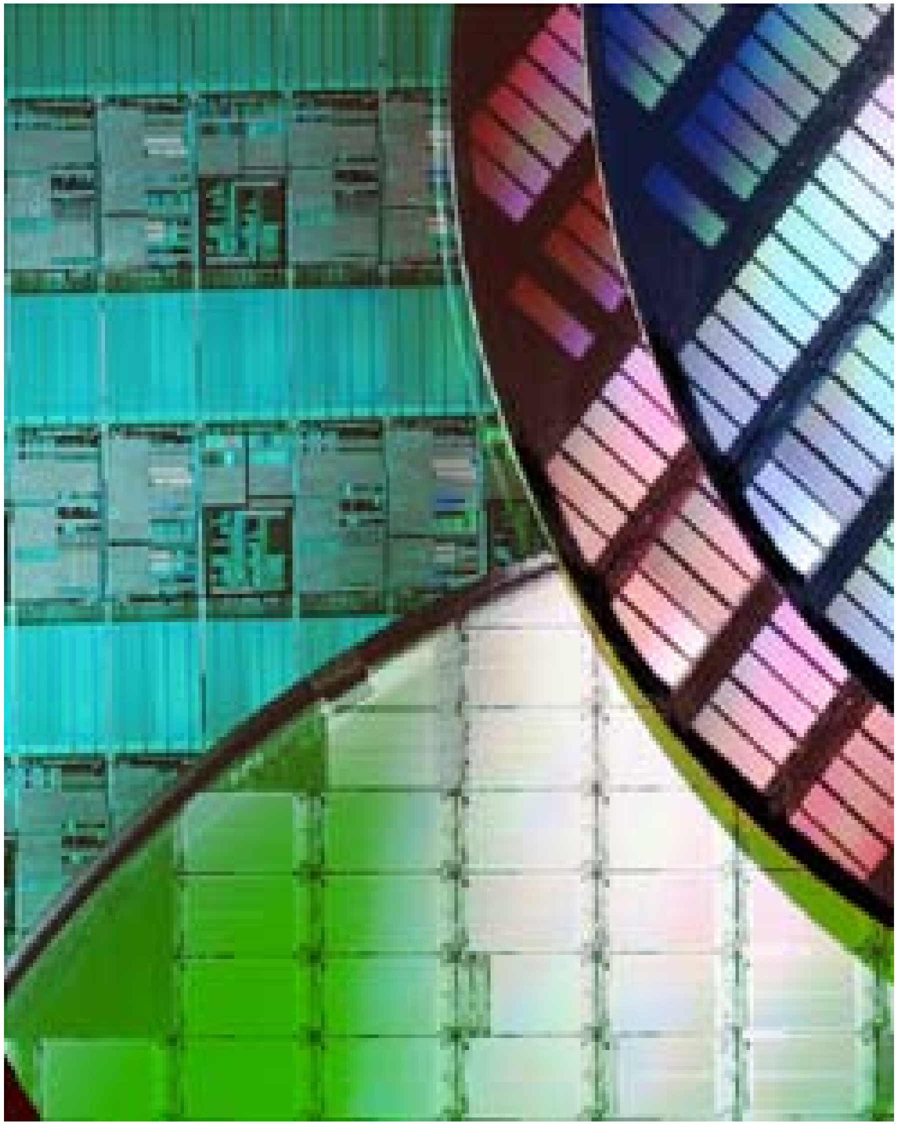
Food Safety and Commercial Products

- Microbial Reduction Services
- Phytosanitation
- Herbs and Spices
- Dried Vegetables
- Government Approved Foods
- Food Packaging Materials
- Cosmetic Products
- Personal Care Products
- Pet Treats and Pet Products

Food Irradiation – Phytosanitary Example Peruvian Asparagus

- Most Peruvian asparagus being treated with Methyl Bromide (> $1B annual revenue)
    - Ozone depleting chemical
    - Damages the asparagus tips
    - Air freighted to reduce time to market
- 400 Gy Dmin is not sufficient to extend shelf-life
    - Asparagus can be shipped by ocean since damage done by MB is eliminated
- Gamma radiation cost versus MB
    - $42 US per tonne vs. $50 (30,000 tonne/a)
    - $12 US per tonne (100,000 tonne/a)

Semiconductor Processing

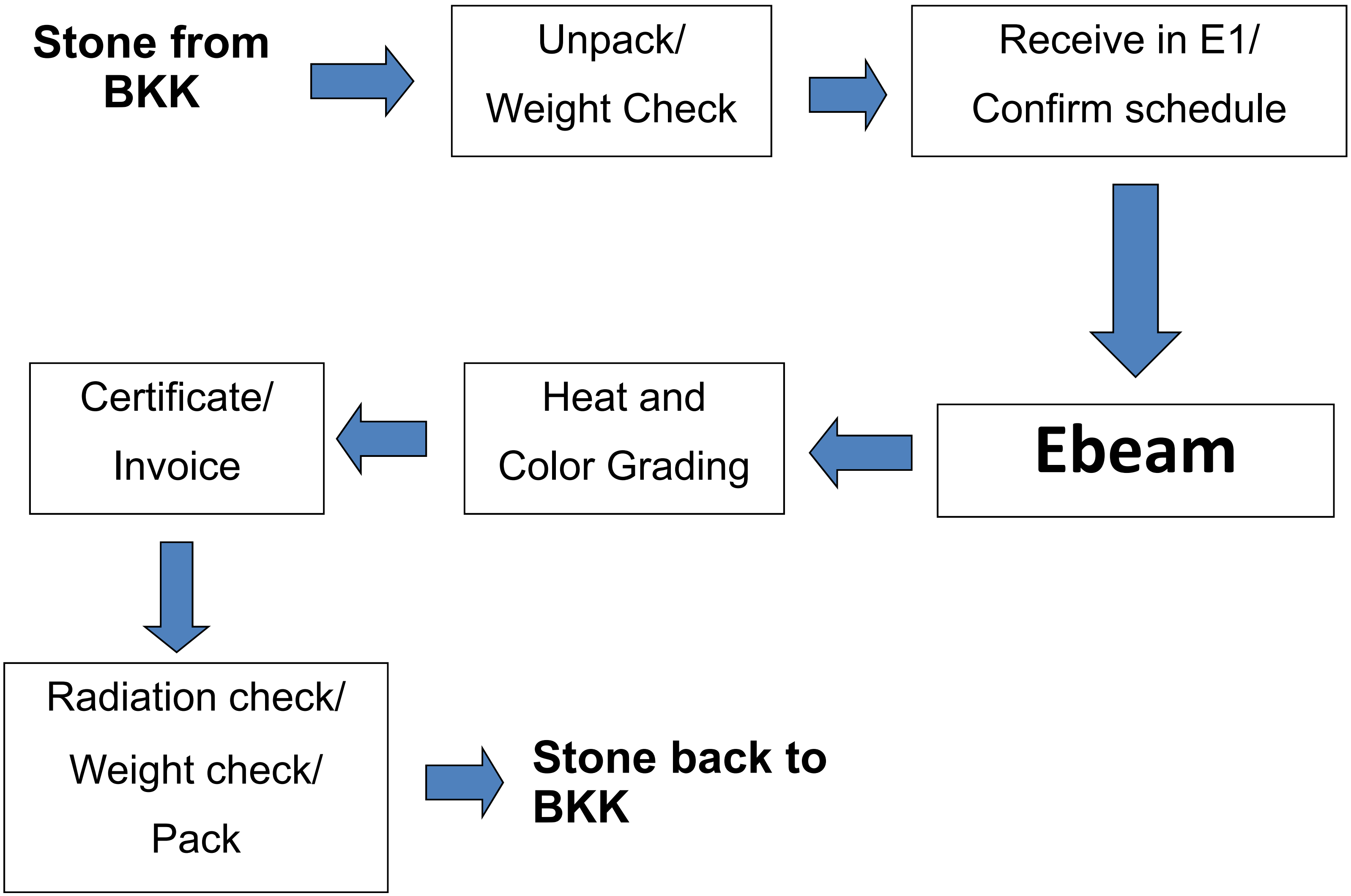


- E-beam process for tailoring switching speeds of many bipolar silicon power semiconductor devices.
- Irradiation to increase switching speed.
- Offers significant advantages over gold or platinum doping, the conventional competitive processes.
- Patented wafer carrier for the processing of stacks of wafers with a uniform dose distribution.

