



In-Training Examination for Radiation Oncology Residents

March 5, 2015

Sponsored by:
Commission on Education

Committee on Residency Training in Radiation Oncology, Biology & Physics

List of Acronyms Meanings

AAPM TG	American Association of Physicists in Medicine Task Group
ABVD	Adriamycin, bleomycin, vinblastine, dacarbazine (chemotherapy)
AFP	α -Fetoprotein
APR	Abdominoperineal resection
AUA	American Urologic Association
BCG	Bacillus Calmette-Guerin
BCNU	Carmustine (chemotherapy)
BCT	Breast Conserving Therapy
β -hCG	β -human chorionic gonadotropin
BrdUrd	5'-Bromodeoxyuridine
CBCT	Cone-beam computed tomography
ChemoRT	Chemoradiation
CEA	Carcinoembryonic antigen
CR	Complete Response
CSF	Cerebral Spinal Fluid
CSI	Cranial Spinal Radiation
CTV	Clinical tumor volume
d_{max}	Depth of Maximum Dose
DCIS	Ductal carcinoma in situ
DLBCL	Diffuse Large B Cell Lymphoma
DM	Distance Metastases
DFS	Disease Free Survival
DSS	Disease Specific Survival
DRE	Digital Rectal Exam
DVH	Dose volume histogram
EBRT	External-beam radiation therapy
EBV	Epstein-Barr virus
ECF	Epirubicin, cisplatin, and 5-FU (chemotherapy)
EGF	Epidermal growth factor
ESR	Erythrocyte Sedimentation Rate
EGFR	Epidermal growth factor receptor
FFF	Flattening Filter Free
FIGO	International Federation of Gynecology and Obstetrics
FSU	Functional subunit
GTV	Gross tumor volume
HCC	Hepatocellular Carcinoma
HDR	High dose rate
HIF	Hypoxia inducible factor
HIV	Human immunodeficiency virus
HNPPCC	Hereditary nonpolyposis colorectal cancer
HPF	High Power Fields
HPV	Human papillomavirus
HSV	Herpes simplex virus
IBTR	Ipsilateral breast tumor recurrence
ICRU	International Commission on Radiation Units and Measurements
IdUrd	5'-Iododeoxyuridine
IFRT	Involved Field Radiation Therapy
IGRT	Image Guided Radiation Therapy
IMRT	Intensity modulated radiation therapy
ITV	Internal target volume
LCIS	Lobular carcinoma in situ
LDH	Lactate dehydrogenase
LET	Linear energy transfer
linac	Linear Accelerator
LDR	Low dose rate

LRC	Local Regional Control
LRR	Local Regional Recurrence
LVI	Lymphovascular invasion
MALT	Mucosa Associated Lymphoid Tumor
MGMT	Methyl-guanine methyltransferase (gene)
MLC	Multileaf collimator
MRS	Magnetic resonance spectroscopy (imaging)
MU	Monitor Unit
MVCT	Megavoltage CT
NCRP	National Council on Radiation Protection and Measurement
NHEJ	Non-Homologous End-Joining
NRC	Nuclear Regulatory Commission
NSCLC	Non-small cell lung cancer
OAR	Organs at risk
OER	Oxygen enhancement ratio
PBSCT	Peripheral blood stem cell transplantation
PFS	Progression Free Survival
PCI	Prophylactic cranial irradiation
PCR	Polymerase chain reaction
PCV	Procarbazine, lomustine (CCNU), and vincristine (chemotherapy)
PDD	Percent depth dose
PFT	Pulmonary function test
PIV	Prescription Isodose Volume
PLD	Potentially lethal damage
PMRT	Post Mastectomy Radiation Therapy
PS	Performance Status
PSA	Prostate specific antigen
PTV	Planning treatment volume
QoL	Quality-of-Life
R ₅₀	Depth of 50% of the dose relative to d _{max}
RBE	Relative biological effectiveness
R-CHOP	Rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone (chemotherapy)
RT	Radiation Therapy
RTOG	Radiation Therapy Oncology Group
SAD	Source-to-axis distance
SBRT	Stereotactic body radiation therapy
SCLC	Small cell lung cancer
SOD	Source-to-detector distance
SIADH	Syndrome of inappropriate antidiuretic hormone
SLD	Sublethal damage
SOBP	Sine Oculis Binding Protein
SBRT	Stereotactic Body Radiation Therapy
SRS	Stereotactic radiosurgery
SSD	Source-to-surface distance
T _{pot}	Tumor potential doubling time
TBI	Total Body Irradiation
TCC	Transitional cell carcinoma
TGF-β	Transforming growth factor beta
TME	Total Mesorectal Excision
TURBT	Transurethral resection of bladder tumor
TV	Target Volume
TVL	Tenth Value Layer
UNSCEAR	United Nations Subcommittee on the Effects of Atomic Radiation
VEGF	Vascular endothelial growth factor
WBRT	Whole-brain radiation therapy
5 FU	5 fluorouracil

1. Which of the following represents primary tumors listed in order of increasing risk of distant metastatic diseases following surgical resection?

- (A) Intrahepatic cholangiocarcinoma, hilar cholangiocarcinoma, adenocarcinoma of the gall bladder
- (B) Hilar cholangiocarcinoma, intrahepatic cholangiocarcinoma, adenocarcinoma of the gall bladder
- (C) Adenocarcinoma of the gall bladder, hilar cholangiocarcinoma, intrahepatic cholangiocarcinoma
- (D) Hilar cholangiocarcinoma, adenocarcinoma of the gall bladder, intrahepatic cholangiocarcinoma

Key: A

Rationale: In the study by Jarnagin et al., the rate of first recurrence including a distant site for adenocarcinoma of the gall bladder was 85% vs. 41% for patients with hilar cholangiocarcinoma. In the study by Weber et al., the rate of first recurrence for an intrahepatic cholangiocarcinoma including a distant site was 25%.

References: Jarnagin WR, et al., Cancer, (2003). Weber SM, et al., Journal of the American College of Surgeons, (2001).

2. Per NCCN guidelines, what is the appropriate adjuvant treatment for a pathologic stage T3N1 urothelial carcinoma of the mid ureter?

- (A) RT alone
- (B) Chemotherapy alone
- (C) Concurrent chemoRT
- (D) Sequential chemotherapy followed by RT

Key: B

Rationale: Radiation therapy is generally not indicated in the adjuvant setting for the treatment of urethral cancer. Per the NCCN recommendations, the standard adjuvant treatment for this patient would be chemotherapy alone.

3. Which of the following radiation toxicities increases over time after accelerated partial breast irradiation?

- (A) Edema
- (B) Breast pain
- (C) Fat necrosis
- (D) Hyperpigmentation

Key: C

Rationale: Hyperpigmentation was shown to decrease from 67% at 6 months to 37% at 5 years. Breast edema decreased from 50% at 6 months to 6% by 5 years. Breast pain was shown to decrease from 27% at 6 months to 8% by 5 years. Both fat necrosis and telangiectasias are toxicities that increase with time. Fat necrosis increased from 1% at approximately 6 months to 11% at 5 years.

4. Which drug has been found to increase the pathologic CR rates when added to standard neoadjuvant systemic therapy in triple negative breast cancer patients?

- (A) Eribulin
- (B) Carboplatin
- (C) Dacarbazine
- (D) Capecitabine

Key: B

Rationale: The additional of carboplatin was found to increase the rates of pathologic CR when added to standard chemotherapy in patients with triple negative breast cancer. Recurrence free and overall survival benefits have not yet been shown.

5. The *in vivo-in vitro* assay involves the irradiation of tumors *in situ*, followed by the tumor cell surviving fraction determined from colony counts in:

- (A) the lung.
- (B) the spleen.
- (C) petri dishes.
- (D) jejunal crypts.

Key: C

Rationale: As the name implies, the *in vivo-in vitro* assay begins with an *in vivo* component where the tumor is irradiated *in situ*, followed by an *in vitro* component where the tumor is excised, the cells separated, and plated into petri dishes for a standard clonogenic assay. The other answer choices refer to colony assays performed *in vivo* only, with no *in vitro* component.

6. What fraction of the maximum energy of the incident electron beam BEST approximates the energy of the bremsstrahlung beam?

- (A) 1/4
- (B) 1/3
- (C) 1/2
- (D) 2/3

Key: B

Rationale: The "1/3 approximation" is a useful estimate of the average energy of a bremsstrahlung beam. For example, a 6 MV linac beam has average photon energy of approximately 2 MeV.

7. According to the 7th edition AJCC staging manual, penile cancer involving bilateral inguinal lymph nodes is staged as:

- (A) N1.
- (B) N2.
- (C) N3.
- (D) M1.

Key: B

Rationale: N1 stage involves only one inguinal lymph node. N2 stage involves more than one inguinal lymph node on the same or contralateral side

8. In the Hopkins rapid autopsy study, what percent of patients with pancreatic cancer died with "locally destructive" disease?

- (A) 10
- (B) 20
- (C) 30
- (D) 40

Key: C

Rationale: According to this rapid autopsy series, locally destructive disease was found in 30% of patients.

References: Iacobuzio-Donohue C., et al, J Clin Oncol.

9. Based on ICRU 83, the near maximum dose, $D_{2\%}$, is BEST defined as the:

- (A) mean dose to 2% of the volume of a structure.
- (B) highest dose to 2% of the volume of a structure.
- (C) volume of a structure receiving 2% of the mean dose.
- (D) volume of a structure receiving the highest 2% of the prescription dose.

Key: B

Rationale: Because of advanced computer-based treatment planning and 3D conformal delivery techniques, ICRU has recommended using Level 2 reporting which is primarily based on volume metrics instead of point dose metrics. The $D_{2\%}$ is best defined as the highest dose to 2% of a given structure.

10. How would a 30-year-old patient presenting with classic Hodgkin with a single left level IIA non-bulky lymph node in the neck, no B symptoms, and normal ESR be classified?

- (A) Favorable early stage HL
- (B) Unfavorable early stage HL
- (C) Favorable advanced stage HL
- (D) Unfavorable advanced stage HL

Key: A

Rationale: This patient would be classified as a favorable early stage HL.

11. For radiation with an LET of 100 keV/ μ m, the average separation between ionization events is closest to the diameter of which of the following cellular components?

- (A) Nucleus
- (B) Ribosome
- (C) DNA helix
- (D) Mitochondria

Key: C

Rationale: 100 keV/ μ m is the LET that yields the highest RBE for the production of biological effects. This is thought to be because the average separation between ionizing events approximates the diameter of the DNA double helix (\sim 2 nm).

12. Which chemotherapy regimen is the MOST appropriate 1st line therapy for an epithelial mesothelioma?

- (A) Cisplatin and Etoposide
- (B) Cisplatin and Pemetrexed
- (C) Carboplatin and Paclitaxel
- (D) Carboplatin and Gemcitabine

Key: B

Rationale: This randomized trial in mesothelioma was a major breakthrough in mesothelioma and should be known by all physicians taken care of this disease. It was the 1st trial to demonstrate a benefit over cisplatin alone in the advanced setting.

13. Which factors predict the outcome of DLBCL patients?

- (A) PS, histology, ESR, mediastinal bulk, number of nodal sites
- (B) B symptoms, age, ESR, mediastinal bulk, number of involved sites
- (C) PS, age > 60 years, LDH, presence of extranodal disease sites, stage
- (D) B symptoms, age, histology, extranodal sites, number of involved sites

Key: C

Rationale: The International Non-Hodgkin's Lymphoma Prognostic Factors Project had outlined the following factors as the most predictive of outcome in patients diagnosed with aggressive non-Hodgkin lymphoma: Age, stage, performance status, extranodal involvement, serum LDH.

14. For a suspected multiple myeloma patient, which test is BEST avoided?

- (A) MRI
- (B) PET/CT
- (C) Skeletal survey
- (D) CT scan with contrast

Key: D

Rationale: Because of renal failure, suspected multiple myeloma patients should not receive CT contrast.

15. What is the purpose of rounded leaf ends on MLCs?

- (A) Reduce radiation leakage
- (B) Reduce internal scatter
- (C) Provide accurate MLC positions, independent of leaf position
- (D) Provide radiation field edge penumbras that are similar, independent of leaf position

Key: D

Rationale: For single-focused MLCs, radiation passes through different thicknesses of material depending on the MLC position. This results in different radiation penumbra depending on position. In order to mitigate this effect, these MLCs are designed with rounded leaf edges.

16. According to 7th edition AJCC staging manual, prostate cancer involving bilateral seminal vesicles is staged as:

- (A) T2c.
- (B) T3a.
- (C) T3b.
- (D) T3c.

Key: C

Rationale: There is no T3c in the current edition. Involvement of both lobes is T2c. Either unilateral or bilateral extracapsular extension is T3a. Either unilateral or bilateral seminal vesicles involvement is T3b.

17. What is the MOST common testicular cancer in men over 50 years old?

- (A) Lymphoma
- (B) Adenocarcinoma
- (C) Testicular seminoma
- (D) Non-seminomatous germ cell tumor

Key: A

Rationale: Lymphoma is the most common testicular cancer after age 50.

18. What is the benefit of PCI for a patient with extensive SCLC who had a good response to chemotherapy?

- (A) Reduction in the incidence of symptomatic brain metastases, but no effect on OS
- (B) Reduction in the incidence of symptomatic brain metastases, and an improvement in OS
- (C) Reduction in the incidence of asymptomatic brain metastases, and an improvement in OS
- (D) No reduction in the incidence of symptomatic brain metastases, but an improvement in OS

Key: B

Rationale: The role of prophylactic cranial irradiation was evaluated by a randomized trial conducted in 186 patients with extensive small cell lung cancer who had had a response to chemotherapy. This study showed that prophylactic cranial irradiation reduces the incidence of symptomatic brain metastases (HR0.27; 95% CI: 0.16–0.44, $p < 0.001$) and prolongs disease-free (14.7 weeks vs 12.0 weeks, $p = 0.02$) and overall survival (6.7 vs 5.4 months, $p = 0.003$) Not only did they show a decrease in CNS metastases but also an improvement of overall survival at 1 year (27% versus 13%). The cumulative risk of brain metastases at 1 year was 40.4% in the observation arm and 14.6% in the therapy arm. Patients in this study did not have routine CNS imaging. brain CT or MRI was done only if patients had symptoms of metastases.

19. According to AAPM TG-142, which statement BEST describes the tolerance values for periodic machine QA tests?

- (A) They are specific to PTV margins used.
- (B) They are independent of treatment techniques.
- (C) They are specific to daily, weekly, and bi-weekly imaging.
- (D) They are specific to non-IMRT, IMRT, and SRS/SBRT treatment techniques.

Key: D

Rationale: An important distinction of the current QA guidance (TG-142) is the use of tolerance values specific to treatment technique.

20. Which measure of central tendency equals the sum of observations divided by the number of observations?

- (A) Mean
- (B) Mode
- (C) Median
- (D) Percentile

Key: A

Rationale: There are three measures of central tendency: mean, median, mode. Mean equals the sum of observations divided by the number of observations. Median equals the observation in the middle when all observations are ordered from smallest to largest. Mode equals the observation that occurs most frequently. Percentile is a measure of dispersion rather than central tendency. The percentile equals the percentage of distribution that is below a specific value. As an example, a child is in 90th percentile for weight if only 10 percent of children the same age weigh more than the child.

21. Which virus is directly involved in carcinogenesis?

- (A) Rhinovirus A
- (B) Human papillomavirus
- (C) Mycobacterium tuberculosis
- (D) Human immunodeficiency virus

Key: B

Rationale: Human papillomavirus is a known cause of cancers of the cervix, anus, and head and neck epithelium. Human immunodeficiency virus is associated with a number of cancers, but is not itself a cause of the disease. Mycobacterium tuberculosis causes tuberculomas, which are benign growths. Rhinovirus A is the cause of the common cold and is not associated with any cancers.

22. In addition to rash, what are the common side effects of cetuximab for the treatment of squamous cell carcinoma of the head and neck?

- (A) Myelosuppression, nausea
- (B) Hyponatremia, nephrotoxicity
- (C) Ototoxicity, peripheral neuropathy
- (D) Hypomagnesemia, infusion reaction

Key: D

Rationale: Common side effects of cetuximab include an acneiform rash, the presence of which is prognostic for better response, hypomagnesemia and an infusion reaction. Nephrotoxicity, ototoxicity, myelosuppression peripheral neuropathy and nausea are common side effects of cisplatin.

23. According to NCCN guidelines, a CT scan of the abdomen and pelvis should be obtained for a patient with intermediate risk prostate cancer when the probability (%) of lymph node involvement is greater than:

- (A) 2.
- (B) 10.
- (C) 15.
- (D) 25.

Key: B

Rationale: Current National Comprehensive Cancer Network (NCCN) guidelines for the management of prostate cancer recommends that if the patient is taken for surgery, a pelvic lymph node dissection (PLND) should be performed at the time of radical prostatectomy in patients who have a the probability of lymph node involvement $\geq 2\%$. A CT scan is recommended when the probability of lymph node involvement $>10\%$. Typically, irradiation of the pelvic lymph nodes are performed when the probability of lymph node involvement $> 15\%$. The criteria for obtaining a bone scan in such patients is not the same as those recommended for obtaining a CT scan. The NCCN recommends obtaining a bone scan in patients with any of the following: T1 disease with a PSA of > 20 ng/mL, T2 disease with a PSA > 10 ng/mL, Gleason Score ≥ 8 , T3 or T4 disease, or symptomatic patients.

24. In agreement states, which two organizations are charged with enforcing radiation safety regulations in the radiation oncology workplace?

- (A) NRC and FDA
- (B) EPA and OSHA
- (C) ICRP and NCRP
- (D) BEIR and UNSCEAR

Key: A

Rationale: The Nuclear Regulatory Commission (NRC) has as part of its responsibilities the regulation of radioactive materials used medically, including diagnostic radionuclides and brachytherapy sources. The Food and Drug Administration is charged with the regulation of "medical devices", including those that produce radiation, such as linear accelerators (and associated treatment planning software).

25. The RTOG breast contouring atlas regarding the CTV lumpectomy cavity recommends a uniform volume expansion (cm) around the lumpectomy GTV of:

- (A) 0.8.
- (B) 1.0.
- (C) 1.5.
- (D) 1.8.

Key: B

Rationale: The RTOG breast contouring atlas and current open cooperative group trials provide target and normal tissue definitions for standardization of contouring as well as dose coverage recommendations and normal tissue constraints for treatment planning. The breast CTV should include the lumpectomy CTV is the Lumpectomy GTV + 1 cm, 3D expansion. Limit the CTV posteriorly at anterior surface of the pectoralis major and anterolaterally 5 mm from skin and should not cross midline. In general, the pectoralis and/or serratus anterior muscles are excluded from the lumpectomy CTV unless clinically warranted by the patient's pathology.

26. The MOST appropriate radiation field after a lateral glossectomy for a clinical T1N0M0, 7 mm thick carcinoma of the oral tongue with negative margins, but positive perineural invasion include:

- (A) bilateral neck.
- (B) oral cavity only.
- (C) ipsilateral neck only.
- (D) oral cavity and bilateral neck.

Key: D

Rationale: The preferred initial modality for a clinical T1N0 oral tongue cancer is resection of the primary and ipsilateral neck dissection when the depth of the tumor invasion is deeper than 4 mm. Since this patient only had partial glossectomy, it would be important to address the neck disease. A staged ipsilateral neck dissection would be appropriate. However, given the presence of perineural invasion and thicker tumor, postoperative radiation should be considered regardless whether an elective neck dissection is performed. A combined series from MSKCC and PMH (I. Ganly et al. 2013) showed a high nodal failure rate for after partial glossectomy and neck dissection even with pathologically negative nodes when the tumor thickness was deeper than 4 mm. With a median follow up exceeding 5 years, 10% patients developed local and 18% developed nodal recurrence. Among patients who developed nodal failures, 61% were in the ipsilateral (dissected neck) and 39% in the contralateral (undissected neck).

27. What was the finding in the phase 3 non-inferiority trial for follicular lymphoma comparing 4 Gy versus 24 Gy RT (FORT trial)?

- (A) 4 Gy had more toxicity
- (B) 4 Gy had equivalent toxicity
- (C) 4 Gy was worse in terms of time to progression
- (D) 4 Gy was better in terms of time to progression

Key: C

Rationale: FORT is a prospective randomized, unblinded phase 3 non-inferiority study comparing 4 Gy vs 24 Gy for follicular lymphoma or marginal zone lymphoma. Time to local progression in the 4 Gy was not non-inferior to 24 Gy. The HR was 3.42 (95% CI 2.09-5.55 $p < 0.0001$), showing the 4 Gy was actually worse (see figure 2A in the study). Toxicity was low in both arms. Lowest was in the 4 Gy arm, as would be expected.

28. For 80 keV/ μm carbon ions, the dose response curve for dicentric chromosome aberrations is:

- (A) linear-quadratic.
- (B) linear and steep.
- (C) linear and shallow.
- (D) initially linear, then threshold.

Key: B

Rationale: Dose response curves for two-hit chromosome aberrations like dicentrics are typically linear-quadratic in shape for low LET radiations like x-rays and linear for high LET radiations like carbon ions. And because high LET carbon ions are more biologically effective per unit dose than low LET x-rays, it follows that the dose response curve for the induction of dicentrics would not only be linear, but also steep.

29. What radiotherapy volume should be recommended for a patient who has undergone complete resection of a stage III neuroblastoma AFTER induction chemotherapy?

- (A) None
- (B) Total body
- (C) Whole abdomen
- (D) Tumor bed with margin

Key: D

Rationale: For patients with stage III who do not have a complete resection at the time of diagnosis, radiotherapy is typically recommended to the primary site. The current sequence of interventions is: biopsy-induction chemotherapy- surgery-high dose chemotherapy-local radiotherapy-maintenance therapy. For patients with metastatic disease, the primary site management is similar and additional selected sites of involvement may be treated.

References: Halperin, Pediatric Radiation Oncology.

30. Which gynecologic malignancy is MOST likely in a 72-year-old woman with 3 months of intermittent vaginal bleeding?

- (A) Ovarian
- (B) Uterine
- (C) Vaginal
- (D) Cervical

Key: B

Rationale: All of these conditions can lead to vaginal bleeding in a postmenopausal woman, however uterine cancer is the most common female reproductive tract malignancy in the United States. There were an estimated 40,000 new cases in 2008 compared to 21,000, 11,000, and 2,000 for ovarian, cervical and vaginal cancers, respectively.

References: Jemal, et. al., Cancer.

31. Regarding rhabdomyosarcoma in children and adolescents:

- (A) it has a slight female predominance.
- (B) it is the least common soft tissue sarcoma.
- (C) it is the most common extracranial solid tumor.
- (D) embryonal and alveolar subtypes are the most common histologic variants.

Key: D

Rationale: The most frequently diagnosed malignancies in order are: leukemia (31%), CNS tumors (21%), neuroblastoma (7%), Wilms tumor (5%), lymphomas (4 & 6%: HL & NHL), RMS (3%) , bone cancers (4%).

References: Egas-Bejar D, Huh WW, Rhabdomyosarcoma in adolescent and young adult patients: current perspectives, (2014).

32. What is an appropriate adjuvant treatment for a Stage IA uterine cancer with < 50% myometrial invasion, incompletely surgically staged, G2 endometrioid adenocarcinoma with high-risk intrauterine features and negative postoperative imaging?

- (A) Chemotherapy
- (B) Vaginal brachytherapy
- (C) Chemotherapy with vaginal brachytherapy
- (D) Chemotherapy with external beam radiation

Key: B

Rationale: A Stage IA, G1-2 (myometrial invasion <50%) that is incompletely surgically staged and has high-risk intrauterine features should undergo post-operative imaging. If the imaging is negative then the patient may be observed or have vaginal brachytherapy with or without EBRT.

33. Based on the EBCTCG meta-analysis, what is the 5-year local recurrence rate (%) for a patient with Stage I breast cancer treated with conservation surgery and irradiation?

- (A) 1
- (B) 3
- (C) 7
- (D) 11

Key: C

Rationale: The EBCTCG meta-analysis demonstrated cause-specific and overall survival advantages with the addition of radiation after BCS. The 5 year local recurrence rate was 7% with BCS+RT versus 26% with BCS alone, resulting in a 5 year local recurrence risk reduction of 19%. The 15 year breast cancer mortality was reduced by 5.4% given a 30.5% reduction with BCS+RT versus 35.9% with BCS alone.

