



31st
Annual

**In-Training Examination
for Radiation Oncology Residents**

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1. According to RTOG 95-01, the addition of cetuximab to radiation significantly increased:
- (A) acute, but not late toxicity.
 - (B) local control, but not median survival.
 - (C) both local control and overall survival.**
 - (D) median survival, but not overall survival.

Rationale: Cetuximab improved the local control, median survival and overall survival compared to radiation alone.

References: Bonner JA, Harari PM, Giralt J, Azarnia N, Shin DM, Cohen RB, et al., Radiotherapy plus cetuximab for squamous-cell carcinoma of the head and neck, (2007) pp. 567-78.

2. Which rhabdomyosarcoma disease site requires pathologic evaluation of clinically and radiographically negative lymph nodes?
- (A) Parameningeal
 - (B) Liver
 - (C) Extremity**
 - (D) Bladder

Rationale: The standard work up that must include pathologic evaluation of clinical uninvolved nodes is delineated in the Children's Oncology Group Protocols, including ARST0531. Because lymph node involvement is less likely for parameningeal, liver and bladder primary sites, pathologic sampling of draining lymph nodes is not required. An additional site that requires LN assessment is paratesticular primaries.

3. Which of the following cysteine-aspartic proteases is an effector caspase?
- (A) Caspase 2
 - (B) Caspase 3**
 - (C) Caspase 8
 - (D) Caspase 9

Rationale: Caspases 2, 8, 9 and 10 are initiator caspases that cleave inactive pro-forms of effector caspases to activate them. The effector caspases (caspases 3, 6, 7), once activated, cleave other protein substrates within the cell that trigger apoptosis. Caspases 4 and 5 are not currently classified as either initiator or effector.

References: Lamkanfi M, et al., Caspases in cell survival, proliferation and differentiation, (2007) pp. 44-55.

4. Annual x-ray/electron output calibration tolerance for a linear accelerator is:

- (A) $\pm 0.1\%$ (absolute).
- (B) $\pm 1\%$ (absolute).**
- (C) $\pm 0.1\%$ (relative).
- (D) $\pm 1\%$ (relative).

Rationale: This tests the knowledge of the output tolerances for linacs. The absolute calibration is measured according to AAPM TG 51 protocol. Annual output is an absolute, not relative measurement.

References: AAPM Task Group 51: protocol for clinical reference dosimetry for high energy photon and electron beams, (1999).

Klein et al., AAPM Task Group 142: Quality Assurance of Medical Accelerators, (2009).

5. What is the risk of pelvic lymph node involvement with a G1 cancer of the uterus confined to the endometrium as seen in GOG 33?

- (A) 0%**
- (B) 3%
- (C) 7%
- (D) 11%

Rationale: GOG 33 studied the risk of lymph node involvement based on the tumor grade and the depth of invasion. None of the patients with grade 1 tumors confined to the endometrium had positive lymph nodes. Grade 1 tumors involving the inner 1/3 and outer 1/3 of the myometrium had pelvic lymph node involvement in 3% and 11% of cases, respectively.

References: Creasman W et al., Creasman W et al., (1987).

6. What is the first assumption in hypothesis testing?

- (A) No errors are possible.
- (B) The null hypothesis is true.**
- (C) The null hypothesis is false.
- (D) The alternative hypothesis is true.

Rationale: The basic and first assumption of hypothesis testing is that the null hypothesis true.

7. Mutations which render the DNA mutation repair mammalian pathway MOST sensitive to ionizing radiation are:

- (A) mismatch repair (MMR).
- (B) base excision repair (BER).
- (C) nucleotide excision repair (NER).
- (D) non-homologous end-joining (NHEJ).**

Rationale: NHEJ mutants (e.g., Ku70/80 deficient, LIG4 deficient, etc.) are deficient in the repair of DNA double strand breaks, the most critical type of DNA lesion induced by ionizing radiation. BER, NER and MMR mutants either display wild-type radiosensitivity or are only slightly radiosensitive.

References: Wilson PF and Bedford JS, Leibel and Philips Textbook of Radiation Oncology, (2010) Chapter 1.

8. The rate of energy loss per unit length of a charged particle is quantified using the:

- (A) linear stopping power.**
- (B) Klein-Nishina cross section.
- (C) linear attenuation coefficient.
- (D) electron-capture cross section.

Rationale: Linear attenuation coefficient describes the attenuation of an uncharged particle. The Klein-Neshina cross section describes the probability of a Compton event for a photon with a free electron. Electron capture transitions are a type of radioactive disintegration.

References: Attix, Introduction to Radiological Physics and Radiation dosimetry, (1986) Chapter 8.

9. A monoenergetic proton Bragg peak is converted to a spread out Bragg peak (SOBP) by:

- (A) changing the beam current.
- (B) modulating the energy of the beam.**
- (C) modulating the frequency of the cyclotron.
- (D) changing the magnetic field of the cyclotron.

Rationale: The location of the narrow Bragg peak for a monoenergetic proton beam is determined by the energy. To spread out the Bragg peak to encompass a target it is necessary to modulate the energy of the beam.

References: McDermott & Orton, The Physics and Technology of Radiation Therapy, (2010) Chapter 20.

10. When do patients with hereditary retinoblastoma develop eye tumors relative to those patients with sporadic retinoblastoma?

- (A) At a younger age
- (B) At the same age
- (C) At an older age
- (D) There is no relationship

Rationale: Patients with hereditary retinoblastoma tend to develop eye tumors at an earlier age than those patients with sporadic retinoblastoma. They also are more likely to develop bilateral and multifocal disease.

References: Halperin, Pediatric Radiation Oncology.

11. During carcinogenesis, mutation of the *KRAS* proto-oncogene at codon 12 will cause which initial cellular response?

- (A) Senescence
- (B) Apoptosis
- (C) Autophagy
- (D) Mitotic catastrophe

Rationale: Several studies have shown that oncogenic stress-induced senescence occurs in vivo in both human tumors and in mouse tumor models. This is consistent with the idea that the process of senescence can function to suppress tumor development.

References: Courtois-Cox et al., Many roads lead to oncogene-induced senescence, (2008) pp. 2801-2809.