Gemstone Color Enhancement

- High-energy electron beam processing can duplicate colors only nature could otherwise provide.
- White topaz, for example, becomes Sky Blue.
- London Blue topaz transforms to Swiss Blue.

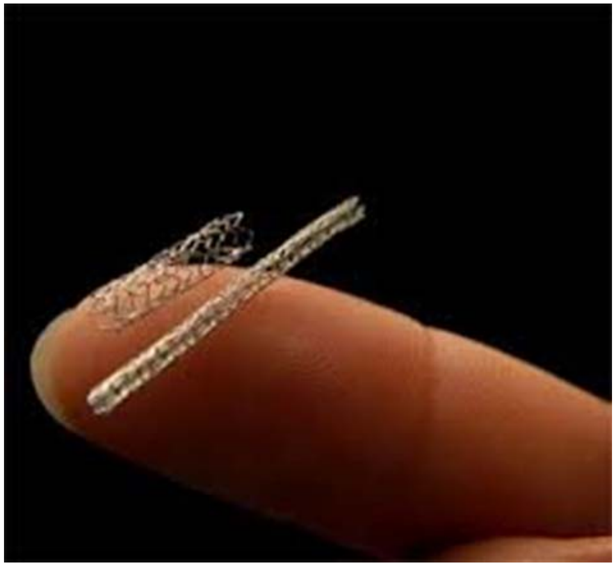
Gemstone Process Flow




White
Post Radiation
Post Heat

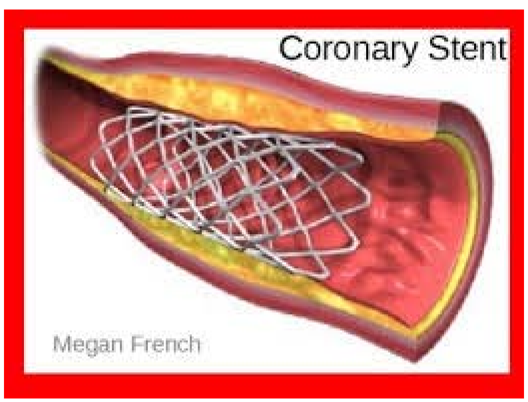
Diverse Applications

Drug –device products

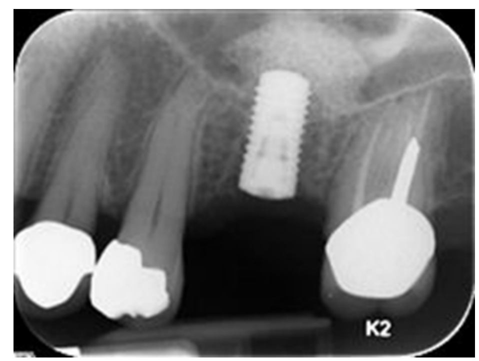


Pharma products

Cardiovascular Stent

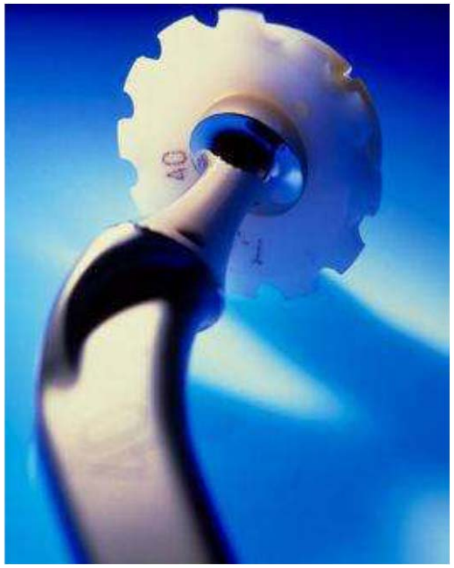


Complex medical devices



Diverse Applications

Hip Joint



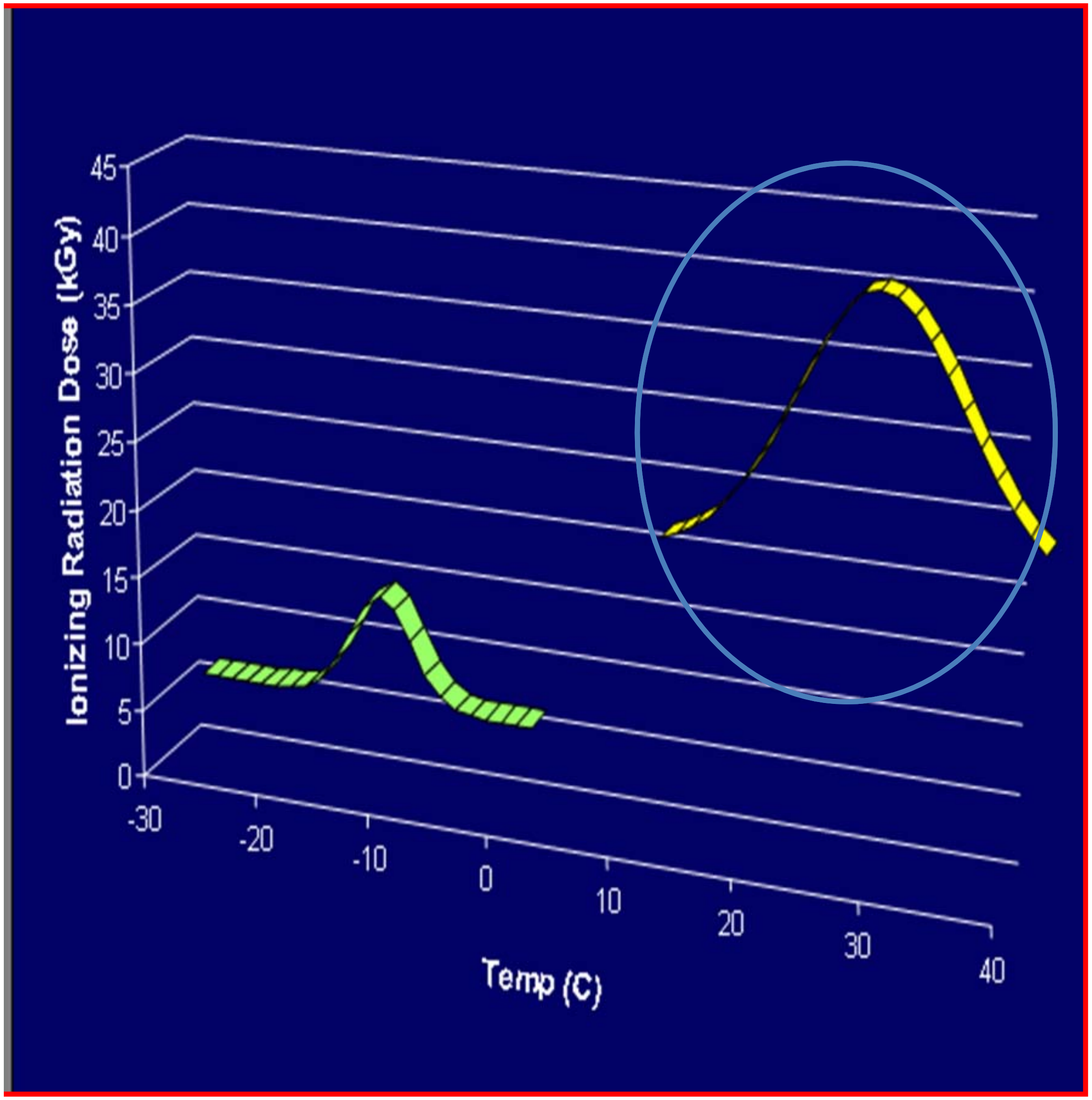
Knee Joint

Tissue Scaffold

