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Guidance for the first FRCR examination

Introduction

The first FRCR examination assesses understanding of the scientific basis of cancer and its treatments, including physics as applied to radiotherapy, radiobiology, cancer biology including molecular biology, the pharmacology of systemic anticancer treatments and medical statistics. This knowledge underpins and is essential to clinical oncology practice, and for this reason should be covered during the oncology common stem (ST3) with the examination passed by the end of ST4.

As detailed in the specialty training curriculum for clinical oncology, the first FRCR examination forms part of the evidence that trainees have met CiP 7 (applying knowledge and understanding of the scientific principles that underpin malignancy for the provision of high-quality and safe patient-centred cancer care). It also covers elements of other CiPs, such as CiP 2 (able to deal with ethical and legal issues related to clinical practice). Please note that the examination is not the only way in which these CiPs are assessed, and it is not designed to cover all aspects of these CiPs. Trainees should ensure that they include other evidence of their progress towards these CIPs in their e-portfolio, as described in the curriculum.

The first FRCR examination is divided into four modules: cancer biology and radiobiology; clinical pharmacology; physics; and medical statistics. The purpose statements, learning outcomes and syllabus of each module are given below to assist candidates, and those involved in their training, in understanding the scope of the first FRCR examination. Further details about the examination can be found on the RCR website.

Cancer biology and radiobiology module

The purpose of the cancer biology and radiobiology module is to ensure that those undertaking specialty training in clinical oncology have an appropriate knowledge of the processes of cancer cell transformation and tumour development, and the response to ionising radiation of cells both individually and grouped as tissues.

Learning outcomes

Candidates should:

1. understand the molecular basis of abnormalities which give rise to dysplasia, invasive cancer and metastases
2. understand the therapeutic effects and toxicity of ionising radiation at the level of cells, organs and organisms

Table 1 provides a guide to the topics through which the learning outcomes may be examined. It is intended as guide to the breadth of topics that may appear in the examination. It is not an exhaustive list or a teaching plan, and the points do not relate to equal amounts of study time.

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Table 1: Topics for the first FRCR cancer biology and radiobiology module

Topic	Further guidance
1.1 Principles of tumour biology	▪ Define and distinguish between different types of growth disorder (e.g. dysplasia and carcinoma in situ) ▪ Describe the cell cycle, basic cell kinetics and control mechanisms ▪ Describe the mechanisms of spread, local invasion/ migration, metastasis ▪ Describe the effects of tumours, including local effects (e.g. pressure) and distant effects (metastatic and non-metastatic) ▪ Discuss the importance of tumour vasculature and angiogenesis ▪ Describe mechanisms of DNA damage and repair: – single strand DNA breaks: base excision repair (BER); nucleotide excision repair (NER); and mismatch repair (MMR) – double strand DNA breaks: non-homologous end joining (NHEJ); and homologous recombination (HR) ▪ Describe the potential role of cancer stem cells ▪ Describe mechanisms of cell death, e.g. apoptosis, autophagy ▪ Describe the molecular targets for anti-cancer therapy
1.2 The genetics of normal and malignant cells	▪ Describe normal chromosomal structure and function, normal gene transcription and its control ▪ Describe polymorphisms and microsatellites ▪ Describe chromatin structure and function ▪ Describe the importance of methylation ▪ Discuss chromosomal and genetic changes in malignancy, point mutations, translocations, deletions, gene amplification and over-expression ▪ Discuss oncogenes, proto-oncogenes, tumour suppressor genes and their mode of action, describing well established examples in each class ▪ Recognise the clinical relevance of genomics in cancer biology and treatment

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Topic	Further guidance
1.3 Normal and aberrant mechanisms of cell growth control	▪ Discuss the control of normal cell growth and behaviour ▪ Contrast autocrine, paracrine and endocrine growth factors ▪ Discuss altered expression, function and control of these mechanisms in malignancy ▪ Describe signal transduction ▪ Describe gene promoters and their activity in normal and malignant cells
1.4 Inherited and non-inherited causation of human cancers	▪ Describe the following non-inherited factors and influences: – environmental – chemical – lifestyle – viral and non-viral infection – inflammatory – ionising and non-ionising radiation ▪ Discuss underlying genetic abnormality, its mechanism of action and associated cancers in: – retinoblastoma – Wilm's tumour – familial adenomatous polyposis coli – hereditary non-polyposis colon cancer – familial breast cancer – Li Fraumeni syndrome – neurofibromatosis 1 – MEN 1 – MEN 2 – xeroderma pigmentosum – ataxia telangiectasia – Peutz-Jeghers' syndrome – Von Hippel-Lindau syndrome – Cowden syndrome