12. How would replacing a tungsten target ($Z = 74$) with a lead target ($Z = 82$) effect the probability of bremsstrahlung production in a linear accelerator?

- (A) Decrease by ~ 8%
- (B) Decrease by ~ 23%
- (C) Increase by ~ 8%
- (D) Increase by ~ 23%

Rationale: The energy loss per atom by electrons depends on the square of the atomic number (Z^2) of the target. Thus, the probability of bremsstrahlung production varies with Z^2 of the target material. Hence, $(82/74)^2 = 1.228 \sim 23\%$.

References: Khan, F.M. The Physics of Radiation Therapy, (2003) Chapter 3.4.

13. The number of pixels in a single CT slice is typically:

- (A) 512.
- (B) 1,024.
- (C) 2,048.
- (D) 260,000.**

Rationale: A typical CT image is 512×512 pixels = 260,000 pixels = 0.26 megapixels. Every resident should easily be able to square 512 without a calculator. Part of the idea is to know what “mega” means and to illustrate how poor CT spatial resolution is in comparison to consumer digital photography.

References: McDermott & Orton. The Physics and Technology of Radiation Therapy, (2010) Chapter 19.

14. What is the accepted dose (Gy) for gross tumor in a thoracic vertebral body Ewing sarcoma?

- (A) 45**
- (B) 54
- (C) 55.8
- (D) 60

Rationale: 55.8 Gy is the recommended dose for gross Ewings sarcoma. One exception is the spine, which is classically 45 Gy. Though, modern treatment planning can allow for higher doses with sparing of the spinal cord.

15. How do the PDD and d_{\max} change relative to a $10 \times 10 \text{ cm}^2$ field for the small photon beam field sizes used in IMRT and SRS?

- (A) Both increase
- (B) Both decrease**
- (C) PDD increases; d_{\max} decreases
- (D) PDD decreases; d_{\max} increases

Rationale: For a given beam energy, d_{\max} increases rapidly with increasing field size at small fields, reaches a maximum around $5 \times 5 \text{ cm}^2$ and then gradually decreases with increasing field size for large fields. This effect at small fields is caused by in-phantom scatter while the large field effect is due to scatter contamination of the primary beam spectra from the linac head. For the PDD, as the field size increases, the Compton photons scattered from the irradiated volume will contribute dose to the central axis. At large field sizes, the effect is greater since the divergence at depth is greater.

References: Sixel KE, Podgorsak EB, Buildup region and depth of dose maximum of megavoltage x-ray beams, (1994) pp. 411-6.

16. Which of the following is considered a T4 glottic cancer?

- (A) **Tracheal invasion**
- (B) Paraglottic space invasion
- (C) Complete vocal cord fixation
- (D) Thyroid cartilage erosion (inner cortex)

Rationale: Trachea invasion is considered T4, the others are all considered T3.

References: AJCC Cancer Staging Manual, (2010).

17. TBI to an absorbed dose equivalent of 3-4 Sv would MOST likely cause which of the following?

- (A) Severe diarrhea within 8 hours
- (B) Neutropenic fever within 3 hours
- (C) **Nausea and vomiting within 2 hours**
- (D) Dry or moist skin desquamation within 24 hours

Rationale: The prodromal radiation syndrome causes a dose-dependent increase in the frequency of nausea/vomiting, fatigue, headaches, fever, and skin reddening. Skin desquamation and neutropenia would take days/weeks to develop, not hours. Finally, doses in the 3-4 Sv range are generally too low to cause early onset, severe diarrhea in exposed individuals.

References: Schrieve, D.C., Loffler, J.S., Human Radiation Injury, (2011) Chapter 11. Donnelly et al, Donnelly et al, (2010) 541-546.

18. A key advantage of proton beams is the sharp dose fall off gradient of the Bragg peak along the central axis of the beam. How does the lateral (perpendicular to central axis) dose fall off gradient compare?

- (A) Same
- (B) Sharper
- (C) **Shallower**
- (D) Sharper only at depth of Bragg Peak

Rationale: The lateral penumbra of proton beams at depth is largely determined by the multiple scattering in the medium. However, as the proton beam loses energy, the multiple scattering at the Bragg Peak causes a lateral broadening of the beam near the end of the range. This causes a much shallower dose fall-off as compared to the central axis fall-off.

References: P Mayles, A Nahum, J.C Rosenwald, Handbook of Radiotherapy Physics, (2007) Chapter 46.3.11.1.

19. What was the frequency of inguinal recurrence at two years in the radiation arm of GOG 37 study for vulvar cancer with pathologically positive inguinal nodes randomized to postoperative radiation to inguinal and pelvic nodes versus pelvic lymphadenectomy?

- (A) 5%
- (B) 10%
- (C) 15%
- (D) 20%

Rationale: GOG 37 demonstrated benefit of postoperative radiation therapy compared to pelvic lymphadenectomy leading to a change in treatment paradigm for patients found to have inguinal node metastases. Postoperative radiation therapy rather than pelvic lymphadenectomy has been incorporated in subsequent trials of radiation therapy and chemotherapy.

References: Homesley HD, Bundy BN, Sedlis A, Radiation therapy versus pelvic node resection for carcinoma of the vulva with positive groin nodes, (1986) pp. 733-740.

20. Which is the graph of a frequency distribution of numerical observations?

- (A) Histogram
- (B) Scatter plot
- (C) F distribution
- (D) Linear regression

References: Dawson B and Trapp RG, Basic and Clinical Biostatistics, (2004) p. 407.

21. The intensity of a radiation beam is measured at a particular distance in air and far from the source. If the distance from the source decreases by 2%, the intensity will increase by:

- (A) 0.25%.
- (B) 0.5%.
- (C) 2%.
- (D) 4%.

Rationale: For small changes in distance, the percentage change in intensity is approximately twice the percentage change in distance, provided the radiation obeys an inverse square law dependence. This can be seen by considering a specific example. The relationship between the intensity I_2 at distance d_2 and intensity I_1 at distance d_1 is $(I_2/I_1) = (d_1/d_2)^2$. If $d_1 = 100$ cm and $d_2 = 98$ cm, then $(I_2/I_1) = 1.041$, a 4.1% increase in intensity.