Heart Valve

Skin Graft

Traditional Radiation Processing

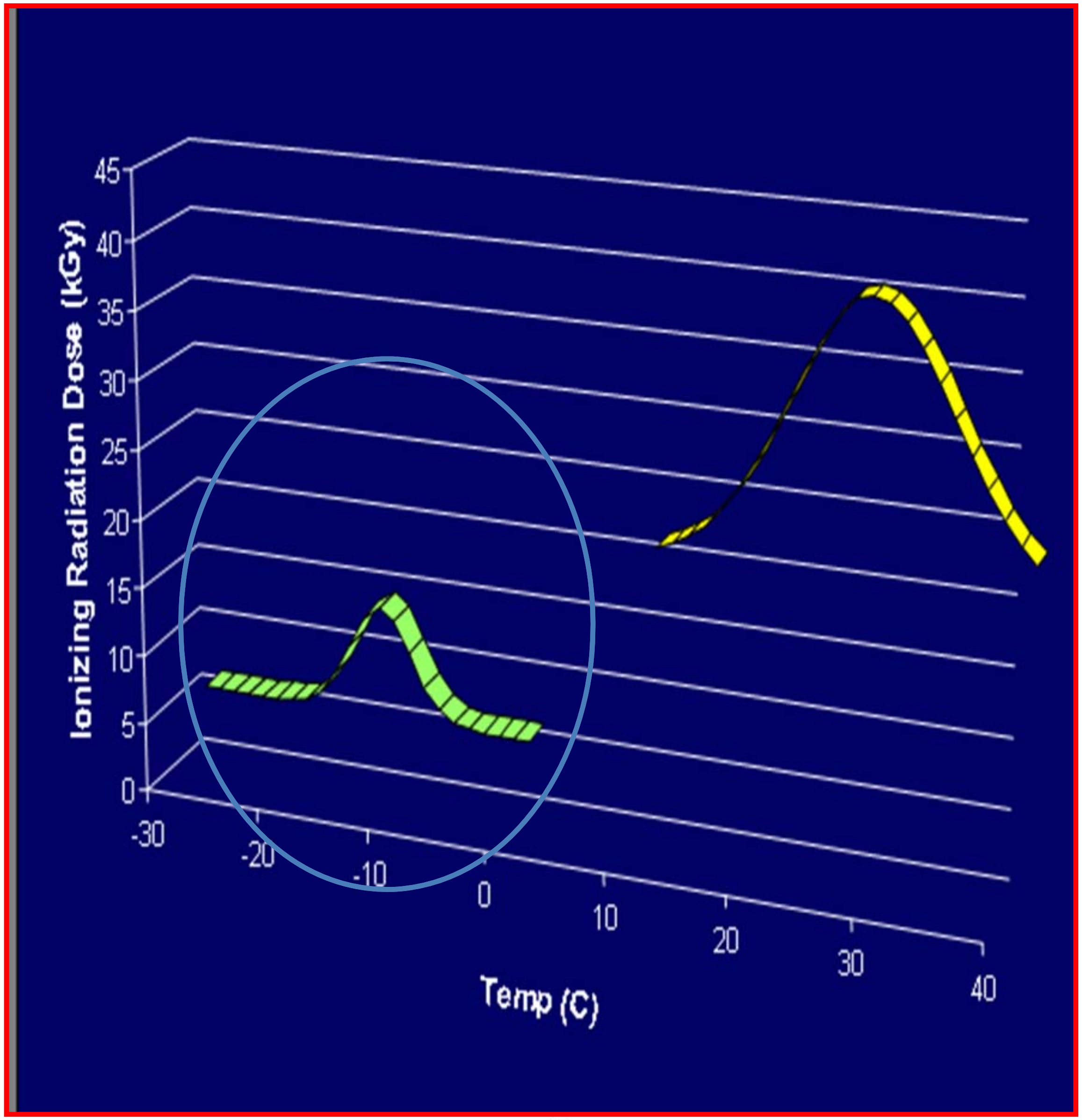


- High minimum doses and wide ranges
  - 25 kGy – 50 kGy
- Ambient conditions during irradiation
  - Temperature rise in product due to absorbed dose
- Large batch volumes, "simple" products

This Generation of Processing

- Low temperature environments will help protect biologic (migration of radiation-induced free radical is mitigated)

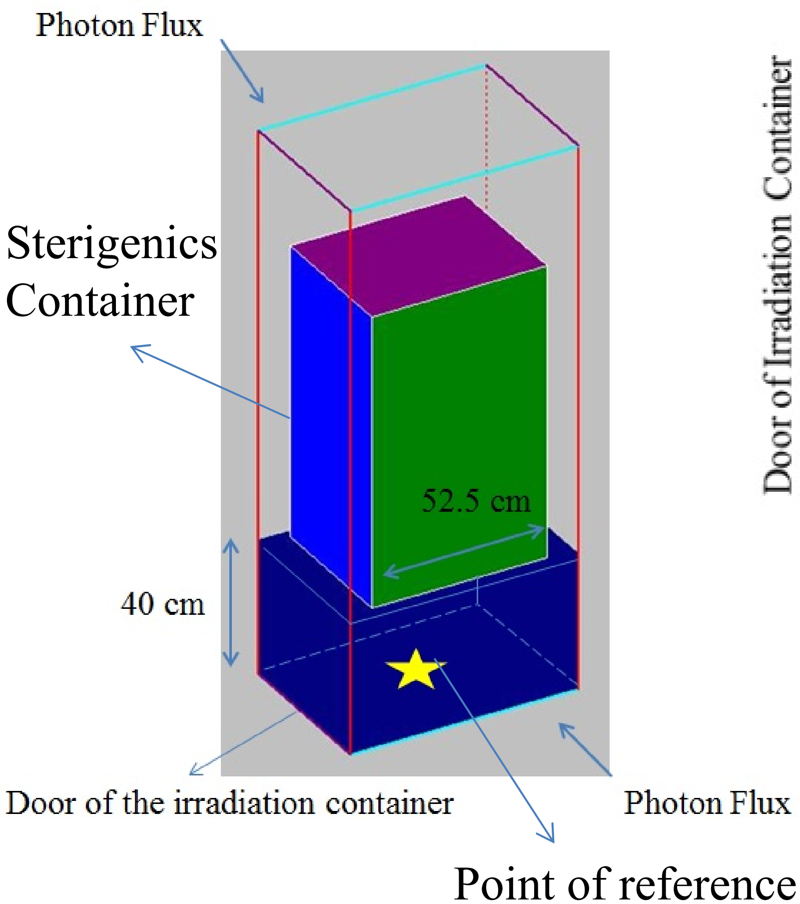
- Potential……
  - Dose Rate Restrictions
  - Inert Atmosphere
  - Temperature Constraints and Cold Chain Management
  - Narrow Dose Range
  - Smaller Product Volumes

