

TEACHING INSTRUCTIONAL DESIGN (BRP)

COURSE

RADIOBIOLOGY

by

Kristina Tri Wigati, M.Si Supriyanto Ardjo Pawiro, Ph.D.

Undergraduate Program in Physics Faculty of Mathematics and Natural Sciences Universitas Indonesia Depok

December 2016

PREFACE

Buku Rancangan Pembelajaran (BRP) ini disusun sebagai panduan kegiatan perkuliahan Radiobiologi bagi mahasiswa semester enam yang telah memperoleh mata kuliah Anatomi dan Fisiologi serta Pendahuluan Fisika Radiologi dan Dosimetri.

Mata kuliah ini memberikan bekal bagi mahasiswa untuk memiliki pengetahuan mengenai efek radiasi pada sel hidup terjadi pada semua aktivitas medis yang memanfaatkan radiasi pengion, dalam bidang Radiologi Diagnostik, Radioterapi, dan Kedokteran Nuklir. Metode pembelajaran dirancang sedemikian rupa agar mahasiswa tidak hanya mampu bekerja mandiri, namun juga dapat bekerja dalam kelompok, untuk menguasai materi secara komprehensif dan integratif.

Semoga BRP ini dapat memberikan arahan dalam proses pembelajaran agar terpenuhi semua sasaran yang diharapkan baik bagi dosen maupun mahasiswa.

Depok, December 2016

Kristina Tri Wigati, M.Si.

Supriyanto Ardjo Pawiro, Ph.D.

I. General Information

1.	Nama of Program / Study Level	:	Physics / Undergraduate
2.	Course Name	:	Radiobiology
3.	Course Code	:	SCFI603915
4.	Semester	:	6
5.	Credit(s)	:	2 credits
6.	Teaching Method(s)	:	Collaborative learning
7.	Prerequisite course(s)	:	Anatomy and Physiology
8.	Requisite for course(s)	:	-
9.	Integration Between Other Courses	:	Introduction to Radiotherapy, Introduction to Medical Imaging and Nuclear Medicine.

:

- 10. Lecturer(s)
- 11. Course Description

: Review radiation interaction with matter, radiation damage on DNA, damage repair of DNA, radiation induced chromosomal damage and reparation, survival curve, cell lethality: concept of cell lethality (apoptosis and reproduction of lethal cell), cellular healing process, cell cycle, response modifiers radiation-sensitizer and protector, RBE, OER, and LET, cell kinetics, radiation damage on tissue, radiation pathology acute and advanced effects, histopathology, tumor radiobiology, TDF (time, dose, and fractionation), radiation genetics: effects of radiation on fertility and mutagenesis, and molecular mechanisms

II. Course Learning Outcome (CLO) and Sub-CLO

A. CLO

After completing this course, students are able to explain various aspects related to Radiobiology and its application in the fields of Diagnostic Radiology, Radiotherapy, and Nuclear Medicine. (ELOs 3,5,6, and 7)

B. Sub-CLO

- 1. Describe the physical and chemical process of radiation absorption in biological cells (C3).
- 2. Studying DNA damage and chromosome aberration (C1).
- 3. Studying normal and tumor cell survival curves (C1).
- 4. Perform calculations of the survival and death of normal and tumor cells (C3).
- 5. Studying radiosensitivity and cell age in the mitotic cycle (C1).
- 7. Study the radiation damage repair and dose rate effects (C1).
- 8. Studying the oxygen effects and reoxygenation (C1).
- 9. Describe Linear Energy Transfer (LET) and Relative Biological Effectiveness (RBE) (C2).
- 10. Understand determining factors of RBE (C4).
- 11. Studying the acute effects of Total-Body Irradiation (TBI) (C1).
- 12. Studying the radioprotector (C1).
- 13. Studying radiation carcinogenesis (C1).
- 14. Studying the heredity effect of radiation (C1).
- 15. Calculating the risk of heredity of radiation (C3).
- 16. Studying the effects of radiation on the embryo and fetus (C1).
- 17. Studying cataracts caused by radiation (C1).

