The Fundamentals of Ionizing Radiation as Applied to Radiation Processing

Kevin O’Hara, Director of Radiation Physics

CIRMS Meeting, April 27, 2015
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

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

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

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

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

- 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

Product Overlapping Source

Typical Product Dimensions
60 cm (l) x 50 cm (w) x 140 cm (h)

Multiple-Pass Irradiator Design

Percentages Denote Approximate Contribution to the Targeted Minimum Absorbed Dose

15% 35% 35% 15%
Precision Dose Delivery
E-beam and X-Ray
## Food Irradiation Applications

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

Stone from BKK → Unpack/Weight Check → Receive in E1/Confirm schedule

Certification/Invoice → Heat and Color Grading

Radiation check/Weight check/Pack → Ebeam

Stone back to BKK
Diverse Applications

Drug –device products

Pharma products

Complex medical devices

Cardiovascular Stent

Coronary Stent

Megan French
Diverse Applications

- Hip Joint
- Heart Valve
- Tissue Scaffold
- Skin Graft
- Knee Joint
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

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pharmaceutical</th>
<th>Biologic</th>
<th>Combination Devices</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active Ingredient</td>
<td>Non-biologically Active</td>
<td>Metabolically active</td>
<td>Delivery device and pharmaceutical or biologic</td>
</tr>
<tr>
<td>Density JIT</td>
<td>&gt; 0.2 g/cc YES</td>
<td>&gt; 0.2 g/cc YES</td>
<td>&lt; 0.2 g/cc YES</td>
</tr>
<tr>
<td>Temperature Restrictions</td>
<td>Yes</td>
<td>Yes</td>
<td>&lt; 40 °C to prevent H$_2$ bond rupture</td>
</tr>
<tr>
<td>Dose Rate Restrictions</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>DUR Constraint</td>
<td>Yes. Processed with refrigerant.</td>
<td>Yes</td>
<td>Typically no. DUR &lt; 1.6</td>
</tr>
<tr>
<td>Batch Volume</td>
<td>Low processing volumes</td>
<td>Low processing volumes</td>
<td>Can be larger volumes</td>
</tr>
<tr>
<td>Other</td>
<td>Radiochemistry driven (small molecule), Ultraclean (&lt; 1 CFU)</td>
<td>Radiochemistry driven. 50 - 2,000 CFU</td>
<td>CFU range typical of disposable device (0.1 to 10$^6$ CFU)</td>
</tr>
</tbody>
</table>
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

Elements of Gamma

System

- Collimator / aperture
- Product stack
- Upper limit of field
- Upper penumbra region
- Lower penumbra region
- Lower limit of field

Source rack

Source

R_s

A

Δr

r

m

n

u

v

C

θ

R_p

L

d
Precision Dose Delivery
Low Temperature Dose Mapping

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

![Graph showing the relative response of alanine dosimeters irradiated to 1, 10, and 30 kGy at temperatures between 80 and 310 K.]

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

Sharpe et al
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 atmosphere, 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

Radiation

1.17 MeV

1.33 MeV

compton scattering

absorption

Polymer

Chain Scission

Ruptured Bonds

Recombination

Cross Linking
Breaking Bonds within a Microorganism
Radiolytic Products of Water

\[ \text{H}_2\text{O} + \text{H} \rightarrow \text{H}_3\text{O}^+ + \text{e}^- \]

\[ \text{H}_2\text{O} \rightarrow \text{H}_2\text{O}^+ \]

\[ \text{e}^-_{\text{aq}} + \text{H}_2\text{O} \rightarrow \text{H}_3\text{O}^+ + \text{OH} \]

\[ \text{H}_2\text{O}^+ + \text{H} \rightarrow \text{H}_3\text{O} + \text{OH} \]

\[ \text{H}_3\text{O}^+ + \text{e}^- \rightarrow \text{H}_3\text{O}^- \]

\[ \text{e}^-_{\text{aq}} + \text{e}^-_{\text{aq}} \rightarrow \text{H}_2 + 2\text{OH}^- \]

“Plus many more chemical reactions...”
Factors Affecting Lethality

- Water and Humidity
- Anoxic Conditions
- Dose Rate
- Laboratory Determination
- Oxygen
Modality Comparison

Kevin O’Hara, Director of Radiation Physics

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

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Gamma</th>
<th>X-Ray</th>
<th>E-Beam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irradiation Parameters</td>
<td>Cycle Time Density</td>
<td>Conveyor Speed Density, Scan Width, Beam Energy</td>
<td>Conveyor Speed, Scan Width, Density, Beam Energy</td>
</tr>
<tr>
<td>Radiation Field</td>
<td>Isotropic</td>
<td>Highly Directional</td>
<td>Highly Directional</td>
</tr>
<tr>
<td>Geometry of Materials and Heterogeneity of Product</td>
<td>Important to Consider</td>
<td>Important to Consider</td>
<td>Critical</td>
</tr>
<tr>
<td>Irradiator Reliability</td>
<td>Excellent</td>
<td>Good</td>
<td>Good to Excellent</td>
</tr>
</tbody>
</table>
## Summary, Irradiation modalities

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Gamma</th>
<th>X-Ray</th>
<th>E-Beam</th>
</tr>
</thead>
<tbody>
<tr>
<td>ISO 11137 Part 1</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Product Treatment</td>
<td>Pallet / Tote</td>
<td>Pallet / Tote</td>
<td>Boxes / Tote</td>
</tr>
<tr>
<td>Dose Rate (Dmin 25 kGy)</td>
<td>Hours</td>
<td>Minutes</td>
<td>Seconds</td>
</tr>
<tr>
<td>Dose Uniformity Ratio (DUR)</td>
<td>Low sensitivity to product thickness</td>
<td>Low sensitivity to product thickness</td>
<td>Sensitive to product thickness</td>
</tr>
<tr>
<td>On/Off Technology</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Flexible Target Dose</td>
<td>No</td>
<td>Yes/No</td>
<td>Yes</td>
</tr>
</tbody>
</table>
## Summary, Irradiation modalities

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Gamma</th>
<th>X-Ray</th>
<th>E-Beam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penetration - Low $\rho$</td>
<td>Good - excellent</td>
<td>Good - excellent</td>
<td>fair - good</td>
</tr>
<tr>
<td>Penetration - High $\rho$</td>
<td>effective</td>
<td>effective</td>
<td>Special processing</td>
</tr>
<tr>
<td>Processing Time</td>
<td>Good</td>
<td>Good</td>
<td>Very Good</td>
</tr>
<tr>
<td>Mechanical Properties of Product</td>
<td>Good</td>
<td>Good to Very Good</td>
<td>Very Good</td>
</tr>
<tr>
<td>Repeatability of Dose Delivery</td>
<td>Excellent</td>
<td>Very Good</td>
<td>Good</td>
</tr>
<tr>
<td>Process Validation</td>
<td>Straightforward</td>
<td>Straightforward</td>
<td>Potentially Complicated</td>
</tr>
</tbody>
</table>