POSTGRADUATE INSTITUTE OF MEDICINE
UNIVERSITY OF COLOMBO

MD (CLINICAL ONCOLOGY) PART I EXAMINATION – AUGUST 2018

Date: 27th August 2018 **Time: 2.00 p.m. – 4.15 p.m.**

PAPER I

If the examiners cannot read your writing, they will be unable to give you full credit for your knowledge.

PHYSICS

Each question carries 100 marks.
Each question to be answered in a separate book.
Question one is compulsory.
Answer five questions of the six questions from 2 to 7.

1.

1.1.

(a) Define the term "Effective Dose" and list the two units used to measure this quantity. (15 marks)

(b) List effective dose limits recommenced for radiation workers and public of Sri Lanka. (10 marks)

1.2.

(a) In terms of Sri Lanka Atomic Energy Act No.40 of 2015, what are the legal requirements to be fulfilled in sequential order to establish a new Radiotherapy facility. (15 marks)

(b) What are the licence periods respectively for a Tele-Gamma Facility and a Linear Accelerator Facility as given in the Atomic Energy (Licence) Rule No. 1 of 2015? (10 marks)

1.3.

(a) What are the aims of radiation protection with regard to radiation effects. (10 marks)

(b) List three exposure categories recognized for radiation protection standards by the ICRP. (15 marks)

1.4.

(a) Briefly explain what is meant by external radiation hazards (10 marks)

(b) List basic methods used to control the external radiation hazards. (09 marks)

(c) Explain one method in 3-4 sentences giving practical examples. (06 marks)

Contd...../2-

2.

2.1. What is meant by the activity of a radionuclide? (10 marks)

2.2. Define the half-life of a radionuclide (15 marks)

2.3. Write down the decay process, photon energies and the half-life of a ^{60}Co radionuclide. (20 marks)

2.4. Briefly explain the main interaction process of ^{60}Co gamma rays in human body. (20 marks)

2.5. List four (04) daily quality control parameters of a ^{60}Co teletherapy machine and give their tolerances. (20 marks)

2.6. Find the number of gamma rays emitted from a ^{60}Co source per minute if the activity is 2 Ci (15 marks)

3.

3.1. Explain the following terms with reference to ICRU report 50

(a) Treated volume (TV) (15 marks)

(b) Irradiated volume (IV) (15 marks)

(c) Organ at risk (OAR) (15 marks)

3.2. Explain how the field size relates to planning target volume and why this is different on a Linac and cobalt teletherapy machine. (15 marks)

3.3. Briefly describe Beams Eye View (BEV) in radiotherapy treatment planning (10 marks)

3.4. (a) What is meant by following terms

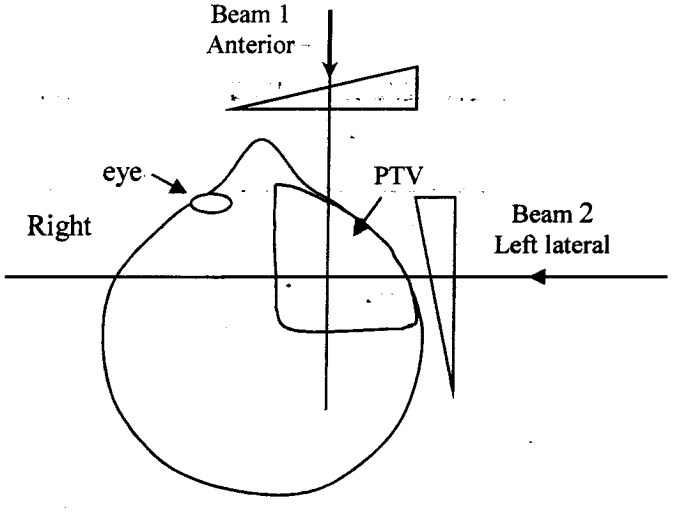
(i) Conformity index (10 marks)

(ii) Integral dose (10 marks)

(b) How are they used in comparing treatment plans? (10 marks)

Contd...../3-

4. A patient with carcinoma of the left maxillary antrum has been planned to deliver a dose of 66 Gy to the PTV in 33 fractions over 6½ weeks from 6 MV photons at 100 cm SAD from a linear accelerator machine as shown in figure below. Patient lies in supine position and a thermoplastic shell is used for immobilization.



