College of Health and Medical Technologies

Department of Radiology Technologies

Radiobiology

The first stage

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Tumor response to radiation

Lecture No.9

The aim of radiotherapy is to annihilate the tumor tissue while minimizing damage to the normal surrounding tissues. Thus, the radio-sensitivities of the tumor and its surrounding tissues are important considerations when determining the best treatment.

It is well known that cells in tumor tissues have chaotic growth patterns and various radio-sensitivities.

Furthermore, tumor cells exhibit a variety of size, chromosome structures, and cytoplasms. However, this is not true of neighboring normal tissue cells.

The principle of *primum non nocere* is always valid in radiotherapy. In light of this principle, several concepts for destroying the tumor while protecting healthy tissues have been developed in the field of radiation oncology.

The therapeutic index

defines how the tumor control probability (TCP) relates to the normal tissue complication probability (NTCP) for different doses. Normal tissues may get damaged by the dose required to control the tumor; on the other hand, the tumor may not receive an adequate dose if the normal tissues require protection.

Achieving the optimal balance between TCP and NTCP is a basic aim of radiotherapy. All new technologies are directed towards this aim.

The therapeutic index (= therapeutic window) increases if the region the between two curves become large, and the expected benefit from treatment increases.

When the fraction dose is increased from 2 to 2.5 Gy, the total dose to control the tumor decreases. Since the maximum tolerable dose is constant, the total dose received by normal tissue increases and the therapeutic window narrows.

Tumor Control Probability (TCP)

The efficacy of radiotherapy treatment is evaluated by the locoregional TCP and the treatment-related NTCP.

TCP is directly proportional to the dose and inversely proportional to the number of cells in the tissue (or the volume of the tumor). The total dose required to control the subclinical disease in epithelial cancers is 40–50 Gy, whereas it is 60–70 Gy for clinically observable gross disease. The most important dose-limiting factor is the tolerance of the surrounding tissues to radiation.

Local tumor control. This is the destruction of tumor cells, where they are determined.

It is also defined as the death of the last clonogenic cancer cell.

Radiation affects tumor cells in a very similar way to normal tissue and organs; its effect is nonspecific.

Tumoral factors affecting the TCP:

1. Intrinsic radiosensitivity
2. Location and size of tumor
3. Cellular type of tumor
4. Effect of oxygen
5. Treatment-related factors affecting the TCP:
6. Dose–time fractionation
7. Radiation quality (RBE, LET)
8. Dose rate
9. Use of radiosensitizers
10. Combination of radiotherapy with surgery and/or chemotherapy
11. Technique (e.g., small field sizes)
12. Treatment modality (e.g., brachytherapy, conformal RT, IMRT, IGRT, targeted RT

The dose needs to be increased threefold to increase the TCP from 10 to 90%.

Normal Tissue Complication Probability (NTCP)

The TCP is a function of the total dose, fraction dose, irradiated volume including the whole tumor, and treatment reproducibility . The NTCP is a function of the total dose, fraction dose, fraction number and the volume of tissue exposed to the radiation.

Factors affecting NTCP :

1. **Factors related to organ tissue**

A. Tissue radiosensitivity
B. The volume of organ tissue within the radiotherapy portal
C. Organ type: serial or parallel

2.Factors related to treatment

A. Dose-time fractionation
B. Quality of radiation (RBE, LET)
C. Dose rate
D. Use of radioprotectors
E. Combination of RT with surgery and/or chemotherapy
F. Technique (e.g., addition of boost field)
G. Treatment modality (e.g., brachytherapy, conformal RT, IMRT, IGRT, targeted RT).

The Clinical Importance of TCP and NTCP

• The TCP and NTCP can be used to estimate the treatment success and side effects in particular.

• Dose–volume histograms created by treatment planning systems (particularly 3D-conformal radiotherapy and IMRT) as well as TCP and NTCP mathematical modeling are very useful for graphically demonstrating normal tissue damage ratios within the treated tumor volume, and can be used to guide clinicians during treatment planning