34. Which of the following parameters predicts a higher risk of local recurrence when using tandem and ovoids for cervical cancer brachytherapy?

- (A) Tandem in midpelvis
- (B) Appropriate vaginal packing
- (C) Symmetrically placed ovoids to tandem
- (D) Displacement of ovoids away from cervix

Key: D

Rationale: Patients with displacement of the ovoids in relation to the cervical os had a significantly increased risk of local recurrence and a lower DFS rate in review of quality for RTOG 0116 and 128. Ideally, the tandem should be in midpelvis and bisect the ovoids. The ovoids should rest against the cervix face. Appropriately placed vaginal packing secures the implant while further displacing the bladder and rectum.

References: Viswanathan, et al, The Quality of Cervical Cancer Brachytherapy Implantation and the Impact on Local Recurrence and Disease Free Survival in Radiation Therapy Oncology Group Prospective Trials 0116 and 0128), (2012).

35. The MOST important prognostic factor for soft tissue sarcoma is:

- (A) age.
- (B) grade.
- (C) lymph node status.
- (D) histologic subtype.

Key: B

Rationale: Histologic grade and tumor size have been consistently found to be independent predictors of prognosis.

36. A fetus that receives 25 cGy of X-rays after the 16th week of gestation is at elevated risk for:

- (A) miscarriage.
- (B) carcinogenesis.
- (C) growth retardation.
- (D) congenital malformations.

Key: B

Rationale: From about 16 weeks gestation until birth, non-cancer health effects in the fetus are very unlikely, especially for doses below ~50 cGy. However, doses to a fetus in the range of 5-50 cGy are associated with an increased risk of childhood cancer (leukemia in particular).

37. In radiation shielding calculations, the use factor (U) is defined as the fraction of time that:

- (A) the beam is turned on in a day.
- (B) the isocenter is not blocked by a primary jaw or MLC.
- (C) a radiation worker may be present when the beam is on.
- (D) the radiation is directed at a particular shielding structure.

Key: D

Rationale: The Use factor (U) is the fraction of time during which the radiation under consideration is directed towards a particular structure.

38. Which method combines pertinent qualitative and quantitative data from selected studies to develop a conclusion that has a greater statistical power?

- (A) Meta-analysis
- (B) Cox regression
- (C) Analysis of variance
- (D) Pearson product-moment correlation coefficient

Key: A

Rationale: A meta-analysis is a method of systematically combining pertinent qualitative and quantitative study data from several selected studies to develop a single conclusion that has a higher statistical power. Cox regression (or proportional hazards regression) is method for investigating the effect of several variables upon the time a specified event takes to happen. In the context of an outcome such as death this is known as Cox regression for survival analysis. Analysis of variance (ANOVA) is a collection of statistical models used to analyze the differences between group means and their associated procedures such as variation among groups. ANOVAs are useful in comparing (testing) three or more means (groups or variables) for statistical significance. Pearson product-moment correlation coefficient is a measure of linear correlation between two variables.

39. What is the advantage of using a parallel-plate ionization chamber over a cylindrical ionization chamber for radiation dose measurement?

- (A) Reduced equipment cost
- (B) Reduced beam direction dependence
- (C) Reduced sensitivity to scatter radiation
- (D) Reduced cavity perturbations due to smaller electrode spacing

Key: D

Rationale: Because of the small electrode spacing (typically $\sim 2\text{mm}$), a parallel-plate chamber minimizes cavity perturbations in the radiation field and serves as a good dosimeter for electron beams and surface dose measurements.

40. 5 Gy of X-rays is delivered to mammalian cells *in vitro* using a megavoltage linear accelerator. What is the MOST likely observation 6 hours after irradiation?

- (A) Approximately 30 γ H2AX subnuclear foci are counted per cell per Gy
- (B) The BRCA1 protein localizes to a subset of the total number of radiation-induced subnuclear foci
- (C) Using the comet assay, the length of the "tail" is reduced in the irradiated cells compared to unirradiated cells
- (D) Using pulsed-field gel electrophoresis, the fraction of DNA released from the agarose plug is at its maximum relative to other time points

Key: B

Rationale: The correct answer is C. The majority of DNA double strand breaks are repaired via non-homologous end-joining, with a minority repaired via homologous recombination. BRCA1, which is involved in homologous recombination repair, localizes to a subset of radiation induced DNA repair foci. Most of the DNA damage capable of being repaired already has been by 6 hours after irradiation. In fact, 40-50% of double strand breaks are repaired within 30 minutes and may not produce radiation-induced foci at all. An average of 20-40 double-strand breaks per Gy is produced initially, however far fewer ionically foci will persist 6 hours post-radiation. Using pulsed-field gel electrophoresis, the maximum DNA released from the agarose plug would occur immediately after radiation before repair occurs, not 6 hours later. The comet assay measures fragmented DNA released from the nucleus when an electric field is applied. A longer comet "tail" reflects more DNA double strand breaks than a shorter tail.

41. What commonly used component of the photon beam delivery system is NOT essential for linac based IMRT delivery?

- (A) Target
- (B) Primary jaw
- (C) Flattening filter
- (D) Monitor chamber

Key: C

Rationale: An IMRT plan modulates the beam intensity to create a non-uniform beam. Therefore a flattening filter, whose purpose is to create uniformly flat beam intensities, is not needed. Flattening filters are still used in some IMRT plans, but they are not required. Although the MLC or a compensator modulates the beam, the primary jaws are still needed to block radiation outside the largest extent of the field. Monitor chambers are used in the treatment head to measure the output of the machine and are used for all external beam RT modalities. Scattering foils are used for electrons.

42. According to RTOG 0129, which patient related characteristics of oropharyngeal squamous cell carcinoma correlates with lowest OS?

- (A) HPV negative, ≤ 10 pky smoking, T2N1M0
- (B) HPV negative, ≤ 10 pky smoking, T4N0M0
- (C) HPV positive, ≤ 10 pky smoking, T2N2bM0
- (D) HPV positive, ≥ 10 pky smoking, T2N2aM0

Key: B

Rationale: Recursive-partitioning analysis was used to identify prognostic factors with the most influential predictive significance in a proportional-hazards model of overall survival and to classify patients into categories of low, intermediate, or high risk of death. The prognostic factors in the analysis were age, tumor stage, nodal stage, race, smoking status, HPV status, anemia status, performance status, treatment assignment, and sex. The 3-year rates of overall survival were 93.0% (95% CI, 88.3 to 97.7) in the low-risk group, 70.8% (95% CI, 60.7 to 80.8) in the intermediate-risk group, and 46.2% (95% CI, 34.7 to 57.7) in the high-risk group. Both options of C and D are low risk groups and A is intermediate risk group. Option B is high risk with expected 3-year survival rate of 46%.

43. Regarding prostate cancer, CT of the pelvis is equivalent or better than MRI for evaluating:

- (A) lymph nodes.
- (B) zonal anatomy.
- (C) neurovascular bundles.
- (D) extracapsular extension.

Key: A

Rationale: MRI has been shown to be superior to CT in identifying prostate zonal anatomy, prostatic apex, neurovascular bundles, ECE, anterior rectal wall, seminal vesicles invasion, penile bulb and local extent of the disease.

44. Which of the following tumors is MOST likely to be associated with long-term diabetes insipidus?

- (A) Pineal germinoma
- (B) Craniopharyngioma
- (C) Pituitary adenoma
- (D) Cavernous sinus meningioma

Key: B

Rationale: Although pineal germ cell tumors may involve suprasellar and third ventricular structures leading to diabetes insipidus, approximately 60% of craniopharyngioma patients will experience long-term diabetes insipidus.

45. Patients with inherited BRCA1 mutations tend to exhibit which breast cancer molecular subtype?

- (A) Her2+
- (B) Basal
- (C) Luminal A
- (D) Luminal B

Key: B

Rationale: The majority of breast cancers arising in BRCA1 mutation carriers exhibit the basal expression subtype. (BRCA2 mutation carriers most frequently develop receptor positive cancers.) Luminal A and B are gene expression subtypes that correspond to estrogen receptor positive cancers of low and high grade, respectively. Her2+ cancers constitute a third subtype in which tumor cells overexpress human epidermal growth factor receptor 2 on their outer cell membranes, which stimulates cell growth and proliferation.

46. Which of the following makes pancreatic cancer unresectable?

- (A) CA 19-9 of 250 ng/mL
- (B) Invasion of the duodenum
- (C) Encasement (270 degrees) of the superior mesenteric artery
- (D) Involvement of peri-pancreatic lymph nodes in the field of resection

Key: C

Rationale: Greater than 180 degree SMA encasement is considered unresectable. Clearly resectable tumors must have an intact fat plane around the SMA. CA 19-9, invasion of the duodenum, and regional lymph node involvement in the field of resection do not make a tumor unresectable.

References: NCCN Clinical Practice Guidelines in Oncology.

47. In the 2014 EBCTCG meta-analysis for effect of PMRT, the RT fields treated in the vast majority of the trials were:

- (A) chest wall and low axilla.
- (B) chest wall, supraclavicular fossa, and undissected axilla.
- (C) supraclavicular and axillary fossa and internal mammary chain.
- (D) chest wall, supraclavicular or axillary fossa or both, and internal mammary chain.

Key: D

Rationale: The EBCTCG meta-analysis of node positive women treated with mastectomy and axillary surgery, radiotherapy data was available for 22 trials in which RT was directed to the chest wall and regional lymphatics (supraclavicular or axillary fossa or both). This included the internal mammary chain in 20 of 22 trials.

48. Which is a recognized risk factor for the development of primary adenocarcinoma of the urinary bladder?

- (A) Cigarette smoking
- (B) Chronic indwelling catheter
- (C) Persistence of an urachal remnant
- (D) Infection with schistosoma haematobium

Key: C

Rationale: adenocarcinoma of the urinary bladder is a rare entity comprising 1-2% of all bladder cancer. It is believed that the cancer may arise in the remnant of the fetal urachus. Both infection with the parasite *Schistosoma haematobium*, primarily in the middle east, and the presence of the irritation associated with a chronic indwelling catheter are associated with squamous cell carcinoma of the bladder (approximately 5% of bladder tumors.) By far the most common histology associated with bladder cancer is transitional cell carcinoma (90% of bladder cancers) for which there is a strong association with cigarette smoking.

49. Desmoid tumors arising in patients with familial adenomatous polyposis predominate in which of the following anatomic sites?

- (A) Thorax
- (B) Abdomen
- (C) Extremities
- (D) Head and neck

Key: B

Rationale: In patients with FAP, intra-abdominal desmoids predominate and tend to be associated with surgical sites and anastomoses following colectomy. In patients with sporadic desmoids, the most common sites are the extremities, the shoulder girdle and the buttock areas.

50. Based on the outcome of the MRC trial TE 10 (1999) which compared para-aortic and ipsilateral pelvic (dog-leg) versus para-aortic only radiation field, it can be concluded that:

- (A) dog-leg field should be used for Stage IA seminoma.
- (B) dog-leg field should be used for Stage IIA seminoma.
- (C) para-aortic fields should be used for Stage IA seminoma.
- (D) para-aortic fields should be used for Stage IIA seminoma.

Key: C

51. Telomere degradation with each subsequent cell division ultimately will result in:

- (A) necrosis.
- (B) apoptosis.
- (C) autophagy.
- (D) senescence.

Key: D

Rationale: As a cell divides, its telomeres are reduced in size until the sequence is no longer able to "cap" the end of the chromosome. Once this occurs, the end of the chromosome may be recognized as an open break end, akin to an unrejoined DNA double stranded break, at which point the cellular repair machinery permanently halts cell cycle progression, causing the cell to senesce.

52. A 10 MV photon beam traverses 12 cm of lung tissue. The approximate correction factor for the increased absorbed dose due to this inhomogeneity is:

- (A) 12%.
- (B) 18%.
- (C) 30%.
- (D) 48%.

Key: C

Rationale: The correction factor for 10 MV radiation traversing lung tissue is approximately 2.5% per cm

53. On the EORTC "non-believers" trial of low grade glioma, early post-operative radiotherapy decreased:

- (A) OS.
- (B) quality of life.
- (C) rate of seizures.
- (D) rate of high grade recurrence.

Key: C

Rationale: The EORTC 22845 'Non-Believers' trial randomized patients with low grade glioma to immediate post-operative 54 Gy vs. observation. Results showed an increase in PFS (median 5.3 years with RT vs. 3.4 years with observation), no increase in OS (7.4 years vs. 7.2 years), no difference in rate of high grade glioma at recurrence (72% with RT and 66% with observation) and a lower rate of seizure at 1 year (25% with RT vs. 41% with observation). Quality of Life was not assessed.

54. Which characteristic makes cancer stem cells an important determinant of resistance to RT?

- (A) Absence from metastatic sites
- (B) Ability to repopulate during treatment
- (C) Presence of multiple DNA repair deficiencies
- (D) Can initiate carcinogenesis following a stem cell transplant

Key: B

Rationale: Cancer stem cells are pluripotent cells with a high replicative potential, that give rise both to more stem cells and to tumor progenitor cells that become heterogeneous genotypically and phenotypically. Not only are they thought to be resistant to conventional therapies, but also they have the ability to repopulate an entire tumor with progenitors. Cancer stem cells are implicated in the metastatic process and may be enriched in sites of metastatic disease, however they have no role in cancers that may arise following a stem cell transplant.

55. Which of the following drugs is associated with an increased risk of cardiac disease when used with trastuzumab?

- (A) Paclitaxel
- (B) Doxorubicin
- (C) Fluorouracil
- (D) Cyclophosphamide

Key: B

Rationale: Doxorubicin is associated with cardiotoxicity. When used in combination with trastuzumab, there is an increased risk of cardiac disease. There is an added concern for higher cardiac toxicity with the addition of radiation. Maximal cardiac sparing is needed to minimize the risk of cardiotoxicity.

56. A 7-year-old undergoes a gross total resection of a classic medulloblastoma. A lumbar puncture obtained 14 days after surgery identifies two metastatic cells. MRI scans of brain and spine show no evidence of metastases. What is an appropriate RT regimen for this patient?

- (A) None
- (B) 23.4 Gy in 13 fractions of CSI followed by 30.6 Gy in 17 fractions to the resection bed plus margin
- (C) 36 Gy in 20 fractions of CSI followed by 18 Gy in 10 fractions to the resection bed plus margin
- (D) 54 Gy in 30 fractions to the resection bed plus margin

Key: C

Rationale: A patient with a positive lumbar puncture has M1 disease and is considered high risk. Therefore, she should receive high dose craniospinal irradiation, 36Gy in 20 fractions, followed by a boost to the primary site to a total dose of 54-55.8Gy.

References: Halperin, Pediatric Radiation Oncology.

57. To limit Grade 3 acute small bowel toxicity to <10% with postoperative pelvic 3DCRT for a cervical cancer, QUANTEC recommends that the V45 not exceed:

- (A) 195 cc.
- (B) 225 cc.
- (C) 250 cc.
- (D) 300 cc.

Key: A

Rationale: The Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC) identifies an increased risk for Grade 3 toxicity if the V45 for small bowel exceeds 195cc. In this case the volume is based on the entire potential space within the peritoneal cavity.

References: Marks, L.B. et al., Use of Normal Tissue Complication Probability Models in the Clinic, (2010).

58. Per NCCN guidelines, which ovarian cancer histology may be considered for RT or platin-based chemotherapy for Stages II to IV tumors?

- (A) Epithelial
- (B) Low malignant potential
- (C) Malignant mixed Mullerian
- (D) Malignant sex cord-stromal

Key: D

Rationale: For patients with Malignant Sex Cord-Stromal Tumors with high-risk stage I (tumor rupture, stage IC, poorly differentiated tumor, tumor size >10-15 cm) recommendations include observation or consideration of platinum based chemotherapy. Those with surgical findings of low risk disease should be observed. For patients with granulosa cell tumors who are being observed inhibin should be followed if they were initially elevated. For patients with Stage II-IV tumors, recommended options include RT for limited disease or platinum-based chemotherapy. However in 2013 the NCCN panel added surveillance recommendations for malignant sex-cord stromal tumors which are based on the SGO recommendations. Prolonged surveillance was recommended for granulosa cell tumors because they recur later (30 years). For recurrences then options include clinical trial or targeted recurrence strategies.

59. In terms of freedom from treatment failure and OS, what was the finding of the German HD10 trial?

- (A) 2 cycles of ABVD and 20 Gy of IFRT was equal.
- (B) 2 cycles of ABVD and 20 Gy of IFRT was worst.
- (C) 2 cycles of ABVD and 30 Gy of IFRT was best.
- (D) 4 cycles of ABVD and 30 Gy of IFRT was better.

Key: A

Rationale: For favorable patients, the German HD 10 showed equivalent outcome at 5 yrs for 2 cycles of ABVD and 20 Gy IFRT compared with 4 cycles of ABVD and 30 Gy IFRT.

60. According to the ACT II study of definitive chemoradiation for anal cancer, the complete response rate (%) at 26 weeks was:

- (A) 60.
- (B) 70.
- (C) 80.
- (D) 90.

Key: D

Rationale: The ACT II study is a 2 × 2 factorial trial which enrolled patients with histologically confirmed squamous-cell carcinoma of the anus without metastatic disease from 59 centres in the UK. Patients were randomly assigned to one of four groups, to receive either mitomycin (12 mg/m²) on day 1) or cisplatin (60 mg/m²) on days 1 and 29), with fluorouracil (1000 mg/m²) per day on days 1-4 and 29-32) and radiotherapy (50.4 Gy in 28 daily fractions); with or without two courses of maintenance chemotherapy (fluorouracil and cisplatin at weeks 11 and 14). With a median follow-up of 5.1 years, maintenance chemotherapy either regimens did not improve progression-free survival compared with no maintenance chemotherapy.

61. According to NCCN guidelines, what is the preferred management of a 3.8 cm pure seminoma without elevation of tumor markers preoperatively, with involvement of the tunica albuginea, no LVSI, and no other abnormalities detected on imaging?

- (A) Observation
- (B) A single dose of carboplatin
- (C) 3 cycles of etoposide and cisplatin
- (D) RT to the para-aortic lymph nodes only to a dose of 20 Gy in 10 fractions

Key: A

Rationale: For a pT1 pure seminoma, the category 1 options for treatment include: Observation, Radiation to a dose of 20 Gy and a single dose of Carboplatin. The disease specific survival is approximately 99% for all options and the relapse rate within 5 years is 15% for observed patients. Patients can be effectively salvaged when they do fail. There is also significant concern for long term toxicities from chemotherapy and radiation, including secondary malignancies. That being said the NCCN now agrees that Observation (Choice A) is the preferred post orchiectomy strategy for pT1a seminoma patients. Multi-chemotherapy regimens (Choice B) are reserved for patients with Stage IIA or greater disease. However, if Etoposide and Cisplatin are used, the recommendation is for 4 cycles.

62. In addition to the nasopharynx and retropharyngeal nodes, what areas should be included in the radiation field for the treatment of a T1N0M0 squamous cell carcinoma of the nasopharynx involving Rosenmüller fossa?

- (A) None
- (B) Bilateral levels 2-4 neck
- (C) Bilateral levels 2-5 neck
- (D) Ipsilateral levels 2-4 neck

Key: C

Rationale: A meta-analysis showed that 85% of NPC cases presented with lymphadenopathy. The most commonly involved regions include retropharyngeal (69%) and level II lymph nodes (70%). The overall probability of levels III, IV, and V nodal involvement are 45%, 11%, and 27%, respectively. Low-risk node groups included the supraclavicular, levels IA/IB and VI nodes, and parotid nodes with involvement rates at 3%, 0%, 3%, 0%, and 1%, respectively. Nodal metastases followed an orderly pattern and the probability of "skip" metastasis between levels varied between 0.5-7.9%.

63. The RTOG 9704 pancreatic cancer study demonstrated that:

- (A) adjuvant chemoradiation improves OS.
- (B) neoadjuvant chemoradiation improves OS.
- (C) adjuvant gemcitabine and 5-FU following chemoradiation show similar efficacy.
- (D) gemcitabine and 5-FU showed similar efficacy as a radiosensitizer during chemoradiation.

Key: C

Rationale: RTOG 9704 tested systemic 5FU vs gemcitabine in the adjuvant setting, after resection of pancreatic cancer. Patients received one month of chemotherapy, followed by chemoradiation followed by an additional 3 months of chemotherapy. The chemoradiation for all patients was infusional 5FU with a total dose of 5040 cGy of radiation. Median OS was 20.5 months with gemcitabine and 17.1 months with 5FU (P=0.12).

References: Regine WF, et al, Ann Surg Oncol, (2011)

64. Stage II tumors of the vulva involve the:

- (A) cervix, vagina, or anus.
- (B) lower urethra, vagina, or anus.
- (C) cervix, lower urethra, or vagina.
- (D) bladder, vagina, or lower urethra.

Key: B

Rationale: Stage II tumors are defined as lesions involving the lower urethra, vagina, or anus.

65. Per NCCN guidelines, what is the appropriate adjuvant therapy for a T1B serous carcinoma of the uterus that has undergone complete surgical staging?

- (A) Vaginal brachytherapy
- (B) Pelvic external beam RT
- (C) Whole abdominopelvic RT
- (D) Chemotherapy with or without tumor directed RT

Key: D

Rationale: Chemotherapy with or without tumor directed radiation is recommended for serous carcinomas as the preferred adjuvant therapy. For the 2014 update, whole abdominopelvic radiation with or without brachytherapy is no longer recommended as a primary treatment option.

Tumor-directed radiation is treatment to sites of known or suspected tumor involvement and may include external beam and/or vaginal brachytherapy.

66. Per consensus guidelines, what comprises the CTV for IMRT pelvic radiotherapy for the definitive treatment of IB2 cervical cancer?

- (A) GTV, cervix, parametrium, upper half of vagina
- (B) GTV, cervix, lower uterine segment, parametrium
- (C) GTV, cervix, entire uterus, parametrium, upper half of vagina
- (D) GTV, cervix, lower uterine segment, parametrium, upper half of vagina

Key: C

Rationale: CTV= entire GTV, entire cervix, entire uterus, entire parametrium including ovaries (include the entire mesorectum if the uterosacral ligament involved), for minimal or no vaginal extension such as this case then the upper half of the vagina is included.

References: Lim, et al., Consensus Guidelines for Delineation of Clinical Target Volume for Intensity-Modulated Pelvic Radiotherapy for the Definitive Treatment of Cervical Cancer, (2011).

67. Historically, HIF-1 α was considered an “un-druggable” target, however, recent data suggest that several agents can inhibit this pathway, including:

- (A) vincristine.
- (B) camptothecin.
- (C) 5-fluorouracil.
- (D) cyclophosphamide.

Key: B

Rationale: Camptothecin, a topoisomerase 1 inhibitor, has been shown to inhibit HIF-1 α by blocking its translation. Similarly, anthracyclines such as doxorubicin also inhibit the actions of HIF-1 α , in this case by blocking its binding to DNA, which in turn prevents the transcription of HIF-1’s target genes (see Lee K et al. PNAS 2009;106(7):2353–2358).

68. Adult survivors of childhood ALL who were treated with cranial RT are more likely to have increased:

- (A) hair.
- (B) intelligence.
- (C) abdominal fat.
- (D) body mass index.

Key: C

Rationale: Body mass index was not increased in a cohort of adult survivors of childhood ALL who received cranial irradiation but abdominal fat was. Hair and intelligence might only be decreased.

69. According to the EORTC 20884 trial (Aleman), which of the following is TRUE regarding patients who received IFRT versus no further treatment after a complete response for stage III or IV Hodgkin lymphoma?

- (A) Improvement in OS
- (B) Significant decrease in fertility
- (C) Improvement in event-free survival
- (D) Significant increase in second cancers

Key: D

Rationale: No overall survival or event-free advantage was observed. However, an almost 2-fold increase in second cancers was noted in those who received IFRT.