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Topic	Further guidance
1.5 The role of the immune system	▪ Outline the basic principles of immunoediting, including elimination, equilibrium, and escape ▪ Outline the basic principles of tumour immunology: – fundamentals of immune response - innate versus adaptive immunity – relevant cell types including T cells (CD4 and CD8), B cells, dendritic cells – antibodies – immune tolerance; self/non-self, danger hypothesis – MHC class I and II – immunomodulation, including co-stimulation and negative regulation. – tumour associated antigens – immune suppression by tumours; tumour infiltrating lymphocytes, regulatory T cells
1.6 Principles of radiobiology	▪ Describe cellular systems (hierarchical, flexible) and their response to radiation ▪ Contrast parallel and serial systems ▪ Outline the principles of cell survival curves ▪ Describe the relevance of Linear Energy Transfer (LET) to cellular damage ▪ Describe radiation damage at the cellular level (including outcome phenotypes, chromosome damage and cell radiosensitivity) ▪ Describe the molecular biology of radiation damage and repair ▪ Compare bystander with direct effects of radiation ▪ Describe interactions between systemic anti cancer therapies and radiotherapy
1.7 Normal tissue radiobiology	▪ Describe normal tissue damage (early and late) ▪ Discuss the concept of normal tissue tolerance ▪ Describe the effects of radiation on different tissues and organs including unplanned whole-body exposure ▪ Discuss organ tolerance to retreatment with radiation

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Topic	Further guidance
1.8 Radiotherapy fractionation	▪ Discuss the concept of lethal, sublethal, potentially lethal damage ▪ Discuss the concept of early and late repair ▪ Describe the effect of cell cycle on radiation sensitivity ▪ Discuss repopulation ▪ Explain the role of the cell survival curve as a basis for fractionation ▪ Describe the linear quadratic model ▪ Define terms describing cellular sensitivity (SF2, α, β, mean inactivation dose) ▪ Discuss the α/β ratio and its relevance to tumours, acute and late responding tissues ▪ Calculate Biological Effective Dose (BED) ▪ Define and use equivalent dose in 2 Gy fractions (EQD2) ▪ Discuss fractionation and its influence on tumour control with different α/β ratio ▪ Define hyperfractionation, accelerated fractionation and hypofractionation ▪ Discuss the influence of gaps in radiotherapy and their management ▪ Describe the influence of dose rate effects, including low, pulsed, medium and high dose rate ▪ Define relative biological effect (RBE) and discuss its relationship to LET ▪ Explain the influence of oxygen on radiosensitivity, including oxygen enhancement ratio (OER) ▪ Explain the role of reoxygenation ▪ Explain the relationship between OER and LET

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Clinical pharmacology module

The purpose of the clinical pharmacology module is to ensure that those undertaking specialty training in clinical oncology have an appropriate understanding of the structure, action, use and evaluation of drugs used in the treatment of a patient with cancer.

Learning outcomes

Candidates should:

1. demonstrate knowledge of the safe, appropriate and effective use of drugs for anti-cancer systemic therapy. The anti-cancer drugs covered in this module are set out in the FRCR anti-cancer drugs list published on the RCR website and updated regularly to reflect current practice.
2. demonstrate knowledge of the symptomatic treatment of cancer, including the use of analgaesia, anti-emetics and anticoagulants.

Table 2 provides a guide to the topics through which the learning outcomes may be examined. It is intended as guide to the breadth of topics that may appear in the examination. It is not an exhaustive list or a teaching plan, and the points do not relate to equal amounts of study time.

Table 2: Topics for the first FRCR clinical pharmacology module

Topic	Further guidance
2.1 The mode of action of cytotoxic drugs	▪ Describe the mechanisms of action for each drug on the FRCR anti-cancer drugs list ▪ Discuss the mechanisms of drug resistance ▪ Describe strategies to optimise efficacy of cytotoxic therapy
2.2 Toxicity of systemic therapies	▪ Describe the dose limiting and common toxicities ▪ Describe dose-related and idiosyncratic toxicity ▪ Define the concepts of acute and long-term toxicity ▪ Discuss the mechanisms of toxicity ▪ Discuss chemical and other factors modifying drug toxicity ▪ Describe the principles of managing cytotoxic extravasation