Machine calibration conditions:
Ionization chamber at 1.5 cm depth in water at 100 cm source chamber distance
Dose rate of 6 MV machine is 1 cGy /MU for 10 cm x 10 cm field size

Description	Beam 1 (Anterior)	Beam 2 (Left Lateral)
Gantry angle	0°	90°
Tissue depth to beam isocenter (cm)	3.5	3.0
Treatment field size (cm)	$X_1 = 3.5, X_2 = 4.5$ $Y_1 = 5.5, Y_2 = 4.5$	$X_1 = 4.0, X_2 = 5.0$ $Y_1 = 5.5, Y_2 = 4.5$
Tissue maximum ratio	0.964	0.982
Wedge transmission factor	0.586	0.588
Collimator scatter factor	0.994	0.997
Phantom scatter factor	0.996	0.998

4.1.

(a) Find the dose rate in water at the points of dose maximum for both wedged beams. (20 marks)

(b) Assuming equal dose contribution to the centre of PTV from both beams; calculate the number of monitor units (MUs) required per field per fraction. (20 marks)

4.2. How will you protect the right eye exposed during the treatment and state the potential issue when doing so? (10 marks)

Contd...../4-

4.3. What are suitable wedge angles for this treatment? (10 marks)

4.4. Illustrate two more field arrangements to treat above patient which may protect the ipsilateral eye. (20 marks)

4.5.

(a) List two dosimeters to be used to measure the dose to lens of the eye. (10 marks)

(b) Give an advantage and a disadvantage for one of the above dosimeters. (10 marks)

5.

5.1. List two advantages and two disadvantages of Intensity Modulated Radiation Therapy (IMRT) compared to 3D CRT. (20 marks)

5.2. Sketch the typical cumulative DVH for an IMRT treatment plan indicating GTV, CTV, PTV and OAR on it. (20 marks)

5.3. Briefly discuss the following IMRT techniques

(i) Static MLC (15 marks)

(ii) Dynamic MLC (15 marks)

5.4. Briefly explain Intensity Modulated Arc Therapy (IMAT). (20 marks)

5.5. Give one advantage and one disadvantage of IMAT. (10 marks)

6. A female patient has undergone a right lumpectomy and a boost dose is planned to be given to the tumour bed from a direct electron beam from a Linear Accelerator machine. The target depth from the skin is 3 cm and the target size is 4 cm x 5 cm.

6.1. What is the most appropriate electron beam energy and applicator size, assuming that there is no skin involvement. If a custom block is used, what is the thickness to be used and what will be the size of the cut-out field for this treatment? Justify your answer. (30 marks)

6.2. Draw two curves of percentage depth dose at 100 cm SSD in the same graph for above electron beam if the beam passes through

(a) a water phantom (10 marks)

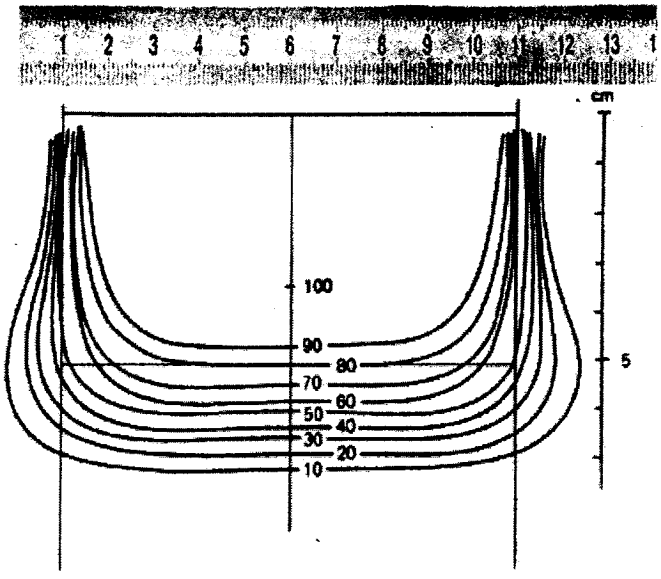
(b) 4 cm lung of the above patient (10 marks)

Contd...../5-

6.3. How does the skin dose vary with electron beam energy? (10 marks)

6.4. List 2 advantages and 2 disadvantages of using an electron beam as compared to a superficial kilovoltage photon beam (DXRT) in treating small fields. (20 marks)

6.4. The following isodose curves were obtained from an electron beam of a Linear Accelerator machine in the principal plane in water at 100 cm SSD. Identify the electron energy of the beam and the field size. Justify your answer. (20 marks)



7.