References: McDermott & Orton, The Physics and Technology of Radiation Therapy, (2010) Chapter 5.

22. Approximately how many ion pairs will be produced in water by a typical Compton recoil electron from a megavoltage photon beam?

- (A) 0
- (B) 10^2
- (C) **10^4**
- (D) 10^6

Rationale: A Compton recoil electron from a megavoltage photon beam has an energy on the order of 1 MeV. The energy necessary to produce an ion pair is approximately 30 eV therefore the number of ion pairs produced is about 3×10^4 .

References: McDermott & Orton, The Physics and Technology of Radiation Therapy, (2010) Chapter 6.

23. Which of the following statements is the MOST accurate in describing follicular lymphoma?

- (A) The disease predominantly affects young adults.
- (B) The disease predominately is localized.
- (C) **BCL-2 gene rearrangement is present in a majority of patients.**
- (D) Without therapy, the median survival of patients is less than 5 years.

Rationale: The majority of patients with follicular lymphoma present with widespread disease and bone marrow involvement. Disease most commonly affects elderly patients and due to its very indolent nature even with observation the median survival of these patients exceeds 5 years. t(14;18) and bcl-2 gene rearrangement is present in majority of patients with follicular lymphoma.

References: Perez & Brady's Principles and Practice of Radiation Oncology.

24. The tolerance for daily output variations of a linear accelerator is:

- (A) 1%.
- (B) **3%.**
- (C) 5%.
- (D) 10%.

Rationale: This question tests the fundamental knowledge of the radiation output stability of medical linear accelerators.

References: Klein et al., AAPM Task Group 142: Quality Assurance of Medical Accelerators, (2009).

25. The EORTC trial demonstrated that PCI for patients with extensive stage SCLC who had a response to chemotherapy:

- (A) increased median OS by 12 weeks.
- (B) had a clinically significant effect on performance status.
- (C) decreased the cumulative risk of brain metastases at 1 year by 15%.**
- (D) prolonged the DFS, but not OS.

Rationale: Prophylactic cranial irradiation reduces the incidence of symptomatic brain metastases and prolongs disease-free and overall survival for patients with extensive-stage small-cell lung cancer who had a response to systemic chemotherapy. The cumulative risk of brain metastases within 1 year was 14.6% in the irradiation group (95% CI, 8.3 to 20.9) and 40.4% in the control group (95% CI, 32.1 to 48.6). Irradiation was associated with an increase in median disease-free survival from 12.0 weeks to 14.7 weeks and in median overall survival from 5.4 months to 6.7 months after randomization. The 1-year survival rate was 27.1% (95% CI, 19.4 to 35.5) in the irradiation group and 13.3% (95% CI, 8.1 to 19.9) in the control group. Irradiation had side effects but did not have a clinically significant effect on global health status.

References: Slotman, B. et al., Prophylactic cranial irradiation in extensive small-cell lung cancer, (2007) pp. 664-72.

26. What is the implication for breast irradiation when early invasive breast cancer is associated with both DCIS and LCIS?

- (A) A boost to 66 Gy is needed
- (B) Re-excision is needed prior to radiation
- (C) Remains a candidate for postoperative radiation**
- (D) Bilateral mastectomy is superior to breast conservation therapy

Rationale: The patient remains a candidate for breast conservation and postoperative radiation. Bilateral mastectomy is one option for treating LCIS but not superior to breast conservation. Recent studies confirm that the presence of LCIS does not significantly change the local control rates after breast-conserving surgery and postoperative radiation. A re-excision or boost to a higher dose than typically used for negative margins is not needed due to the presence of DCIS or LCIS.

References: Ciocca et al., Presence of Lobular Carcinoma In Situ Does Not Increase Local Recurrence in Patients Treated with Breast-Conserving Therapy, (2008) pp. 2263-2271.
Ben-David et al., Is lobular carcinoma in situ as a component of breast carcinoma a risk factor for local failure after breast-conserving therapy? Results of a matched pair analysis, (2006) pp. 28-34.

27. When taking weekly portal films for positioning verification, a double exposure method is used because:

- (A) a double exposure provides higher spatial resolution.
- (B) a single exposure is more susceptible to motion artifact.
- (C) a single exposure would have insignificant soft tissue contrast.
- (D) the treatment port provides insufficient anatomical information.**

Rationale: In most cases, the actual treatment port is too small to provide enough anatomical information for accurate determination of positioning. The "open" field is used to provide this information.

28. The standard format for the transfer and communication of images between computer devices in radiation oncology is:

- (A) hospital information system (HIS).
- (B) joint photographic experts group (JPEG).
- (C) picture archiving and communication system (PACS).
- (D) digital imaging and communications in medicine (DICOM).**

Rationale: The DICOM standard format was developed to enable communication of images between different devices and software. An extension of the DICOM format, DICOM-RT is specifically for use in radiation oncology.

References: McDermott & Orton, The Physics and Technology of Radiation Therapy, (2010) Chapter 19.

29. The Philadelphia chromosome is MOST often found in which of the following forms of leukemia?

- (A) ALL
- (B) AML
- (C) CLL
- (D) CML**

Rationale: The Philadelphia chromosome $t(9;22)(q34;q11)$ is associated with chronic myelogenous leukemia.

References: DeVita et al., Cancer: Principles and Practice of Oncology, (2011).

30. The TD 5/5 in Gy for the whole kidney is which of the following?

- (A) 17.5
- (B) 23**
- (C) 30
- (D) 45

Rationale: Knowledge of dose constraint limits are crucial to defining treatment fields and surrounding organs at risk, especially with IMRT planning. The TD5/5 in Gy is 17.5 for lung, 23 for kidney, 30 for liver and 45 for brain when looking at whole organ dose.

References: Hall, E.J., Radiobiology for the Radiologist, (2012) Chapter 19.

