Practical radiobiologic concepts all physicists should know well

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What we will cover

- Total dose versus dose per fraction: $\alpha/\beta$, BED, EQD2
- Incomplete repair
- Account for time between fractions $<24$ h
- Account for extended delivery times for each fraction
- Changes in overall time
- Gamma values
- Retreatment – review chapter 23 in BCR 5
Thames et al.  
*Int J Radiat Oncol Biol Phys*  
1982;8:219
**EQD2**

**Equivalent Dose in 2-Gy fractions**

\[
\text{EQD2} = D \left( \frac{d + \alpha}{\beta} \right)
\]

**BED = EQD0 = D \left( 1 + \frac{d}{\alpha/\beta} \right) = EQD2 \left( 1 + \frac{2}{\alpha/\beta} \right)\]

EQD2 is recommended by ICRU (Bentzen et al 2012)
Patient has metastatic bone pain localized to the 5\textsuperscript{th} thoracic vertebra. Propose palliative treatment of $4 \times 5$ Gy which includes spinal cord. Is this safe?

Take $\alpha/\beta = 2$ Gy for radiation myelopathy

$$\text{EQD2} = 20 \left( \frac{5 + 2}{2 + 2} \right) = 35$$

Currently accepted limit on spinal cord dose from QUANTEC: \textbf{50 Gy} in \textbf{2-Gy} fractions
Incomplete repair

2 fractions per day

\[
\text{EQD2} = D \left( \frac{d \left(1 + H_m\right)}{2 + \frac{a}{b}} \right)
\]

\[
H_m = \exp\left(\frac{T \ln 2}{T_{1/2}}\right)
\]

e.g. if \(\Delta T = T_{1/2}\) \(H_m = 0.5\)

if \(\Delta T = 24\) h \(H_m < 0.04\)
Repair $T_{1/2}$: CHART head and neck

Laryngeal Edema  
Telangiectasia  
s.c. Fibrosis

Incidence of laryngeal oedema (%)  
Incidence of skin telangiectasia (%)  
Incidence of subcutaneous fibrosis (%)

4.9 h (3.2–6.4)  
3.8 h (2.5–4.6)  
4.4 h (3.8–4.9)

Slow repair in late reacting tissues

- Do **NOT** do 3 fractions per day, even avoid 2
- If 2 per day, space as far apart as possible (max 12 h)
- Avoid 2 per day more than once per week
  - do it on Friday
  - safer to give the extra fraction on the Saturday
- Leave longer times between larger dose fractions
  - safer to do SBRT no quicker than 3 × per week
Dose rate effect: variation in $\alpha/\beta$

$\alpha/\beta = 10 \text{ Gy}, \quad T_{1/2} = 1 \text{ h}$

$\alpha/\beta = 3 \text{ Gy}, \quad T_{1/2} = 1 \text{ h}$
Low $\alpha/\beta$: variation in $T_{1/2}$

$\alpha/\beta = 3$ Gy,
$T_{1/2} = 1$ h

$\alpha/\beta = 3$ Gy,
$T_{1/2} = 4$ h
Dose rate effect

- For **short** repair half-times (<1.5 h), $\alpha/\beta$ is more important
- For **longer** repair halftimes (>1.5 h), $\alpha/\beta$ is less important and effectiveness is dominated by $T_{1/2}$
Loss in effective dose:
- Acute to 60 min: 8%
- 5 min to 45 min: 6%
- 5 min to 30 min: 4%

\[ \alpha/\beta = 8.7 \text{ Gy} \]
\[ T_{1/2} = 26.7 \text{ min} \]

Glioblastoma HGL21

Loss in effective dose:
- Acute to 60 min: 18%
- 5 min to 45 min: 12%
- 5 min to 30 min: 7%

Surviving Fraction vs Time (min)

- $\alpha/\beta = 0.6$ Gy
- $T_{1/2} = 69.5$ min

2 Gy in 6 “fields”

Avoid long dose delivery times

• Patient inconvenience
• Can be significant loss in effective dose
• Tumor loses more effective dose (short $T_{1/2}$)
• Late effects lose less effective dose (long $T_{1/2}$)
• More variability in treatment outcome
Overall treatment time: SCC head and neck

Split course treatment

Protraction of overall treatment time is detrimental

Bentzen and Overgaard (1996)
Lost dose from overall treatment time extension

<table>
<thead>
<tr>
<th>Tissue Type</th>
<th>$D_{\text{prolif}}$ (Gy day$^{-1}$)</th>
<th>$T_k$ (days)</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Head &amp; Neck</td>
<td>0.64</td>
<td>30</td>
<td>Hendry et al</td>
</tr>
<tr>
<td>NSCLC</td>
<td>0.60</td>
<td>30?</td>
<td>Bentzen et al</td>
</tr>
<tr>
<td>Oesphagus</td>
<td>0.59</td>
<td></td>
<td>Geh et al</td>
</tr>
<tr>
<td>Prostate</td>
<td>0.24</td>
<td>52</td>
<td>Thames et al</td>
</tr>
<tr>
<td>Breast</td>
<td>0.60</td>
<td></td>
<td>Haviland et al</td>
</tr>
<tr>
<td>Medulloblastoma</td>
<td>0.52</td>
<td>21</td>
<td>Hinata et al</td>
</tr>
<tr>
<td>GBM</td>
<td>0.30</td>
<td>37</td>
<td>Pedicini et al</td>
</tr>
</tbody>
</table>

Note: $D_{\text{prolif}}$ is shown here in EQD2
Conversion of dose to effect: Gamma

Normalized dose response gradient, $\gamma$:

$$P \approx \frac{D}{D}$$

1% change in dose gives increase in response $= \gamma \%$

Usually defined at the steepest part of curve:
With Poisson model, at Response $= 37\% (0.3679\ldots, e^{-1})$

Bentzen SM. Radiother Oncol 1994;32:1-11
Very important principles

• Never extend overall time
• Avoid unscheduled gaps during treatment
• If gaps occur, compensate without extending overall time
• Automatic treatment acceleration (gaining effective dose) usually occurs with hypofractionation/SBRT
• Retreatment – ask an expert!
What we have covered

• Total dose versus dose per fraction – Know $\alpha/\beta$, use EQD2
• Incomplete repair – Avoid it if possible
• Account for it if time between fractions <24 h
• Avoid long delivery times for each fraction
• Never extend overall time
• Using Gamma can shock you!