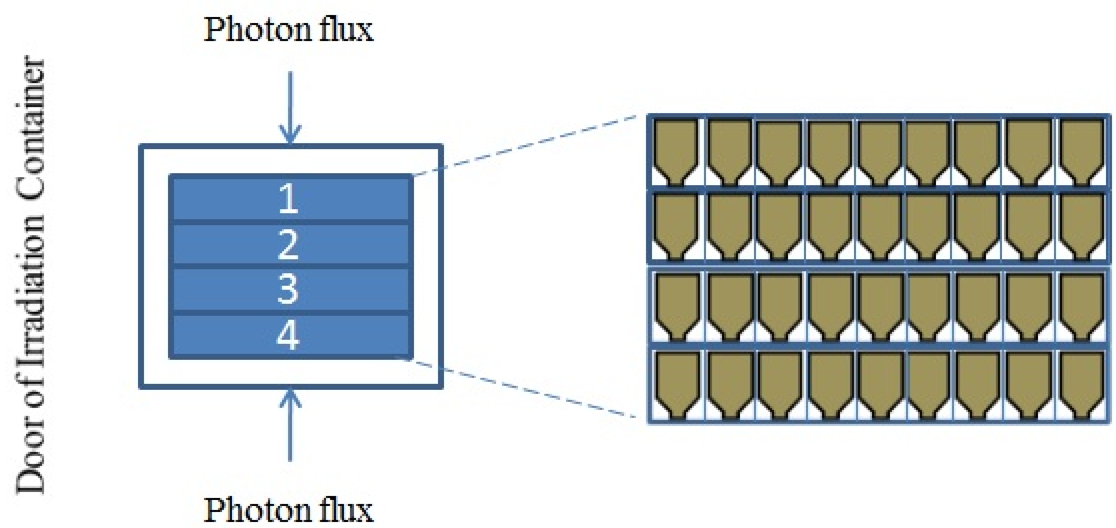


Product Characteristics

Characteristic	Pharmaceutical	Biologic	Combination Devices
Active Ingredient	Non-biologically Active	Metabolically active	Delivery device and pharmaceutical or biologic
Density JIT	> 0.2 g/cc YES	> 0.2 g/cc YES	< 0.2 g/cc YES
Temperature Restrictions	**Yes**	**Yes**	< 40 °C to prevent H_2 bond rupture
Dose Rate Restrictions	**Yes**	**Yes**	No
DUR Constraint	**Yes.** Processed with refrigerant.	Yes	Typically no. DUR < 1.6
Batch Volume	**Low processing volumes**	**Low processing volumes**	Can be larger volumes
Other	Radiochemistry driven (small molecule), Ultraclean (< 1 CFU)	Radiochemistry driven. 50 - 2,000 CFU	CFU range typical of disposable device (0.1 to 10^6 CFU)

Pharma Product





Gamma
Pharma product

20 ml powder filled vials

Below -15°C (storage / irradiation)

~ 10,000 vials per run
(dummy material added)

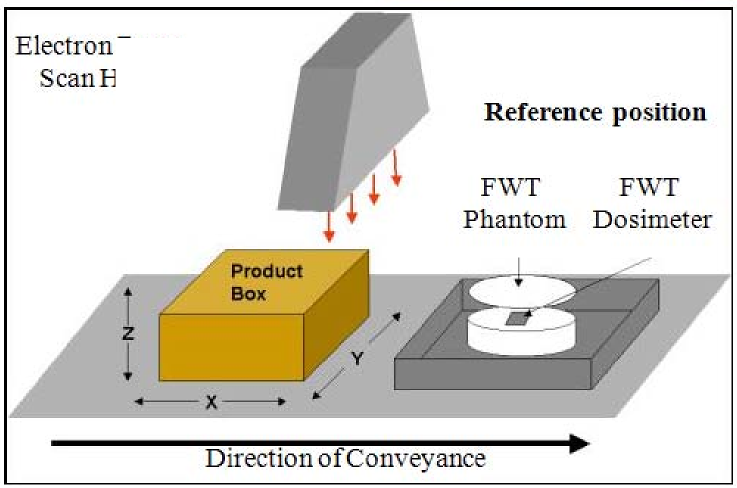
DUR ≈ 1.2

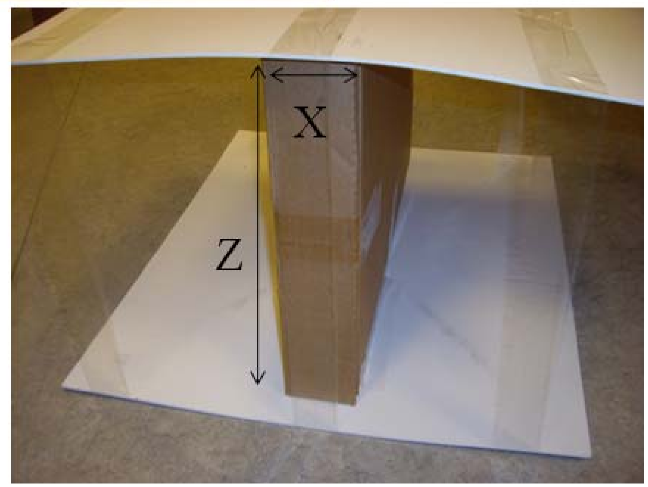
E-beam Example

10 MeV Electron beam

2-sided exposure

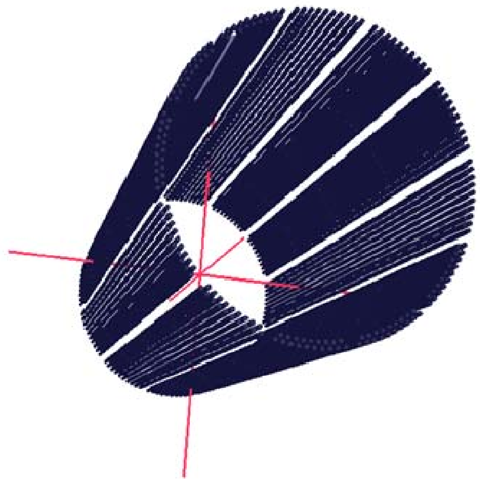
DUR < 1.3

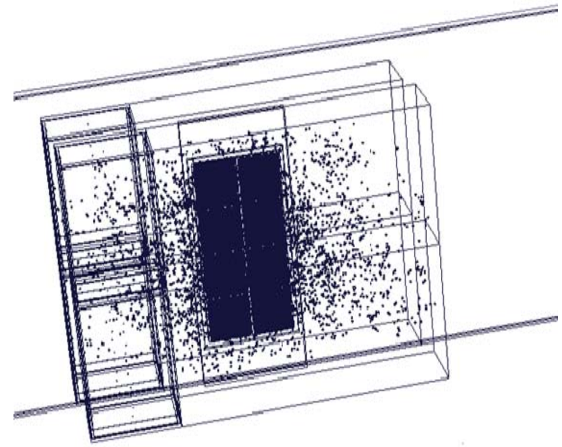


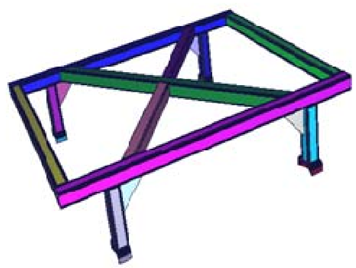


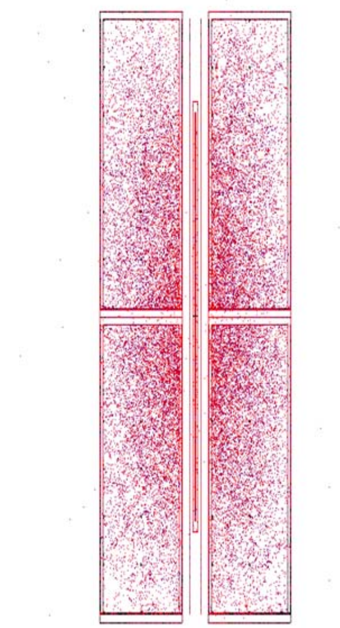
Mathematical Modelling (ISO 11137 Parts 1, 3)

- Bringing the physics to life.
- Ability to model actual product by AutoCad 3D input file.
- Virtual validation of a process or change.

