Dosimetry and process control for using low energy electron beams for sterilization or decontamination of surfaces

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Introduction

• Low energy electron beams are used in different applications, including:
  – Curing / crosslinking of polymers
  – Disinfection / sterilisation of surfaces

• Pharmaceutical manufacture requires aseptic filling processes
  – Disinfection / sterilisation of the outside of tubs containing syringes of vaccines, for example
Pharmaceutical tubs

Sterilised with empty syringes, and then filled under aseptic conditions
Pharmaceutical filling line
Pharmaceutical tub filling line
Placement of dosimeters on product

• Think like an electron...!

• How do electrons get into those hidden corners?
Electron beams...

Low energy electrons scatter more than high energy electrons.

They behave more like a cloud as they scatter...
Range of electrons

- **10 MeV electrons:**
  - Water: 5 cm
  - Air: 35 m

- **80 keV electrons:**
  - Water: 0.14 mm
  - Air: 10 cm

Ti window and air

Product: 99%

Ti window: 41%

Air: 35%

Product: 24%
Depth-dose distributions

Normalised depth - dose distribution in water

Dose normalised to surface

Depth, µm, water

80 keV
125 keV
150 keV
200 keV
Depth-dose distributions

Normalised depth - dose distribution in water

Average response in dosimeter will not reflect dose at surface

Problem gets worse as dosimeter thickness increases

18 µm B3
50 µm FWT-60
135 µm alanine (density 1.35)

Dose normalised to surface

Depth, µm, water

Dose normalised to surface
Measuring the depth-dose distribution

Stack of dosimeter film

Dosimeter film under a stack of e.g. Mylar.

Beam

Dosimeter films

Thin Mylar films

Dosimeter film

• Enables us to measure $D\mu$ (absorbed dose in first $\mu$m) and relate this to apparent dose measured in reference dosimeters (e.g. alanine, thickness 135 $\mu$m)

• $D\mu$ gives traceability to national standards of absorbed dose via calibration of alanine dosimetry system
Measuring the depth-dose distribution

Depth-dose stack (here, B3)

Scan and then analyse using RisøScan
Measuring the depth-dose distribution

Measured depth dose curve

Extrapolate to surface for $D_{\mu}$ (Depth 0.5 µm)

Polynomial fit to measured doses

Here, stack of B3 films

1st measurement
2nd measurement
3rd measurement
Convert to surface dose $D_{\mu}$ (1)

- Calibration verifications carried out with alanine film dosimeters over several doses
  - Cover the range of doses expected to be used
  - Cover the range of dosimeters to be used
Convert to surface dose $D_\mu$ (2)

- Note: Dose response is *nonlinear for alanine!*
  - At high surface dose, response curve through alanine film is complex
  - Alanine response also changes with temperature
  - Alanine response measured using ESR spectrometer

- For these reasons, these calibrations are carried out by calibration laboratories

- Enables use of B3 / GEX DoseStix for routine process monitoring of surface treatment

- Uncertainty is currently quite large!
Routine process dosimetry

• Use (e.g.) GEX DoseStix
  – B3 in identified card holder

• Use reference dosimetry tub
  – Maintains distance from emitter to dosimeter, so that dosimeter does not saturate

• Use measured and otherwise identified uncertainty components to set process limits on current and conveyor speed to achieve required doses
## Example Uncertainty Budget

### Calibration

<table>
<thead>
<tr>
<th>Reference dosimeter - Alanine film</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Calibration</td>
<td>1.51</td>
</tr>
<tr>
<td>Measurement</td>
<td>1.77</td>
</tr>
<tr>
<td>Determination of $D_\mu$ (at 150 keV)</td>
<td>5.00</td>
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<tr>
<td>Alanine films total uncertainty</td>
<td>5.30</td>
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</table>

### Routine process measurement

<table>
<thead>
<tr>
<th>Routine dose - DoseStix</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Calibration</td>
<td>5.3</td>
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<tr>
<td>Dosimeter reproducibility</td>
<td>1.0</td>
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<tr>
<td>E-beam facility variability</td>
<td>7.1</td>
</tr>
<tr>
<td>Routine dose uncertainty</td>
<td>7.4</td>
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<tr>
<td>Routine dose total uncertainty</td>
<td>9.5</td>
</tr>
</tbody>
</table>

### Dose mapping

<table>
<thead>
<tr>
<th>Dose map - Risø B3 / RisøScan</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Calibration</td>
<td>6.1</td>
</tr>
<tr>
<td>Dosimeter reproducibility</td>
<td>2.00</td>
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<tr>
<td>E-beam facility variability</td>
<td>7.1</td>
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<tr>
<td>Minimum dose uncertainty</td>
<td>10.9</td>
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<tr>
<td>Minimum dose total uncertainty</td>
<td>12.5</td>
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</tbody>
</table>
Dose limits – minimum dose

• Sterilisation or disinfection
  – No measurement of bioburden is possible!
  – Device has been sterilised prior to arrival at filling line
  – It is then removed from sterile packaging and placed into filling line machinery

• Acceptance criteria for minimum dose: Usual recommendations:
  – Measured dose at minimum dose locations on the surface of the irradiated tubs must exceed 15 kGy
  – Average minimum dose should exceed 25 kGy
Dose limits

- Acceptance criteria for maximum dose:
  - Most of tub is constructed from polystyrene of about 1mm thickness
  - Maximum dose of significantly above 100 kGy will not cause problems
  - However, dose under Tyvek lid / liner should be below 2 kGy
  - Maximum dose to the top of the Tyvek lid is therefore measured to be below 100 kGy
Improvements and developments

- Currently, development is under way with UK National Physical Laboratory (NPL) of a new graphite calorimeter
  - Measure directly energy in graphite from low energy electrons (80 – 200 keV)
  - Relate response in alanine at low energies to response in this calorimeter

- Significantly reduce the uncertainty in measurement of $D\mu$
Risø Courses in 2017: see
http://www.nutech.dtu.dk/english/Products-and-Services/Dosimetry/HDRL/HDRL_Courses