31. Which of the following factors is LEAST important for AJCC staging in a well-differentiated thyroid cancer?

- (A) Number of involved lymph nodes**
- (B) Age at diagnosis
- (C) Extrathyroidal extension
- (D) Tumor size

Rationale: Patients younger than 45 years have better prognosis. They are staged as stage I without distant metastases or stage II with distant metastases, regardless the T stage and N stage. Size of the primary tumor and the presence of extrathyroid extension are important for T stage. The involved lymph node level is used for N stage but not the number of lymph node involved. Involved node(s) limited in level VI is staged N1A, and outside level VI is staged N1B.

References: Hay ID, Petersen IA, Foote RL. Thyroid cancer, (2012) In: Gunderson LLG, Tepper JE (eds). Clinical Radiation Oncology. 3rd edition. 2012; Saunders. p.710, AJCC Cancer Staging Manual, (2010).

32. Regarding on-board cone beam kV CT systems mounted on linac, the low contrast resolution of these systems is inferior to conventional helical CT due to:

- (A) increased energy.
- (B) increased scatter dose.**
- (C) faster image acquisition time.
- (D) increased spatial resolution.

Rationale: The large cone angle and lack of detector grid used by CBCT imaging systems allow x-ray scatter to contribute undesirable signals to the reconstructed images. As a result, x-ray scatter reduces soft tissue contrast and increases image noise.

References: Imaging for Treatment Verification Work Group Task Group #179.

33. The region of sharp increase in dose at the end of a proton beam's path is called the:

- (A) **Bragg peak.**
- (B) tissue maximum ratio.
- (C) exit dose.
- (D) Lorentzian dilation.

Rationale: The region of high dose at the end of a proton's range is called the Bragg peak.

References: Khan, Physics of Radiation Therapy, (2003) p. 56.

34. Bujold et al. recently reported the phase I/II experience of liver SBRT for treatment of unresectable, locally advanced hepatocellular carcinoma (HCC) from University of Toronto (JCO, 2013). What was the reported 1 year overall survival rate (%)?

- (A) 35
- (B) 45
- (C) **55**
- (D) 65

Rationale: In this study, 102 patients with locally advanced HCC and Childs Pugh class A liver function were treated to doses of 30-54 Gy in 6 fractions. The 1-year local control rate was 87%, and 1 year OS was 55%.

References: Bujold et al., Sequential phase I and II trials of SBRT for locally advanced HCC, (2013) pp. 1631-9.

35. Which of the following is a CONTRAINDICATION for bladder preservation approach with chemoradiotherapy?

- (A) T2 tumor on cystoscopy
- (B) Tumor on the lateral bladder wall
- (C) 4 cm unifocal tumor
- (D) **Maximal TURBT cannot be performed**

Rationale: In patients who undergo a bladder conservation approach, maximal transurethral resection of the tumor should occur before proceeding with chemoradiation.

References: NCCN Clinical Practice Guidelines in Oncology, Version 1.2013 – Bladder Cancer.

36. Which of the following strategies is recommended for a patient with inflammatory breast cancer whose tumor has had a complete clinical response to chemotherapy?

- (A) Modified radical mastectomy + RT to chest wall
- (B) No breast surgery + RT to breast and regional LNs
- (C) Skin sparing mastectomy + RT to chest wall and regional LNs
- (D) Modified radical mastectomy + RT to chest wall and regional LNs**

Rationale: Management guidelines are for patients to receive neoadjuvant chemotherapy consisting of both an anthracycline and taxane agent. Trastuzumab should be given with patients having Her2+ disease. Operable patients should be treated with modified radical mastectomy. Radiation should be given to the chest wall and regional lymphatics. The dose of radiation to the initial fields should be 50 Gy with a boost to the chest wall to 60-66Gy, depending on extent of any residual disease.

References: Perez & Brady's Principles and Practice of Radiation Oncology, p. 1157, NCCN Clinical Practice Guidelines in Oncology, 2013.

37. What is the radiation weighting factor for protons used to calculate equivalent dose?

- (A) 1
- (B) 2**
- (C) 20
- (D) 50

Rationale: The equivalent dose adjusts physical dose to take into account the greater relative biological effectiveness (RBE) of different radiations. This is done by multiplying the dose by a radiation weighting factor (WR). These factors are somewhat arbitrary and have been assigned by the ICRP as 1 for photons, electrons and muons, 2 for protons and charged pions, and 20 for alpha particles, fission fragments and heavy ions.

References: Hall, E.J., Radiobiology for the Radiologist, (2012) Chapter 17.

38. Which of the following is NOT part of the routine work-up for a 5-year-old boy with a prostate embryonal rhabdomyosarcoma?

- (A) Chest CT
- (B) Bone scan
- (C) CSF cytology**
- (D) Bilateral bone marrow aspiration/biopsy

Rationale: The standard work up for a child with a prostate embryonal rhabdomyosarcoma is delineated in the Children's Oncology Group Protocols, including ARST0531, and include chest CT, bilateral bone marrow aspiration/biopsy, and bone scan, but NOT lumbar puncture with cytology.

39. What component of a linac is responsible for creating a relatively uniform electron fluence across the treatment field?

- (A) Bending magnet
- (B) Scattering foil**
- (C) Flattening filter
- (D) Multileaf collimator (MLC)

Rationale: The scattering foil is used to spread the very thin beam of electrons and make a uniform, large beam that is more valuable for treatment. The MLC is typically only used to collimate an x-ray beam, the flattening filter is used to flatten the x-ray beam as it exits the target while the bending magnet is used to steer the electron beam from the accelerating guide to the target in x-ray beam production, or the scattering foil in electron beam production.

References: Khan, Physics of Radiation Therapy, (2003) p. 45.

40. For HDR brachytherapy, what is required by the NRC's 10CFR Part 35 at the end of every treatment after the source retracts?

- (A) Radiation survey of the patient**
- (B) Patient identification verification
- (C) Well chamber measurement of the source
- (D) Written directive update by the authorized user

Rationale: This item requires knowledge of required safety measures to minimize unintentional irradiation of the patient. Out of the provided options, 10CFR35 specifically requires that post-treatment radiation survey of the patient be performed.

References: U.S.NCR, NRC: 10 CFR Part 35 - Medical Use of Byproduct Material.