70. Which of the following is associated with superior survival in patients with glioblastoma?

- (A) Inclusion of edema on T2 or FLAIR in the initial GTV
- (B) Presence of isocitrate dehydrogenase (IDH) 1-mutation
- (C) Escalation of radiation dose above 60 Gy in 30 fractions
- (D) Addition of bevacizumab to radiotherapy and temozolomide

Key: B

Rationale: Glioblastoma studies, including the Stupp trial, using gross tumor volumes excluding edema have had similar survival outcomes compared to those studies using gross tumor volumes including edema. Addition of bevacizumab has not been shown to improve survival in patients with glioblastoma. Dose escalation beyond 60 Gy has not shown to improve survival in glioblastoma patients in phase III trials.

71. Which treatment option offers the strongest evidence for the management of metastatic clear cell renal cell carcinoma?

- (A) Prophylactic cranial irradiation
- (B) Conventional multi-agent chemotherapy
- (C) SBRT to the primary tumor and sites of oligometastasis
- (D) Cytoreductive nephrectomy followed by systemic therapy

Key: D

Rationale: Renal Cell Carcinoma is relatively resistant to conventional chemotherapy (Choice B) with poor response rates (Choice B). Although renal cell carcinoma can cause brain metastasis they are often solitary and prophylactic cranial irradiation (Choice A) would not be reasonable treatment for anything other than small cell lung cancer. Stereotactic radiotherapy (Choice D) is often used to treat intracranial metastasis from renal cell carcinoma as well as other sites of metastasis, however Stereotactic radiotherapy to the renal primary is only in its infancy and is yet to be rigorously tested. Multiple studies have demonstrated the benefits of Cytoreductive nephrectomy followed by systemic therapy (Choice C) with primarily biologic agents such as Interferon, IL-2, and more recently anti-angiogenic agents.

72. An electron passes through a potential difference of 120 V, causing the electron to acquire a kinetic energy equal to:

- (A) 120 J.
- (B) 120 eV.
- (C) 120 MV.
- (D) 120 kVp.

Key: B

Rationale: This question requires knowledge of energy units commonly used in radiation therapy.

73. What is the recommended minimal surgical margin in fixed tissue for excision of a squamous cell carcinoma of the vulva?

- (A) 2 mm
- (B) 4 mm
- (C) 8 mm
- (D) No tumor at ink

Key: C

Rationale: A tumor free gross surgical margin of ≥ 1 cm is required due to shrinkage of normal tissue margins consequent to fixation that has been estimated at 20%. Therefore, an 8 mm margin in fixed tissue will correspond to an approximate clinical margin of 1 cm in vivo. For patients with tumor at or < 8 mm, re-excision is advocated. If re-excision is not feasible then radiation is an alternative.

74. The Ku proteins involved in NHEJ are:

- (A) DNA ligases.
- (B) protein kinases.
- (C) metalloproteases.
- (D) DNA binding proteins.

Key: D

Rationale: The eukaryotic Ku protein is a heterodimer of Ku70 (XRCC6) and Ku80 (XRCC5) that participates in NHEJ, although is not a DNA repair protein per se. Instead, Ku functions as a molecular scaffold to which other proteins involved in NHEJ can bind, including the main repair protein, DNA-PKcs. Ku binds to and forms a sheath around the DNA that is capable of sliding along the helix as repair progresses. It also acts to stabilize and align broken DNA ends so that they don't unwind or mis-rejoin.

75. According to INT 0116, adjuvant chemoradiotherapy for gastric cancer is MOST appropriate for which of the following?

- (A) pT3N1 disease, D0 dissection, diffuse type
- (B) pT3N1 disease, D1 dissection, diffuse type
- (C) pT1N0 disease, D1 dissection, intestinal type
- (D) pT3N1 disease, D1 dissection, intestinal type

Key: D

Rationale: Most patients on the INT0116 trial had a D1 or less dissection. Although adjuvant chemoradiation is an appropriate option for patients with D2 dissection, subsequent trials in D2 patients have since shown that adjuvant chemotherapy alone can also achieve comparable improvements in survival. Therefore, adjuvant chemoradiation is especially appropriate for D1-resected patients, since the chemotherapy-alone regimens do not necessarily apply. The updated analysis of INT0116 indicated that there was no benefit to chemoradiation in diffuse-type cancer. T1N0 patients were not eligible for inclusion on the INT0116 trial.

References: Smalley, SR, J Clin Oncol, (2012).

76. Which of the following ABVD agents causes pulmonary toxicity?

- (A) Bleomycin
- (B) Dacarbazine
- (C) Doxorubicin
- (D) Vinblastine

Key: A

Rationale: Bleomycin can cause pulmonary toxicity.

77. If a tertiary MLC is added to a linear accelerator to enable the IMRT delivery, the improvement in the physical penumbra will likely be due to a decrease in which component of the penumbra?

- (A) Scatter
- (B) Leakage
- (C) Geometric
- (D) Transmission

Key: C

Rationale: The physical penumbra is the composite of the scatter, geometric and transmission penumbras. By adding a tertiary MLC, the source to diaphragm distance (SDD) increases and thereby reduces the geometric penumbra in the patient.

78. Compared to CT-based IGRT, what is an advantage of integrated MRI-external beam radiotherapy?

- (A) Increased RBE due to MR field
- (B) Decreased treatment delivery time
- (C) Image guidance with improved spatial resolution
- (D) Image guidance with improved soft tissue visualization

Key: D

Rationale: MRI guided RT provides better soft tissue visualization. There is no increased RBE from MR. The treatment delivery is not effected by the presence of the MRI. Spatial resolution of MRI is not an advantage compared to CT based IGRT.

79. Regarding the use of an intention-to-treat analysis:

- (A) the benefits of randomization are lost.
- (B) subjects that are lost to follow up are optimally accounted for.
- (C) participants are analyzed according to the assigned randomized group.
- (D) it will not account for factors that can influence the outcomes of prescribed treatment.

Key: C

Rationale: The central principle underlying intention-to-treat analysis is that study participants should be analyzed according to the groups in which they were randomized, even if they did not receive or comply with treatment. Such analysis is contrasted to "as treated" analysis, in which subjects are analyzed according to the actual treatment they received. The theoretical advantage of intention-to-treat analysis is that it preserves the benefits of randomization. For example, it is possible that patients who complied with treatment differed in some important ways than those who did not. Another way to consider the advantage of intention-to-treat analysis is that it better accounts for factors that can influence the outcomes of a prescribed treatment, not just the effects on those who adhered to it. A drug which has serious side-effects but is highly effective, for example, might look favorable in an "as treated" analysis but less favorable in an intention-to-treat analysis if the majority of patients could not tolerate it. Although conceptually simple, analyzing according to intention-to-treat principles can be complex. For example, optimal methods to account for subjects who were lost to follow-up remain uncertain. Such patients could be considered as treatment failures, however, such an approach can be overly punitive for an otherwise promising therapy. Because of these complexities, studies that reported that they performed an intention-to-treat analysis, may not have always done so or have modified the approach in some way.

80. Regarding von Hippel-Lindau (VHL) for renal cell carcinoma, it is:

- (A) an autosomal recessive germline mutation.
- (B) a VHL protein not involved in angiogenesis.
- (C) associated with papillary renal cell carcinoma.
- (D) caused by germline mutation on chromosome 3p.

Key: D

Rationale: VHL is autosomal dominant and caused by germline mutation of the VHL tumor suppressor gene located on chromosome 3p25-26. VHL protein is involved in cell cycle regulation and angiogenesis. VHL is associated with clear cell renal cell carcinoma.

81. Which of the following is the MOST appropriate treatment for intermediate and high grade chondrosarcomas?

- (A) Surgical excision
- (B) Definitive radiation therapy
- (C) Neoadjuvant chemotherapy followed by surgery
- (D) Neoadjuvant chemoradiation followed by surgery

Key: A

Rationale: Surgery is the treatment of choice for intermediate and high grade tumors.

82. A 71-year-old with deep myometrial invasion is considered what endometrial risk stratification (GOG)?

- (A) Low
- (B) Low-Intermediate
- (C) High-Intermediate
- (D) High

Key: C

Rationale: Low risk defines women with G1 endometrial cancer confined to the endometrium and are at a very low risk for cancer recurrence following surgery alone. Intermediate risk patients have cancers that invade the myometrium or demonstrate occult cervical stromal invasion. Other adverse prognostic factors are used to stratify them into low- and high- intermediate risk. These factors include outer 1/3 myometrial invasion, grade 2 or 3 differentiation, or the presence of LVI in the cancer. High-intermediate risk is based on a combination of age and number of prognostic factors present. High-intermediate risk==per GOG if they are ≥ 70 with one risk factor, 50-69 with 2 risk factors or ≥ 18 with all 3 factors. Otherwise they are classified as low-intermediate if they meet some of the criteria but do not fully fit these criteria. A high risk patient is one with Stage III disease regardless of histology or grade in addition to uterine serous carcinoma or clear cell at any stage. NCCN guidelines for adjuvant therapy recommendations for Stage I cancers considers the adverse risk factors.

83. In a phase II trial, it has been determined that the data do NOT follow a normal distribution. What test could the researchers use to help analyze the data?

- (A) T-test
- (B) Z-test
- (C) Chi-square test
- (D) Wilcoxon rank sum test

Key: D

Rationale: A chi-square test checks for independence, a t-test compares the mean from a normal distribution from a small number of samples, a z-test is like a t-test but for a large number of samples, the Wilcoxon rank sum test is used when the distribution is NOT normal.

References: Dawson B and Trapp RG, Basic and Clinical Biostatistics, (2004) -Pages 134 and 162.

84. In a Phase I-II dose escalation SBRT trial for prostate cancer, what percent of the rectal wall circumference receiving 39 Gy was correlated with Grade 3 or higher late rectal toxicity?

- (A) 15
- (B) 25
- (C) 35
- (D) 45

Key: C

Rationale: In this recently reported Phase I-II dose escalation SBRT trial for prostate cancer, more than 35% of the rectal wall circumference receiving 39 Gy and more than 3cc of rectal wall volume receiving 50 Gy were correlated with Grade 3 or higher late rectal toxicity.

85. Which is the CORRECT match between whole body dose and likely outcome?

- (A) 2 Sv – epilation within a week
- (B) 9 Sv – brain edema within minutes
- (C) 5 Sv – low red blood cell count within a month
- (D) 7 Sv – nausea, vomiting, and diarrhea within hours

Key: D

Rationale: A dose of 7 Sv will cause severe nausea and vomiting as well as diarrhea, typically within a couple of hours of radiation exposure. Doses greater than 8 Gy are usually lethal (although there have been exceptions), but not because of brain edema, but rather because of the gastrointestinal syndrome. The cerebrovascular syndrome, which would cause brain edema as a major symptom, has a much higher threshold dose than 9 Gy. A dose of 5 Gy is a high enough dose to elicit the hematopoietic syndrome; however red blood cell counts are typically the least affected by radiation exposure. A dose of 2 Gy is at or near the threshold dose to cause epilation, but even if it did occur, it would take longer than a week to manifest.

86. In a perfectly calibrated CT scanner, water is assigned a value of how many Hounsfield units?

- (A) -1,000
- (B) 0
- (C) 100
- (D) 1,000

Key: B

Rationale: CT numbers are all relative to the value of water that is defined as 0.

87. Regarding the use of adjuvant chemotherapy following surgical resection for lung cancer:

- (A) there is an improvement in OS of 10%, based on the LACE meta-analysis.
- (B) the combination of cisplatin and vinorelbine demonstrated the largest benefit in OS.
- (C) in the absence of nodal involvement, CALGB 9633 demonstrated an improvement in OS.
- (D) the combination of carboplatin and paclitaxel has the largest relative improvement in OS.

Key: B

Rationale: In the most recent update of CALGB 9633, which was the only phase III trial to test the combination of carboplatin and paclitaxel, there was no difference in outcomes for tumors > 3 cm without nodal involvement. There is a suggestion of an improvement in patients with tumors > 4 cm but this was based on an unplanned subset analysis. The survival benefit of adjuvant chemotherapy based on the LACE meta-analysis was 4% with the largest improvement seen in patients treated with cisplatin and vinorelbine.

88. According to TROG 96-06, the only factor predictive of OS for node-positive melanoma patients treated with surgery and postoperative radiation was:

- (A) extracapsular extension.
- (B) presence of a known primary.
- (C) location of nodal involvement.
- (D) number of positive lymph nodes.

Key: D

Rationale: The 5-year overall survival was 35%. On subset analysis, the only factor that adversely impacted overall survival and progression-free survival was ≥ 3 positive lymph nodes (P = .01 and P = .03, respectively).

89. A poor candidate for the bladder preservation approach (combined TURBT and chemoRT) has:

- (A) extensive CIS.
- (B) T2 or T3 tumor.
- (C) good bladder capacity.
- (D) no tumor associated hydronephrosis.

Key: A

Rationale: Ideal candidate has unifocal T2-T3a tumors, tumor less than 5cm, no extensive CIS, no ureteral obstruction or tumor associated hydronephrosis, good bladder capacity and renal function as well as visibly complete TURBT.

90. Genetic deficiency in which of the following components of the NHEJ machinery results in severe combined immunodeficiency (SCID) in humans?

- (A) ATM
- (B) RPA
- (C) Rad50
- (D) Artemis

Key: D

Rationale: Non-homologous end-joining (NHEJ) through V(D)J recombination is a critical pathway to provide genetic diversity in T cell receptors and immunoglobulins. The RAG nucleases create hairpins in V, D, and J segments that are cleaved by Artemis before end-joining occurs. Artemis deficiency therefore results in severe combined immunodeficiency due to defective V(D)J recombination. Genetic deficiency of ATM results in ataxia telangiectasia but not SCID. The RPA protein binds single stranded DNA and plays an important role in homologous recombination (HR), but not NHEJ. Deletion of RPA is embryonic lethal in mice, as is the deletion of RAD50, which is involved in both HR and NHEJ.

91. What is an unfavorable risk factor for early stage Hodgkin lymphoma?

- (A) Bulky
- (B) Normal ESR
- (C) Less than 2 nodal sites involved
- (D) Asymptomatic presentation (i.e., no B symptoms)

Key: A

Rationale: Bulky presentation is considered an unfavorable risk factor per GHSG, EORTC, NCIC, and NCCN.

92. What is the TNM stage for a 2.5 cm tumor of the AE fold with paraglottic space invasion and 3.5 cm ipsilateral level II node without evidence of distant disease?

- (A) T2N1M0, Stage III
- (B) T2N2aM0, Stage IVa
- (C) T3N1M0, Stage III
- (D) T3N2aM0, Stage IVa

Key: D

Rationale: Paraglottic space invasion moves a cancer from T2 to T3 and a single lymph node greater than 3 cm is N2a. A paretic vocal cord without paraglottic space invasion is T2.

93. What is the MOST appropriate radiation dose and volume for an 11-year-old with a grossly resected supratentorial PNET and no evidence of dissemination?

- (A) 18 Gy CSI followed by boost to 54-55.8 Gy
- (B) 36 Gy CSI followed by boost to 54-55.8 Gy
- (C) 23.4 Gy CSI followed by boost to 54-55.8 Gy
- (D) Radiation to tumor bed with 1.5 cm margins to 54-55.8 Gy

Key: B

Rationale: Recent clinical trials for high-risk medulloblastoma include all patients with PNET regardless of extent of resection or dissemination. These protocols include full dose (~36 Gy) craniospinal radiation therapy.

94. The 10-year results of the EORTC 24891 trial comparing total laryngectomy versus chemoRT for locally advanced hypopharyngeal cancer showed that chemoRT:

- (A) improved OS.
- (B) had a PFS rate of 30%.
- (C) reduced DM as site of first failure.
- (D) had a 70% rate of larynx preservation.

Key: C

Rationale: The hypopharyngeal cancer has poor prognosis. The 10-year OS rate was 13.8% in the surgery arm and 13.1% in the chemotherapy arm. The 10-year PFS rates were 8.5% and 10.8%, respectively. In the chemotherapy arm, the 10-year survival with a functional larynx (SFL) rate was 8.7%. Use of chemoRT did result in a significant reduction in distant metastasis as site of first failure compared to surgery.

95. Which provides a direct measure of tumor oxygenation?

- (A) Interstitial oximetry
- (B) Pimonidazole immunohistochemistry
- (C) Carbonic anhydrase IX (CA-IX) immunohistochemistry
- (D) Epstein-Barr virus-encoded RNA (EBER) immunohistochemistry

Key: A

Rationale: While both CA-IX and pimonidazole are used as markers of hypoxia within tissues, only interstitial oximetry can directly measure oxygen levels within a tissue. EBER staining is a marker used for the diagnosis of Epstein Barr Virus-associated cancers. Studying tumor hypoxia remains important as tumors containing a viable, radiobiologically hypoxic fraction are expected to be 2-3 fold more resistant to radiation than fully oxygenated tumors. However, measuring tumor hypoxia has not yet found its way into routine clinical practice.

96. If the temperature is 2% higher and the pressure is 1% lower than standard conditions, the reading of an open-air ion chamber will be:

- (A) 3% lower.
- (B) 1% lower.
- (C) 1% higher.
- (D) 3% higher.

Key: A

Rationale: Radiation measurements in open-air ion chambers must always be corrected for changes in temperature and pressure. The signal from an ion chamber is proportional to the number of air molecules in the chamber available to be ionized. Increasing the temperature and decreasing the air pressure both serve to reduce the number of air molecules in the chamber, reducing the reading from the ion chamber proportionally.

97. Which pathological feature BEST predicts nodal failure in the absence of adjuvant RT for a pathologic T1-2N0 oral tongue squamous cell carcinoma?

- (A) Pathologic T2
- (B) Perineural invasion
- (C) Poorly differentiated
- (D) Tumor thickness ≥ 4 mm

Key: D

Rationale: In the combined database of patients from MSKCC and PMH (Ganly, 2013), 164 patients with oral tongue squamous cell carcinoma treated with surgery without post-operative radiation therapy were reviewed. Amongst the patient, tumor, and treatment related characteristics reviewed, only tumor thickness ≥ 4 mm was significant in multivariate analysis for neck recurrence (regional recurrence rate 5.7 vs 24%; 5 year neck recurrence free survival 93.5 vs 71.9, $p=0.037$).

98. The MOST likely primary site for a TxN2bM0 head and neck squamous cell carcinoma in a non-smoker is the:

- (A) larynx.
- (B) oropharynx.
- (C) hypopharynx.
- (D) nasopharynx.

Key: B

Rationale: Squamous cell carcinoma of unknown primary in the neck in a non-smoker is most likely to be an HPV related oropharyngeal cancer. Vent, et al. reports that HPV DNA in the metastatic LN resulted in the primary cancer more frequently found in the oropharynx.

99. Regarding postoperative IMRT for cervical cancer with concurrent weekly cisplatin chemotherapy (RTOG 0418), which median percentage of bone marrow volume receiving treatment is the BEST predictor of higher hematological toxicity?

- (A) V10 > 96%
- (B) V20 > 84%
- (C) V30 > 61%
- (D) V40 > 37%

Key: D

Rationale: The median percentage of bone marrow receiving 10, 20, 30, 40 Gy was 96%, 84%, 61%, and 37% respectively. Among cervical cancer patients with a $V40 > 37\%$, 75% had grade 2 or higher hematologic toxicity compared with 40% of patients with a $V40 \leq 37\%$. Cervical cancer patients with a median marrow dose of >34.2 Gy had higher rates of grade 2 hematologic toxicity than those ≤ 34.2 Gy. The authors concluded that the V40, rather than the V10 or V20 is the best predictor of hematologic toxicity in patients receiving pelvic IMRT and chemotherapy.

References: Klopp, et al, Hematologic Toxicity in RTOG 0418: A Phase 2 Study of Postoperative IMRT for Gynecologic Cancer, (2013)

100. What is the recommended treatment for a 3-year-old patient with good vision in the left eye, but a large right eye retinoblastoma that has involvement of the anterior chamber?

- (A) Enucleation
- (B) Brachytherapy
- (C) Intravenous chemotherapy
- (D) External beam radiotherapy

Key: A

Rationale: In an older patient, with unilateral locally advanced retinoblastoma with a none to low chance of vision preservation, enucleation is the best option.

References: Halperin, Pediatric Radiation Oncology.

101. According to EORTC analysis, which is TRUE concerning the use of boost treatment for patients with Stage I-II breast cancer?

- (A) Local control for node positive patients was decreased.
- (B) Local control does not impact mastectomy-free survival.
- (C) Impact of boost decreases with increasing age at diagnosis.
- (D) Local control was improved for patients with close surgical margins.

Key: C

Rationale: All age groups had improvement in local control with the use of boost. The cumulative incidence of LR was 10% vs. 6% for no boost vs. boost. Younger women had a greater benefit than older patients. The absolute risk reduction at 10 years per age group was the largest in patients less than or equal to 40 years of age (23.9% to 15.5% [$p=.0014$]). For women <40 , the local recurrence rate was 13% vs. 3.8% for women > 60 . All patients in this study had microscopically negative margins. There was no difference in SCF or axillary events as site of first recurrence between the boost vs. no boost groups. No specific analysis is reported for node positive vs. node negative patients.

102. A 10-year-old boy with headaches is found to have a pineal mass. Serum and CSF marker levels are: HCG = 30 IU (NL 0-5) and AFP is below detection limit. What is the MOST likely type of tumor and does it require biopsy?

- (A) Pure germinoma and does require biopsy
- (B) Pure germinoma and does not require biopsy
- (C) Non-germinomatous germ cell tumor and does require biopsy
- (D) Non-germinomatous germ cell tumor and does not require biopsy

Key: B

Rationale: Based on an elevated B-HCG (but not above 75-100) without an elevated AFP, in the setting of a pineal region mass, is nearly certainly to have a pure germinoma. Non-metastatic patients with pure germinoma have long-term disease control rates of 80-95% with management strategies of radiation alone, or chemotherapy (carboplatin and etoposide, most commonly) and reduced-dose radiation.

References: Halperin, Pediatric Radiation Oncology.

103. What percent of long-term survivors of bladder preservation therapy with TURBT and chemoRT will maintain an intact bladder?

- (A) 50
- (B) 65
- (C) 80
- (D) 95

Key: C

Rationale: Up to about 80% of long term survivals of bladder conservation therapy will maintain an intact bladder, with other patients ultimately requiring a radical cystectomy.

104. What is the maximum recommended single fraction dose (Gy) for a 2.8 cm brain metastasis according to RTOG 90-05?

- (A) 15
- (B) 18
- (C) 21
- (D) 24

Key: B

Rationale: Per RTOG 90-05, the maximum tolerated doses of single fraction radiosurgery were defined for this population of patients as 24 Gy, 18 Gy, and 15 Gy for tumors < 20 mm, 21–30 mm, and 31–40 mm in maximum diameter.

105. The radiation dose used by TROG 96-07 for high-risk Merkel cell carcinoma of the skin was:

- (A) 50 Gy.
- (B) 60 Gy.
- (C) 66 Gy.
- (D) 70 Gy.

Key: A

Rationale: Patients were eligible if they had disease localized to the primary site and nodes, and were required to have at least one of the following high risk features: recurrence after initial therapy, involved nodes, primary tumor size greater than 1 cm, gross residual disease after surgery, or occult primary with nodes. Radiation was delivered to the primary site and nodes to a dose of 50 Gy in 25 fractions over 5 weeks with carboplatin and etoposide. This study showed high levels of locoregional control (75% at 3 years) and survival (76% at 3 years) have been achieved with the addition of chemotherapy to radiation treatment for high-risk MCC of the skin. The role of chemoradiotherapy for high-risk MCC warrants further investigation.

106. Neglecting heterogeneity corrections in the dose calculation for a tangent breast treatment results in:

- (A) overestimation of skin dose.
- (B) underestimation of skin dose.
- (C) overestimation of dose in the breast near the chest wall.
- (D) underestimation of dose in the breast near the chest wall.

Key: C

Rationale: Without accounting for the low density of the lung tissue, the dose to the chest wall will be over calculated. The presence of the air in the lung results in less in-scatter dose to the chest wall area. The skin area is not significantly affected by the heterogeneity since it is farther away.