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Topic	Further guidance
2.3 Pharmacokinetics and pharmacodynamics	▪ Discuss the principles of pharmacokinetics and interpret pharmacokinetic data ▪ Explain the role of the route and timing of administration ▪ Discuss the importance of plasma concentration and its relationship to drug actions ▪ Define Area Under Curve (AUC) and discuss its importance ▪ Discuss drug activation, metabolism and clearance ▪ Discuss the importance of protein and tissue binding ▪ Describe the importance of drug concentration at target site
2.4 The principles of clinical use of systemic therapies	▪ Describe dose response curves ▪ Explain the concept of dose intensity ▪ Discuss the effects of single agent and combination therapy ▪ Discuss the interactions of systemic therapy with other modalities of treatment ▪ Describe the principles of regional therapy ▪ Describe safe practice in intrathecal treatment ▪ Outline the principles of high dose therapy
2.5 Clinical pharmacology of supportive therapies	▪ List the classes of anti-emetics and discuss their use ▪ Discuss the use of steroids ▪ Discuss use of haemopoietic growth factors ▪ Discuss the use of anticoagulants, including mechanisms of action, pharmacological properties, indications, adverse events, interactions and monitoring
2.6 Clinical pharmacology of analgesics	▪ Outline the clinical pharmacology of analgesics and co-analgesics ▪ Discuss the use of drug combinations for pain management ▪ Describe different formulations and their use

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Topic	Further guidance
2.7 Drug interactions in cancer treatment	▪ Discuss common or important interactions between drugs used in cancer therapy and other commonly used drugs

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Medical statistics module

The purpose of the medical statistics module is to ensure that those undertaking specialty training in clinical oncology have an appropriate understanding of the medical statistics relevant to clinical trials and assessment of results, and to the epidemiology of cancer.

Learning outcomes

Candidates should demonstrate the statistics knowledge necessary to:

1. understand the design of trials
2. read and use a trial protocol
3. present and interpret data
4. interpret results of clinical trials
5. critically review and evaluate papers

Table 3 provides a guide to the topics through which the learning outcomes may be examined. It is intended as guide to the breadth of topics that may appear in the examination. It is not an exhaustive list or a teaching plan, and the points do not relate to equal amounts of study time.

Table 3: Topics for the first FRCR medical statistics module

Topic	Further guidance
3.1 Types of data	▪ Present and summarise individual variables ▪ Recognise categorical data (nominal, ordinal) ▪ Recognise discrete and continuous numerical data ▪ Recognise symmetric and skewed distribution ▪ Describe the normal distribution ▪ Interpret bar charts and histograms ▪ Define and apply measures of central tendency and spread
3.2 Sampling	▪ Describe the concept of a source population ▪ Explain random sampling ▪ Explain estimation of population statistics ▪ Describe standard error of a sample mean and of a proportion, and their differences ▪ Define and use confidence intervals ▪ Explain reference ranges

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Topic	Further guidance
3.3 Principles of statistical inference	▪ Explain hypothesis testing and estimation ▪ Contrast Type I and II errors ▪ Interpret p-values and confidence intervals ▪ Define and identify the difference between statistical and clinical significance ▪ Explain the concept of and correction for multiple testing (e.g., false discovery rate, Bonferroni correction)
3.4 Tests used to compare two or more groups	▪ Interpret tests comparing means and percentages
3.5 Association between variables	▪ Interpret the meaning of correlation and regression analysis ▪ Interpret the meaning of scatter plots
3.6 Screening tests	▪ Calculate and interpret the meaning of sensitivity, specificity, positive and negative predictive values and accuracy
3.7 Survival analysis	▪ List types of time-to-event data ▪ Interpret and describe the principles of Kaplan-Meier and actuarial survival curves ▪ Understand censorship ▪ Understand how the KM curves can be derived using algorithms and how to input the data ▪ Describe the possible methods of summarizing survival data ▪ Interpret and describe methods used to compare groups: – logrank test for two or more groups, including ordered groups – Cox's proportional hazards regression model – hazard ratios and their interpretation