41. What parameter is the MOST common descriptor of beam quality for megavoltage photon beams?

- (A) MU
- (B) HVL
- (C) TVL
- (D) PDD**

Rationale: This item requires knowledge of PDD, which is commonly used in hand calculations and determining energies and treatment depths. HVL is a beam quality descriptor for kilovoltage photons, TVL is used for shielding, and monitor units are not related to beam quality.

References: Khan, Physics of Radiation Therapy, (2003) Chapter 7.

42. According to the AJCC 7th edition staging manual for lung cancer, which of the following is classified as a T3 tumor?

- (A) Malignant pleural effusion
- (B) Tumor > 7 cm in greatest dimension**
- (C) Separate tumor nodule(s) in the same lung, different lobe
- (D) Involvement of the main bronchus, ≥ 2 cm distal to the carina

Rationale: Pertinent changes to the lung staging system from the 6th to 7th edition include (1) more discrete stratification of tumors by size and partitioning of larger (>7 cm) tumors into T3, (2) downstaging of multiple nodules to T3 (same lobe), T4 (same lung), and M1a (contralateral lobe), and (3) upstaging of malignant pleural effusion from T4 to M1a

References: AJCC Cancer Staging Manual, (2010).

43. Male breast cancer is MOST commonly associated with:

- (A) BRCA1.
- (B) BRCA2.**
- (C) Lynch syndrome.
- (D) Cowden syndrome.

Rationale: BRCA1 mutations are more common in women. In the Myriad Genetics series, two thirds of mutations found in families with male breast cancer were in BRCA2. The remaining portion was in BRCA1. Cowden's syndrome is an autosomal dominant condition where 80% of persons with the disorder have PTEN mutations. Patients have hamartomatous lesions, early onset breast cancer and thyroid cancer. There is a common history of breast biopsies with benign findings, including atypical hyperplasia, intraductal papillomatosis, adenosis, lobular atrophy, fibroadenomas and fibrocystic changes. There is an associated incidence of bilateral findings for both benign and malignant conditions.

Lynch Syndrome is a variant of hereditary nonpolyposis colon carcinoma. This condition is associated with multiple skin tumors, multiple benign and malignant tumors of the upper and lower GI tract and genitourinary tracts. Breast cancers associated with this syndrome tend to be in postmenopausal women.

References: Harris, J et.al, Diseases of the Breast, 4th edition, (2010) Epidemiology and Assessing and Managing Risk, p. 209-223. Gene Arrays, Prognosis, and Therapeutic Interventions, p. 463-465.

44. Based on increasing volume, which is the correct sequence?

- (A) CTV, PTV, ITV, GTV
- (B) PTV, CTV, ITV, GTV
- (C) GTV, CTV, ITV, PTV**
- (D) GTV, CTV, PTV, ITV

Rationale: The GTV is the smallest volume and represents the actual tumor that can be seen. The CTV contains an extra margin over the GTV to account for unseen micro-extensions. The ITV is grown from the CTV to account for motion and the PTV includes yet another margin to account for positioning/setup uncertainties.

References: ICRU 50: Prescribing, Recording and Reporting Photon Beam Therapy, (1993).

45. Which of the following chemotherapy regimens is MOST active for the treatment of unresectable mesothelioma?

- (A) Cisplatin and etoposide
- (B) Cisplatin and pemetrexed**
- (C) Carboplatin and paclitaxel
- (D) Cisplatin and methotrexate

Rationale: In a meta-analysis of phase II trials conducted between 1965 and 2001, cisplatin was the most active single agent for the treatment of unresectable pleural mesothelioma. Cisplatin has served as the backbone of most doublet regimens. In 2003, a phase III randomized trial compared cisplatin alone versus cisplatin plus pemetrexed in untreated malignant pleural mesothelioma.⁴² With the combination, the response rate was 41.3% compared to 16.7% for cisplatin alone (P, .0001). Median time to progression was 5.7 vs 3.9 months, (P 5 .001), and median overall survival was 12.1 vs 9.3 months (P 5 .02), both in favor of the combination arm. As a result, the combination of cisplatin and pemetrexed is considered standard first-line therapy for unresectable pleural mesothelioma. It has also become a standard recommendation in the adjuvant combined modality approach to resectable disease.

References: N/A, (2002) pp. 111-121, N/A (2), (2003) pp. 2636-2644.

46. For TBI treatments, a beam spoiler is used to:

- (A) decrease surface dose.
- (B) increase surface dose.**
- (C) decrease exit dose.
- (D) increase exit dose.

Rationale: Knowledge of how accessories affect the beam for TBI treatments is needed for this item.

References: Van Dyk, AAPM Report 55 (TG-29), The physical aspects of total and half body photon irradiation, (1986).

Khan, Physics of Radiation Therapy, (2003) Chapter 18.

47. Based on Casarett's classification system for tissue radiosensitivity, which of the following classes of cells is the MOST radioresistant?

- (A) **Fixed postmitotic**
- (B) Reverting postmitotic
- (C) Vegetative intermitotic
- (D) Differentiating intermitotic

Rationale: Fixed postmitotic cells are terminally differentiated and therefore have lost the ability to divide. And because radiation-induced cell killing is, in most cases, linked to cell division, these cells tend to be the most radioresistant. Vegetative intermitotic cells divide regularly, but do not undergo differentiation (i.e., stem cell-like). These are the most radiosensitive cell types. Differentiating intermitotic cells still proliferate, but with increasing differentiation between successive cell divisions, and are somewhat less radiosensitive. Reverting postmitotic cells are differentiated (at least to some extent) and normally do not divide, but can be recruited back into the active cell cycle in response to a tissue injury. Once the injury is resolved, these cells revert back to being differentiated and stop dividing, making them more radioresistant.

References: Hall, E.J., Radiobiology for the Radiologist, (2012) -Chapter 20; pp. 331-332.

48. For patients younger than 10 years of age who received a cumulative dose of 500-600 mSv from head CT scanning, about how many scans are projected to cause one excess case of leukemia and one excess brain tumor per year 10 years after the initial scan?