107. Which technique allows for biopsy of a level 6 mediastinal lymph node?

- (A) Endoscopic ultrasound
- (B) Cervical mediastinoscopy
- (C) Endobronchial ultrasound
- (D) Anterior (Chamberlin) mediastinoscopy

Key: D

Rationale: It is helpful to know the differences between the various techniques for mediastinal lymph node staging. Endobronchial ultrasound can usually sample levels 2L, 2R, 4L, 4R, 7, and 10R and 10L. Endoscopic ultrasounds can usually sample 4L, 4R, 7, 8, 9. Cervical mediastinoscopy can usually sample 2L, 2R, 4L, 4R, 7, and 10R and 10L. Anterior mediastinoscopy is very useful for 4L, 5, 6, and 7. It is one of few techniques that can reach level 6.

108. Which normal tissue has the HIGHEST tolerance to re-irradiation?

- (A) Skin
- (B) Kidney
- (C) Bladder
- (D) Spinal cord

Key: A

Rationale: Retreatment tolerance is governed by the total dose of radiation delivered as the initial treatment, the initial treatment volume, the ability of the tissue at risk of injury to recover, and the time interval elapsed since the initial round of radiotherapy. Of the tissues listed above, radiation-induced skin damage has been studied the most, and shows restoration of almost full radiation tolerance, provided at least a couple of months has passed since the first treatment course. Spinal cord and lung are also able to recover partial retreatment tolerance, particularly for lower initial radiation doses, and provided more than 6 months has elapsed since the initial treatment. Kidney and bladder have significant difficulty recovering from late functional damage, even when the initial total dose delivered is not to full tolerance.

109. According to QUANTEC, what is the amount of normal liver (mL) that should be spared at LEAST 15 Gy in a liver SBRT plan for treatment of hepatic metastases?

- (A) 100
- (B) 400
- (C) 700
- (D) 1,000

Key: C

110. What is the BEST initial treatment for osseous plasmacytomas?

- (A) RT
- (B) Surgery
- (C) Cetuximab
- (D) Rituximab

Key: A

Rationale: The NCCN Panel recommends that primary radiation therapy (45 Gy or more) to the involved field is the initial treatment and is potentially curative.

111. Regarding ependymoma:

- (A) there is a male predilection.
- (B) in adults, most occur in the supratentorial region.
- (C) it is more common in Caucasians than in African Americans.
- (D) the most common site of subependymoma is the ventricular system.

Key: D

Rationale: There is no sex difference for ependymoma. It occurs more commonly in African Americans. In adults, a majority of ependymomas occur in the spine.

112. Which cell surface antigen is targeted by britumomab tiuxetan (Zevalin®)?

- (A) PD-1
- (B) CD4
- (C) CD20
- (D) CD30

Key: C

Rationale: The correct answer is C. Zevalin is a monoclonal antibody with a conjugated Y-90 radionuclide that targets the C20 antigen on normal and malignant B cells. B cell lymphomas are generally C20 positive. CD30 positivity is a marker of Hodgkin subtype, which can be targeted with brentuximab. PD-1 is the target of nivolumab. CD4 is the target of zanolimumab, which is currently under development for cutaneous and peripheral T-cell lymphomas.

113. The RICOVER-RT-60 trial demonstrated:

- (A) RT after R-CHOP improved hazard ratio for OS.
- (B) patients younger than 60 years old benefited from RT.
- (C) only disease ≤ 7.5 cm benefited with the addition of RT.
- (D) patients without B symptoms benefited from RT after R-CHOP.

Key: A

NOTE: This item was 0-weighted for scoring purposes upon post-exam statistical item analysis (did not count for or against candidate in calculation of test scores).

Rationale: RICOVER RT 60 was designed to look at the benefit of RT after R-CHOPx6+2R for elderly patients between 61-80 with initial bulky disease (≥ 7.5 cm) and extralymphatic disease. This arm was compared with RICOVER noRT arm. The findings were that in a per-protocol analysis, RT for bulky (≥ 7.5 cm) improved HR for EFS, PFS, and OS; This was not the case when all eligible patients were included (including the 11 patients that did not get RT per trial design). Thus, answers A, B, and C are incorrect.

114. Which of the following doses is MOST appropriate for definitive local RT for an L1 Ewing sarcoma?

- (A) 41.4 Gy in 23 fractions
- (B) 45 Gy in 25 fractions
- (C) 55.8 Gy in 31 fractions
- (D) 61.2 Gy in 34 fractions

Key: B

Rationale: 41.4 Gy is an insufficient dose. Dose is constrained by risk of spinal cord myelitis. The current Children's Oncology Group protocol AEWS 1031 uses 45 Gy to the pre-chemotherapy extent of disease plus margin. A boost of 5.4 to the pre-operative bone extent/post-chemotherapy soft tissue extent of disease can be considered if feasible with spinal cord tolerance.

References: Halperin, Pediatric Radiation Oncology.

115. From which study population was the genetic doubling dose estimate for humans derived?

- (A) Irradiated mice
- (B) Irradiated *Drosophila*
- (C) Radiation therapy patients
- (D) Japanese atomic bomb survivors

Key: A

Rationale: Genetic doubling dose estimates were derived from mouse studies, with the data corrected as much as possible for differences between mice and humans. The present-day consensus is that these estimates were too low, however human data on radiation's hereditary risk are not sufficiently robust to provide a better estimate of genetic doubling dose.

116. Which paraneoplastic disorder is commonly seen in patients with thymomas?

- (A) Hypercalcemia
- (B) Red cell aplasia
- (C) Alcohol-induced pain
- (D) Lambert-Eaton syndrome

Key: B

Rationale: Of all the choices, Red Cell aplasia is the best answer. The others are not seen with thymomas but other cancers (LES with SCLC, Hypercalcemia with NSCLC (SCCA), and EtOH induced pain is associated with lymphomas.

117. Under which irradiation conditions will protons have a high LET?

- (A) All irradiation conditions
- (B) Irradiation in the initial half of the SOBP
- (C) If the proton energy drops below 10 MeV
- (D) If the cells being irradiated are defective in HR

Key: C

Rationale: Proton beams at clinical energies are low LET, averaging 2-3 keV/ μm in the center of the spread out Bragg peak (SOBP). However, proton energy decreases toward the end of the range of the SOBP, and very low energy stopping protons do have a high LET. DNA repair defects may alter the relative biological effectiveness (RBE) of protons but not the LET.

118. Annihilation coincidence detection is employed in PET scans in order to:

- (A) provide SUV data.
- (B) reject scattered photons.
- (C) improve detection efficiency.
- (D) shorten the time of the scan.

Key: B

Rationale: Scattered photons would detract from the contrast in the PET image and make quantitative assessment difficult. Annihilation coincidence insures that only unscattered annihilation photons are counted. Photons not detected within the coincidence time window are not counted.

119. If two posterior spinal fields are used in CSI, the junction of these fields is matched at the:

- (A) anterior extent of the thecal sac.
- (B) posterior extent of the thecal sac.
- (C) posterior extent of the spinal cord.
- (D) anterior extent of the vertebral body.

Key: A

Rationale: In order to prevent overlap of the 2 posterior spinal fields, and resulting overdose of the spinal cord, the match point is at the anterior thecal sac (ie. the posterior vertebral body). A match at the posterior spinal cord and at the posterior extent of the thecal sac would lead to overdose of the spinal cord.

120. The mutation in chromosome 13 found in patients with retinoblastoma leads to:

- (A) decreased retinal maturation.
- (B) increased cholesterol deposition.
- (C) increased tumor promoter activity.
- (D) decreased tumor suppressor activity.

Key: D

Rationale: The RB1 gene located on chromosome 13 is a tumor suppressor gene which codes for a protein that controls cell growth and division. It also stops other proteins from triggering DNA replication.

References: Valverde et al, RB1 gene mutation up-date, a meta-analysis based on 932 reported mutations available in a searchable database, (2005). Halperin, Pediatric Radiation Oncology.

121. What were the results of the Digital Mammographic Imaging and Screening Trial (DMIST) comparing full field digital mammography (FFDM) to screen film mammography (SFM)?

- (A) SFM resulted in higher biopsy rates.
- (B) Overall diagnostic accuracy of FFDM was significantly better.
- (C) FFDM has significantly greater sensitivity for women under 50 years old.
- (D) FFDM has significantly greater specificity for women with dense breast tissue.

Key: C

Rationale: The overall diagnostic accuracy of digital and film screen mammography was equivalent in both sensitivity and specificity. However, in women less than age 50, premenopausal or perimenopausal women, and women with heterogeneously or extremely dense tissue, FFDM had statistically significant greater sensitivity (70% vs.51% $p=.002$) with no difference in specificity compared to SFM. There was no variation in recall rates or biopsy rates between the two techniques.

122. When comparing a traditional chemotherapy agent to a nanoparticle formulation of the same agent, all of the following properties will change, EXCEPT:

- (A) clearance rate.
- (B) biodistribution.
- (C) circulating time.
- (D) mechanism of action.

Key: D

Rationale: Nanoparticles can be used as drug delivery vehicles for traditional chemotherapy agents. Nanoparticle formulations are advantageous in terms of changing the drug's biodistribution, increasing its circulation time, and changing its clearance rate. However, nanoparticles do not change the drug's mechanism of action.

123. The results of ECOG 5194 (Local Excision Alone Without Irradiation for DCIS of the Breast) indicated a higher risk of ipsilateral breast events associated with which findings?

- (A) Lesion size and margin width
- (B) Nuclear grade and lesion size
- (C) Nuclear grade and patient age
- (D) Clinical mass vs. mammographic detection

Key: C

Rationale: The 5 year rates of ipsilateral breast events (IBE) in relation to individual patient, tumor and treatment characteristics were analyzed with a Cox proportional hazards model with grade as the only covariate (low/intermediate vs. high). Grade was significantly related to the risk of IBE ($p=0.024$). Separate models were created to examine the impact of other features on risk of IBE. Lesion size, margin width, age at last surgery, intent to use tamoxifen or not and tamoxifen use or not were analyzed. The only significant variable was age in the high-grade group, with a hazard ratio of 0.95. (95% CI 0.91-0.99, $p = 0.016$).

124. Regarding historical controls:

- (A) blinding is feasible.
- (B) outcomes are assumed to change over the time period.
- (C) it will be possible to separate the effect of the intervention from possible confounding.
- (D) discrepancies are possible between their characteristics and the current treatment group.

Key: D

Rationale: Baseline differences will be difficult to determine, since the historical controls might not have the same baseline characteristics and prognostic factors with the intervention group; therefore, it will be impossible to separate the effect of the intervention from possible confounding. Blinding is not feasible when historical controls are used. Time trends can cause outcomes to change with time for reasons that cannot be predicted. When using historical controls, we assume the outcome keep same.

125. What is the MOST common presenting symptom of oligodendroglioma?

- (A) Seizures
- (B) Projectile vomiting
- (C) Altered mental status
- (D) Focal neurologic deficits

Key: A

Rationale: Altered mental status, projectile vomiting and focal neurologic deficits can occur in patients with oligodendroglioma but none of those are as common as seizures.

126. In comparing the Chernobyl and Fukushima nuclear power plant accidents, which statement is TRUE?

- (A) Faulty design contributed to the Chernobyl accident, but not the Fukushima accident.
- (B) There were approximately 30 acute radiation deaths at Chernobyl, and 10 at Fukushima.
- (C) The psychosocial and economic impacts of both accidents are the worst of the "radiation effects".
- (D) The maximum dose rate detected at or near the damaged reactors was higher in Fukushima than Chernobyl.

Key: C

Rationale: Arguably, the socioeconomic and psychological impacts of the Chernobyl accident have long since exceeded the impact of the several thousand childhood thyroid cancer cases that were induced. To date, this is also true of the Fukushima accident, although it is still too early to tell whether excess cases of cancer will develop. However, most experts feel that radiation-induced cancer cases will be far fewer in Fukushima, not only because the amount of radiation released in the accident was much smaller, but also because, especially with respect to thyroid cancer in children, possibly contaminated milk was immediately embargoed, unlike in Chernobyl.

127. Which of the following types of HPV are considered high-risk for oropharyngeal carcinoma?

- (A) 6 and 16
- (B) 6 and 22
- (C) 11 and 18
- (D) 16 and 18

Key: D

Rationale: HPVs are a group of more than 150 related viruses. More than 40 of these viruses can be easily spread through direct skin-to-skin contact during vaginal, anal, and oral sex. Sexually transmitted HPVs fall into two categories:

- Low-risk HPVs, which do not cause cancer but can cause skin warts (technically known as condylomata acuminata) on or around the genitals or anus. For example, HPV types 6 and 11 cause 90 percent of all genital warts.
- High-risk or oncogenic HPVs, which can cause cancer. At least a dozen high-risk HPV types have been identified. Two of these, HPV types 16 and 18, are responsible for the majority of HPV-caused cancers.

The incidence of HPV-associated oropharyngeal cancer has increased during the past 20 years, especially among men. It has been estimated that, by 2020, HPV will cause more oropharyngeal cancers than cervical cancers in the United States.

128. Which molecular marker is associated with increased radiosensitivity of cancer cells?

- (A) Loss of p53
- (B) Amplification of *KRAS*
- (C) Overexpression of p16
- (D) Nuclear localization of HIF-1 β

Key: C

Rationale: Overexpressed p16 can be a marker of an HPV infection, which in turn is associated with tumor radiosensitivity. Patients, especially those with lung and GI cancers, who have *KRAS* gene mutations or amplification have worse outcomes and exhibit resistance to some cancer treatments. HIF-1 β is one of the subunits of the HIF-1 transcription factor and is constitutively bound to DNA, so as such, is always localized to the nucleus. Finally, loss of the p53 tumor suppressor protein frequently increases cellular radioresistance, not radiosensitivity.

129. Which statement is MOST accurate for a 50-year-old woman with a gastric MALT?

- (A) Multiagent chemotherapy and IFRT
- (B) Local RT 30 Gy for H. Pylori negative
- (C) Multiagent chemotherapy for H. Pylori negative
- (D) H. Pylori treatment and monitoring for at least 6 months before considering RT

Key: B

Rationale: Anti-H. Pylori therapy is the most effective for H. Pylori positive cases. Radiotherapy is one of the most effective modality in treating gastric MALT for H. Pylori negative cases or for persistent disease.

130. For a TBI treatment, a 75 cm x 50 cm field is required. The maximum field size setting on the accelerator is 40 cm x 40 cm. What is the minimum SSD needed?

- (A) 155 cm
- (B) 164 cm
- (C) 188 cm
- (D) 210 cm

Key: C

Rationale: The field size increases linearly with SSD. The 40x40 cm field size is defined at 100 cm SSD, so to treat this patient, the SSD must increase to $(75 \text{ cm} / 40 \text{ cm}) * 100 \text{ cm} = 187.5 \text{ cm}$.

131. What were the findings of ECOG 5194 (Local Excision Alone Without Irradiation for DCIS of the Breast)?

- (A) The median lesion size was 12 mm.
- (B) Detection was by mammogram screening only.
- (C) The population consisted of post-menopausal women only.
- (D) The study excluded patients with a history of bloody nipple discharge.

Key: B

Rationale: The study included both pre and post-menopausal women. Median lesion size was 6 mm. All lesions were detected by mammography screening only. Patients with bloody nipple discharge were included but represented only ~2.5% of the patient population. This study is important because it was used to validate the Oncotype DX DCIS score™.

132. The majority of the vulva's first line of lymphatic drainage is to which nodal group?

- (A) Obturator
- (B) External iliac
- (C) Deep inguinal
- (D) Superficial inguinal

Key: D

Rationale: The majority of the vulva is drained by lymphatics that pass laterally to the superficial inguinal nodes then the flow is to the deep inguinal group. The clitoris and anterior labia minora may also drain directly to the deep inguinal or external iliac lymph nodes. While vulvar cancer most commonly spreads initially to the superficial inguinal nodes immediately lateral to the pubic tubercles, formal evaluation of the distribution of sentinel lymph nodes in patients with vulvar cancer show that 100% of sentinel lymph nodes lie over or medial to the femoral vessels. In one study that included 59 women with a vulvar cancer <4 cm, the sentinel nodes were superficial in about 85% and in 15% laid deep to the cribriform fascia. These observations have important implications for the extent of inguinofemoral lymphadenectomy as well as the selection of radiotherapeutic target volumes and techniques.

133. ^{125}I and ^{131}I are examples of:

- (A) isobars.
- (B) isomers.
- (C) isotones.
- (D) isotopes.

Key: D

Rationale: Isotopes are atoms that have the same number of protons but different numbers of neutrons. The "A" in the notation AX represents the total number of nucleons (protons + neutrons) and since both are iodine, they have the number of protons, but with different number of neutrons in nucleus.

134. Regarding the role of surgery following chemoRT for stage III non-small cell lung cancer:
- (A) 60 Gy is required to demonstrate an improvement in OS with surgery.
 - (B) surgery improves OS in all resectable patients based on level 1 evidence.
 - (C) a lobectomy improves local control and OS based on an unplanned subgroup analysis of the intergroup trial.
 - (D) a pneumonectomy demonstrates a local control and OS for left side tumors based on an unplanned subgroup analysis of the intergroup trial.

Key: C

Rationale: The Intergroup experience published by Albain demonstrated a significant improvement in local regional control with the addition of surgery following chemo radiotherapy over radiotherapy alone although this did not translate into a survival advantage related to the mortality of surgery – primarily the right sided pneumonectomies. An unplanned analysis of this data suggested that patients undergoing a lobectomy had less morbidity/mortality and subsequently this group of patients had a survival advantage.

135. What is the appropriate RT regimen for a 4-year-old who undergoes a gross total resection of a 4th ventricular grade III non-metastatic ependymoma?
- (A) No role of radiation therapy
 - (B) Resection bed plus margin radiation to 54-59.4 Gy in 30-33 fractions
 - (C) 36 Gy in 20 fractions to the craniospinal axis followed by 18 Gy in 10 fractions to the resection bed plus margin
 - (D) 23.4 Gy in 13 fractions to the craniospinal axis followed by 30.6 Gy in 17 fractions to the resection bed plus margin

Key: B

Rationale: Patients with non-metastatic infratentorial Grade II and Grade III ependymomas should receive adjuvant conformal radiation to the resection margin.

References: Merchant, et. al., Lancet Onco, (2009) Pages 258-266.
Halperin, Pediatric Radiation Oncology.

136. Regarding the use of Oncotype DX DCIS score™, it:
- (A) predicts risk of DCIS only.
 - (B) predicts risk of invasive recurrence.
 - (C) is validated from NSABP B-17 and B-24.
 - (D) includes ER and Her-2 in the gene analysis.

Key: B

Rationale: The Oncotype DX DCIS score™ is validated from ECOG 5194. The DCIS score predicts risk for both non-invasive and invasive disease. ER and Her-2 are not included in the 12 gene analysis but PR is.

137. What is the likelihood (%) of conversion of solitary osseous plasmacytoma to multiple myeloma at 10 years?

- (A) 10
- (B) 25
- (C) 50
- (D) 75

Key: C

Rationale: Multiple myeloma was more likely to develop in patients with osseous versus non-osseous tumors (54% vs. 11% at 10 years, 100% vs. 33% at 15 years, $p = 0.03$).

138. B symptoms for pediatric Hodgkin lymphoma include all of the following EXCEPT:

- (A) pruritus.
- (B) drenching night sweats.
- (C) fever (temperature $> 38^{\circ}\text{C}$).
- (D) unexplained loss of more than 10% of body weight within 6 months preceding diagnosis.

Key: A

Rationale: B symptoms do not include pruritus, though patients may experience this as a presenting symptom. B symptoms are not different between adults and children.

References: Terezakis SA, et al, ACR Appropriateness Criteria Pediatric Hodgkin Lymphoma, (2014).

139. What total dose in Gy of CSI is recommended for a child with persistent CSF involvement after chemotherapy for B-cell ALL?

- (A) 12
- (B) 18
- (C) 24
- (D) 30

Key: C

Rationale: Typically leukemia is quite sensitive to radiotherapy. 24 Gy is an adequate dose for high risk patients with recurrent or persistent disease. 18Gy has been used for elective cranial irradiation and doses as low as 12Gy have been used with intrathecal chemotherapy.

References: Halperin, Pediatric Radiation Oncology.

140. WBRT in the management of solitary brain metastasis following complete surgical resection:

- (A) improves OS.
- (B) reduces local and distant CNS failures.
- (C) increases the risk of neurologic death.
- (D) reduces extracranial recurrences by stimulating the patient's immune system.

Key: B

Rationale: Patchell's classic paper demonstrated a significant reduction in local, distant and any where in the CNS failures with the addition of radiotherapy which translated into a decrease in the risk of neurologic death but no difference in survival due to the progression outside of the brain.

141. A 7-year-old boy undergoes gross total resection of left cerebellar pilocytic astrocytoma. What is an appropriate RT regimen at this time?

- (A) No RT
- (B) 50.4 Gy to the posterior fossa
- (C) 54 Gy to the resection bed plus margin
- (D) 23.4 Gy CSI followed by 30.6 Gy to the resection bed plus margin

Key: A

Rationale: Patients with grossly totally resected cerebellar pilocytic astrocytomas have an excellent progression free survival without further therapy. There is no role for craniospinal irradiation in non-metastatic low grade gliomas.

References: Gajjar, et al., J Clin Oncol, (1997). Halperin, Pediatric Radiation Oncology.

142. What is the AJCC stage for a 5 cm adenocarcinoma starting from the GE junction, extending into the gastric cardia, with extension into but not through the muscularis propria and three suspicious peritumoral nodes?

- (A) T2N1 gastric cancer
- (B) T2N2 gastric cancer
- (C) T2N2 esophageal cancer
- (D) T3N2 esophageal cancer

Key: C

Rationale: In the 7th edition AJCC staging manual, cancers involving the GE junction and extending into the stomach are staged as esophageal cancers if the epicenter of the tumor is within 5cm of the GE junction. Extension into muscularis propria represents T2 disease, and involvement of 3-6 nodes represents N2 disease.

References: Rice, TW, Ann Surg Oncol, (2010).

143. For TBI in preparation for a bone marrow transplant, radiation is delivered at a low dose rate in order to:

- (A) allow time for hypoxic stem cell niches to reoxygenate fully.
- (B) reduce the incidence of early and late effects in normal tissues.
- (C) take advantage of DNA repair deficiencies common to many tumor cells.
- (D) increase the sensitivity of hematopoietic stem cells by cell cycle redistribution.

Key: B

Rationale: When radiation is used for bone marrow ablation prior to a transplant, the radiation is delivered at a low dose rate (and/or fractionated) in order to reduce the incidence of early and late effects in normal tissues. In the early days of bone marrow transplantation for example, radiation-induced lung fibrosis was a frequent and sometimes fatal complication observed when the treatment was at the more standard, higher dose rates used for radiotherapy. In addition, some patients would begin to manifest symptoms associated with the whole body irradiation syndromes, including fairly prompt nausea and vomiting that could interfere with subsequent treatment.

144. A flattening filter is designed to produce a uniform dose in field at:

- (A) d_{max} .
- (B) 5 cm depth.
- (C) 10 cm depth.
- (D) the surface.

Key: C

Rationale: Flattening filters preferentially attenuate the center of the forward-peaked photon beam emerging from the target, but create a beam that is softer (containing more low-energy photons) the farther you get from the central axis. The beam therefore attenuates at a different rate depending where you are radially in the beam. Flattening filters are tuned to be flat at a depth of 10 cm. Upstream of this depth, the edges of the beam will have a higher dose than the center. Downstream of this depth, the edges of the beam will become rounded and lower than the central axis dose.

145. The oxygen-regulated protein lysyl oxidase (LOX) is involved in:

- (A) sprouting angiogenesis.
- (B) cell death by autophagy.
- (C) invasion and metastasis.
- (D) cytotoxic T-cell activation.

Key: C

Rationale: The correct answer is C. Lysyl oxidases are extracellular copper enzymes that catalyze the cross-linking of collagen and elastin in the extracellular matrix (ECM). This facilitates the detachment of cells from the ECM, as well as cell motility and migration. In cancer cells, upregulation of the HIF-1 target gene LOXL2 in response to tumor hypoxia enhances invasion and metastasis. Increased LOX expression is associated with disease progression, metastasis, and poor overall survival in breast cancer and head and neck cancers.