18. Studying dosage and risk in Diagnostic Radiology, Interventional Radiology and Cardiology, and Nuclear Medicine (C1).

- 19. Studying radiation protection (C1).
- 20. Studying the normal tissue model in Radiotherapy (C1).
- 21. Studying the tumor cell model in Radiotherapy (C1).
- 22. Studying time, dose, and fractionation (TDF) in Radiotherapy (C1).
- 23. Perform TDF calculation in Radiotherapy (C3).
- 24. Studying alternative modalities of cancer therapy (C1).

III. Teaching Plan

Week	Sub-CLO	Study Materials	Teaching Method	Time Required	Learning Experience (*O-E-F)	Sub-CLO Weight on Course (%)	Sub-CLO Achievement Indicator	References
1	1	Physics and chemistry of radiation absorption	Lecturing	100 minutes	50% O, 0% E, 50% F	4	To describe types of ionizing radiation, absorption of X-rays, direct and indirect action of radiation, absorption of neutrons, and difference between neutrons and photons. Menjelaskan jenis radiasi pengion, absorpsi sinar-X, efek radiasi langsung dan tidak langsung, absorpsi neutron, dan perbedaan antara neutron dan foton.	1 and 2
2, 3	2,3,4	DNA damage and chromosomal aberrations; Cell survival curves	Lecturing	200 minutes	50% O, 0% E, 50% F	8	To describe DNA strand breaks, measurements of DNA strand breaks, chromosomes and cell division, the role of telomers, radiation-induced chromosome aberrations, examples of radiation-induced aberrations, chromosome aberrations in human lymphocytes; To describe reproductive integrity, the <i>in vitro</i> survival curve, the shape of survival curve, mechanisms of cell killing, survival curves for various mammalian cells in culture, survival curve shape and mechanisms of cell death, oncogenes and radioresistance, genetic control of radiosensitivity, intrinsic radiosensitivity and cancer stem cells, effective survival curve for a multifraction regimen, calculation of tumor cell kil, the radiosensitivity of	1 and 2

							mammalian cells compared with	
4,5	5,6	Radiosensitivity and cell age in mitotic cycle; Fractionated radiation and the dose-rate effect	Lecturing	200 minutes	50% O, 0% E, 50% F	8	microorganisms To describe the cell cycle, synchronously dividing cell cultures, the effects of X-rays on synchronously dividing cell cultures, molecular checkpoint genes, the effect of oxygen at various phases of the cell cycle, the age-response function for a tissue <i>in</i> <i>vivo</i> , variation of sensitivity with cell age for neutron radiation, mechanisms for the age-response function, and the possible implications of the age- response function in radiotherapy; To describe operational classifications of radiation damage, lethal damage, mechanism of sublethal damage repair, repair and radiation quality, the dose- rate effect, examples of the dose-rate effect <i>in vitro</i> and <i>in vivo</i>	1 and 2
6,7	7,8,9	Oxygen effect and reoxygenation; Linear Energy Transfer (LET) and Relative Biological Effectiveness (RBE)	Lecturing	200 minutes	50% O, 0% E, 50% F	8	To describe the nature of the oxygen effect, the time at which oxygen acts and the mechanism of the oxygen effect, the concentration of oxygen required, chronic and acute hypoxia, the first experimental demonstration of hypoxic cells in a tumor, proportion of hypoxic cells in various animal tumors, evidence for hypoxia in human tumors, techniques to measure tumor oxygenation, reoxygenation, time sequence of reoxygenation, mechanism of reoxygenation, the importance of reoxygenation in radiotherapy, hypoxia and tumor progression; To describe the deposition of radiant energy, LET, RBE, RBE and fractionated doses, RBE for different cells and tissues, RBE as a function of LET, the optimal LET, factors that	1 and 2