- (A) 100
- (B) 1,000
- (C) **10,000**
- (D) 100,000

Rationale: A recent epidemiological study by Pearce et al. examined cancer incidence, mortality, and loss to follow-up in a large cohort of UK pediatric patients examined with head CT from 1985 to 2008. A positive association between radiation dose and excess relative risk for leukemia and brain tumors was noted. Since the absolute risks for such cancers are low, the additive risk for leukemias and brain tumors after a cumulative dose of 500-600 mSv would be one excess case of each cancer type per 10,000 head CT scans.

References: Pearce, M.S., et al., Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: A retrospective cohort study, (2012) pp. 499-505.

49. Which trial would be used to determine the BEST method for administering a new drug?

- (A) **Phase 1**
- (B) Phase 2
- (C) Phase 3
- (D) Phase 4

Rationale: A Phase 1 investigation is devoted to discovering if a treatment is safe and gaining enough understanding of the treatment to design formal studies. A Phase 2 investigation is a preliminary investigation of the effectiveness of treatment. A Phase 3 investigation is a large-scale verification of the early findings, the step from “some evidence” to “proof”. A Phase 4 investigation evaluates an established treatment to detect any changes in the treatment or population of patients that would affect its use.

References: Riffenburgh RH, Statistics in Medicine, p. 5.

50. Which of the following histologic variants of central nervous germ cell tumors carries the BEST prognosis in children?

- (A) Yolk sac tumor
- (B) **Pure germinoma**
- (C) Choriocarcinoma
- (D) Embryonal carcinoma

Rationale: Germinoma carries the best prognosis compared to non-germinomatous histologies and patients have a >90% overall survival rate in comparison to the non-germinomatous variants where survival is lower at 60-70%.

References: Echevarría ME, Fangusaro J, Goldman S., Pediatric central nervous system germ cell tumors: a review., (2008) pg. 690-9

51. What wedge angle should be used to make the dose distribution uniform in the region of beam overlap when treating with two beams, separated by 120° ?

- (A) 15
- (B) **30**
- (C) 45
- (D) 60

Rationale: The ideal wedge angle (WA) for a given hinge angle (HA) between two beams is defined as $WA = 90^\circ - HA/2$.

References: Khan, Physics of Radiation Therapy, (2003).

52. Which of the following constitute International Prognostic Factors for advanced Hodgkin lymphoma?

- (A) Serum albumin < 4 g/dl, Stage IV, female sex, hemoglobin < 10.5 g/dl
- (B) Serum albumin > 4 g/dl, "B" symptoms, male sex, age > 45
- (C) Serum albumin > 4 g/dl female sex, "B" symptoms, hemoglobin < 10.5 g/dl
- (D) Serum albumin < 4 g/dl, Stage IV, male sex, age > 45**

Rationale: The following factors constitute International Prognostic Factors for Advanced Hodgkin Lymphoma: Stage IV, male sex, age >45, serum albumin <4 g/dl, hemoglobin <10.5 g/dl, lymphocyte count <600/mm³.

References: Hasenclever, D. & Diehl, V. A prognostic score for advanced Hodgkin's disease. International Prognostic Factors Project on Advanced Hodgkin's Disease, (1998) p. 1506-14.

53. When would whole-abdominal radiation be indicated for a patient with favorable histology Wilms tumor?

- (A) Tumor involving the renal hilum
- (B) After an open biopsy of renal mass without rupture
- (C) Peritoneal seeding noted at surgery**
- (D) Tumor involvement of regional lymph nodes

Rationale: The "SPAR" mnemonic for indications for whole-abdominal radiation include: diffuse Spillage during surgery across, Peritoneal seeding, Ascites and preoperative Rupture.

54. In the Polish randomized trial of long-course vs. short-course preoperative radiotherapy for rectal cancer, long-course radiation was associated with significantly increased rates of:

- (A) local control.
- (B) late toxicity.
- (C) sphincter preservation.
- (D) pathologic complete response.**

Rationale: In the Polish trial of short-course radiation (5Gy in five fractions) vs. long-course chemoradiation (50.4Gy in 28 fractions with concurrent chemotherapy), long-course chemoradiation demonstrated higher rates of acute toxicity and no significant difference in local control or sphincter preservation. The rate of pathologic complete response was significantly higher (16.1% vs. 0.7%).

References: Bujko K. et al., Long-term results of a randomized trial comparing preoperative short-course radiotherapy with preoperative conventionally fractionated chemoradiation for rectal cancer, (2006) pg. 1215-1223.

55. What is the FIGO stage of a papillary serous carcinoma of the uterus confined to less than half of the myometrium, with negative pelvic and para-aortic LNs but has positive peritoneal washings?

- (A) IA
- (B) IIA
- (C) IIIA
- (D) IVA

Rationale: The most recent AJCC manual no longer considers positive peritoneal washings in the staging of endometrial cancer. In the previous edition, this would be considered stage IIIA disease. Since the tumor is confined to the uterus and is limited to the endometrium, it should be staged IA.

References: AJCC Cancer Staging Manual, (2010) -6th and 7th editions.

56. As defined by the ICRU, exposure is a measure of:

- (A) charged particle dose in a known volume of air.
- (B) photon dose produced in a known volume of air.
- (C) ionization by photons produced in a known volume of water.
- (D) **ionization by charged particles produced by photons in a known volume of air.**

Rationale: Understanding the limitation of exposure measurements is important. Exposure and roentgen is only defined for x and gamma ray radiation. Exposure is the measured of the total charge in air (ionization) of all electrons and positrons liberated by photons in a known volume of air.

References: International Commission on Radiation Units and Measurements, Radiation quantities and units, (1980).

57. What percent of patients with an urothelial carcinoma of the renal pelvis will have an urothelial carcinoma of the bladder?

- (A) 4
- (B) 12
- (C) 22
- (D) **50**

Rationale: Approximately 50% of patients with a urothelial cancer of the renal pelvis will have a urothelial cancer of the bladder.

References: Olgac S, Mazumdar M, Dalbagni G, Reuter VE., Urothelial carcinoma of the renal pelvis: a clinicopathologic study of 130 cases, (2004) pp. 1545-52.