146. What were the results of NSABP R-04, which evaluated the use of four chemotherapy regimens with preoperative radiation therapy for Stage II and III rectal cancer?

- (A) Toxicities were similar with the addition of oxaliplatin to capecitabine.
- (B) The addition of oxaliplatin to capecitabine improved sphincter sparing surgery.
- (C) Capecitabine was superior to continuous infusion 5-FU for surgical downstaging.
- (D) The addition of oxaliplatin to capecitabine did not improve pathological complete response rates.

Key: D

Rationale: Patients with clinical stage II or III rectal cancer who were undergoing preoperative RT were randomly assigned to: continuous intravenous infusional fluorouracil with or without intravenous oxaliplatin or oral capecitabine with or without oxaliplatin. Before random assignment, the surgeon indicated whether the patient was eligible for sphincter-sparing surgery based on clinical staging. 1,608 patients were randomly assigned. No significant differences in the rates of pCR, sphincter-sparing surgery, or surgical downstaging were identified between the CVI FU and capecitabine regimens or between the two regimens with or without oxaliplatin. Patients treated with oxaliplatin experienced significantly more grade 3 or 4 diarrhea.

147. What is the observed rate of pathologic complete response after chemoradiation for esophageal cancer?

- (A) 10-15%
- (B) 25-30%
- (C) 40-45%
- (D) 55-60%

Key: B

Rationale: The rate of pathologic complete response was 29% in the chemoradiation arm of the CROSS trial. The U. Michigan trial (Urba SG, J Clin Oncol 2001; 19:305-313) had a 28% pCR rate. An EORTC trial (Bosset J, New Engl J Med 1997; 337:161-70) had a 26% pCR rate.

References: Van Hagen, P. et.al, New Engl J Med, (2012).

148. Which of the following drugs selectively targets anaplastic lymphoma kinase (ALK) mutated NSCLC?

- (A) Gefitinib
- (B) Erlotinib
- (C) Lapatinib
- (D) Crizotinib

Key: D

Rationale: Crizotinib is an oral tyrosine kinase inhibitor targeting ALK rearranged NSCLC. In heavily pretreated patients it was associated with a 57% overall response rate, and a estimated 6 month progression free survival of 72%. Erlotinib and gefitinib are EGFR inhibitors. Lapatinib is a mixed EGFR and Her2 inhibitor.

149. For a patient with extensive stage SCLC receiving cisplatin/etoposide, the expected response rate (RR) and the median OS associated with this regimen is:

- (A) RR of 30-50% and median OS of 4-5 months.
- (B) RR of 30-50% and median OS of 7-9 months.
- (C) RR of 60-80% and median OS of 7-9 months.
- (D) RR of 60-80% and median OS of 18-24 months.

Key: C

Rationale: Chemotherapy is the standard treatment for extensive-disease small cell lung cancer. The combination of cisplatin and etoposide (EP) or carboplatin and etoposide (EC) up to 4–6 cycles remains the most widely used regimen, with an ORR ranging from 60% to 80%. However, the median OS is still 7– 9 months, and only 2% of patients survive for 5 years.

150. Which of the following represents a dosimetric predictor of duodenal toxicity after IMRT for treatment of para-aortic nodes in gynecologic cancers?

- (A) V40 > 15 cm³
- (B) V45 < 15 cm³
- (C) V50 < 15 cm³
- (D) V55 > 15 cm³

Key: D

Rationale: 3-year actuarial rates of duodenal toxicity with V55 above and below 15 cm³ were 48.6% and 7.4%, respectively (p < .01). In Cox, univariate analysis of dosimetric variables, V55 was associated with duodenal toxicity (P=0.29). In recursive partitioning analysis, V55 less than 13.94% segregated all patients with duodenal toxicity.

References: Verma, et. al, Dosimetric predictors of duodenal toxicity after intensity modulated radiation therapy for treatment of the para-aortic nodes in gynecologic cancer, (2014).

151. What further treatment is recommended for a pathologic stage T1b1N1 cervical cancer treated with radical hysterectomy, pelvic lymph node dissection, and para-aortic lymph node sampling?

- (A) No further treatment
- (B) Adjuvant RT
- (C) Adjuvant chemoRT
- (D) Adjuvant chemotherapy

Key: C

Rationale: Patients with clinical stage IA(2), IB, and IIA carcinoma of the cervix, initially treated with radical hysterectomy and pelvic lymphadenectomy, and who had positive pelvic lymph nodes and/or positive margins and/or microscopic involvement of the parametrium were eligible for this study. Patients were randomized to receive RT or RT + CT. Patients in each group received 49.3 GY RT in 29 fractions to a standard pelvic field. Chemotherapy consisted of bolus cisplatin 70 mg/m² and a 96-hour infusion of fluorouracil 1,000 mg/m²/d every 3 weeks for four cycles, with the first and second cycles given concurrent to RT. Between 1991 and 1996, 268 patients were entered onto the study. Two hundred forty-three patients were assessable (127 RT + CT patients and 116 RT patients). Progression-free and overall survival are significantly improved in the patients receiving CT. The hazard ratios for progression-free survival and overall survival in the RT only arm versus the RT + CT arm are 2.01 (P = .003) and 1.96 (P = .007), respectively. The projected progression-free survivals at 4 years is 63% with RT and 80% with RT + CT. The projected overall survival rate at 4 years is 71% with RT and 81% with RT + CT.

References: Peters, et al, Concurrent chemotherapy and pelvic radiotherapy compared with pelvic radiation therapy alone as adjuvant therapy after radical surgery in high-risk early stage cancer of the cervix, (2000).

152. What is the appropriate recommendation for treatment of inflammatory breast cancer?

- (A) Mastectomy, adjuvant chemotherapy, and PMRT
- (B) Neoadjuvant chemotherapy, modified radical mastectomy, and PMRT
- (C) Neoadjuvant chemotherapy, modified radical mastectomy with immediate reconstruction, and PMRT
- (D) Neoadjuvant chemotherapy, skin sparing mastectomy and axillary lymph node dissection, and PMRT

Key: B

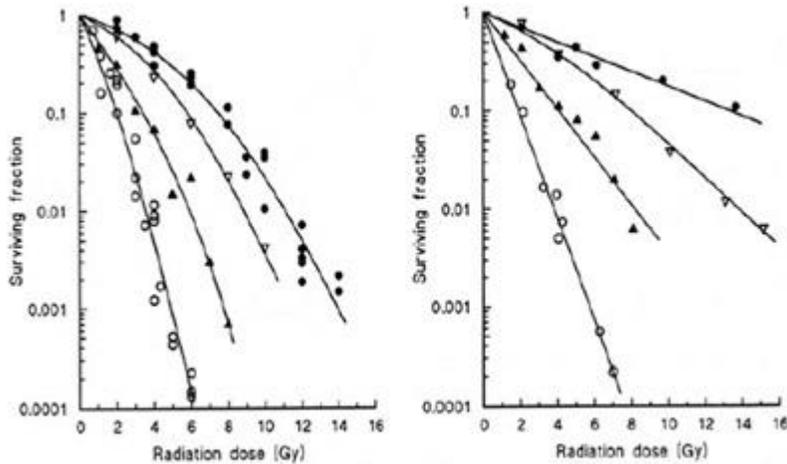
Rationale: The treatment of choice for inflammatory breast cancers is trimodality therapy with chemotherapy, mastectomy and post mastectomy radiation. Immediate reconstruction and skin sparing mastectomy should not be performed in the setting of inflammatory breast cancer.

153. Independent of hypoxia, tumor cells can regulate HIF-1 α in response RT by:

- (A) upregulating its activity, making tumor cells more radioresistant.
- (B) upregulating its activity, making tumor cells more radiosensitive.
- (C) downregulating its activity, making tumor vasculature more radioresistant.
- (D) downregulating its activity, making surrounding normal tissue more radioresistant.

Key: A

Rationale: The correct answer is A. Tumor cells upregulate HIF-1 α activity in response to radiotherapy, which makes them more radioresistant. (This is also true for vascular endothelial cells, which can add to tumor resistance.)



154.

Single-dose, x-ray survival curves for four different human tumor cell lines are shown in the left panel of the above image. Survival curves for the same cells under different treatment conditions are shown in the right panel. Compared to the left panel, the cells in the right panel have:

- (A) become hypoxic during irradiation.
- (B) had key excision repair genes silenced.
- (C) been irradiated over an extended period.
- (D) been irradiated with neutrons instead of x-rays.

Key: C

Rationale: Compared to acute dose survival curves, protracted irradiation (i.e., fractionated or continuous low dose rate irradiation over an extended period) produces survival curves that are roughly exponential, and shallower. Sublethal damage recovery (SLDR) occurring during protracted irradiation accounts for this change in survival curve shape. Had key repair genes been silenced in the cell lines, survival curves would likely become exponential, however they would also be steeper, not shallower. This would also be the case for irradiation with high LET neutrons. Had the cell cultures gradually become hypoxic during irradiation, a biphasic dose response would have been expected.

155. Regarding limited stage SCLC, chemoRT demonstrated:

- (A) a 5.4% improvement in OS compared with RT alone.
- (B) a 5.4% improvement in OS compared with cisplatin-based chemotherapy alone.
- (C) a 5.4% improvement in LRC, but no improvement in OS compared with RT alone.
- (D) a 5.4% improvement in LRC, but no improvement in OS compared with cisplatin-based chemotherapy alone.

Key: B

Rationale: Due to high locoregional failure rates after chemotherapy alone, thoracic radiation in combination with chemotherapy was investigated for patients with limited stage disease. Several randomized studies compared chemotherapy alone to chemotherapy and radiation.

156. If a study has a negative result, which of the following should be considered to determine whether the study had adequate power?

- (A) Chance
- (B) Type II errors
- (C) Power calculations
- (D) Confidence interval

Key: D

NOTE: This item was 0-weighted for scoring purposes upon post-exam statistical item analysis (did not count for or against candidate in calculation of test scores).

Rationale: Whether a study has a positive or negative result, one or more of the following four possible explanations will explain the outcome:

- Truth — The conclusion of the study may accurately reflect the answer to the underlying question that was being asked.
- Bias — There may be one or more errors in the way the study was performed that distorted the results and affected the conclusions.
- Confounding — There may be one or more variables that are associated both with the exposure being studied and also with the outcome of interest that affected the results of the study.
- Chance — Random variations that occurred within the sample of the population being studied may lead to erroneous conclusions. If random chance leads to a mistaken conclusion that there was an effect, the mistake is called a type 1 error (alpha error); if random chance leads to a mistaken conclusion that there was no effect, the mistake is called a type 2 error (beta error).

Power is the statistical probability of avoiding a type 2 error in a study. That is, it is the probability that a study will not mistakenly accept the null hypothesis and conclude that there was no effect or difference when there really was one. Whenever a study finds no statistically significant difference, the issue of whether there was "adequate power" is raised, since one possible explanation for the result was that a small sample size and/or random chance led to a failure to detect a difference that really existed. This issue feels particularly pressing when the point estimate found in the study appears clinically important. It is possible to calculate the power a study has to find a given result (for instance a 25 percent reduction in mortality) given a particular sample size (and also given the underlying variation in the population). Power calculations are useful in the design of studies to decide whether a study is large enough to have a reasonable chance of finding a positive result or to calculate the number of patients required to achieve a certain power. However, when papers try to deal with the issue of "adequate power" after a negative study result by performing a power calculation using the point estimate found in the study, the result is meaningless. The power in such a calculation will always be less than 50 percent. Instead, as discussed above, the way to decide after the fact whether a negative study had sufficient power is to look at the confidence intervals and see whether clinically important values exist within the range of the statistically likely values represented by the confidence interval.

157. According to ACOSOG Z1071 (Sentinel Node Biopsy After Neoadjuvant Chemotherapy in Patients with Node Positive Breast Cancer), the minimum number of sentinel nodes sampled to give a 9% false negative rate is:

- (A) 1.
- (B) 2.
- (C) 3.
- (D) 4.

Key: C

Rationale: The endpoint of this study was to determine the number of SLNs needed to equate the 9% FNR of sentinel node biopsy in the clinically negative axilla. The minimum number of sentinel nodes sampled to provide a false negative rate of 9% is 3. When one sentinel node was removed, the false negative rate was 32% and with 2 sentinel nodes it was 21%. ACOSOG recommends at least 3 sentinel nodes should be sampled for accurate axillary evaluation after neoadjuvant chemotherapy in the setting of clinically positive nodes. The SENTINA study (SLN Detection Rates Pre- vs. Post-Chemo) showed similar findings. 1 SLN sampled - FNR was 24%, 2 SLN – 19% and 3 SLN sampled 7.3%. Greater than 4 SLN sampled - FNR was 6%.

158. According to the combined analysis of EORTC 22931 and RTOG 9501 for head/neck cancer, post-operative chemoRT improved loco-regional disease control in patients with the risk factors of:

- (A) vascular embolisms and perineural invasion.
- (B) positive margins and/or extracapsular extension.
- (C) perineural invasion and multiple positive lymph nodes.
- (D) stage III-IV disease, and multiple positive lymph nodes.

Key: B

Rationale: Extracapsular extension and/or microscopically involved surgical margins were the only risk factors that impacted significantly on overall survival in both trials. There was also a trend in favor of chemoRT in the group of patients who had stage III–IV disease, perineural infiltration, vascular embolisms, and/or clinically enlarged level IV–V lymph nodes secondary to tumors arising in the oral cavity or oropharynx. Patients who had two or more histopathologically involved lymph nodes without ECE as their only risk factor did not seem to benefit from the addition of chemotherapy in this analysis.

159. The lytic bone lesions caused by multiple myeloma are due to the over-expression of:

- (A) beta-2 microglobulin.
- (B) sedimentation factor.
- (C) Receptor Activator for Nuclear Factor k B Ligand (RANKL).
- (D) Receptor Activator for Nuclear Factor Amyloid Ligand (RANAL).

Key: C

Rationale: Beta-2 microglobulin is a prognostic test used in multiple myeloma whereas Receptor Activator for Nuclear Factor Amyloid Ligand and Sedimentation Factor do not exist. Receptor Activator for Nuclear Factor k B Ligand (RANKL) activates osteoclasts which resorb bone.

160. The NRC exposure limits for the total effective dose for occupational workers and for individual members of the public are:

- (A) 5 mSv, 1 mSv.
- (B) 50 mSv, 1 mSv.
- (C) 50 mSv, 5 mSv.
- (D) 500 mSv, 50 mSv.

Key: B

Rationale: The NRC establishes regulatory limits on the amount of radiation that both occupational workers and individual members of the public may receive.

161. In which type of interaction is an orbital electron ejected as a result of the absorption of a photon?

- (A) Pair production
- (B) Compton scattering
- (C) Coherent scattering
- (D) Photoelectric effect

Key: D

Rationale: During a photoelectric reaction, a photon is absorbed and causes an orbital electron to be ejected from the atom.

162. What type of trial is used to investigate the efficacy of a new drug?

- (A) Phase I
- (B) Phase II
- (C) Phase III
- (D) Phase IV

Key: B

Rationale:

- Phase I: Researchers test a new drug or treatment in a small group of people for the first time to evaluate its safety, determine a safe dosage range, and identify side effects.
- Phase II: The drug or treatment is given to a larger group of people to see if it is effective and to further evaluate its safety.
- Phase III: The drug or treatment is given to large groups of people to confirm its effectiveness, monitor side effects, compare it to commonly used treatments, and collect information that will allow the drug or treatment to be used safely.
- Phase IV: Studies are done after the drug or treatment has been marketed to gather information on the drug's effect in various populations and any side effects associated with long-term use.

References: <http://www.nlm.nih.gov/services/ctphases.html>.

163. What is the optimal cycle of chemotherapy to start concurrent thoracic radiation for a healthy patient with limited stage SCLC?

- (A) 2
- (B) 3
- (C) 4
- (D) 5

Key: A

Rationale: The current standard of care is concurrent chemotherapy and radiation, with radiation being delivered in the first two courses of chemotherapy. LRC and survival is better with concurrent rather than sequential therapy but at the cost of increased toxicity. Sequential therapy is acceptable for patients who may not tolerate the added toxicity of concurrent therapy or have large tumor volumes and/or poor pulmonary function. Volume reduction with chemotherapy may allow for sparing of normal tissue and better therapy tolerance.

164. A 10-year-old female presents with clinical stage IIIB mixed cellularity Hodgkin lymphoma with partial response at completion of 5 cycles ABVE-PC chemotherapy. What is the MOST appropriate next step?

- (A) No RT
- (B) 12 Gy IFRT
- (C) 25 Gy IFRT
- (D) 36 Gy IFRT

Key: C

Rationale: Patients with no adverse prognostic factors (advanced stage, bulky disease, four or more involved sites, B symptoms) and a good response to chemotherapy can be treated with an attenuated regimen. The German approach has suggested that elimination of radiotherapy may be feasible, but the Stanford data does not confirm that CT response is adequate to eliminate RT.

References: Terezakis SA, et al, ACR Appropriateness Criteria Pediatric Hodgkin Lymphoma, (2014).

165. When used in patient-specific QA to compare planned and measured dose distributions, what does the gamma analysis consider?

- (A) Absolute dose deviation at each point
- (B) Dose deviation and distance to agreement
- (C) Maximum dose deviation in a region of interest
- (D) Root mean square difference in dose distributions

Key: B

Rationale: The gamma evaluates not only the accuracy of the dose agreement at each point but also compared the distance to agreement for each point in the dose distribution.

166. Regarding NSABP R-03:

- (A) there was no improvement in DFS with preoperative chemoradiation.
- (B) there was a significant improvement in OS with preoperative chemoradiation.
- (C) the chemotherapy used concurrently with radiation was 5-FU and leucovorin.
- (D) it compared preoperative radiotherapy to preoperative chemoradiation therapy for rectal cancer.

Key: C

Rationale: Patients with clinical T3 or T4 or node-positive rectal cancer were randomly assigned to preoperative or postoperative chemoradiotherapy. Chemotherapy consisted of fluorouracil and leucovorin with 45 Gy in 25 fractions with a 5.40-Gy boost within the original margins of treatment. The 5-year DFS for preoperative patients was 64.7% v 53.4% for postoperative patients ($P = .011$). The 5-year OS for preoperative patients was 74.5% v 65.6% for postoperative patients ($P = .065$). A complete pathologic response was achieved in 15% of preoperative patients. No preoperative patient with a complete pathologic response has had a recurrence.

167. Which OAR dose constraint to pharyngeal constrictors reduces long-term dysphagia while maintaining control of oropharyngeal squamous cancer?

- (A) V20
- (B) V30
- (C) V40
- (D) V50

Key: D

Rationale: Eisbruch, et al. identified anatomic structures that contributed to swallowing that could be spared with IMRT. He compared 3D-CRT to two IMRT strategies: RTOG 0022 dose constraints +/- minimizing volume of pharyngeal constrictors and larynx receiving >50 Gy. Mean pharynx/larynx dose was significantly decreased with the optimized technique that included the V50 dose objective. Feng, et al. prospectively tested the use of this IMRT technique including the pharyngeal constraint in 73 oropharyngeal cancer patients. Achieving adequate target dose superseded sparing of any organ except the spinal cord. At 12 months, HRQOL swallowing and eating scores were minimally worse than baseline and videofluoroscopy scores minimally worsened from baseline. 3-yr DFS was 88% and LRFS was 96%, showing that the technique did not compromise disease control.

168. Which term represents the incidence in exposed individuals divided by the incidence in unexposed individuals?

- (A) Odds ratio
- (B) Relative risk
- (C) Absolute risk
- (D) Number needed to treat

Key: B

Rationale: These terms are used to describe the magnitude of an effect. The relative risk or risk ratio equals the incidence in exposed individuals divided by the incidence in unexposed individuals. The odds ratio equals the odds that an individual with a specific condition has been exposed to a risk factor divided by the odds that a control has been exposed. The relative risk and odds ratio provide an understanding of the magnitude of risk compared to a standard. The absolute or attributable risk is calculated by subtracting the incidence of a disease in non-exposed persons from the incidence of disease in exposed persons. The number to treat is the reciprocal of the absolute risk reduction---an example "This study suggests that I would have to treat 5 patients with radiation to prevent one death".

169. Which statement regarding the autophagy-associated protein beclin is TRUE?

- (A) Genetic knockdown of beclin increases the toxicity of chemotherapy.
- (B) Homozygous deletion of the BECN1 gene in mice causes cancer proneness.
- (C) Beclin participates in the final step of autophagy, the degradation of the autophagosomes.
- (D) Monoallelic disruption of the BECN1 gene occurs in about 10% of human breast, ovarian, and prostate tumors.

Key: A

Rationale: Genetic knockdown of beclin increases the toxicity of chemotherapy, suggesting a role for autophagy in chemotherapy resistance. Homozygous deletion of the BECN1 gene in mice is embryonic lethal. Monoallelic disruption of the BECN1 gene occurs in 40-70% of human human breast, ovarian and prostate tumors. Beclin participates in the initial step of autophagy, the formation of the autophagosomes.

170. Which of the following is the MOST common site of Ewing sarcoma?

- (A) Rib
- (B) Tibia
- (C) Pelvis
- (D) Femur

Key: C

Rationale: The pelvis accounts for approximately a quarter of all Ewing sarcomas, followed by the femur (one fifth), and the Rib, Tibia and Fibula (about 10% each). Overall, extremities account for a slight majority of primary sites of disease.

References: Pizzo, Pediatric Oncology.

Halperin, Pediatric Radiation Oncology.

171. Among elderly women, which of the following cancers confers the HIGHEST risk of pelvic fracture following pelvic irradiation?

- (A) Anal
- (B) Colon
- (C) Rectal
- (D) Cervical

Key: A

Rationale: Pelvic irradiation significantly increases the long-term risk of pelvic fractures. A SEER database study (Baxter et al, JAMA (294(20):2587-93, 2005) found that women who underwent radiation therapy were more likely to have a pelvic fracture than women who did not undergo radiation therapy (cumulative 5-year fracture rate, 14.0% vs 7.5% in women with anal cancer, 8.2% vs 5.9% in women with cervical cancer, and 11.2% vs 8.7% in women with rectal cancer). The impact of irradiation varied by cancer site: treatment for anal cancer was associated with a higher risk of pelvic fractures (hazard ratio, 3.16; 95% confidence interval, 1.48-6.73); than for cervical cancer (hazard ratio, 1.66; 95% confidence interval, 1.06-2.59); or rectal cancer (hazard ratio, 1.65; 95% confidence interval, 1.33-2.05). This is likely due to the inclusion of inguinal lymph nodes in the radiation treatment field, which may inadvertently increase dose to the femoral heads.

172. Which agent is used as a hypoxic cell radiosensitizer in the treatment of squamous cell cancers of the head and neck?

- (A) Cetuximab
- (B) Nimorazole
- (C) Mitomycin C
- (D) Tirapazamine

Key: B

Rationale: Nimorazole is an oxygen-mimetic hypoxic cell radiosensitizer used in Europe in combination with radiotherapy for the treatment of select head and neck cancers. Tirapazamine and mitomycin C are bioreductive drugs preferentially toxic to hypoxic cells (the former much more than the latter) and have been used to treat head and neck cancers, however mechanistically-speaking, they are not hypoxic cell radiosensitizers. Cetuximab is also used in combination with radiotherapy for head and neck cancer treatment, but does not specifically target tumor hypoxia.

173. According to Mirels' criteria, which feature is the MOST critical in determining the need for surgical intervention of a metastasis to a long bone?

- (A) Functional pain
- (B) Location in the distal femur
- (C) Tumor appears primarily blastic
- (D) 25% of the cortical bone is destroyed

Key: A

Rationale: Mirels criteria has been used by orthopedic oncologist for several decades which predict for fracture following patients treated with radiotherapy alone. There is point scoring system that was developed where 4 components are evaluated, each scored from 1 to 3. The components considered for the highest score are location in the femoral neck, patients with functional pain, tumors that are primarily lytic as opposed to blastic and the size of of the cortical involvement with the highest measured as $> 2/3$ of the cortex destroyed.

174. Retrospective data from MDACC indicates which of the following 10-year LRR rates with and without PMRT for patients with Stage III breast cancer having pathologic CR after neoadjuvant chemotherapy?