							determine RBE, the oxygen effect and	
							LET, radiation weighting factor	
8					Mid-Term Exam			
9, 10	10,11,12	Acute radiation syndrome, Total Body Irradiation (TBI); Radioprotector; Radiation carcinogenesis	Lecturing	200 minutes	50% O, 0% E, 50% F	8	To describe early lethal effects, the prodromal radiation syndrome, the gastrointestinal syndrome, the hematopoietic syndrome, average lethal dose and bone-marrow transplantation, treatment of radiation accident victims exposed to dose close to the LD _{50/60} , survivors of radiation accidents, radiation emergency assistance center; To describe the discovery of radioprotectors, mechanism of action, development of more effective compounds, amifostine (WR-2721) as a radioprotector in radiotherapy, and radioprotector and chemotherapy; To describe deterministic and stochastic effects, the human experience of carcinogenesis, the latent period, assessing the risk, committees concerned with risk estimates and radiation protection, leukemia, thyroid cancer, breast cancer, lung cancer, bone cancer, skin cancer, quantitative risk estimates for radiation-induced cancer, dose and dose-rate effectiveness factor, second malignancies in radiotherapy patients, cancer risks in nuclear industry workers, childhood cancer after radiation exposure in utero.	1 and 2
11,12	13,14,15,16	Heritable effects of radiation; Effects of radiation on the embryo and fetus; Radiation	Lecturing	200 minutes	50% O, 0% E, 50% F	6	To describe germ cell production and radiation effects on fertility, mutations, absolute and relative mutation risks, radiation-induced heritable effects in mice, radiation-induced heritable effects in humans, estimates of	1 and 2

		cataractogenesi					hereditary risks; To describe overview of radiation effects on the embryo and fetus, data from mice and rats, experience in humans, survivors of the A-bomb attacks on Hiroshima and Nagasaki irradiated in utero, exposure to medical radiation, comparison of human and animal data, occupational exposure of women, the pregnant or potentially pregnant patient; To describe cataracts of the ocular lens, lens opacification in experimental	
13	17,18,19	Dose and risks in Diagnostic Radiology, Interventional Radiology and Cardiology, and Nuclear Medicine;	Lecturing	200 minutes	50% O, 0% E, 50% F	6	animals, radiation cataracts in humans, dose-response relationship for cataracts in humans To describe doses from natural background radiation, comparison of radiation doses from natural sources and human activities, diagnostic radiology, interventional radiology and cardiology, nuclear medicine, medical irradiation of children and pregnant women; To describe national council on radiation protection, quantities and units, dose, radiation weighting factor, equivalent dose, effective dose, principles of radiation protection, basis for exposure limits, limits for occupational exposure, As Low As Reasonably Achievable (ALARA),	1 and 2
		Radiation protection; Radiobiology in radiotherapy – part I					protection of the embryo / fetus, emergency occupational exposure, exposure of persons younger than 18 years, exposure of members of the public, exposure to indoor radon ; comparison between National Council on Radiation Protection and Measurements (NCRP) and International Commission on Radiation Protection (ICRP); To describe dose-	

							response relationship for model normal tissues, mitotic death and apoptosis, dose-response relationships, clinical response of normal tissue, cell and tissues, early and late effects, functional subunits in normal tissues, the volume effects in radiotherapy, radiation pathology of tissues, classification of tissue radiosensitivity, growth factors, specific tissues and organs	
14	20,21,22, 23,24	Radiobiology in radiotherapy – part II; Radiobiology in radiotherapy – part III	Lecturing	200 minutes	20% O, 60% E, 20% F	8	To describe model tumor systems, transplantable solid tumor systems, tumor growth measurements, Tumor Cure (TCD ₅₀) assay, dilution assay technique, lung colony assay, <i>in vivo /</i> <i>in vitro</i> assay, xenografts of human tumors, spheroids: an <i>in vitro</i> model tumor system, spheroids of human tumor cells, comparison of the various model tumor systems, apoptosis in tumors, cell, tissue, and tumor kinetics, time, dose and fractionations in radiotherapy, the 5Rs of radiobiology (Repair, Repopulation, Radiosensitivity, Redistribution, Reoxygenation), isoeffect curve, Linear-Quadratic (LQ) parameter, Biological Effective Dose (BED), Linear-Quadratic Equivalent Dose (LQED), residue damage and treatment repetition, accelerating repopulation in normal and tumor cells, time factor in radiotherapy, the concept of Tumor Control Probability (TCP) and Normal Tissue Complication Probability	1 and 2