58. An advantage of flattening filter free (FFF) beams for IMRT delivery is:

- (A) **higher dose rate.**
- (B) decreased dose to normal structures.
- (C) increased variation in energy spectrum available in the field.
- (D) more uniform dose distribution in the central 80% of the beam.

Rationale: Removing the flattening filter from photon beam allows for a higher dose rate. The other options are not characteristics of FFF beams. The beam is strongly forward peaked, but since the beam is modulated anyway there is no for flat beam exiting the linac. FFF beams display reduced energy variation across the field since there is not beam hardening by the filter. The dose distribution to normal structures is determined by the IMRT optimization and is not a direct function of the presence or absence of a flattening filter.

References: Georg, Knoos and McClean, Current status and future perspective of flattening filter free photon beams, (2011) Volume 35.

59. What is the recommended PTV margin around the nodal CTV for IMRT in postoperative pelvic radiation for cervical cancer?

- (A) 5 mm
- (B) **7 mm**
- (C) 10 mm
- (D) 15 mm

Rationale: A PTV margin of 7 mm around the nodal CTV was agreed upon and in line with the previous recommendations in the postoperative cervix cancer setting (RTOG 0418).

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) pp. 348-355.

60. Which of the following descriptions accurately defines a Kaplan-Meier analysis?

- (A) Simultaneously accounts for multiple variables
- (B) Applies a logistic regression to a complication that occurs or does not occur
- (C) **Measures the ratio of surviving patients to total number at risk for the outcome**
- (D) Time to be included as a variable and patients are counted only during the time observed

61. NSABP analysis shows patients with T3N0 breast cancer treated with mastectomy, chemotherapy and no radiation have a 10-year LRR rate of:

- (A) 5%.
- (B) 7%.**
- (C) 9%.
- (D) 11%.

Rationale: The local regional recurrence rate was 7%

References: Taghian, A. G. et al., Low local regional recurrence rates among node negative breast cancer patients with tumors 5 cm or larger treated by mastectomy and without radiotherapy: results from NSABP randomized clinical trials, (2006) pp. 3927-3932.

62. When treating cervical cancer with EBRT and HDR brachytherapy the EQD2 D2cc for the bladder (the minimum dose in the MOST irradiated 2 cm³ normal tissue volume) should not exceed:

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

Rationale: For normal tissues it is recommended that for each fraction of brachytherapy, the DVH values be calculated and summed. The EQD2 D2cc of bladder is ≤ 90 Gy.

References: Viswanathan, et al., American Brachytherapy Society consensus guidelines for locally advanced carcinoma of the cervix. Part II: High-dose-rate brachytherapy, (2012) pp. 47-52.

63. The MOST common form of secondary leukemia caused by either chemotherapy or radiation is:

- (A) AML.**
- (B) ALL.
- (C) CML.
- (D) CLL.

Rationale: 90% of secondary leukemias in patients with a history of radiation or chemotherapy treatments are AML.

References: DeVita et al, DeVita et al, (1993) p. 2405.

64. In the CROSS study, what was the neoadjuvant chemoradiation treatment regimen for resectable esophageal cancer?

- (A) 41.4 Gy with 5-FU/cisplatin
- (B) 50.4 Gy with 5-FU/cisplatin
- (C) 41.4 Gy with carboplatin/paclitaxel**
- (D) 50.4 Gy with carboplatin/paclitaxel

Rationale: Although in the US, neoadjuvant chemoradiation is standardly prescribed to 50.4 Gy, the CROSS regimen consisted of radiation prescribed to 41.4 Gy administered with concurrent carboplatin and paclitaxel.

References: Van Hagen et al., Preoperative Chemoradiotherapy, (2012) pp. 2074-2084.

65. Which protein kinase does NOT phosphorylate histone H2AX at sites of DNA double strand breaks?

- (A) mTOR**
- (B) ATM
- (C) DNA-PK
- (D) ATR

Rationale: Of the four PI3K-like serine/threonine protein kinases mentioned, only mTOR has not been shown to phosphorylate histone H2AX at serine 139.

References: Wilson PF and Bedford JS, Leibel and Philips Textbook of Radiation Oncology, (2010) Chapter 1.

66. If the sample mean of a data set is 200 and the sample standard deviation is 20, what percent of the data would you expect to fall between 160 and 240, assuming a normal distribution?

- (A) 50%
- (B) 67%
- (C) 95%**
- (D) 99%

Rationale: In a normal distributed population, 67% of values will within 1 standard deviation of the mean, 95% of values within 2 standard deviations, and 99% within 3 standard deviations.

67. For melanoma patients harboring BRAF oncogene mutations, treatment with RAF inhibitors typically yields which type of therapeutic response?

- (A) No therapeutic response
- (B) Accelerated tumor growth
- (C) Tumor regression initially, followed by accelerated tumor regrowth**
- (D) Tumor regression in most cases, including some cures

Rationale: In clinical trials of targeted inhibitors of oncogenic protein kinases such as mutated BRAF (found in more than 50% of melanomas), rapid and dramatic tumor regression is frequently observed. However – typically within a year of the start of treatment – such tumors invariably become resistant to these inhibitors and recur. Genetic mechanisms of acquired resistance to targeted kinase inhibitors include: additional mutations affecting the target kinase that allow it to function even in the presence of inhibitors; or alterations of other genes in the target signaling pathway that compensate for or bypass the inhibited oncoprotein.

References: Wagle N, et al., Dissecting therapeutic resistance to RAF inhibition in melanoma by tumor genomic profiling, (2011) pp. 3085-3096

68. What is the TNM stage for a resected 2.5 cm extrahepatic cholangiocarcinoma with invasion through the bile duct but without involvement of nearby organs or blood vessels, and 4/15 lymph nodes positive?

- (A) T2N1M0**
- (B) T3N1M0
- (C) T3N2M0
- (D) T4N1M0

Rationale: AJCC staging: A primary tumor that extends beyond the bile duct wall but not into any surrounding organs or blood vessels is a T2. Lymph node involvement is N1.

References: AJCC Cancer Staging Manual, (2010).