- (A) 3% vs. 16%
- (B) 7% vs. 33%
- (C) 14% vs. 40%
- (D) 20% vs. 26%

Key: B

Rationale: In a retrospective review of patients at MDACC who achieved a pCR following neoadjuvant chemotherapy, there was no difference in LRR rates with use of PMRT in stage I or II patients, (10 yr LRR rates were 0% in both). In stage III patients however, 10 yr LRR rates were 7% with PMRT vs 33% ($p=0.04$). Within this cohort, use of RT was also associated with improved DSS and OS.

175. Which of the following gastric lymph node stations is dissected in a D2 dissection?

- (A) Mesenteric
- (B) Para-aortic
- (C) Retropancreatic
- (D) Common Hepatic

Key: D

Rationale: D2 dissection includes dissection of L gastric, celiac, common hepatic, splenic hilum, and splenic artery.

176. Compared with other subtypes of breast cancer, triple negative disease is more commonly associated with:

- (A) BRCA 2 mutation.
- (B) detection by physical examination.
- (C) higher frequency of positive axillary nodes.
- (D) increasing rate of relapse and death beyond 18 years.

Key: B

Rationale: 60-70% of BRCA 1 breast cancers are triple negative and approximately 10-20% of unselected triple negative breast cancer patients are BRCA1 positive. They are less likely to be diagnosed with mammography screening. Some studies show triple negative cancers have no difference in rates of positive nodes; however, the NCCN reports a lower frequency of positive nodes in triple negative disease (HR <0.88, p=<.001). There is increased relapse until 5-6 years (peak within first 3 years), then sharp decrease and virtually no relapses after 8 years. 70% of deaths occur within the first 5 years. There are almost no deaths after 10 years.

177. CML is marked by the presence of which gene protein products?

- (A) RB
- (B) KRAS
- (C) BRCA 1
- (D) BCR-ABL

Key: D

Rationale: The BCR-ABL proteins are the result of the translocation t(9,22) or the Philadelphia chromosome.

178. What is the MOST common radiation regimen for Graves ophthalmopathy?

- (A) 10 Gy in 10 fractions
- (B) 20 Gy in 10 fractions
- (C) 30 Gy in 10 fractions
- (D) 30 Gy in 15 fractions

Key: B

Rationale: 20 Gy in 10 fractions was utilized in most of the randomized trials evaluating fractionated radiation therapy to treat Grave's disease ophthalmopathy.

179. Medical misadministration involving a linac is defined by:

- (A) FDA.
- (B) NRC.
- (C) state regulations.
- (D) federal regulations.

Key: C

Rationale: The NRC regulates the medical use of radiation from radioactive isotopes, which does not apply to radiation produced by a linear accelerator. State laws regulate the medical use of radiation produced by a linac.

180. To date, the MOST effective application of PARP inhibitors in the clinic is for:

- (A) radioprotection.
- (B) radiosensitization.
- (C) chemoprevention.
- (D) chemosensitization.

Key: D

Rationale: The PARP-1 protein is an abundant nuclear enzyme involved in both DNA SSB repair and base excision repair. PARP-1 is overexpressed in, among others, human breast and prostate cancers. Inhibition of PARP produces synthetic lethality in cells with a preexisting DNA repair defect (as is the case for many tumor cells), which can sensitize them to other DNA toxins like ionizing radiation and chemotherapy. In clinical trials, PARP inhibitors have been most efficacious to date as chemosensitizers.

181. The 2014 EBCTCG meta-analysis reports which of the following findings for the addition of PMRT for breast cancer patients with 1-3 positive nodes?

- (A) Reduction in LRR, any recurrence, and breast cancer mortality
- (B) No reduction in LRR, any recurrence, or breast cancer mortality
- (C) Reduction in LRR, but not any recurrence or breast cancer mortality
- (D) Reduction in LRR and any recurrence, but not breast cancer mortality

Key: A

Rationale: The EBCTCG meta-analysis of node positive women treated with mastectomy and axillary surgery showed a reduction in recurrence (loco regional and any) and breast cancer mortality in women with 1-3 and 4 + nodes, including in trials in which systemic therapy was given. This reduction in recurrence and breast cancer mortality was not seen in node negative women.

182. Which is NOT a radiosensitizer?

- (A) Nimorazole
- (B) Gemcitabine
- (C) Glutathione
- (D) Tirapazamine

Key: C

Rationale: Glutathione is a naturally-occurring antioxidant/free radical scavenger capable of protecting cells against radiation damage. All of the remaining answer options are radiosensitizers: gemcitabine is used in concurrent chemoradiotherapy regimes as a radiosensitizer, nimorazole is an hypoxic cell radiosensitizer, and tirapazamine is a bioreductive drug selectively toxic to hypoxic cells.

183. A linear accelerator electron scattering foil:

- (A) spreads out the narrow raw electron beam.
- (B) filters bremsstrahlung x-ray contamination.
- (C) collimates the beam and reduces penumbra.
- (D) converts the high energy photons to electrons.

Key: A

Rationale: The purpose of the scattering foil is to spread out the very narrow raw electron beam that emerges from the accelerator wave guide. The foil should be thin enough to avoid significant bremsstrahlung production but it does not filter this contamination.

184. Cutaneous squamous cell carcinoma of the head and neck region:

- (A) is more indolent with desmoplastic histologic variant.
- (B) has the same prognosis regardless of the depth of invasion.
- (C) has an increased risk of regional and DM with perineural invasion.
- (D) has an increased risk of regional, but not distant metastasis with perineural invasion.

Key: C

Rationale: Thickness of skin SCC is an important predictor of metastasis. The thicker tumor increases the risk of nodal metastasis (Rowe ED, et al. J of the Am Academy of Derm. 1992;6:976-990). Desmoplastic is an aggressive histologic variant of SCC and is associated higher risk of nodal disease especially with increasing tumor thickness. Perineural invasion occurs in about 5% of cutaneous SCC and is associated with higher risk for both regional and distant metastasis (Breuninger H. et al. 1990 Am J of Clin Path; 94:6)

185. For squamous cell carcinoma of the esophagus, what is the expected benefit of surgical resection after achieving a clinical response to concurrent chemoradiotherapy?

- (A) Decreased local recurrence, improved survival
- (B) Decreased local recurrence, unchanged survival
- (C) Unchanged local recurrence, improved survival
- (D) Unchanged local recurrence, unchanged survival

Key: B

Rationale: In two randomized trials of chemoradiation with or without surgery (the other is Stahl M, J Clin Oncol 2005; 23:2310-2317), the addition of surgery led to no significant improvement in overall survival, but a decrease in rate of locoregional relapse. The Bedenne trial included mostly squamous carcinoma patients and the Stahl trial only included squamous carcinoma, therefore these conclusions are not necessarily applicable to adenocarcinoma.

References: Bedenne, L. et. al, J Clin Oncol, (2007) -

186. According to the 2007 WHO classification, what is a histologic criterion for a Grade II atypical meningioma?

- (A) Brain invasion
- (B) Rhabdoid features
- (C) 0 to 3 mitotic figures per 10 HPF
- (D) 20 or more mitotic figures per 10 HPF

Key: A

Rationale: 0-3 mitotic figures per 10 high power fields is a grade I meningioma. Greater than 20 mitotic figures per 10 high power fields or rhabdoid features are among the criteria for a grade III (anaplastic/malignant) meningioma.

187. What is the MOST common type of childhood leukemia?

- (A) Acute myelogenous
- (B) Acute promyelocytic
- (C) Acute B cell lymphoblastic
- (D) Acute T cell lymphoblastic

Key: C

Rationale: ALL makes up 25% of all childhood cancer diagnosis with B cell ALL comprising 82-85% of the ALL cases.

References: Halperin, Pediatric Radiation Oncology.

188. Which factor is MOST important in WHO histopathologic classification of nasopharyngeal cancer?

- (A) Mucin
- (B) Keratin
- (C) EBV antibody
- (D) Lymphoid infiltration

Key: B

Rationale: Histology is an important prognosticator in nasopharynx cancer. The World Health Organization (WHO) classification is based on the tumor's keratin production.

189. During DNA single strand break repair, which step occurs first?

- (A) Resection by the MRN complex
- (B) Gap filling by DNA polymerase β
- (C) End processing by polynucleotide kinase
- (D) End recognition by the Ku/DNA-PKcs complex

Key: C

Rationale: The correct answer is C. End processing by polynucleotide kinase occurs before gap filling by DNA polymerase β . The other answer options are steps that occur during DNA double strand break repair.

190. Regarding RTOG 0617, which evaluated (1) the benefit of an additional 14 Gy to the standard dose of 60 Gy and (2) the benefit of the addition of cetuximab to the chemotherapy?

- (A) No difference in OS was seen between all four treatment arms.
- (B) There was an OS benefit in the 60 Gy arm with either chemotherapy combination.
- (C) There was an OS benefit in the 74 Gy arm with either chemotherapy combination.
- (D) The OS benefit in the 74 Gy arm was limited to chemotherapy without cetuximab.

Key: B

Rationale: The RTOG 0617 trial was a phase III study with a double randomization comparing (1) 60 vs. 74 Gy, and chemotherapy consisting of carbo/paclitaxel alone vs. carbo/paclitaxel with cetuximab. The median survival times and 18-month OS rates for the 60 Gy and 74 Gy arms were 28.7 vs 19.5 months, and 66.9% vs 53.9% respectively ($p < 0.001$). Unfortunately, and surprisingly, not only was there no benefit to escalating doses to 74 Gy, this arm did statistically worse.

191. Which histologic subtype of sarcoma has the lowest risk of lymph node metastasis?

- (A) Liposarcoma
- (B) Angiosarcoma
- (C) Clear cell sarcoma
- (D) Epithelioid sarcoma

Key: A

Rationale: Increased risk in clear cell sarcoma (28%), angiosarcoma (23%), epithelioid sarcoma (20%), rhabdomyosarcoma (15%), synovial sarcoma (14%). (Mnemonic: SCARE for synovial, clear cell, angio, rhabdo, epithel.)

192. For locally advanced rectal cancer, a UK + NCIC trial comparing preoperative RT (25 Gy/5fx) to selective postoperative chemoRT (45 Gy/25 fx) showed that:

- (A) TME reduced local recurrence.
- (B) preoperative therapy improved OS.
- (C) preoperative therapy improved DFS.
- (D) negative circumferential margins were improved with preoperative therapy.

Key: C

Rationale: This study found a reduction of 61% in the relative risk of local recurrence for patients receiving preoperative radiotherapy (hazard ratio [HR] 0.39, 95% CI 0.27–0.58, $p < 0.0001$), and an absolute difference at 3 years of 6.2% (95% CI 5.3–7.1) (4.4% preoperative radiotherapy vs 10.6% selective postoperative chemoradiotherapy). It showed a relative improvement in disease-free survival of 24% for patients receiving preoperative radiotherapy (HR 0.76, 95% CI 0.62–0.94, $p = 0.013$), and an absolute difference at 3 years of 6.0% (95% CI 5.3–6.8) (77.5% vs 71.5%). Overall survival did not differ between the groups (HR 0.91, 95% CI 0.73–1.13, $p = 0.40$). The rate of circumferential resection margin involvement and the proportion of patients with pathological stage III disease did not differ between the two groups ($p = 0.12$ and $p = 0.29$, respectively). 93% of patients had TME.

193. For which electron beam energies is the 80% depth dose invariant as the field size decreases from 10 x 10 cm² to smaller field sizes?

- (A) ≤ 6 MeV
- (B) ≤ 9 MeV
- (C) ≥ 12 MeV
- (D) ≥ 18 MeV

Key: A

Rationale: Rationale has a graphs and this tab does not support it. However, explanation says "as the electron beam energy increases over ~ 9 MeV, the d80% becomes more sensitive to field size and will decrease (become shallower) as the field size is reduced. Because of this, potential underdosing to the treatment volume may occur if high energies and small field sizes are used for treatment."

194. What is the reason why two fractional regimens, 60 Gy in 30 fractions and 60 Gy in 3 fractions, respectively, are isoeffective?

- (A) Most of the tumors are hypoxic.
- (B) The 20 Gy fractions are ablative.
- (C) The α/β ratio of the tumor is infinite.
- (D) There is a dosimetric error in the 30 fraction regimen.

Key: C

Rationale: Tumors with an infinite α/β ratio (i.e., $\beta = 0$) would be insensitive to fractionation. However, for a tumor with an α/β ratio of 10 Gy, the 3 fraction regimen would be more biologically effective. Had the 3 fraction schedule been ablative, it should have had a greater effect than the 30 fraction schedule, not an equal effect. The presence of tumor hypoxia could have limited the efficacy of the 3 fraction regimen due to the lack of sufficient overall treatment time for reoxygenation to occur. If so, the 3 fraction schedule could have had less of an effect than the 30 fraction schedule.

195. A 10 MeV photon in water undergoes Compton scattering through an angle of 90 degrees. The kinetic energy of the recoil electron is approximately:

- (A) 8.0 MeV.
- (B) 8.5 MeV.
- (C) 9.0 MeV.
- (D) 9.5 MeV.

Key: D

Rationale: High energy photons scattered through 90 degrees have a final energy of 0.511 MeV. This leaves an approximate total of 9.5 for the recoil electron. This is important to know for shielding considerations. Scatter radiation from patients that is incident on walls results from scattering at approximately 90 degrees.

196. Which study design starts with an exposure and moves forward to the outcome of interest even if the data are collected retrospectively?

- (A) Cohort
- (B) Phase III
- (C) Phase IV
- (D) Case-control

Key: A

Rationale: A cohort study starts with an exposure and moves forward to the outcome of interest even if the data are collected retrospectively. A case-control study starts with an outcome of interest and works backward to the exposure. Phase III trials compare the results of people taking a new treatment with the results of people taking the standard treatment (for example, which group has better survival rates or fewer side effects). In most cases, studies move into phase III only after a treatment seems to work in phases I and II. A phase IV trial studies the side effects of a treatment after it has been approved and is being marketed and sometimes are called post-marketing surveillance trials.

197. Which of the following subtypes is NOT a form of classical Hodgkin Lymphoma?

- (A) Mixed cellularity
- (B) Nodular sclerosis
- (C) Lymphocyte depleted
- (D) Nodular lymphocyte predominant

Key: D

Rationale: Nodular Lymphocyte Predominant is not a classical subtype of HL. They tend to be CD 15 and CD 30 negative, but CD 20 and CD 45 positive. Their clinical behavior is different from the classical subtypes of HL.

198. Radiation-induced cellular senescence:

- (A) cannot be reversed using any known intervention.
- (B) can be reversed by the addition of fibroblast growth factor.
- (C) can be reversed by the addition of hepatocyte growth factor.
- (D) can be reversed by the addition of vascular endothelial growth factor.

Key: A

Rationale: The senescent phenotype is characterized by an irreversible cellular growth arrest. Senescence is a process through which normal cells lose the ability to divide, typically after about 50 cell divisions in vitro. However, a senescent-like phenotype also occurs secondary to oncogenic stress or irreparable DNA damage, which in turn permanently activates cell cycle checkpoints. (This is more properly called "permanent growth arrest" than senescence however, because it is not a normal process.)

199. According to ICRU 78, the RBE of protons is approximately:

- (A) 0.6.
- (B) 1.1.
- (C) 1.5.
- (D) 2.1.

Key: B

Rationale: The RBE of protons is similar to that of photons. It is approximately 1.1.

200. Which term describes the measure of variability of data around the mean?

- (A) Range
- (B) Percentile
- (C) Prevalence
- (D) Standard deviation

Key: D

Rationale: Standard deviation, percentile and range are measures of dispersion while prevalence is used to describe the frequency of an event. The standard deviation measures the variability of data around the mean. It provides information on how much variability can be expected among individuals within a population. The range equals the difference between the largest and smallest observation. The percentile equals the percentage of a distribution that is below a specific value. As an example, a child is in the 90th percentile for weight if only 10% of children the same age weigh more. Prevalence refers to the number of individuals with a given disease at a given point in time divided by the population at risk at that point in time.

201. A rectangular 10 x 15 cm² field is approximately equivalent to a square field with a side of:

- (A) 11 cm.
- (B) 12 cm.
- (C) 13 cm.
- (D) 14 cm.

Key: B

Rationale: Using Sterling's approximation, a rectangular field is equivalent to a square field if they have the same area to perimeter ratio. The side(s) of an equivalent square field is calculated by $4 \times (\text{Area}/\text{Perimeter})$. In this case it is $(150/50) \times 4 = 12$

202. Adjuvant RT after prostatectomy has demonstrated OS benefit in cases exhibiting:

- (A) post-op PSA > 0.2.
- (B) peri-neural invasion.
- (C) Gleason > 8 disease.
- (D) extra-capsular extension.

Key: D

Rationale: The only study showing survival benefit of adjuvant RT after prostatectomy is SWOG 8794 in which the inclusion criteria was extra-capsular extension, seminal vesicle invasion and positive margin.

203. In a typical diagnostic x-ray tube, what percent of the incident electron energy is emitted as photons?

- (A) 0.01
- (B) 0.1
- (C) 1
- (D) 10

Key: C

Rationale: The efficiency of photon generation through the bremsstrahlung process increases with increasing electron energy. For relatively low energies found in diagnostic x-ray tubes, only 1% of the incident energy goes into photon production. At megavoltage energies, such as those found in therapeutic linear accelerators, around 30% of the energy is radiated as photons. The remaining energy is dispersed as heat.

204. The advantage of CBCT or MVCT over portal images is:

- (A) shorter acquisition time.
- (B) three-dimensional information.
- (C) use of the treatment beam energy.
- (D) correction for gantry sag during rotation.

Key: B

Rationale: CBCT is a three dimensional imaging modality. As such it provides information about translational shifts in three directions and rotations about three axes. Acquisition time is longer for CBCT. Although choice D is correct, this is not an advantage. CBCT usually employs kilovoltage energy.

205. What is the MOST appropriate treatment strategy for a 50-year-old, otherwise healthy male with a T1N1M0 squamous cell carcinoma of the nasopharynx?

- (A) Concurrent chemoRT
- (B) Definitive radiation only
- (C) Induction chemotherapy followed by radiation
- (D) Concurrent chemoRT followed by chemotherapy

Key: D

Rationale: Concurrent chemoRT followed by adjuvant chemotherapy remains the standard of care for most nasopharyngeal cancer except for T1N0 disease which can effectively treated with radiation alone.

206. According to ACT II trial, what is the impact of maintenance chemotherapy on OS following definitive chemoradiation for anal cancer?

- (A) improved with 5-FU and Cisplatin
- (B) no impact with 5-FU and Cisplatin
- (C) improved with 5-FU and Mitomycin-C
- (D) no impact with 5-FU and Mitomycin-C

Key: B

Rationale: The ACT II study is a 2 × 2 factorial trial which enrolled patients with histologically confirmed squamous-cell carcinoma of the anus without metastatic disease from 59 centres in the UK. Patients were randomly assigned to one of four groups, to receive either mitomycin (12 mg/m²) on day 1) or cisplatin (60 mg/m²) on days 1 and 29), with fluorouracil (1000 mg/m²) per day on days 1-4 and 29-32) and radiotherapy (50.4 Gy in 28 daily fractions); with or without two courses of maintenance chemotherapy (fluorouracil and cisplatin at weeks 11 and 14). With a median follow-up of 5.1 years, maintenance chemotherapy either regimens did not improve progression-free survival compared with no maintenance chemotherapy.

207. Which type of tumor has the lowest risk of leptomeningeal dissemination?

- (A) Pineoblastoma
- (B) Medulloblastoma
- (C) Ependyoblastoma
- (D) Hemangioblastoma

Key: D

Rationale: Hemangioblastoma is a WHO grade I neoplasm with a low risk of dissemination. The other tumors listed generally require prophylactic treatment of the craniospinal axis.

208. When planning CSI, the inferior aspect of the thecal sac in adults typically ends at:

- (A) L2.
- (B) L3.
- (C) S2.
- (D) the coccyx.

Key: C

Rationale: As determined by a sagittal T2 weighted MRI, the thecal sac ends at S2 in over 95% of adults. Therefore, the inferior border of a spinal CSI field is typically near S3. The spinal cord (not the thecal sac) ends at L2-3.

209. Retrospective studies reporting an OS benefit of primary tumor excision in the setting of metastatic breast cancer have found benefit:

- (A) regardless of surgical margin status.
- (B) was best in cases with bone metastases only.
- (C) when local surgery included axillary dissection.
- (D) was best with smaller number of metastatic sites.

Key: B

Rationale: Overall survival benefits were reported best in cases with bone metastases only and negative surgical margins. Addition of axillary surgery did not improve survival.

210. A brain MRI should be done in patients with bilateral retinoblastoma to rule out the presence of:

- (A) Lisch nodules.
- (B) optic nerve atrophy.
- (C) a pineal gland tumor.
- (D) contralateral eye involvement.

Key: C

Rationale: There is a small number of patients with bilateral retinoblastoma who will have a pineoblastoma as well. This is known as trilateral retinoblastoma and has a very poor prognosis. An MRI is performed for evaluation of the pineal gland.

References: Halperin, Pediatric Radiation Oncology.

211. A recommended risk-reducing strategy for women without gene mutations but who are considered at high risk for developing breast cancer is:

- (A) low fat, isocaloric diet in adulthood.
- (B) low fat, isocaloric diet in adolescence.
- (C) weight reduction in premenopausal women.
- (D) weight reduction in postmenopausal women.

Key: D

Rationale: High lifetime physical activity is associated with a lower risk of breast cancer. During adolescence, physical activity is associated with delayed menarche and delay in the establishment of regular ovulatory cycles. Later in life, a beneficial effect of physical activity has been observed. Postmenopausal obesity should be modified. High risk women who are obese should be directed toward weight control, because the combination of increased physical activity and caloric restriction are likely to have beneficial effects on both breast cancer risk and overall health. Among the reproductive risk factors, lactation has a protective effect. Women who accumulate a life-time exposure to lactation of at least 15 months have a lower risk for breast cancer after adjusting for other risk factors. Every 12 month period of lactation decreases risk by 4.3%. Obesity in premenopausal women has not been associated with a higher risk of breast cancer.

212. Which of the following patients would benefit from ^{131}I after total thyroidectomy?

- (A) 36-year-old female with T2N0M0 follicular carcinoma
- (B) 47-year-old female with T2N1aM0 papillary carcinoma
- (C) 52-year-old male with T2N1bM0 anaplastic carcinoma
- (D) 80-year-old female with T2N0M0 Hurthle cell carcinoma

Key: B

Rationale: Papillary thyroid carcinoma is likely to be iodine-avid, and a positive margin in a patient >45 yr old is at higher risk for recurrence and death from thyroid cancer. RAI ablation will treat known persistent disease. Anaplastic thyroid cancer is not treated with RAI. A 36 yr old patient with completely resected N0 disease is a Stage I cancer and a very low risk for recurrence, thus RAI not indicated. Hurthle cell carcinoma has variable iodine avidity and in an 80 yr old patient who has undergone complete resection of a small tumor, RAI is unlikely to benefit.

213. The health care communication standard for medical images is:

- (A) HL7.
- (B) 4DCT.
- (C) JPEG.
- (D) DICOM.

Key: D

Rationale: DICOM is the common format for digital images. It stands for Digital Imaging and Communications in Medicine. HL7 is a standard code for information interchange and is the principle code for patient information used in admissions, discharges and transfers. JPEG is a compressed file format for digital images. 4DCT is an abbreviation for a 4 dimension CT scan that is often used in radiation therapy planning.

214. What is the appropriate clinical T-stage for a 2.5 cm palpable mass in the oral tongue with severely limited tongue mobility?

- (A) T2
- (B) T3
- (C) T4a
- (D) T4b

Key: C

Rationale: Oral cavity primary cancers are staged according to both size and extent of involvement. T1 tumors are classified as being ≤ 2 cm, whereas T2 tumors are > 2 cm but ≤ 4 cm. T3 tumors are > 4 cm in size. T4 tumors invade adjacent structures; T4a represents tumor invasion of adjacent structures only (including cortical bone, deep muscles of the tongue, maxillary sinus, and skin of face), whereas T4b signifies invasion of the masticator space, pterygoid plates, base of skull, or encasement of the internal carotid artery. In this patient, although a 2.5 cm tumor would seem to be consistent with a T2 tumor, given the patient presenting with dysarthria and had poor tongue protrusion on exam signifies the patient has deep tongue muscle involvement, which is most consistent with T4a disease.