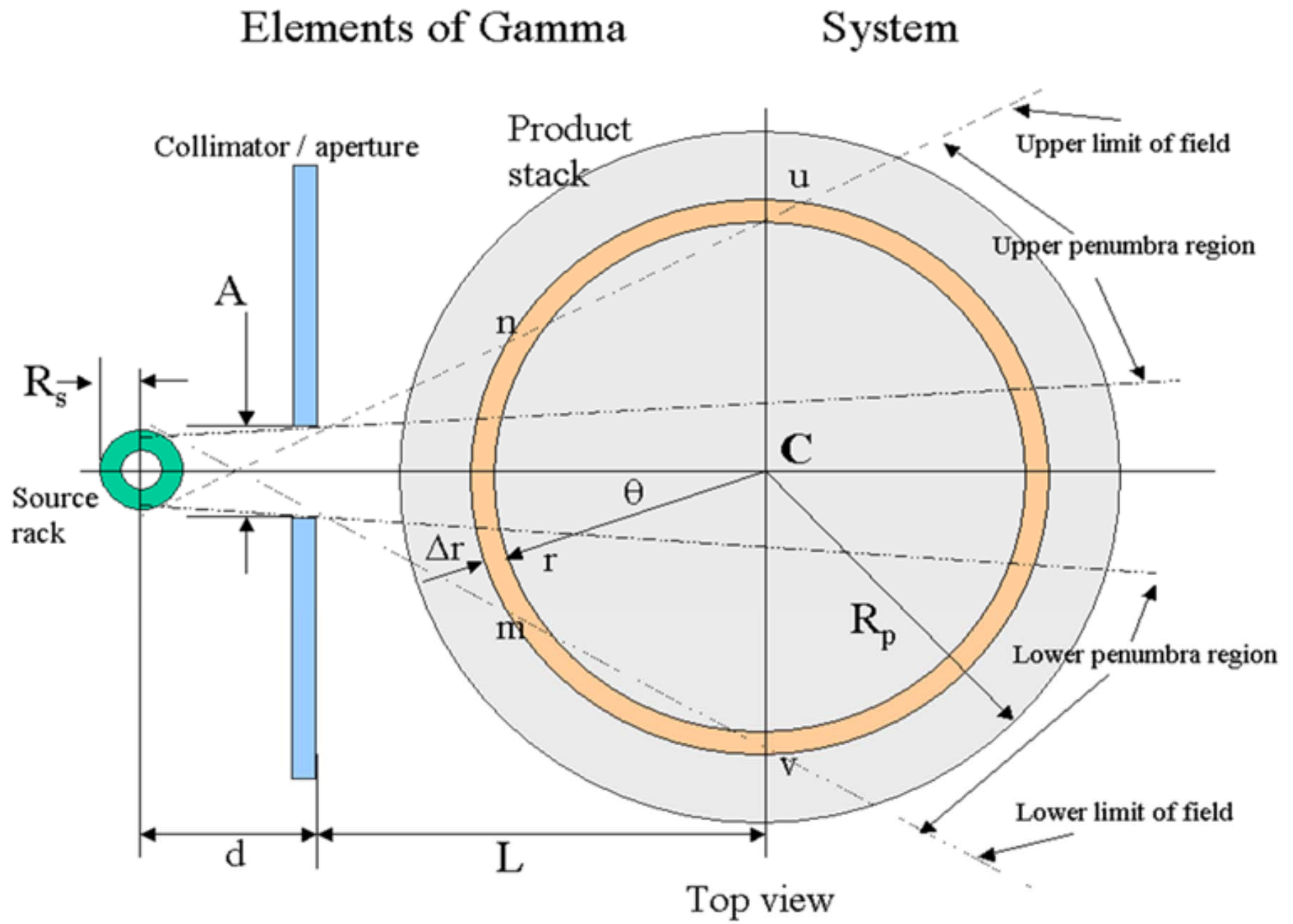








Precision Dose Delivery



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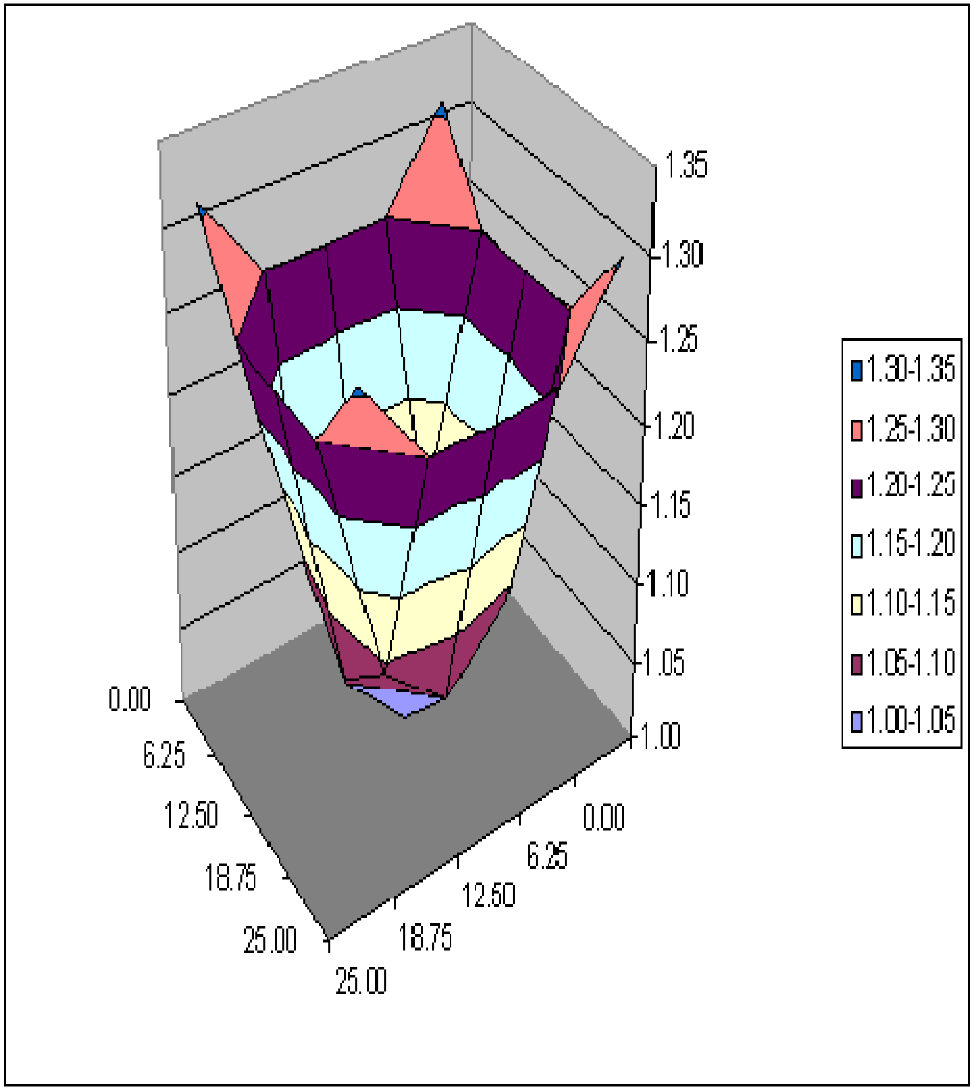
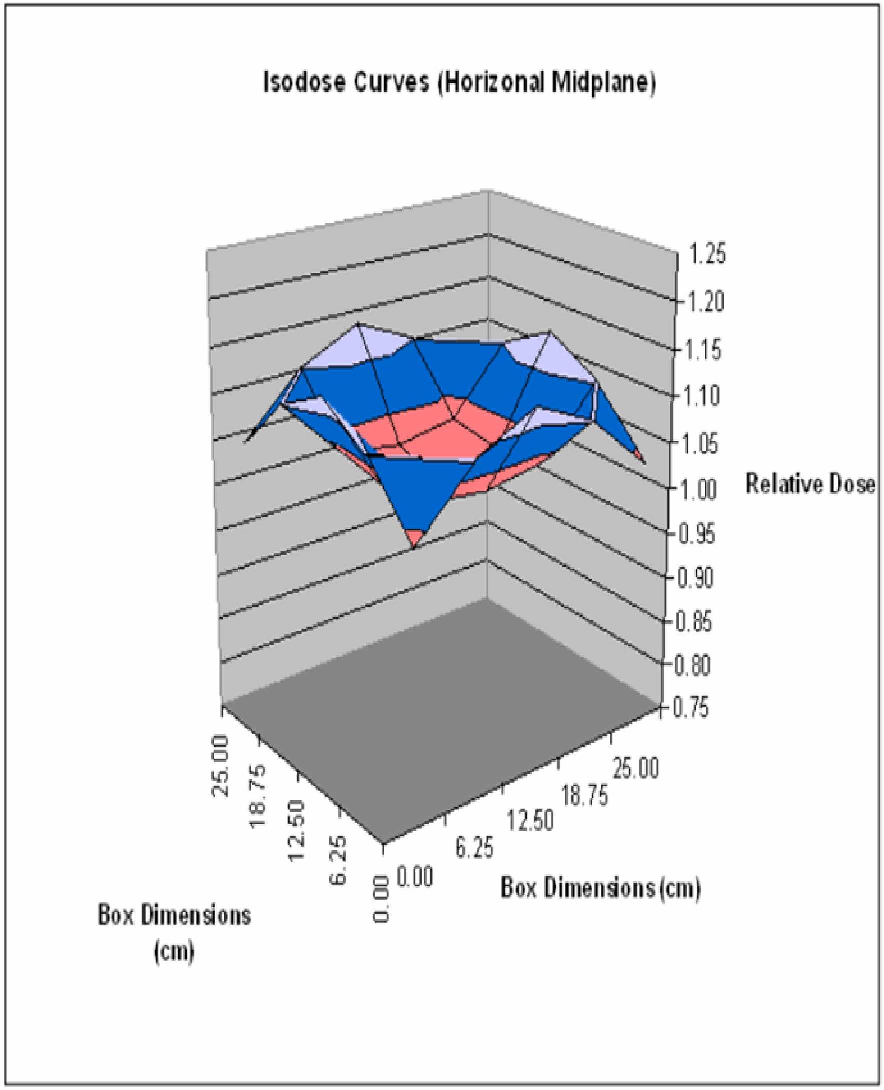