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Topic	Further guidance
3.8 Design and analysis of clinical trials	▪ Compare the design and role of phases I-IV of clinical trials ▪ Explain the need for randomization and the problems with non-randomised studies and historical controls ▪ Describe the methods of randomisation (simple, block, stratified, minimisation) ▪ Explain the concepts of blinding/masking ▪ Describe the possible trial designs: parallel group, cross-over, factorial ▪ Describe the contents of a trial protocol ▪ Discuss the ethical basis for research of what constitutes informed consent and reporting adverse events ▪ Describe the possible measures of response including: – tumour regression – quality of life – toxicity – local and regional recurrence – distant metastases – death – cause specific death – disease free survival – progression free survival ▪ Outline the principles of: – sample size calculation – interim analyses – intent-to-treat analysis – early stopping rules ▪ Outline the role and basic principles of meta-analysis and systemic reviews
3.9 Collection and use of epidemiological data	▪ Contrast the design and interpretation of cross-sectional case control and cohort studies ▪ Define the principles, calculate and interpret odds ratios and risk ratios ▪ Define incidence, prevalence, mortality rates and standardised mortality rates

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Physics module

The purpose of the physics module is to ensure that those undertaking specialty training in clinical oncology can apply physical principles and methods in clinical radiotherapy and have an appropriate understanding of the physical basis of the therapeutic uses of radioactive isotopes, radiation hazards and protection.

Learning outcomes

Candidates should demonstrate knowledge and understanding of:

- the interaction of ionising radiation with matter
- how a desired dose distribution is produced, calculated and quality assured
- how the dose of unintended radiation can be minimised for patients and staff

Table 4 provides a guide to the topics through which the learning outcomes may be examined. It is intended as guide to the breadth of topics that may appear in the examination. It is not an exhaustive list or a teaching plan, and the points do not relate to equal amounts of study time.

Table 4: Topics for the first FRCR physics module

Topic	Further guidance
4.1 Physics relevant to radiotherapy	▪ Describe atomic structure, atomic and mass numbers ▪ Describe electron shells and energy levels ▪ Describe electromagnetic radiation and the electromagnetic spectrum ▪ Explain the relationship between wavelength, frequency and energy ▪ Describe an x- or gamma-ray beam (quality, energy, intensity, size) ▪ Explain the basic principles of production of x- or gamma-rays ▪ Contrast continuous and discrete spectra ▪ Describe attenuation, absorption, scattering of x-rays ▪ Define attenuation coefficients and half value layer

Topic	Further guidance
4.2 Electromagnetic radiation and its interaction with matter	▪ Discuss the nature of the following effects and their dependence on the properties of the irradiated material (e.g. density, atomic number), their variation with energy and their relative importance in therapy and imaging: – Compton effect – photoelectric effect – pair production – scattered radiation – secondary electrons – linear energy transfer
4.3 Interaction of subatomic particles with matter	▪ Discuss ionisation and excitation due to charged particles ▪ Discuss the interactions of electrons with matter: – collision loss – radiative loss – stopping power due to each and total stopping power – particle range ▪ Explain the principle of Bremsstrahlung ▪ Discuss the interactions of neutrons with matter: elastic and inelastic collisions ▪ Discuss the principles of heavier charged particle therapy including proton beam therapy: – ionisation profile – Bragg peak

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Topic	Further guidance
4.4 Radiation dosimetry	▪ Discuss variation of absorbed dose in different tissues and materials ▪ Explain the concept of exposure and KERMA ▪ Describe the principles of the relationship between exposure, KERMA and absorbed dose ▪ Describe the physical principles underlying radiation dose measurement ▪ Describe methods of measurement, including the advantages and disadvantages of the following: – ionisation methods (ionisation chamber, Geiger counter, diodes) – thermoluminescence (TLD) – calorimetry ▪ Discuss calibration standards (local and national) ▪ Discuss practical dose measurements – derivation of isodose curves – central axis depth dose profiles – use of phantoms
4.5 The physics of teletherapy beams	▪ Describe energy ranges of x-rays used in clinical practice ▪ Discuss the dose distribution for therapeutic x-rays noting the effects on the isodose curve (% depth dose and beam profile) of: – energy – FSD (Focus to Skin Distance) – beam modifying devices such as wedges – build-up and skin sparing – field size – surface obliquity – inhomogeneous media ▪ Understands the concept of monitor units ▪ Describe beam geometry – penumbra – field size definition