215. Per NCCN guidelines, what is the MOST appropriate postoperative care for a Stage I endometrial stromal sarcoma?

- (A) Observation
- (B) Chemotherapy
- (C) Brachytherapy
- (D) External beam radiation

Key: A

Rationale: Observation is recommended for postoperative stage I ESS. Postoperative hormone therapy (with or without radiation) is recommended for stages II-IV ESS. Radiation is considered an option (category 2 B) for stage I only. Typical hormonal therapy includes megestrol acetate or medroxyprogesterone. Hormonal therapy is also recommended for recurrence or unresectable disease. Series of ESS suggest long DSF in the absence of specific therapy and offer less support for the use of adjuvant radiation. Adjuvant radiation has been demonstrated to reduce local recurrence rates with limited effect on survival.

216. Clinical group IIA rhabdomyosarcoma consists of:

- (A) completely resected localized disease.
- (B) incomplete resection with gross residual disease.
- (C) grossly resected tumor with microscopic residual disease, without involved regional lymph nodes.
- (D) grossly resected tumor with involved regional nodes resected with no microscopic residual disease.

Key: C

Rationale: Group IIA RMS includes patients where there has been a complete resection of the primary tumor with no evidence of LN or metastatic involvement. Microscopic positive margins may be present.

References: Egas-Bejar D, Huh WW, Rhabdomyosarcoma in adolescent and young adult patients: current perspectives, (2014).

217. According to the ASTRO guidelines, which of the following is an “unsuitable” factor when selecting patients for accelerated partial breast irradiation?

- (A) Tumor size 3 cm
- (B) Invasive lobular cancer
- (C) Presence of extensive LVSI
- (D) Less than 2 mm surgical margin

Key: C

Rationale: The ASTRO consensus statement defines patients for APBI as “suitable”, “cautionary”, or “unsuitable”. Close margins (less than 2 mm), invasive lobular cancer, and a tumor 3 cm or less are all criteria in the cautionary category. Extensive LVSI is considered an unsuitable criterion.

218. Which of the following clinical stages would have been eligible for the SWOG 9416/INT0160 study of superior sulcus tumors?

- (A) T2N1
- (B) T2N2
- (C) T3N2
- (D) T4N1

Key: D

Rationale: The SWOG 9416/INT 0160 was a phase II study examining neoadjuvant chemotherapy and radiation for patients with superior sulcus tumors. Eligible stages were T3-4N0-1. Patients were treated to 45 Gy with concurrent cisplatin and etoposide. The rate of complete resection was 76%. 5 year overall survival was 44%.

219. Which treatment is associated with a survival benefit for painful bony metastases from castrate resistant prostate cancer?

- (A) Treatment with ^{223}Ra
- (B) Treatment with ^{153}Sm
- (C) 30 Gy in 10 fractions to all painful sites
- (D) SBRT to 30 Gy in 5 fractions to all painful sites

Key: A

Rationale: Radium 223 is an alpha emitter that selectively targets bone metastases with alpha particles. A recently completed phase III study in men with castration-resistant metastatic prostate cancer compared treatment with Radium 223 to placebo, in addition to the best standard of care and revealed a survival benefit of 14 months vs 11.2 months for men with Radium-223. Radium 223 differs from standard external beam radiotherapy and treatment with beta-emitting agents such as samarium 153 in this setting because these treatments are not associated with a survival advantage.

220. An adenoid cystic carcinoma of the salivary glands:

- (A) is rarely associated with perineural invasion.
- (B) is commonly associated with lymph node metastasis.
- (C) has worse prognosis with increased solid component.
- (D) is the predominant malignant histologic type in the parotid salivary gland.

Key: C

Rationale: Adenoid cystic carcinoma is the predominant malignant histologic type in submandibular and minor salivary gland tumors. The cribriform pattern represents differentiated component whereas the solid component are undifferentiated features. In a mixed tumor with both components, the degree of solid component (>30%) would have poorer prognosis. Lymph node spread is rare (<5%).

221. What is the clinical stage for a patient with a 1 cm palpable breast mass having no palpable local or regional adenopathy and an enlarged ipsilateral internal mammary lymph node on CT?

- (A) IB
- (B) IIA
- (C) IIB
- (D) IIIA

Key: D

Rationale: As per the staging guidelines, this patient has a T1b (1 cm mass in greatest dimension) and an N2b (ipsilateral internal mammary node in the absence of any other clinically evident nodes in Level I and II axilla). Clinical Stage is IIIA.

222. An ipsilateral RT is MOST appropriate for which carcinoma of the tonsil?

- (A) HPV negative T2N1 limited to the tonsillar fossa
- (B) HPV negative T1N2b with 2 positive level II nodules
- (C) HPV positive T3N0 extending 1.5 cm onto the soft palate
- (D) HPV positive T2N0 extending 1.2 cm onto the base of tongue

Key: A

Rationale: According to the most recent ACR appropriateness criteria published in Head and Neck (Yeung, 2012), bilateral radiation was recommended for any patient with ≥ 1 cm of invasion into either the soft palate or base of tongue, or nodal stage N2b or greater. Insufficient data was present to make a definitive conclusion regarding the role of HPV status in evaluating patients for ipsilateral RT.

223. What is the appropriate clinical stage for a 2.5 cm nasopharyngeal cancer with parapharyngeal extension and a 3.5 cm right supraclavicular lymph node without distant disease?

- (A) T1N2M0
- (B) T1N3M0
- (C) T2N2M0
- (D) T2N3M0

Key: D

Rationale: The primary T-stage is determined entirely by extent of the primary lesion, and not the size. In particular, T1 tumors are confined to the nasopharynx, and may extend to the oropharynx and/or nasal cavity. T2 tumors include those with parapharyngeal extension (posterolateral tumor infiltration). The nodal staging for nasopharyngeal cancer is also different from other head and neck cancers. Notably, supraclavicular lymph nodes are considered as regional nodes, and whose borders are defined by superior margin of the sternal end of the clavicle, the superior margin of the lateral end of the clavicle, and the point where the neck meets the shoulder. N1 denotes unilateral cervical lymph node(s) ≤ 6 cm and/or unilateral or bilateral retropharyngeal lymph node(s) ≤ 6 cm. N2 denotes bilateral cervical lymph node involvement ≤ 6 cm. N3 includes lymph nodes > 6 cm and/or lymph node metastasis to the supraclavicular fossa, which are designated N3a and N3b, respectively.

224. For a linear accelerator with FFF mode, how does the average energy of its 6 MV FFF beam compare to the average energy of its flattened 6 MV beam?

- (A) Lower
- (B) Equal
- (C) Higher
- (D) Double

Key: A

Rationale: The flattening filter preferentially filters out low energy photons, increasing the average energy of the beam. FFF modes do not have a flattening filter, so, even though the nominal accelerating energy is the same, the average beam energy is lower.

225. According to the recently updated results of RTOG 91-11, the 10-year larynx preservation rate was:

- (A) the same between RT alone versus sequential chemoRT.
- (B) the same between sequential versus concurrent chemoRT.
- (C) better with concurrent chemoRT versus sequential chemoRT.
- (D) better with sequential chemoRT versus concurrent chemoRT.

Key: C

Rationale: Concurrent chemoRT resulted in significantly improved laryngeal preservation and locoregional control over sequential chemoRT and radiation alone. Both chemo regimens significantly improved 10-year laryngectomy-free survival over RT alone.

226. Which agent can be used to abrogate internal radionuclide contamination?

- (A) Polyethylene glycol (PG)
- (B) Fibroblast growth factor (FGF)
- (C) Adenosine monophosphate (AMP)
- (D) Diethylenetriamine pentaacetate (DTPA)

Key: D

Rationale: DTPA is a chelating agent that can bind to radioisotopes and facilitate their clearance from the body.

227. A Kaplan-Meier analysis:

- (A) is similar to logistic regression analysis.
- (B) permits time to be included as a variable.
- (C) allows patients to be counted only for the period of time that they are observed.
- (D) measures the ratio of surviving patients to total number of patients at risk for outcome.

Key: D

Rationale: There are two very common methods of survival analysis utilized in medical literature. These are Kaplan-Meier analysis and Cox proportional hazards analysis. Kaplan-Meier analysis measures the ratio of surviving patients (or those free from an outcome) divided by the number of patients at risk for the outcome. Every time a patient has an outcome, the ratio is recalculated. Using these calculations, a curve can be generated that graphically depicts the probability as time passes. Whereas Cox proportional hazard analysis (like logistic regression analysis) can account for many variables that are relevant for predicting a dichotomous outcome. Cox permits time to be included as a variable (unlike logistic regression analysis) and for patients to be counted only for the period of time in which they are observed.

228. Regarding thymomas/thymic carcinomas:

- (A) pericardial invasion is considered unresectable disease.
- (B) there is no role for chemotherapy in the management of thymomas.
- (C) involvement of mediastinal lymph nodes is considered stage IVB disease.
- (D) thymoma-associated myasthenia gravis is readily reversed with surgical resection.

Key: C

Rationale: In the modified Masaoka staging system, LN+ disease is considered stage IVB. Other statements are incorrect. Pericardial invasion is still considered resectable, often done with induction chemotherapy followed by maximum resection. Surgery does not reverse MG related symptoms right away, and may require continued therapies. Thymomas are sensitive to platinum agents, and CAPP is often employed as induction chemotherapy prior to surgical resection for bulky disease.

229. What is the MOST common solid tumor in children?

- (A) Brain tumor
- (B) Wilms tumor
- (C) Neuroblastoma
- (D) Rhabdomyosarcoma

Key: A

Rationale: The most frequently diagnosed malignancies in order are: leukemia (31%), CNS tumors (21%), neuroblastoma (7%), Wilms tumor (5%), lymphomas (4 & 6%: HL & NHL), RMS (3%), bone cancers (4%).

References: Egas-Bejar D, Huh WW, Rhabdomyosarcoma in adolescent and young adult patients: current perspectives, (2014).

230. In the original GITSG 9173 study of adjuvant chemoradiation, chemoradiation with 5-FU improved:

- (A) median OS from 11 months to 20 months.
- (B) median OS from 22 months to 40 months.
- (C) progression-free survival from 11 months to 20 months.
- (D) progression-free survival from 22 months to 40 months.

Key: A

Rationale: The original GITSG 9173 trial of adjuvant chemoradiation showed a survival benefit in the 21 patients randomized to adjuvant chemoradiation over the 22 patients randomized to no adjuvant treatment. Adjuvant treatment was weekly bolus 5FU with radiation delivered in two 2000 cGy two-week intervals with a two-week break in between. Median survival was 20 months with chemoradiation and 11 months with observation. (P=0.03)

References: Kalser MH, Ellenberg SS., Arch Surg, (1985).

231. What is the 5-year rate of isolated vaginal recurrences for high-intermediate risk endometrial cancer treated with adjuvant vaginal brachytherapy (PORTEC-2)?

- (A) 1.6%
- (B) 1.8%
- (C) 2.1%
- (D) 5.1%

Key: B

Rationale: PORTEC-2 randomized high-intermediate risk endometrial carcinoma patients to pelvic radiation or vaginal brachytherapy. The primary endpoint of vaginal recurrence risk was not statistically significant between the two groups at 1.8% (vaginal brachytherapy) and 1.6% (pelvic radiation). The 5 year local regional relapse (pelvic, vaginal or both) was 5.1% (vaginal brachytherapy) and 2.1% (pelvic radiation). The interpretation was that vaginal brachytherapy is effective in ensuring vaginal control, with fewer GI toxic effects than with external beam. The authors concluded that vaginal brachytherapy should be the adjuvant treatment of choice for patients with endometrial cancer of high-intermediate risk.

References: Nout RA, et al., None Given, (2010).

232. In comparison to glioblastoma with unmethylated MGMT promoter, glioblastoma with methylated MGMT promoter:

- (A) carries a worse prognosis.
- (B) presents a target for therapeutic intervention.
- (C) has less benefit with the addition of temozolomide to radiotherapy.
- (D) has an increased risk of pseudoprogression after chemoradiotherapy.

Key: D

Rationale: Methylated MGMT promoter tumors carries a more favorable prognosis. Patients with methylated MGMT promoter glioblastoma derive significant benefit from addition of temozolomide to radiotherapy. To this day, MGMT methylation status is found to have predictive, but not prognostic, and no therapeutic interventions have been found yet.

233. How do protons predominately interact with matter?

- (A) Coulomb forces
- (B) Photoelectric effects
- (C) Pair and triplet production
- (D) Rayleigh and Compton scattering

Key: A

Rationale: It is important to understand that charged particles (such as protons) interact primarily by excitation and ionization due to Coulomb interactions with orbital electrons and atomic nuclei. Photoelectric, Compton and pair production are all interactions between photons and matter.

234. In the postoperative management of rectal cancer, the NCCTG 86-47-51 trial demonstrated that:

- (A) semustine and 5-FU before and after chemoradiation improved OS.
- (B) bolus 5-FU caused more hand-foot syndrome and diarrhea compared to protracted venous infusion 5-FU.
- (C) bolus 5-FU concurrent with RT reduced local tumor relapse rates compared to protracted venous infusion 5-FU.
- (D) protracted venous infusion 5-FU with concurrent RT had superior OS compared to bolus 5-FU with RT.

Key: D

Rationale: Patients who received a protracted infusion of fluorouracil had a significantly increased time to relapse ($P = 0.01$) and improved survival ($P = 0.005$), and reduced tumor relapse rates. There was no evidence of a beneficial effect in the patients who received semustine plus fluorouracil. PVI resulted in more diarrhea and bolus 5-FU resulted in more leukopenia.

235. What is the mechanism of action of Temsirolimus in the treatment of renal cell carcinoma?

- (A) A monoclonal antibody directed against the EGFR
- (B) An inhibitor of the mammalian target of Rapamycin (mTOR) protein
- (C) A recombinant humanized monoclonal antibody that binds and neutralizes circulating VEGF
- (D) A small molecule inhibitor of the VEGF receptor and platelet derived growth factor receptor tyrosine kinases

Key: B

Rationale: Temsirolimus is a competitive inhibitor of the mammalian target of Rapamycin (mTOR) protein. The mTOR pathway regulates cell growth, cell proliferation, cell motility and survival. Agents that inhibit the activation of mTOR have activity in patients with advanced or metastatic renal cell cancer, particularly in patients with poor prognostic features.

236. The dose in the buildup region in an electron beam will increase due to:

- (A) an increase in SSD.
- (B) a decrease in beam energy.
- (C) a significant increase in field size.
- (D) a significant reduction in field size.

Key: C

Rationale: The surface dose increases. Decreasing beam energy results in lower dose in buildup region. Increasing the SSD will result in lower dose.

237. What structures are MOST likely involved by a tumor in a patient with Parinaud syndrome?

- (A) Medulla
- (B) Dorsal midbrain
- (C) Cavernous sinus
- (D) Suprasellar region

Key: B

Rationale: Parinaud syndrome is a constellation of disorders of eye movement and pupillary dysfunction related to dorsal midbrain dysfunction. Oncologic causes include tumors of the pineal region and associated hydrocephalus but stroke and MS can lead to similar symptoms.

238. Why does the build-up incorporated into diode dosimeters used for routine in-vivo dosimetry consist of high density materials such as brass or tungsten?

- (A) These materials provide increased conductivity
- (B) To limit bremsstrahlung production in the diode
- (C) To compensate for p-n junction energy dependence
- (D) So that the diode can be made reasonably compact in size

Key: D

Rationale: Tissue density build-up would require up to 3 – 4 cm thickness, which is impractical. Diodes are usually calibrated to measure the dose at a depth of d_{max} .

239. For IMRT, treatment plan quality is relatively independent of beam energy provided that:

- (A) number of beams is sufficient.
- (B) only coplanar beams are used.
- (C) image guidance is used in delivery.
- (D) full heterogeneity corrections are applied.

Key: A

Rationale: A low energy beam has a higher proximal dose and a lower dose distal to the target. When a small number of low energy beams are used to treat a deep target, the proximal dose must be high to deliver the required dose at depth. As the number of beams increases the proximal dose will be diluted. Heterogeneity corrections, IGRT and beam arrangement should not influence energy choice.

240. Prevalence of which interaction in kV imaging is responsible for improved bone/soft-tissue contrast compared to a MV portal image?

- (A) Compton
- (B) Photoelectric
- (C) Pair production
- (D) Bremsstrahlung

Key: B

Rationale: The photoelectric effect is proportional to the cube of the atomic number (Z) and inversely proportional to the cube of the photon energy (E). The high Z dependence makes photoelectric interactions very sensitive to small changes in material composition, but the strong E dependence means photo electric only makes a significant contribution at lower photon energies. In tissue, the photoelectric effect is approximately equal to the Compton effect at about 30 keV, with the prevalence of photoelectric interactions decreasing rapidly for the higher energies found in megavoltage beams.

241. In 3D conformal planning, beam apertures are designed to frame the PTV with an additional margin to account for:

- (A) patient motion.
- (B) internal scatter.
- (C) beam penumbra.
- (D) setup uncertainties.

Key: C

Rationale: The CTV accounts for option A, while the PTV accounts for options B and C. Due to beam penumbra, beam apertures need an additional margin for PTV coverage.

242. What is the assumption of the null hypothesis?

- (A) There is a statistical probability of avoiding a Type II error.
- (B) There is a positive correlation between the variables tested.
- (C) No random variations will occur within the sample population.
- (D) There is no relationship or difference between the variables tested.

Key: D

Rationale: The null hypothesis is the assumption that there is no relationship between two measured phenomena.

243. Patients receiving an immunotherapy checkpoint blockade agent can safely receive palliative RT under which condition?

- (A) RT should be hyperfractionated
- (B) RT should be standard fractionation
- (C) RT should be hypofractionated
- (D) RT should not be given with immunotherapy

Key: C

NOTE: This item was 0-weighted for scoring purposes upon post-exam statistical item analysis (did not count for or against candidate in calculation of test scores).

Rationale: Immunotherapy and radiotherapy can behave synergistically under certain conditions. Preclinical data suggest that hypofractionated radiosurgery with concurrent immunotherapy is the best treatment option.

244. Which is an initiator caspase?

- (A) Caspase 3
- (B) Caspase 6
- (C) Caspase 7
- (D) Caspase 9

Key: D

Rationale: The correct answer is D. Caspases, which are cysteine proteases, are broadly divided into initiator (apical) caspases and effector (executioner) caspases. Initiators (like caspases 2, 8, 9 and 10) cleave inactive pro-forms of effector caspases to activate them. In contrast, effector caspases cleave other protein substrates that trigger apoptosis.

245. Regarding the role of adjuvant RT following complete surgical resection (negative margins) in a patient with NSCLC with evidence mediastinal lymph node involvement?

- (A) There is no role for RT following adjuvant chemotherapy.
- (B) RT should be delivered sequentially to decrease the morbidity.
- (C) The total dose should be 60 Gy since the tumor bed has been devascularized.
- (D) Chemotherapy should be administered concurrently to get the best local control and OS.

Key: B

Rationale: Based on retrospective analyses through SEER (Lally) and ANITA, PORT has demonstrated substantial benefits in the adjuvant chemotherapy era. All the data demonstrating a benefit was seen in the sequentially treated patients suggesting high complication rates related to concurrent approach (ECOG). Doses > 54 Gy have been shown to increase complications (Dautzenberg and Machtay).

246. What is the QUANTEC-defined cardiac dose for conventional fractionated 3D conformal radiation that results in < 1% risk of long term cardiac mortality?

- (A) V25 < 10%
- (B) V30 < 55%
- (C) V40 < 15%
- (D) Mean < 40 Gy

Key: A

Rationale: The correct answer is V25 < 10% will result in a less than 1% risk of long term cardiac mortality. A Mean dose to the heart (pericardium) of < 26 Gy is associated with a <15% of pericarditis as is a V30 of <46% is also associated with a <15% risk of pericarditis.

247. The 5-year pelvic control rate for Stage I squamous cell carcinoma of the mid-vagina treated with definitive radiation is:

- (A) 60%.
- (B) 72%.
- (C) 86%.
- (D) 94%.

Key: C

Rationale: The 5year pelvic control rates were 86%, 84% and 71% for stages I, II and III-IV, respectively.

References: Frank, S.J. et al., Frank, S.J. et al., 62:138-47.

248. A posterior hypopharyngeal wall squamous cell carcinoma MOST frequently involves which groups of the nodes?

- (A) I, II, III
- (B) II, III, IV
- (C) Retropharyngeal, III, IV
- (D) Retropharyngeal, II, III

Key: D

Rationale: Primary lymphatic drainage of the posterior hypopharyngeal wall includes the retropharyngeal and bilateral level II and III lymph nodes. Levels I and V are less likely to be involved until nodal disease is very advanced. The retropharynx is at higher risk for lymphatic spread than level IV for a posterior pharyngeal wall location, thus D is a better answer than A. Level IV and paratracheal nodes may be at risk for post-cricoid and piriform sinus primary locations.

249. Which type of study begins with the absence or presence of an outcome and then looks backward in time to detect possible causes or risk factors?

- (A) Cohort
- (B) Case series
- (C) Case control
- (D) Cross sectional

Key: C

Rationale: A case series study is a simple descriptive account of characteristics observed in a group. A cross sectional study is meant to analyze data at one time to determine what is happening at the moment. A cohort study is a group with something in common suspected of being a precursor or risk factor to something that might happen in the future.

References: Dawson B and Trapp RG, Basic and Clinical Biostatistics, (2004) Pages 8 to 11.

250. According to AJCC guidelines, invasion of which anatomical structure is considered T2 disease for urethral cancer?

- (A) Bladder neck
- (B) Prostatic capsule
- (C) Corpus cavernosum
- (D) Corpus spongiosum

Key: D

251. With the addition of volumetric imaging systems placed on linear accelerators (i.e., CBCT), the recommended testing frequency and tolerance difference between the mechanical and imaging isocenters are:

- (A) daily, $\leq 2\text{mm}$.
- (B) daily, $\leq 4\text{mm}$.
- (C) monthly, $\leq 1\text{mm}$.
- (D) monthly, $\leq 2\text{mm}$.

Key: A

Rationale: Since volumetric imaging systems are used to position patients on a daily basis, the coincidence between the mechanical isocenter and the imaging isocenter must be validated each day prior to patient treatment. The recommended tolerance for linear accelerators, not used for stereotactic deliveries, is $\leq 2\text{mm}$.

252. Which of the following is the optimal donor for an 8-year-old patient with ALL who requires a bone marrow transplant?

- (A) 3/6 HLA matched parent
- (B) 6/6 HLA matched fraternal twin
- (C) 6/6 HLA matched identical twin
- (D) 10/10 HLA matched unrelated donor

Key: B

Rationale: A matched sibling donor is the best match. An identical twin match (syngeneic) may not allow adequate graft vs leukemia effect since the bone marrow would be identical to the diseased patient marrow.

References: Halperin, Pediatric Radiation Oncology.

253. The MOST likely effect of an HDM2 (human equivalent of MDM2) inhibitor on normal cells is:

- (A) apoptosis.
- (B) mitotic catastrophe.
- (C) neoplastic transformation.
- (D) epithelial-mesenchymal transition.

Key: A

Rationale: The HDM2 protein is a negative regulator of p53, meaning that its inhibition would cause p53 to accumulate in excess, which in turn would trigger apoptosis (or, in some cases, senescence).

254. In a woman undergoing hypofractionated breast-conserving RT following lumpectomy, patchy moist desquamation under the breast should be scored as:

- (A) dose limiting toxicity.
- (B) serious adverse event.
- (C) grade II adverse event (CTCAE).
- (D) grade III adverse event (RTOG scale).

Key: C

Rationale: Moist desquamation in a skin fold is considered a grade 2 reaction, while confluent moist desquamation outside a skin fold is scored as grade 3. Grade 2/3 skin reactions are expected side effects and do not qualify as serious events or dose limiting toxicities.

