Isoeffective Dose Display (EQD2) for Composite Plan of Radiosurgery and Conventional 3D Radiotherapy

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Problem

Direct addition of doses between plans with different fractionation fails to provide accurate dose-response information to anticipate clinical outcome.
To consider cumulative dose for multiple courses of treatment:

- **Direct / Linear Addition of Dose**
  - Acceptable when comparing similar fraction sizes

- **Conversion to BED**
  - Provides accurate biological effects to predict outcomes, but…

  *Nobody thinks in BED* – decades of experience administering 2 Gy fractions
Solution

We desired a method to display combined volumetric dose distributions across different modalities and fractionation schemes that would be meaningful to those interpreting it.

1. **Calculate a factor** for each treatment course based on biological effect compared to 2 Gy fractions

2. **Scale RTDose distributions** using this factor and MIM software

3. **Fuse images** from each treatment course

4. **Combine RTDose distributions** for easy viewing and DVH information
BED – Biologically Effective Dose

BED (Gy) is a single quantity which may be used to compare dose given:

- at different dose rates
- to different tissues with different repair times
- or, with different fractionation schemes

\[
BED = Nd \left( 1 + \frac{d}{\alpha / \beta} \right)
\]

where:
- \( N \) is the number of fractions
- \( d \) is the dose per fraction
- \( \alpha / \beta \) ratio is associated with tissue sensitivity and repair
EQD2 – Equivalent Dose in 2 Gy Fx

EQD2 is the BED value converted back to an equivalent dose in traditional 2 Gy fractions:

\[
BED = EQD \times 2 \times \left(1 + \frac{2}{\alpha / \beta}\right)
\]

or, combining equations:

\[
Nd = EQD \times 2 \times \frac{\left[1 + \frac{2}{\alpha / \beta}\right]}{1 + \frac{d}{\alpha / \beta}}
\]
EQD2 – Equivalent Dose in 2 Gy Fx

To make it simple, consider a “2 Gy fraction conversion factor”, C:

$$EQD_2 = Nd \times C$$

which will depend on the fraction size and \(\alpha/\beta\) ratio for each case.
EQD2 – Equivalent Dose in 2 Gy Fx

Ideally, each voxel would have its own conversion factor based on:

- Dose received at that voxel
- $\alpha/\beta$ of the specific tissue in the voxel

Instead, we used a single conversion factor based on:

- Prescription dose – conservative outside target volume
- $\alpha/\beta$ of the tissue of concern – early or late effects
Patient Case #1

GammaKnife to Cerebellum

- 18 Gy x 1 fraction
- December 2011

Whole Brain RT

- 3 Gy x 10 fractions
- February 2012
Whole Brain
3 Gy x 10
Feb. 2012
$\alpha/\beta = 2.5$
$C = 1.22$

GammaKnife
18 Gy x 1
Dec. 2011
$\alpha/\beta = 2.5$
$C = 4.56$
Whole Brain
3 Gy x 10
Feb. 2012
\(\alpha/\beta = 2.5\)
\(C = 1.22\)
\(\text{EQD}_2 = 36.6 \text{ Gy}_2\)

GammaKnife
18 Gy x 1
Dec. 2011
\(\alpha/\beta = 2.5\)
\(C = 4.56\)
\(\text{EQD}_2 = 82.1 \text{ Gy}_2\)
**Linear Dose Summation**
Max Dose = 60.5 Gy
Max Brainstem EQD2 = 28.1 Gy

**EQD2 Dose Summation**
Max EQD2 = 178.5 Gy
Max Brainstem EQD2 = 46.7 Gy
Patient Case #2

CyberKnife to Sacrum

- 15 Gy x 1 fraction
- January 2009

3D Bilateral Pelvis

- 3 Gy x 10 fractions
- June 2010

CyberKnife to Sacrum

- 10 Gy x 1 fraction
- November 2010
Cyberknife Sacrum
15 Gy x 1
Jan. 2009
$\alpha/\beta = 2.5$
$C = 3.89$

L/R Pelvis
3 Gy x 10
Jun. 2010
$\alpha/\beta = 2.5$
$C = 1.22$

Cyberknife Sacrum
10 Gy x 1
Nov. 2010
$\alpha/\beta = 2.5$
$C = 2.78$
Cyberknife Sacrum
15 Gy x 1
Jan. 2009
α/β = 2.5
C = 3.89
EQD2 = 58.4 Gy

L/R Pelvis
3 Gy x 10
Jun. 2010
α/β = 2.5
C = 1.22
EQD2 = 36.6 Gy

Cyberknife Sacrum
10 Gy x 1
Nov. 2010
α/β = 2.5
C = 2.78
EQD2 = 27.8 Gy
EQD2 Dose Summation
Max EQD2 = 132.9 Gy
Max Sacral Nerve EQD2 = 87.8 Gy

Linear Dose Summation
Max Dose = 55.5 Gy
Max Sacral Nerve EQD2 = 28.8 Gy
Improvements to the Method

1. Automated workflow in MIM

2. Voxel-by-voxel calculation

3. Overestimation of BED at high dose per fraction
   - LQL model
   - gLQ model

4. Incorporation of repair time
   - Between courses of treatment (months – years)
   - Within course of treatment (daily, EOD, BID)
   - Within fraction (treatments lasting > 15 minutes)
Conclusions

1. **Successful method to display dose based on equivalent biological effect** in 2 Gy fractions

2. **Generally conservative outside the target region** (<Rx dose), and underestimates hot spots within the target ( >Rx dose).

3. **Depends greatly on** $\alpha/\beta$, so create a distribution for early effects ($\alpha/\beta \sim 10$) and late effects ($\alpha/\beta \sim 2.5$)

4. **Somewhat laborious process** that would be improved with a workflow script