7.1. Write down the distribution rules for a single plane implant in Manchester system as regards to interstitial Brachytherapy. (15 marks)

7.2. List important four (04) physical properties of ^{192}Ir that makes it suitable for temporary implants in Brachytherapy. (20 marks)

7.3. Why is ^{226}Ra no longer used in Brachytherapy? (15 marks)

7.4. Give two advantages and two disadvantages of HDR Brachytherapy compared to LDR Brachytherapy. (20 marks)

7.5. The exposure rate in air at 1m from a ^{137}Cs source is 2 R/hr (HVL of Lead is 6mm for ^{137} Cs source).

(a) Find the exposure rate in air at 20 cm from the source (15 marks)

(b) What would be the thickness of Lead required to reduce the exposure rate to 6.25 R/hr at 20cm distance? (15 marks)

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MD (CLINICAL ONCOLOGY) PART I EXAMINATION – AUGUST 2018

Date: 27th August 2018 **Time: 4.30 p.m. – 5.15 p.m.**

PAPER I

If the examiners cannot read your writing, they will be unable to give you full credit for your knowledge.

MEDICAL STATISTICS

Each question carries 100 marks.
Each question to be answered in a separate book.
Answer TWO (02) questions of the THREE (03) questions given below.

1. A matched case-control study was conducted involving 500 patients with breast cancer and 500 controls to determine risk factors for breast cancer. The results are given below.

Logistic regression analysis of breast cancer-related factors

Variables	Unadjusted OR	95% CI		Adjusted OR	95% CI		p
Family history of breast cancer	1.88	1.33	2.65	2.42	1.36	4.29	0.003
Menopause	1.72	1.33	2.23	1.98	1.36	2.89	<0.001
Present life satisfaction: Low	1.95	1.66	2.29	1.85	1.44	2.39	<0.001

1.1. Outline the steps in designing the above study. (20 marks)

1.2. Propose a suitable control group for the above study. Justify your answer. (20 marks)

1.3. State one advantage and one disadvantage of matching. (10 marks)

1.4. List two types of information bias and briefly explain how you would minimize such bias. (20 marks)

1.5. Briefly explain how you would calculate unadjusted odds ratio. (10 marks)

1.6. Interpret the adjusted odds ratio for family history of breast cancer and corresponding 95% confidence interval. (20 marks)

Contd...../2-

2. Cancer patients with psychological distress were randomized into two interventions, 'Mindfulness-based cognitive therapy' (MBCT) and 'treatment as usual' (TAU). The primary outcome was psychological distress measured by the Hospital Anxiety and Depression Scale (the total score ranged 1 to 30). Compared with TAU, patients reported significantly less psychological distress after MBCT ($p < 0.001$). In addition, post-treatment prevalence of psychiatric diagnosis was lower with MBCT (33%; $p = 0.03$) in comparison with TAU (16%).

2.1. State the objective of the above study. (20 marks)

2.2. Explain how you would allocate the patients into two groups to minimize selection bias. (20 marks)

2.3. What would be the effect of blinding for the results of the trial? (20 marks)

2.4. What is meant by 'primary outcome'? (10 marks)

2.5. Name a statistical test to compare psychological distress levels. (10 marks)

2.6 What is the conclusion of this trial? (20 marks)

3. Write notes on the following

3.1. Validity of a screening test (25 marks)

3.2. Kaplan-Meier survival curve (25 marks)

3.3. Non-parametric tests (25 marks)

3.4. External validity (25 marks)

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MD (CLINICAL ONCOLOGY) PART I EXAMINATION – AUGUST 2018

Date: 28th August 2018 **Time: 9.00 a.m. – 9.45 a.m.**

PAPER II

If the examiners cannot read your writing, they will be unable to give you full credit for your knowledge.

PATHOLOGY

Each question carries 100 marks.
Each question to be answered in a separate book.
Answer TWO (02) questions of the THREE (03) questions given below.

1. 64-year-old female has a pigmented lesion on the forehead suspicious of a malignant melanoma.

   1.1. What clinical features would make the lesion suspicious for the above diagnosis? (20 marks)

   1.2. Name two other lesions that can clinically mimic a malignant melanoma. (20 marks)

   1.3. State four main histological subtypes of malignant melanoma. (20 marks)

   1.4. What two methods are used to indicate the depth of invasion of malignant melanoma in a pathology report? (20 marks)

   1.5. Name two immunohistochemical markers that are utilized to confirm the above diagnosis. (20 marks)

Contd...../2-

2. A 10-year old boy presents with an intra abdominal mass.
A core biopsy of the mass reveals a malignant small round cell tumour.