255. What is the likelihood ratio for a positive test if the sensitivity is 75% and the specificity is 65%?

- (A) 0.35
- (B) 1.15
- (C) 2.14
- (D) 2.60

Key: C

Rationale: The likelihood ratio is defined as the sensitivity divided by the false-positive rate. (The false-positive rate is $1 - \text{specificity}$.)

References: Dawson B and Trapp RG, Basic and Clinical Biostatistics, (2004) Page 309.

256. According to ICRU-62, an ITV is created by adding a margin to:

- (A) GTV.
- (B) CTV.
- (C) PTV.
- (D) PIV.

Key: B

Rationale: ICRU report 62 recommends that an internal margin be added to the CTV to compensate for internal physiological movements.

257. A patient presents with an anterior mediastinal mass. What is the MOST appropriate first step?

- (A) PET/CT
- (B) Bone marrow biopsy
- (C) Inquire about associated symptoms
- (D) Fine-needle aspirate of the mass lesion

Key: C

Rationale: While all the procedures are appropriate depending on the etiology of the mass, the most appropriate next step is more history about the symptoms to rule in and out various potential disease, before launching a more thorough workup.

258. RTOG 9804 (Phase III Trial of Observation +/- Tamoxifen vs. RT +/- Tamoxifen for Good Risk DCIS) found which of the following 7-year local recurrence rates?

- (A) 1% with RT
- (B) 3% with RT
- (C) 8% without RT
- (D) 10% without RT

Key: A

Rationale: 7 year recurrence rate is 0.9% with RT and 6% without RT.

259. Which of the following is elevated in patients with Cushing disease?

- (A) Cortisol
- (B) Prolactin
- (C) Thyroid stimulating hormone (TSH)
- (D) Insulin-like growth factor 1 (IGF-1)

Key: A

260. What is the likely diagnosis for a 2-year-old presenting with bilateral orbital bruising, weight loss, and bone pain?

- (A) Wilms tumor
- (B) Histiocytosis
- (C) Neuroblastoma
- (D) Rhabdomyosarcoma

Key: C

Rationale: Bilateral orbital ecchymosis (raccoon eyes) is a classic presenting symptoms for neuroblastoma involvement of the orbital bone. Bone pain and loss of weight would suggest bony and systemic involvement.

References: Halperin, Pediatric Radiation Oncology.

261. According to RTOG 98-11, the 5-year OS for patients with T4, node positive anal canal cancer is:

- (A) 20%.
- (B) 40%.
- (C) 60%.
- (D) 80%.

Key: B

Rationale: The long-term update of RTOG 98-11 found that concurrent chemoradiation with 5-FU and MMC had a significant impact of DFS and OS over 5-FU and cisplatin. In a recent secondary analysis, TN category has a statistically significant impact on overall survival, disease-free survival, and colostomy failure. Among all patients with T4, node positive disease, the 5-year overall survival was 42%.

262. Separate tumors in the same lobe are considered to signify what AJCC stage of disease?

- (A) T2
- (B) T3
- (C) T4
- (D) M1a

Key: B

Rationale: Two tumor nodules in the same lobe are considered T3 disease. Two tumor nodules in separate but ipsilateral lobes are T4 disease, and a separate tumor nodule in a contralateral lobe is considered M1a disease.

263. The angle of photon scattering that results in the largest energy transfer to a Compton recoil electron is:

- (A) 0 degrees.
- (B) 45 degrees.
- (C) 90 degrees.
- (D) 180 degrees.

Key: D

Rationale: In Compton scattering, when a photon is backscattered, it transfers the maximum fraction of its energy to the recoil electron.

264. What was the 5-year OS rate in the SWOG 9416/INT0160 trial for superior sulcus tumors?

- (A) 32%
- (B) 44%
- (C) 56%
- (D) 68%

Key: B

Rationale: The SWOG 9416/INT 0160 was a phase II study examining neoadjuvant chemotherapy and radiation for patients with superior sulcus tumors. Eligible stages were T3-4N0-1. Patients were treated to 45 Gy with concurrent cisplatin and etoposide. The rate of complete resection was 76%. 5 year overall survival was 44%.

265. Compared to Iodine-125 brachytherapy seeds, Palladium-103 seeds are characterized by:

- (A) longer half-life and lower average energy.
- (B) longer half-life and higher average energy.
- (C) shorter half-life and lower average energy.
- (D) shorter half-life and higher average energy.

Key: C

Rationale: Compared to I-125, Pd-103 has a shorter half-life (17 days vs. 60 days) and a lower average energy (21 keV vs. 28 keV). Pd-103 seeds are used in many of the same applications as I-125, including prostate seed implant and eye plaque therapy.

266. Potentially lethal damage is said to be "fixed" when cell survival *in vitro*:

- (A) decreases as the interval between two radiation doses increases.
- (B) decreases after a drug is added immediately following irradiation.
- (C) increases with increasing delay in subculture following irradiation.
- (D) increases after adding oxygen to the culture medium immediately following irradiation.

Key: B

Rationale: Potentially lethal damage (PLD) is either recovered or "fixed" (i.e. the damage is fixed in place) by conditions following irradiation. If a drug interferes with lesion repair it will fix PLD. Changes in survival following split doses reflects sublethal damage repair. An increase in survival following delayed post-irradiation subculture is an example of PLD repair. The addition of oxygen after irradiation is unlikely to improve cell survival.

267. In stereotactic radiotherapy, the Winston-Lutz test is used to verify the:

- (A) constancy of beam energy.
- (B) constancy of machine output.
- (C) accuracy of the MLC leaf motion with respect to isocenter.
- (D) alignment of patient positioning lasers with the radiation isocenter.

Key: D

Rationale: In the Winston Lutz, a pointer is set up using the lasers and the pointer is irradiated to verify the alignment of the lasers to the radiation field.

268. What were the findings of Chemotherapy for Isolated Locoregional Recurrence of Breast Cancer: A Randomised Trial (CALOR)?

- (A) Radiation was given to 80% of patients
- (B) Adjuvant chemotherapy improved DFS and OS
- (C) Adjuvant chemotherapy improved DFS but not OS
- (D) Most recurrences were after primary treatment with mastectomy

Key: B

Rationale: Most recurrences occurred in the setting of breast conservation therapy (60% BCT vs. 40% mastectomy). The study required negative surgical margins. Adjuvant chemotherapy improved 5 year DFS (69% vs. 57%, $p=0.046$) and overall survival (88% vs 76%, $p=0.024$). There was superior DFS for patients with ER negative breast cancer compared with patients with ER positive disease. ER negative patients had 5 year DFS 67% with vs 35% without chemotherapy. For ER positive patients, the 5 year DFS was 69% with vs. 70% without chemotherapy. The ER sensitivity was measured on the recurrent disease. There was no association with the ER status of the primary disease.

269. Which of the following brachytherapy dose calculation factors is often approximated by either a point or line source?

- (A) Geometry factor
- (B) Air kerma strength
- (C) Dose rate constant
- (D) Radial dose function

Key: A

Rationale: Geometry factor accounts for dose variation due to spatial distribution within the source (ignoring scatter and attenuation in the source.) It is often approximated by either a point or line source. The air kerma strength is a measure of source strength. The dose rate constant converts the strength to dose in water at a distance of 1 cm on the transverse axis. The radial dose function accounts for effects of absorption and scatter in medium along the transverse axis of the source.

270. Localization digitally reconstructed radiographs (DRRs) are principally generated to mimic the spatial geometry of a(n):

- (A) CT simulator.
- (B) diagnostic CT.
- (C) treatment accelerator.
- (D) traditional (kV) simulator.

Key: C

Rationale: DRRs are generated in a virtual environment by creating a planar radiograph using the patient volumetric information (CT) and a ray tracing algorithm that accounts for beam attenuation (ignoring scatter) through the CT of the patient. The geometry of the virtual source and detector pair that creates the DRR is that of the linear accelerator since the DRR is compared to the actual MV EPID or kV planar verification image for positioning purposes.

271. How does lower third vaginal involvement affect radiation field planning for cervical cancer?

- (A) Superior border should be raised to L3VB
- (B) Superior border should be raised to L1 VB
- (C) The inguinal lymph nodes should be included
- (D) A four field pelvic box technique should be used

Key: C

Rationale: The distal vagina drains to the inguinal nodes and should be included in the treatment for external beam therapy.

272. Which statement about the response of cells to hyperthermia is TRUE?

- (A) Cells maintained at low pH are resistant to hyperthermic killing.
- (B) Cells with a low energy charge are resistant to hyperthermic killing.
- (C) Hypoxic cells are more resistant to hyperthermia than aerated cells.
- (D) The age response for heat-induced cell killing is complementary to that for radiation.

Key: D

Rationale: The cell cycle age response for heat-induced cell killing is complementary to that for radiation, that is, that S phase cells are most sensitive to hyperthermic killing, but most resistant to radiation-induced cell killing. Maintaining cells at low pH or in a state of nutrient/energy deprivation sensitizes them to hyperthermic killing. Further, hypoxic cells, which are resistant to radiation killing, are equally sensitive as aerobic cells to hyperthermic killing.

273. Which agent improves cognitive function when added to WBRT?

- (A) Carbogen
- (B) Memantine
- (C) Bevacizumab
- (D) Pentoxifylline

Key: B

Rationale: RTOG 0614 randomized patients treated with whole brain irradiation to placebo vs. 6 months of memantine. The trial was underpowered for the primary endpoint of delayed recall, but patients had better overall cognitive function over time.

274. In the Korean ARTIST trial of adjuvant therapy in gastric cancer resected with D2 dissection, what was the impact of chemoradiation on DFS?

- (A) Benefit in all patients
- (B) No benefit in any subset
- (C) Benefit in node-negative patients only
- (D) Benefit in node-positive patients only

Key: D

Rationale: There was no statistically significant benefit in disease-free-survival with chemoradiation in the ARTIST trial as a whole. However, in the subset of patients with node-positive disease (86% of the cohort), DFS was significantly improved.

References: Lee, J., J Clin Oncol, (2012).

275. BRAF mutation is MOST associated with which type of tumor?

- (A) Uveal melanoma
- (B) CNS melanocytoma
- (C) Cutaneous melanoma
- (D) Acral lentiginous melanoma

Key: C

Rationale: Non-cutaneous melanomas and especially uveal melanoma primary tumors rarely harbor BRAF mutations and thus are not likely to respond to BRAF inhibitors such as vemurafenib. In fact, the first case report of BRAF mutation in uveal melanoma was in 2006. Acral lentiginous melanomas demonstrate BRAF mutations in about 20% of patients. CNS melanocytomas are benign tumors that do not harbor BRAF mutations.

276. After treatment of a plasmacytoma, which surveillance test is MOST appropriate?

- (A) M-protein
- (B) P-protein
- (C) Cytogenetics
- (D) Beta-2 microglobulin

Key: A

Rationale: Follow-up and surveillance tests for both solitary plasmacytoma and extra-osseous plasmacytoma consist of blood and urine tests. Serial and frequent measurements of M-protein are required to confirm disease sensitivity.

277. Which clinical observation is consistent with the 1906 "laws" formulated by Bergonié and Tribondeau regarding tissue radiosensitivity?

- (A) Kidneys are radiosensitive
- (B) Glioblastoma is radioresistant
- (C) Testicular cancer is radiosensitive
- (D) Small cell lung cancer is radioresistant

Key: C

Rationale: The "Laws of Bergonie and Tribondeau" state that a tissue would be expected to be radiosensitive if it contained a significant fraction of cells with a high mitotic rate, a long mitotic future, and that were poorly- or undifferentiated. The only answer option that fits these criteria is the finding that testicular cancer is especially radiosensitive. The other answer options would be considered exceptions to the laws, e.g., a non- or slowly-proliferating organ like the kidney being highly radiosensitive instead of resistant, or rapidly growing tumors with high mitotic indices – like small cell lung cancer or glioblastoma – being resistant instead of sensitive.

278. ONE of the main reasons that nanoparticle therapeutics tend to accumulate in tumors is that:

- (A) they are biologically-targeted to tumor cells.
- (B) tumor vasculature is leaky and allows them to extravasate into tumors.
- (C) tumor cells preferentially take up nanoparticles compared to small molecules.
- (D) they are more easily taken up in acidic microenvironments common to many tumors.

Key: B

Rationale: Tumors' leaky vasculature allow macromolecules, including nanoparticles, to extravasate into tumor interstitium. Due to the poor lymphatic drainage which has difficulty clearing macromolecules, nanoparticles become concentrated in tumors. This effect is generally referred to as Enhanced Permeability Effect (EPR).

279. Regarding brachytherapy for prostate cancer, a high initial International Prostate Symptom Score (IPSS) and an enlarged prostate volume is associated with:

- (A) increased post-implant urinary bother.
- (B) increased post-implant rectal bleeding.
- (C) decreased post-implant erectile function.
- (D) decreased post-implant biochemical control.

Key: A

Rationale: Both high pre-implant IPSS and enlarged prostate volume are associated with increased post-implant urinary bother. Patients with these factors are not good candidates for brachytherapy and sometimes they receive few months of androgen ablation before brachytherapy.

280. Myxopapillary ependymoma:

- (A) is most often extradural.
- (B) can be observed after a gross total resection.
- (C) is a World Health Organization (WHO) grade 2 tumor.
- (D) occurs most commonly in the cervicomedullary junction.

Key: B

Rationale: Myxopapillary ependymoma most commonly occurs in the conus medullaris-cauda equina-filum terminale region of the spinal cord and is a WHO grade 1 tumor, exhibiting a slow growth pattern. After complete surgical resection of cauda equina myxopapillary ependymoma, close observation can be offered.

281. What is the appropriate clinical stage of a rectal adenocarcinoma that invades through the muscularis propria, with 4 suspicious lymph nodes on imaging?

- (A) T3N1, stage IIIB
- (B) T3N1, Stage IIIC
- (C) T3N2, Stage IIIB
- (D) T3N2, Stage IIIC

Key: C

Rationale: T3= invasion through muscularis propria N1=1-3 LN N2=4 or more LN, N2a= 4-6 LN, N2b = 7 or more LN T3N2a= IIIB.

282. In a multicenter, phase III trial (BC2001) of bladder preservation, what was the effect of the concurrent chemoRT (5FU and mitomycin C) arm when compared to the RT alone arm?

- (A) Equivalent outcome in DSS
- (B) Significant improvement in LR
- (C) Significant improvement in OS
- (D) Significant increase in adverse events

Key: B

Rationale: Concurrent chemotherapy (5FU and mitomycin C) with radiotherapy significantly improved locoregional control of bladder cancer with no significant increase in adverse events.

283. The MOST frequent leukemia seen after prior radiation exposure is:

- (A) ALL.
- (B) CML.
- (C) AML.
- (D) CLL.

Key: C

Rationale: AML and ALL are commonly associated with prior radiation exposure, but AML is seen more often.

284. Regarding early stage NSCLC eligible for treatment with SBRT:

- (A) local control decreases if more than 5 fractions are given.
- (B) adjuvant chemotherapy improves DFS and OS following SBRT.
- (C) there is level 1 evidence that SBRT has equivalent OS in comparison to surgery.
- (D) a BED of 100 Gy is an important dose to achieve high local control rates > 90%.

Key: D

Rationale: According to Japanese data, if the BED is ≥ 100 Gy, then the 5-yr LC rate is 92% and the 5-yr OS is 71%. However, if the BED is < 100 Gy, then the 5-yr LC rate is 57% and the 5-yr OS is 30%. There is no data suggesting a benefit of adjuvant chemotherapy following SBRT. There are no phase III trials that have been reported to date comparing surgery and SBRT for early lung cancer.

285. SSO-ASTRO Consensus Guidelines regarding surgical margins after breast-conserving surgery apply for patients receiving:

- (A) neoadjuvant chemotherapy.
- (B) accelerated partial breast irradiation.
- (C) whole breast irradiation for pure DCIS.
- (D) whole breast irradiation for invasive carcinoma.

Key: D

Rationale: The guidelines are evidence based for patients undergoing standard conservation surgery followed by whole breast irradiation for invasive carcinoma. The evidence examined did not include review of surgical margins in other treatment settings.

286. Which of the following is considered an aggressive form of NHL?

- (A) MALT
- (B) DLBCL
- (C) Mycosis fungoides
- (D) Follicular (grade 1 or 2)

Key: B

Rationale: DLBCL is an aggressive form of NHL. Mycosis Fungoides, MALT, and Follicular are considered indolent lymphomas.

287. Intraoperative tumor spillage occurs when a 2-year-old girl undergoes resection of a right-sided, non-metastatic favorable histology Wilms tumor. The Children's Oncology Group stage of her disease is:

- (A) I.
- (B) II.
- (C) III.
- (D) V.

Key: C

Rationale: Green, et al, reported lower rates of recurrence free survival and overall survival in Stage II patients treated with dactinomycin and vincristine in NWTS-4. Therefore, the Children's Oncology Group now classifies patients with intraoperative tumor spill as having stage III disease. Stage I disease is confined to the kidney and completely resected. Stage II disease may extend beyond the kidney, but is complete resected without evidence of tumor spill, metastatic disease or lymph node involvement. Stage V disease refers to bilateral disease. Favorable/Unfavorable histology does not affect staging, although it affects treatment algorithm.

References: Green, et. al, <http://www.cancer.org/cancer/wilmstumor/detailedguide/wilms-tumor-staging>, (2014).

288. Which action decreases the risk of radiation pneumonitis?

- (A) Hypofractionation
- (B) Continued smoking
- (C) Concurrent chemotherapy
- (D) Concurrent immunotherapy

Key: B

Rationale: Continued smoking after treatment is associated with a decreased risk for radiation pneumonitis, possibly because it suppresses radiation-induced inflammation. Chemotherapy, immunotherapy and hypofractionation could increase the likelihood of pneumonitis, not decrease it.

289. What is the clinical stage of a cervical cancer that is a 2.5 cm visible lesion with superficial invasion?

- (A) IA1
- (B) IA2
- (C) IB1
- (D) IB2

Key: C

Rationale: All macroscopically visible lesions even with superficial invasion are allotted to stage IB carcinomas. A Stage IA1 has stromal invasion ≤ 3 mm in depth and extension ≤ 7 mm. A Stage IA2 has measured stromal invasion > 3 mm and not > 5 mm with an extension of not > 7 mm. IB classification is divided into 2 categories IB1 clinically visible lesion ≤ 4 cm and IB2 clinically visible lesion > 4 cm.

References: Staging Manual.

290. Which of the following is included in the definition of smoldering myeloma?

- (A) Creatinine > 2 mg/dl
- (B) Calcium > 11.5 mg/dl
- (C) Hemoglobin < 10 g/dl
- (D) Bence-Jones protein > 1 g/24 hours

Key: D

Rationale: Bence-Jones protein > 1 g/24 hours is the only criterion that belongs to the definition of smoldering myeloma. All of the rest are part of the definition of active myeloma.

291. The cumulative cochlear dose (Gy) for a child receiving 54-59.4 Gy of radiation for posterior fossa tumor should be less than:

- (A) 15.
- (B) 25.
- (C) 35.
- (D) 45.

Key: C

Rationale: Sensorineural hearing loss is a common late effect of radiation therapy for children with posterior fossa tumors. The location of the cochlea relative to posterior fossa tumors makes 35 Gy a reasonable goal.

References: Hau, et. al., Int J Radiat Oncol Biol Phys, (2008) Pages 892 – 899.

292. Where is the optic chiasm anatomically located?

- (A) Lateral to the carotid artery
- (B) Anterior to the pituitary stalk
- (C) Inferior to the pituitary gland
- (D) Posterior to the pituitary stalk

Key: B

Rationale: As an aid in contouring the organs at risk for radiotherapy planning, the chiasm is located anterior to the pituitary stalk, superior to the pituitary gland and sella, medial to the carotid arteries bilaterally.

293. Which treatment scenario would shift the normal tissue complication probability (NTCP) curve for salivary glands to the right?

- (A) Increasing the dose per fraction
- (B) Increasing the irradiation volume
- (C) Decreasing the overall treatment time by a week
- (D) Performing a salivary gland stem cell transplant after irradiation

Key: D

Rationale: Shifting of the NTCP curve to the right suggests that the tissue at risk has increased its radiation tolerance. Transplantation of salivary gland stem cells after irradiation would have the greatest potential for increasing radiation tolerance and shifting the NTCP curve to the right, although at present, this is not done clinically. Note however that transplanting stem cells does not affect the actual radiosensitivity of cells, but rather would "simulate" an increase in tissue tolerance due to the proliferation of newly-added cells. Hypofractionation, decreasing overall treatment time, and increasing treatment volume would all have the net effect of sensitizing the tissue, not protecting it, meaning that the NTCP curve would move to the left, not the right.

294. Which of the following surgical approaches for a cervical cancer would remove the uterosacral ligaments near the sacral origin?

- (A) Simple hysterectomy
- (B) Radical hysterectomy
- (C) Simple trachelectomy
- (D) Modified radical hysterectomy

Key: B

Rationale: A simple trachelectomy and a simple hysterectomy divide the ligaments at the cervical border; a modified radical partially resects the ligaments; a radical hysterectomy divides the ligaments at the sacral origin. This information is used in postoperative treatment planning.

References: See Table: NCCN Guidelines Version 1.2014 Cervical Cancer: Principles of Evaluation and Surgical Staging.

295. A Kaplan-Meier survival curve has a 5-year survival probability of 0.60 and a standard error of 0.06. The 95% confidence interval for the 5-year survival probability is approximately:

- (A) 0.54 to 0.66.
- (B) 0.48 to 0.72.
- (C) 0.42 to 0.79.
- (D) 0.35 to 0.85.

Key: B

Rationale: The limits of the 95% Confidence Interval is equal to the mean \pm 1.96*SE.

296. The approximate incidence of mucosal emergence 5 years after comprehensive radiation for squamous cell carcinoma metastatic to a cervical lymph node of unknown primary origin is:

- (A) 10%.
- (B) 20%.
- (C) 30%.
- (D) 40%.

Key: A

Rationale: The risk of primary emergence is generally considered low after radiation.

297. What is the T stage for an ulcerated skin melanoma, Clarks level 3, Breslow depth 3.5 mm with 5 mitoses/mm²?

- (A) T2b
- (B) T3a
- (C) T3b
- (D) T4a

Key: C

Rationale: Breslow depth 2.01-4 mm is T3. Presence of ulceration makes T stage "b" rather than "a". Mitoses impacts T1 staging, where 1 or more mitoses/mm² increases stage to T1b.

298. In the management of a high risk low grade glioma (RTOG 98-02), the addition of PCV to radiotherapy increased:

- (A) OS.
- (B) cognition.
- (C) late radiation toxicity.
- (D) transformation to high grade glioma.

Key: A

Rationale: Updated results of RTOG 98-02 (after initial publication in JCO 2012), show a significant improvement in overall survival for those who received PCV chemotherapy plus radiation therapy (13.3 years median survival time) compared to those receiving radiation therapy alone (7.8 years median survival time). Late RT toxicity was not increased.

299. Mice bearing tumors containing 10^8 clonogenic cells receive a course of radiation therapy that reduces the cell surviving fraction by 8 logs. If the total number of mice irradiated was 10, about how many animals will be cured?

- (A) 0
- (B) 2
- (C) 4
- (D) 8

Key: C

Rationale: The correct answer is C. For a tumor initially containing 10^8 clonogenic cells, but that then suffers an 8 log survival decrement, approximately one surviving tumor cell should remain. Based on Poisson statistics, tumors that contain, on average, a single surviving cell have about a 37% probability of being cured.

300. What is an advantage of an active scanning versus a passive scattering delivery system for proton beam radiotherapy?

- (A) Reduced delivery time
- (B) Reduced neutron dose to patient
- (C) Reduced sensitivity to patient motion
- (D) Reduced maximum depth of proton Bragg peak

Key: B

Rationale: Reference: In an active scanning system, the proton beam is steered using a magnetic field-based system. Because of this, there is no need to have scattering foils or compensators in the beamline thereby reducing the neutron dose production in these components. Additionally, because the proton beam is not attenuated in a scanning system, the depth of the Bragg peak is not modified prior to patient entrance. However, since most active scanning approaches utilize a spot scanning technique, there is an increase in sensitivity to patient motion.