Clinical Radiobiology of Brachytherapy

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Brachytherapy

• Temporal insertion of one radioactive source in or close to the tumour.
  - afterloading techniques using various applicators.

• Permanent insertion of radioactive sources in or close to the tumour
Brachytherapy

Rationale:

• steep dose gradient outside the tumour
• small or no margin needs to be added to the CTV

=> a high dose to the tumour while sparing organs at risk

=> potential for radiobiological optimisation
Main sources used today

In afterloaders (3.5 x 1 mm)
  Ir-192
  Co-60

Seeds (4-5 x 1 mm)
  I-125
  Pd-103
Applicators
Permanent implant
Dose distributions
Dose distributions
Dose distributions
Dose distributions

Dose-volume histogram for PTV / CTV

- **PTV - EBRT**
- **CTV - EBRT**
- **CTV - BT**
- **PTV - BT**
Dose distributions

Dose-volume histogram for urinary bladder

- **external beam therapy**
- **brachytherapy**

- absorbed dose [% of prescribed dose]
- urinary bladder volume [%]
Dose delivery

LDR

HDR

PDR

pLDR
The linear-quadratic model

Absorbed dose is not proportional to biological effect!

Fractionation sensitivity:

$$EQD_2 = D \left( \frac{d + \alpha/\beta}{2 + \alpha/\beta} \right)$$

$\alpha/\beta$ is a tissue specific parameter

$\approx 3$ Gy for normal tissue

$\approx 10$ Gy for most tumours
The linear-quadratic model
Fractionation sensitivity:

![Graph showing total dose required to deliver EQD2 = 50 Gy3 versus number of fractions.](chart.png)
The linear-quadratic model

Dose rate effect:

\[ EQD_2 = D \left( \frac{gD + \alpha/\beta}{2 + \alpha/\beta} \right) \]

\[ g = 2 \left( \frac{\mu t - 1 + e^{-\mu t}}{(\mu t)^2} \right) \]

Recovery half time:

0.5 – 6 hours in normal tissue

\[ \mu = \frac{\ln(2)}{T_{1/2}} \]
The linear-quadratic model
Dose rate effect:

total dose to deliver $\text{EQD}_2 = 30 \text{ Gy10 (T1/2 = 1.5 h)}$
The linear-quadratic model

PDR

solvable using $\alpha/\beta$ and $T_{1/2}$
The dose distribution is inhomogeneous in the PTV.
The dose distribution is inhomogeneous in the PTV

- MRI-based brachytherapy for cervical cancer
- 25-28x1.8 + 4x7.0 Gy
- Analysing $D_{90\%}$

Radiotherapy & Oncology 2009
Dimopoulos et al (Vienna)
Dose-effect relationship for local control of cervical cancer by magnetic resonance image-guided brachytherapy.

EQD2 [Gy10]
The dose distribution is inhomogeneous in organs at risk close to the PTV.
The dose distribution is inhomogeneous in organs at risk close to the PTV.

- MRI-based brachytherapy for cervical cancer
- 25+28x1.8+4x7.0 Gy
- rectal toxicity
- bladder toxicity

EQD2 [Gy3]

D2cc [Gy]

Probability of rectum side effects G2.4
The dose can be delivered in a number of different ways

Prostate cancer...

EBRT: 39x2.0 (probably...)
EBRT+BT: 23x2.0 + 2x9.5 Gy
pLDR BT: 120 Gy with Pd-103
HDR BT: 4x9.5 Gy

EBRT+PDR BT: 28x1.8 + 3x6.0 Gy
(40-80 minutes to give 6 Gy)

Mohammed et al (WBH)
COMPARISON OF ACUTE AND LATE TOXICITIES FOR THREE MODERN HIGH-DOSE RADIATION TREATMENT TECHNIQUES FOR LOCALIZED PROSTATE CANCER

Radiotherapy and Oncology (2006)
Izard et al
SIX YEAR EXPERIENCE OF EXTERNAL BEAM RADIOTHERAPY, BRACHYTHERAPY BOOST WITH A 1Ci 192 Ir SOURCE, AND NEOADJUVANT HORMONAL MANIPULATION FOR PROSTATE CANCER
Wrap up

Tumour control probability

• make sure to cover the tumour with adequate dose (minimum dose)
• can we use the LQ-model to optimise our fractionation schedules at high doses per fraction?
Wrap up

Normal tissue complication probability

The Quantec issue of the Red Journal in 2010


INTRODUCTORY PAPER

USE OF NORMAL TISSUE COMPLICATION PROBABILITY MODELS IN THE CLINIC

Lawrence B. Marks, M.D., Ellen D. Yorke, Ph.D., Andrew Jackson, Ph.D.,
Randall K. Ten Haken, Ph.D., Louis S. Constine, M.D., Avraham Eisbruch, M.D.,
Søren M. Bentzen, Ph.D., Jiho Nam, M.D., and Joseph O. Deasy, Ph.D.
Wrap up

Normal tissue complication probability

The Quantec issue of the Red Journal in 2010
Wrap up

Normal tissue complication probability

Evolving Fractionation Schedules

RT-induced normal tissue responses are fraction size dependent. Throughout the QUANTEC reviews, this variable is acknowledged and, where possible, considered by making adjustments for fraction size based on the linear quadratic (LQ) model. Nevertheless, $\alpha/\beta$ ratios are uncertain. Particular care must be taken when QUANTEC information is applied to stereotactic RT, where the fraction size is much different than that in the cited literature. For very novel fractionations, even the validity of the LQ model is questioned (2).
Wrap up

Normal tissue complication probability

- LQ-model?
- Addition of EBRT & BT?