Low Temperature Dose Mapping

- Temperature Response of Dosimetry
- Potential Variation of Mass
- Heterogeneous Mass Distribution
- Internal Monitoring Locations

Impact on Radiation Dosimetry

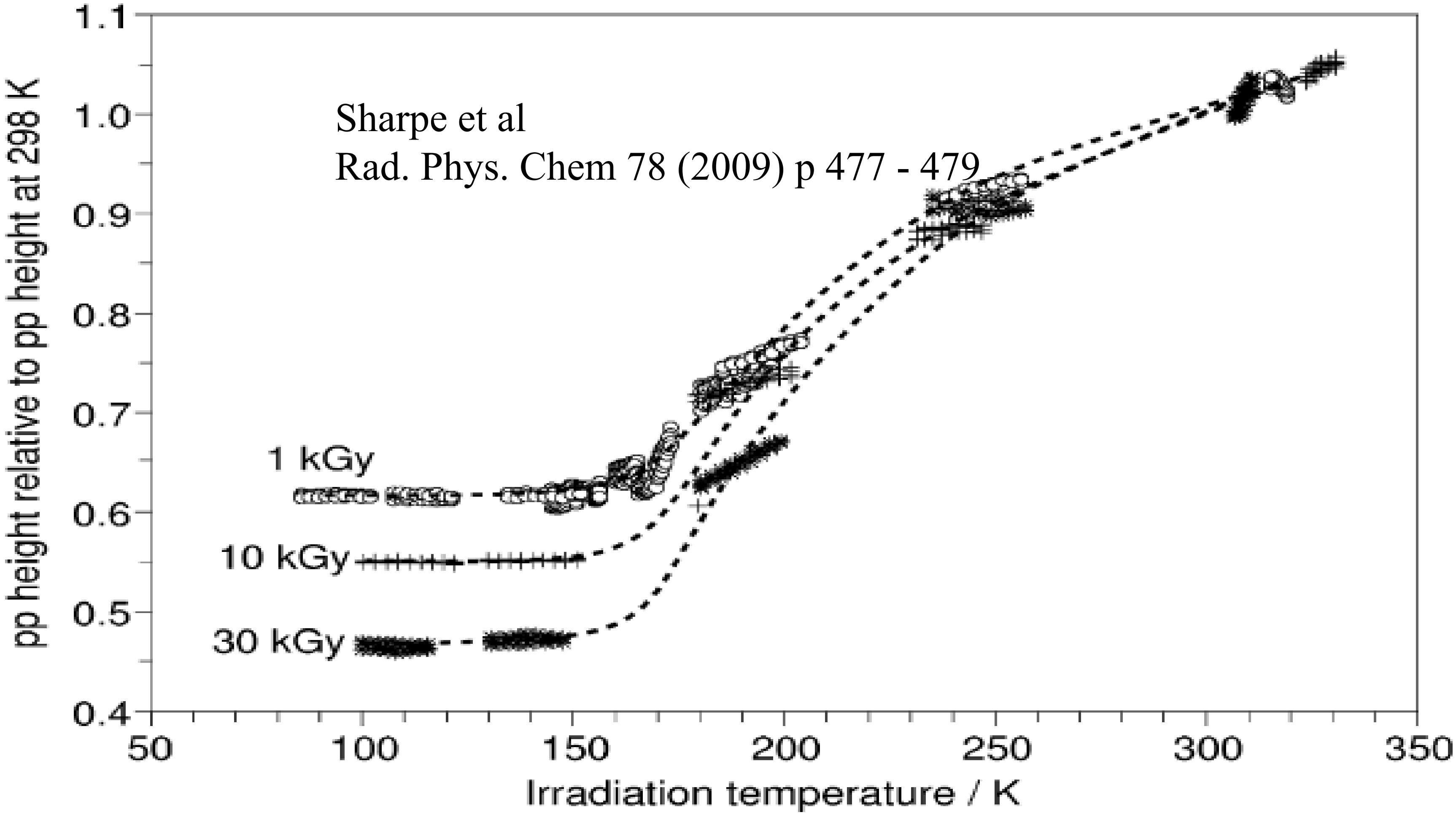


Fig. 3. Relative response of alanine dosimeters irradiated to 1, 10 and 30 kGy at temperatures between 80 and 310 K.