Topic	Further guidance
4.6 Electron beam physics	▪ Describe the dose distribution of electron beams used in clinical practice noting the effect on the isodose curve (% depth dose and beam profiles) of: – energy – tissue factors affecting dose at depth (e.g. lung) – field size – build up and skin sparing – surface obliquity and inhomogeneities – shielding
4.7 Principles of radiotherapy treatment planning	▪ Discuss the techniques available to optimise patient set-up ▪ Discuss the effects of patient and organ movement ▪ Describe the methods of tumour volume definition: clinical examination, radiograph, CT, MRI, ultrasound, functional imaging ▪ Explain the concept of planning volumes: – gross tumour volume (GTV) – clinical target volume (CTV) – planning target volume (PTV): internal target volume (ITV); set-up margin (SM) – treated volume – irradiated volume – organs at risk (OAR) – planning organ at risk volume (PRV) ▪ Explain the methods of planning volume localisation: – clinical mark-up – CT scanning ▪ Compare fixed FSD versus isocentric planning ▪ Describe isodose distributions, their uses and critical assessment in each of the following situations: – single field – multifield (coplanar and non-coplanar) – arc and rotational therapy – weighting

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Topic	Further guidance
4.7 Principles of radiotherapy treatment planning (continued)	▪ Outline the principles of beam shaping including conformal therapy, IMRT and VMAT ▪ Outline the principles of forward and inverse planning ▪ Discuss dose prescription including the ICRU reference point ▪ Outline the principles of dose calculations in the presence of extensive shielding ▪ Explain the principles of field matching ▪ Describe the principles of plan evaluation and verification using isodose display, dose volume histograms (DVH, cumulative and frequency) and digitally reconstructed radiographs (DRR)
4.8 Principles of beam therapy equipment	▪ Outline the principles of superficial and orthovoltage x-ray production ▪ Outline the principles of the linear accelerator, including: – electron beam production – x-ray production, beam control and stability – output – IMRT and VMAT ▪ Describe the concept and definition of the isocentre ▪ Describe the techniques for defining the beam geometry: – collimators – applicators – multileaf collimators ▪ Explain the factors influencing penumbra ▪ Define beam quality ▪ Describe the shielding techniques available and the materials used in their construction ▪ Explain the concepts of transmission, scatter and doses under shields

Topic	Further guidance
4.8 Principles of beam therapy equipment (continued)	▪ Discuss the factors involved in accurately irradiating the target: – the treatment couch (including modern techniques of couch movements and the concept of 6 degrees of freedom) – positioning of the patient – lasers – light fields – monitoring radiation output ▪ Describe the functioning of multileaf collimators: – edge definition – leaf leakage – influence of leaf size ▪ Outline the principles of stereotactic ablative radiotherapy (SABR) – Understands the role of 4D imaging – Understands and discusses the advantages and disadvantages of SABR delivery platforms including standard external beam linacs, CyberKnife and Tomotherapy – Understands the concepts of conformity index and gradient index in SABR plan appraisal – Understands the difference in homogeneity of dose seen in SABR compared to conventional radiotherapy – Understands the principles of quality assurance of SABR ▪ Recognise motion management techniques for SABR including – active breathing control – abdominal compression – gating – fiducial implantation

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Topic	Further guidance
4.9 Quality assurance in radiotherapy	▪ Define quality assurance and quality control in radiotherapy ▪ Describe the processes that are undertaken to ensure that the prescription is correctly implemented: – the role of computer verification – manual checking – monitoring accuracy of treated volume: offline and online IGRT – monitoring accuracy of positioning (lasers, light-fields, tolerances) – in vivo dosimetry ▪ Outline monitoring to assure accuracy of: – radiation output – symmetry – field flatness – beam energy – field size ▪ Describe the rules for reporting near misses and errors including the legal requirements
4.10 Radioactive sources in therapy	▪ Describe the basic principles of gynaecological brachytherapy (Manchester and three- dimensional image guided) ▪ Describe the basic principles of prostate brachytherapy using permanent seeds ▪ Describe the basic principles of radioactivity including: – definitions and units of activity and half-life including physiological and biological half life of 192Ir, 131I, 125I, and 60Co – inverse square law – hazards with sealed and unsealed sources – source strength – afterloading

Topic	Further guidance
4.11 Principles of radiation protection	▪ Explain radiation protection mechanisms, including time, distance, shielding ▪ Discuss quality factors and dose equivalent ▪ Discuss background radiation ▪ Describe the statutory framework for radiation protection ▪ Describe the classification of staff, designated areas ▪ Outline the principles of : – IR(ME)R – ARSAC – local rules – controlled areas ▪ Explain the design of treatment rooms: – primary/secondary barriers – transmission through barriers – mazes, doors and interlocks – leakage and scattered radiation ▪ List the methods of monitoring of personnel e.g.: – TLD badge – direct reading dosemeter