	(NTCP) model, fractionation modification (hiper-, hipo-, accelerated, concomitant boost; To describe alternative radiation modality, radiosensitizer and bioreductive drugs, gene therapy, chemotherapy agent from hyperthermia radiobiologist				
	perspective				
15	Final Exam				

*) O : Orientation

- E : Exercise
- F : Feedback

References:

1. G. Gordon Steel (Editor). Basic Clinical Radiobiology, Edward Arnold, London, UK, 1993.

2. Eric J. Hall . Radiobiology for the Radiologist. 5th ed., Lippincott Williams and Wilkins, Philadelphia, PA, 2000.

IV. Assignment Design

Week	Assignment Name	Sub-CLO	Assignment	Scope	Working Procedure	Deadline	Outcome
1	Tugas Mandiri 1	1	Problem Set	Physics and chemistry of radiation absorption	Individual homework	1 week	Answer sheet
2	Tugas Mandiri 2	2,3,4	Problem Set	DNA damage and chromosomal aberrations; Cell survival curves	Individual homework	1 week	Answer sheet
3	Tugas Mandiri 3	5,6	Problem Set	Radiosensitivity and cell age in mitotic cycle; Fractionated radiation and the dose-rate effect	Individual homework	1 week	Answer sheet
4	Tugas Mandiri 4	7,8,9	Problem Set	Oxygen effect and reoxygenation; Linear Energy Transfer (LET) and Relative Biological Effectiveness (RBE)	Individual homework	1 week	Answer sheet

5		Mid-Term Exam							
5	Tugas Mandiri 5	10,11,12	Problem Set	Acute radiation syndrome, Total Body Irradiation (TBI); Radioprotector; Radiation carcinogenesis	Individual homework	1 week	Answer sheet		
6	Tugas Mandiri 6	13,14,15,16	Problem Set	Heritable effects of radiation; Effects of radiation on the embryo and fetus; Radiation cataractogenesis	Individual homework	1 week	Answer sheet		
7	Tugas Mandiri 7	17,18,19	Problem Set	Dose and risks in Diagnostic Radiology, Interventional Radiology and Cardiology, and Nuclear Medicine; Radiation protection; Radiobiology in radiotherapy – part I	Individual homework	1 week	Answer sheet		
8	Tugas Mandiri	20,21,22,23, 24	Problem Set	Radiobiology in radiotherapy – part II; Radiobiology in radiotherapy – part III	Individual homework	1 week	Answer sheet		
9	Final Exam								

Evaluation Type	Sub-CLO	Assessment Type	Frequency	Evaluation Weight (%)
Quiz	1-23	Quiz	4	20
Individual Assignment	1-23	Problem Set	14	20
Mid-Term Exam	1-9	Essay	1	30
Final Exam	10-24	Essay	1	30
	Total		•	100

V. Assessment Criteria (Learning Outcome Evaluation)

VI. Rubrik

A. Criteria for Individual Assignment

Score	Presentation Delivery
>90	Students can solve more than 90% of the problem correctly
70-89	Students can solve between 70% to 89% of the problem correctly
60-69	Students can solve between 60% to 69% of the problem correctly
55-59	Students can solve between 55% to 59% of the problem correctly
50-54	Students can solve between 50% to 54% of the problem correctly

B. Quiz, Mid-Term Exam, and Final Exam

- [1] Able to express ideas in solving problems (25%)
- [2] Able to determine the right basic concepts in solving problems (35%)
- [3] Able to formulate final solutions (30%)
- [4] Able to use appropriate units and significant figures (10%)