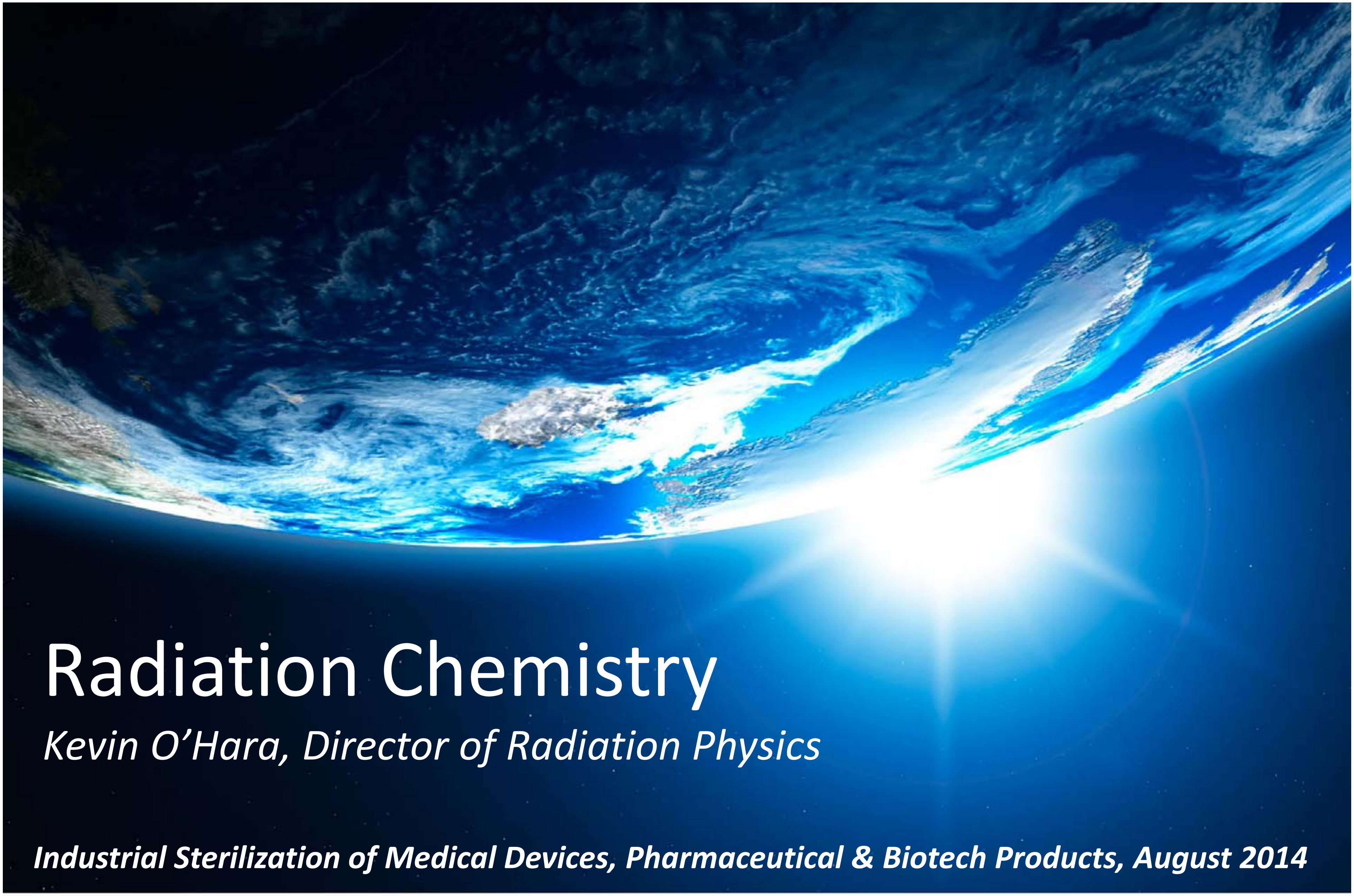
Summary

- Radiation-processing world is more and more complex
  - Customized solutions are becoming more common
  - Techniques to minimise radiation damage (e.g. low temperature, inert atomosphere, dose sculpting)
  - New methods for establishing a sterilisation dose to minimise radiation damage of the product

- Mathematical Modelling and Specialized Irradiators

- Discussion

Thank you

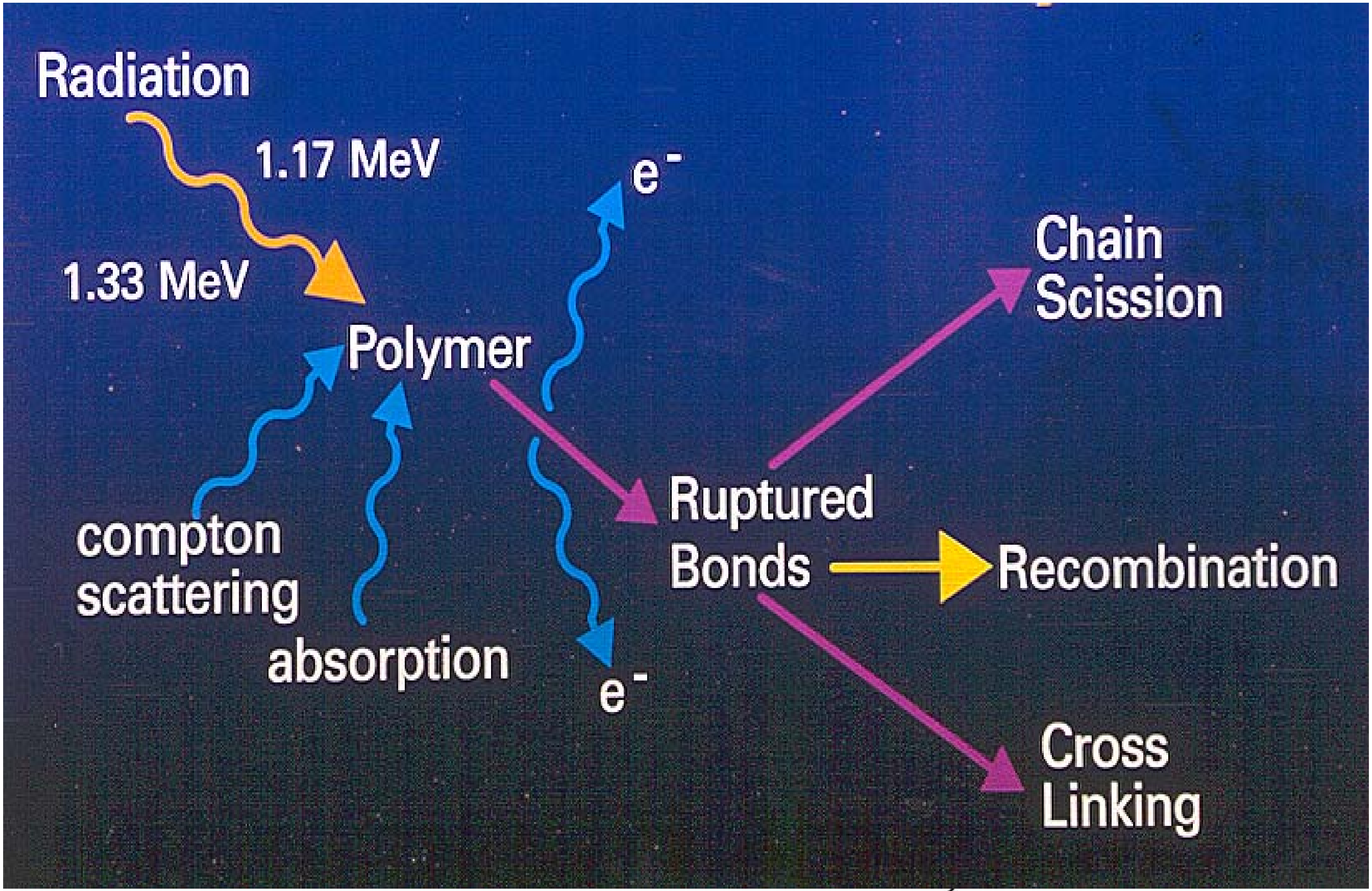


Radiation Chemistry

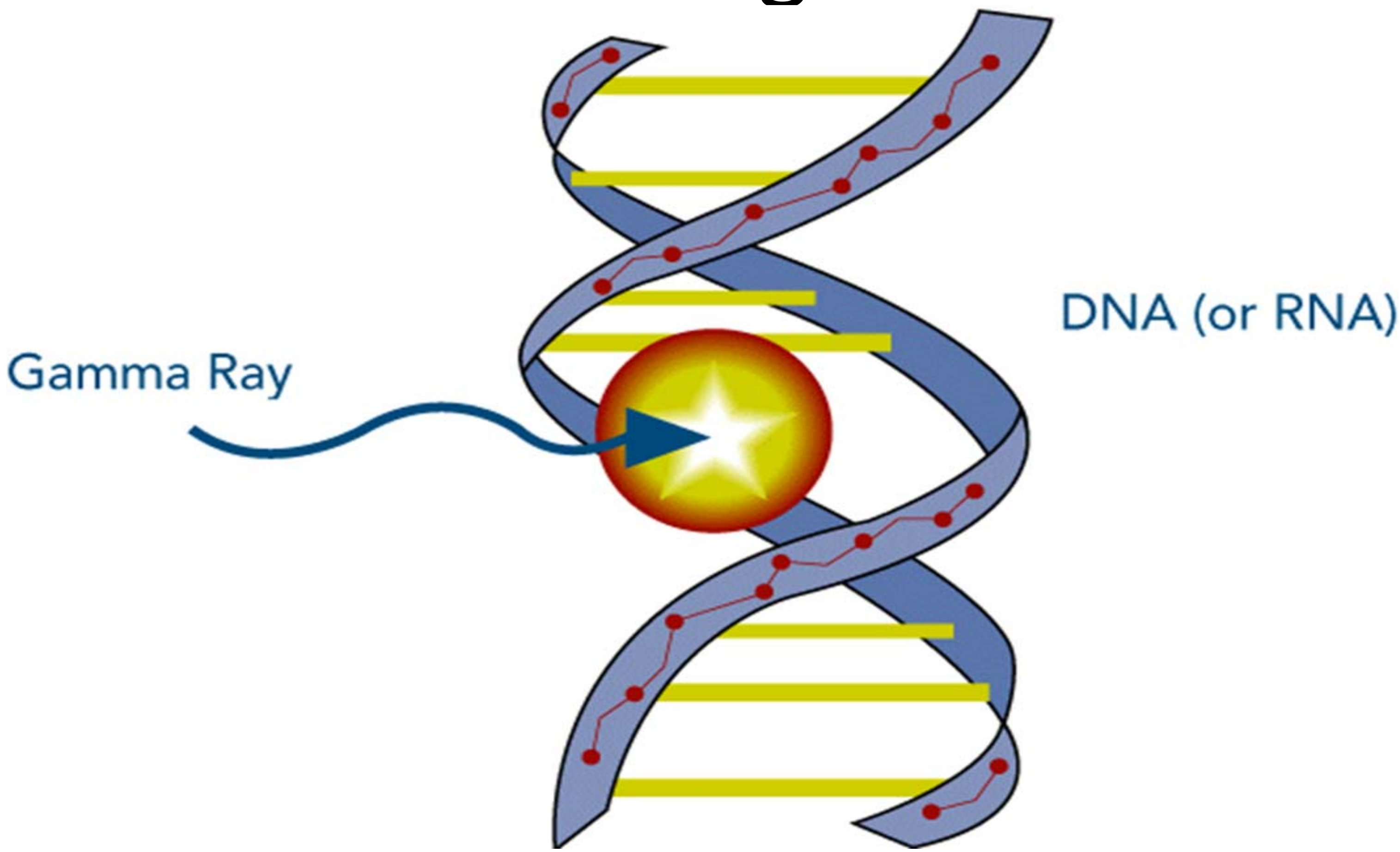
Kevin O'Hara, Director of Radiation Physics