2.1. Having excluded lymphoma state four (04) possible differential diagnoses. (20 marks)

2.2. For each of the tumours stated in 2.1 describe how immunohistochemistry would help in making a definitive diagnosis. (40 marks)

2.3. Describe the histopathological parameters in the FNCLCC (Federation Nationale des Centres de Lutte Contre le Cancer) grading system of sarcomas. (40 marks)

3. Write short notes to include clinical presentation, histological features, immunohistochemistry (where relevant) and prognostic factors on

3.1. Burkitt lymphoma (25 marks)

3.2. Phyllodes tumour of breast (25 marks)

3.3. Pilocytic astrocytoma. (25 marks)

3.4. Clear cell carcinoma of the kidney (25 marks)

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MD (CLINICAL ONCOLOGY) PART I EXAMINATION – AUGUST 2018

Date: 28th August 2018 **Time: 10.00 a.m. – 10.45 a.m.**

PAPER II

If the examiners cannot read your writing, they will be unable to give you full credit for your knowledge.

RADIOBIOLOGY

Each question carries 100 marks.
Each question to be answered in a separate book.
Answer TWO (02) questions of the THREE (03) questions given below.

1.

1.1. (a) Write the steps involved in producing biological damage by the indirect action of x rays. (10 marks)

(b) List three possible outcomes of cell irradiation. (10 marks)

1.2. Differentiate between the phenomena of i) "potentially lethal damage repair" and ii) "sublethal damage repair" in cells after irradiation. (10 marks)

1.3. Draw a cell survival curve for cells in the different phases of the cell cycle irradiated with low LET radiation. (20 marks)

1.4.

(a) Define the oxygen enhancement ratio (OER) and give an OER value for low LET radiation. (10 marks)

(b) Explain the mechanisms of the radiosensitization effect of oxygen. (10 marks)

(c) Propose three strategies by which hypoxia may be overcome during radiotherapy. (10 marks)

Contd...../2-

1.5.

(a) Graphically represent OER and RBE as a function of LET (10 marks)

(b) Explain what happens to RBE when LET is increased above 100 KeV/μm. (10 marks)

2.

2.1. List the 5Rs that summarize the radiobiological basis of fractionation. (10 marks)

2.2.

(a) Differentiate between

(i) hyperfractionation,

(ii) accelerated radiotherapy

(iii) hypofractionation (15 marks)

(b) List an advantage of each type of radiotherapy listed under (a). (15 marks)

2.3. Define the "α/β ratio" applicable to the Linear Quadratic model. (20 marks)

2.4. If 10^8 cells were irradiated according to single hit kinetics so that the average number of hits per cell is one, how many cells would survive? (20 marks)

2.5. Discuss the relative effect on expected cell kill when treating a tumour with low α/β ratio with high and low LET radiation. (20 marks)

Contd...../3-

3.

3.1.

(a) What are the symptoms of the prodromal syndrome after total body irradiation. (10 marks)

(b) Discuss effects and appropriate treatment for victims of whole body radiation after a dose of:

(i) 2Gy (10 marks)

(ii) 6Gy (10 marks)

(iii) 10Gy (10 marks).

(c) Explain the consequences of whole body radiation of 20 Gy. (10 marks)

3.2. Discuss the risk of therapeutic radiation during each trimester of pregnancy. (30 marks)

3.3. Give four examples of second cancers induced by radiation therapy. (20 marks)

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MD (CLINICAL ONCOLOGY) PART I EXAMINATION – AUGUST 2018

Date: 28th August 2018 **Time: 11.00 a.m. – 11.45 a.m.**

PAPER II

If the examiners cannot read your writing, they will be unable to give you full credit for your knowledge.

CHEMOTHERAPY (PHARMACOLOGY)

Each question carries 100 marks.
Each question to be answered in a separate book.
Answer TWO (02) questions of the THREE (03) questions given below.

1. A phase 1 clinical trial is planned to develop a new drug for treatment of breast cancer following successful preclinical studies.