Industrial Sterilization of Medical Devices, Pharmaceutical & Biotech Products, August 2014

Radiation Effects on Materials



Breaking Bonds within a Microorganism



Radiolytic Products of Water

$H_2O + H \rightarrow H_3O^+ + e^-$

$H_2O \rightarrow H_2O^+$

$e^-_{aq} + H_2O \rightarrow H_3O^+ + OH$

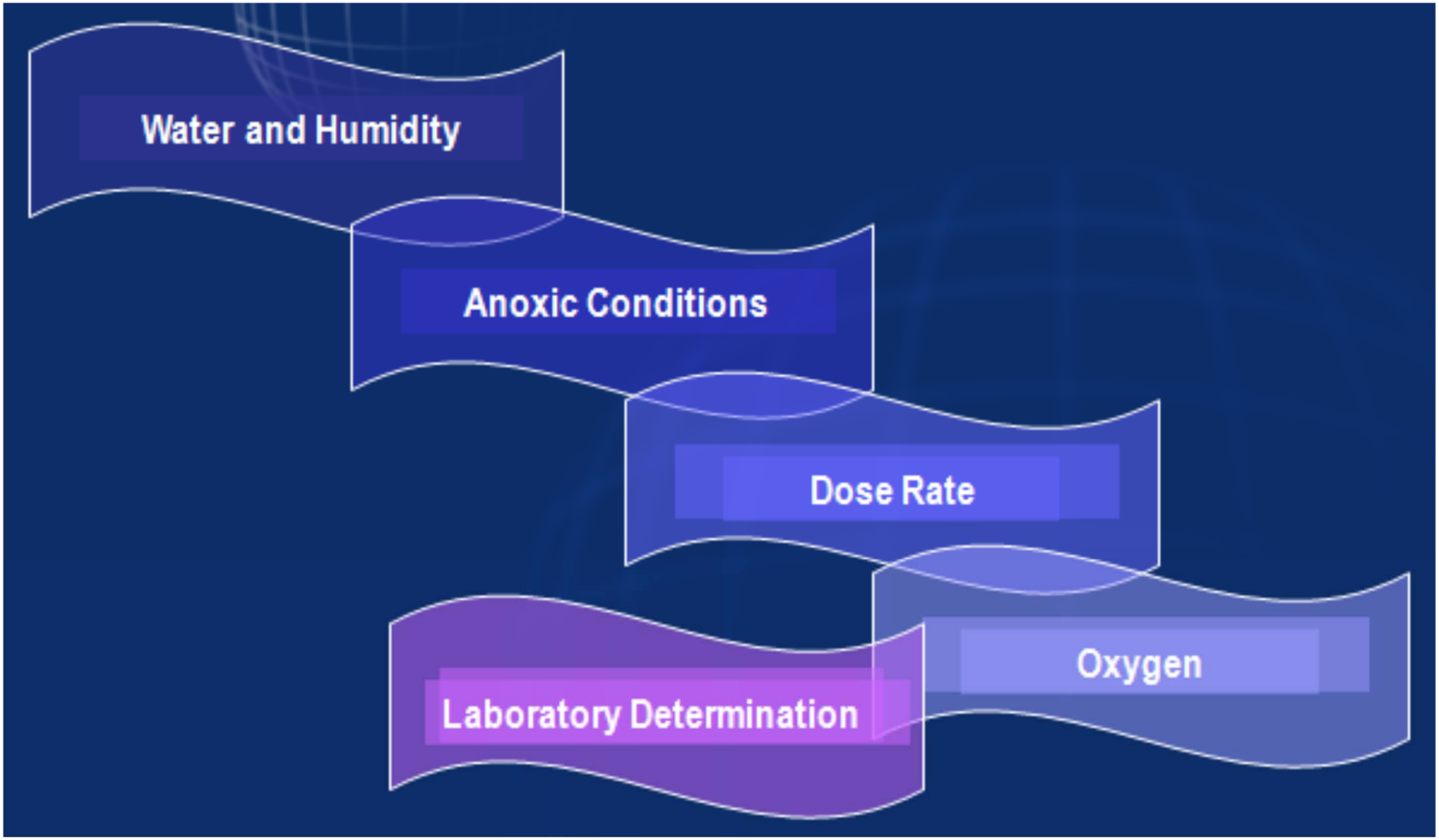
$H_2O^+ + H \rightarrow H_3O + OH$

$H_3O^+ + e^- \rightarrow H_3O^-$

$e^-_{aq} + e^-_{aq} \rightarrow H_2 + 2\,OH^-$

“ Plus many more chemical reactions… ”

Factors Affecting Lethality



Modality Comparison

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Modality Summary

Parameter	Gamma	X-Ray	E-Beam
Irradiation Parameters	Cycle Time Density	Conveyor Speed Density Scan Width Beam Energy	Conveyor Speed Scan Width Density Beam Energy
Radiation Field	Isotropic	Highly Directional	Highly Directional
Geometry of Materials and Heterogeneity of Product	Important to Consider	Important to Consider	Critical
Irradiator Reliability	Excellent	Good	Good to Excellent

Summary, Irradiation modalities

Attribute	Gamma	X-Ray	E-Beam
ISO 11137 Part 1	Yes	Yes	Yes
Product Treatment	Pallet / Tote	Pallet / Tote	Boxes / Tote
Dose Rate (Dmin 25 kGy)	Hours	Minutes	Seconds
Dose Uniformity Ratio (DUR)	Low sensitivity to product thickness	Low sensitivity to product thickness	Sensitive to product thickness
On/Off Technology	No	Yes	Yes
Flexible Target Dose	No	Yes/No	Yes

Summary, Irradiation modalities

Attribute	Gamma	X-Ray	E-Beam
Penetration - Low ρ	Good - excellent	Good - excellent	fair - good
Penetration - High ρ	effective	effective	Special processing
Processing Time	Good	Good	Very Good
Mechanical Properties of Product	Good	Good to Very Good	Very Good
Repeatability of Dose Delivery	Excellent	Very Good	Good
Process Validation	Straightforward	Straightforward	Potentially Complicated