   1.1. Briefly explain the characteristics of research subjects who are suitable to be recruited into this clinical trial. (20 marks)

   1.2. What are the key differences between the research subjects and the protocol used for the above trial and a phase 1 trial for a new anti-diabetic agent. (20 marks)

   1.3. Explain the ethical issues in phase 1 clinical trials in oncology. (20 marks)

   1.4. What is the primary objective of this phase I trial? (10 marks)

   After successful completion of phase 1 and 2 studies, this drug is now going to be tested in a phase 3 trial

   1.5. List three (3) characteristics of an ideal phase 3 clinical trial. (10 marks)

   1.6. List the endpoints that should be considered to evaluate efficacy and safety of the new anticancer drug given above. (20 marks)

Contd...../2-

2.

2.1. List three (3) advantages of combination chemotherapy. (15 marks)

2.2. A 63-year-old Mrs. S was diagnosed to have node-positive invasive ductal breast cancer in December 2010. The tumour was hormone receptor-positive and HER2-negative. After a lumpectomy, she received adjuvant docetaxel, doxorubicin, and cyclophospamide followed by radiotherapy and anastrozole

Explain the mechanisms of action of

(a) Docetaxel (20 marks)

(b) Cyclophospamide (20 marks)

(c) Anastrozole (20 marks)

2.3. Briefly explain the role of chemotherapy with an example in the following settings.

(a) Neoadjuvant (05 marks)

(b) Adjuvant (05 marks)

(c) Palliative (05 marks)

(d) Chemoradiation (05 marks)

(e) Curative (05 marks)

3.

3.1. Explain linear and non-linear pharmacokinetics. (20 marks)

3.2. Outline the sources of pharmacokinetic variability of anticancer agents. (30 marks)

3.3. List four (04) possible consequences of pharmacokinetic variability of anticancer agents. (20 marks)

3.4. Outline the minimal data required to estimate a drug's volume of distribution and half-life. (10 marks)

3.5. Give two (02) examples for each of the following

(a) Drugs which inhibit hepatic drug metabolizing enzymes. (05 marks)

(b) Drugs which induce hepatic drug metabolizing enzymes. (05 marks)

(c) Highly emetogenic anti-cancer agents (05 marks)

(d) Minimal emetic risk anti-cancer agents (05 marks)

POSTGRADUATE INSTITUTE OF MEDICINE
UNIVERSITY OF COLOMBO

MD (CLINICAL ONCOLOGY) PART I EXAMINATION – AUGUST 2018

Date: 28th August 2018 **Time: 12.00 noon – 12.45 p.m.**

PAPER II

If the examiners cannot read your writing, they will be unable to give you full credit for your knowledge.

CANCER BIOLOGY

Each question carries 100 marks.
Each question to be answered in a separate book.
Answer TWO (02) questions of the THREE (03) questions given below.

1.

1.1. Name the cell cycle check point which prevents progression of the cell cycle if

(a) DNA replication is not completed.

(b) Chromosomes are not aligned on the mitotic spindle (10 marks)

1.2. Describe how Anaphase Promoting Complex (APC) brings about sister chromatid separation. (30 marks)

1.3. Explain how retinoblastoma (Rb) protein prevents progression of the cell cycle. (30 marks)

1.4. List three (03) features of epithelial mesenchymal transition. (15 marks)

1.5. Micrometastases do not always progress to macroscopic metastatic tumours. List three (03) factors that may be responsible for this phenomenon. (15 marks)

Contd...../2-

2.

2.1. Explain why the following mutations in tumour suppressor genes lead to cancer. (20 marks)

(a) Nonsense mutation

(b) Missense mutation

2.2. Name two (02) factors that activate *TP53 (P53)* gene expression. (10 marks)

2.3. State the mechanisms by which TP53 (P53) protein prevents carcinogenesis. (40 marks)

2.4. PARP inhibitors are useful in the treatment of *BRCA 1 or BRCA 2* mutation positive breast cancer. Explain. (30 marks)

3.

3.1.

3.1.1. What is a chimeric antigen receptor (CAR) T cell? (10 marks)

3.1.2. How does a CAR T cell function? (10 marks)

3.1.3. How are these cells produced for clinical use? (10 marks)

3.1.4. Give two (02) examples of their clinical use. (10 marks)

3.2.

3.2.1. What is a monoclonal antibody? (10 marks)

3.2.2. Give four (04) examples of currently used monoclonal antibodies in cancer therapy and their mechanisms of action. (20 marks)

3.3. List three (03) intrinsic mechanisms of immune evasion and briefly describe one (01) of these. (30 marks)