69. Which statistical method is used for measuring the reliability between different and independent raters?

- (A) McNemar's test
- (B) Chi-square test
- (C) Kappa coefficient**
- (D) One way analysis of variance

Rationale: The Kappa coefficient is a widely used statistic for measuring the degree of reliability between different and independent raters. It compares the agreement against that which might be expected by chance. The Kappa coefficient ranges from 1 (perfect agreement) to -1 (complete disagreement). Here is one possible interpretation of Kappa. • Poor agreement = Less than 0.20 • Fair agreement = 0.20 to 0.40 • Moderate agreement = 0.40 to 0.60 • Good agreement = 0.60 to 0.80 • Very good agreement = 0.80 to 1.00

References: Lloyd D. Fisher and Gerald van Belle, Biostatistics: A methodology for the health sciences, (1993) Chapter 7.

70. Which term represents the percentage of subjects with a positive test who have the disease?

- (A) Sensitivity
- (B) Specificity
- (C) Predicted value of a negative test
- (D) Predicted value of a positive test**

Rationale: The sensitivity is the percentage of subjects with disease who are classified as having disease and the specificity is the percentage of subjects without disease who are classified as not having disease. The predicted value of a positive test is the percentage of subjects with a positive test who have the disease and the predicted value of a negative test is the percentage of subjects with a negative test who do not have the disease.

References: Lloyd D. Fisher and Gerald van Belle, Biostatistics: A methodology for the health sciences, (1993) Chapter 6.

71. What is the BEST treatment option for a healthy patient with a limited stage SCLC?

- (A) Chemotherapy alone
- (B) Chemotherapy followed by thoracic irradiation
- (C) Concurrent chemotherapy and thoracic irradiation**
- (D) Thoracic irradiation after complete response to chemotherapy

Rationale: Although complete remission rates were not significantly different between the two arms, progression-free survival ($P = .036$) and overall survival ($P = .008$) were superior in the early thoracic irradiation arm. Patients in the late thoracic irradiation arm had a higher risk of brain metastases ($P = .006$). A small but significant improvement in 2-year OS for early radiotherapy versus late radiotherapy in limited stage small cell lung cancer was observed.

References: Fried, D.B. et al., Systematic review evaluating the timing of thoracic radiation therapy in combined modality therapy for limited-stage small-cell lung cancer, (2004) pp. 4837-45.

Murray, N. et al., Importance of Timing for Thoracic Irradiation in the, (1993) pp. 336-344.

72. RTOG 9903, a randomized trial assessing the benefit of erythropoietin (Epo) for anemic patients with head and neck cancer, demonstrated the addition of Epo to the radiation:

- (A) **had no benefit.**
- (B) improved local control.
- (C) improved overall survival.
- (D) improved progression-free survival.

Rationale: A total of 148 patients were enrolled; 141 were evaluable. Median pretreatment hemoglobin was 12.1 g/dL. Hemoglobin levels at 4 weeks rose by an average of 1.66 g/dL in the Epo arm, compared with an average 0.24 g/dL decrease in the control arm ($p = 0.0001$). Median follow-up was 2.5 years (3.1 years for surviving patients). There was no statistically significant difference in the primary endpoint of local-regional failure (LRF) rate between the treatment arms. The 3-year LRF rate was 36% for control and 44% for Epo ($p = 0.56$). There were also no significant differences in local-regional progression-free survival (LRPFS), patterns of failure, overall survival, or toxicity. The 3-year LRPFS rate was 52% for control and 47% for Epo. The overall survival rate was 57% and 56%, respectively.

The addition of Epo to definitive radiotherapy for SCCHN did not improve outcomes. The study was not specifically designed to detect a potential negative association between Epo and tumor progression/survival

References: Machtay, M. et al., Radiotherapy with or without erythropoietin for anemic patients with head and neck cancer: a randomized trial of the Radiation Therapy Oncology Group (RTOG 99-03), (2007) -1008-17.

73. Which of the following treatment programs is recommended for initial management of localized giant cell bone tumors?

- (A) Denosumab
- (B) **Surgical excision**
- (C) Radiation therapy
- (D) Serial embolization

Rationale: Wide excision and intralesional curettage are the two surgical treatment options for patients with resectable tumors. Wide excision is associated with a lower risk of local recurrence than intralesional curettage, with the local recurrence rates ranging from 0%-12% for wide excision and 12%-65% for intralesional curettage. RT has been used as a primary treatment or in combination with surgery to improve local control and DFS for patients with marginally resected, unresectable, progressive or recurrent disease. Denosumab is an option for treatment of unresectable disease.

References: NCCN Clinical Practice Guidelines in Oncology.

74. Which distribution gives the probability that an outcome occurs a specified number of times when the number of trials is large and the probability of any one occurrence is small?

- (A) **Poisson**
- (B) Binomial
- (C) Gaussian
- (D) Chi-square

References: Dawson B and Trapp RG, Basic and Clinical Biostatistics, (2004) p. 76.

75. Which tumor marker is used to follow granulosa cell ovarian cancers if elevated at diagnosis?

- (A) AFP
- (B) CEA
- (C) CA 19-9
- (D) **Inhibin**

Rationale: For patients with granulosa cell tumors who are being observed, inhibin levels are followed if initially elevated at presentation.

References: NCCN Ovary.

76. What is the sensitivity of a screening test administered to 500 patients, 100 of whom are known to have the disease? This test was positive in 50 of the 100 patients with the disease and in 20 patients who do NOT have the disease.

- (A) **50%**
- (B) 71.4%
- (C) 88.4%
- (D) 95%

Rationale: Screening refers to the application of test to people who as yet have no symptoms of a particular disease. It is classified as having a positive (disease likely) or negative (disease unlikely) finding. Diagnostic tests tell whether or not a subject actually has the disease. The performance of a screen test is considered by the sensitivity and specificity. The sensitivity is the percentage of subjects with disease who are classified as having disease and the specificity is the percentage of subjects without disease who are classified as not having disease. Those subjects with the disease should all be classified as having disease, and those subjects without the disease should be classified as not having disease. Therefore a highly sensitive and specific test is preferred.

		Disease Status	
		Present	Absent
Test Result	Positive	50	20
	Negative	50	380

Sensitivity= $50/(50+50)*100\%=50\%$.

References: Mausner, J.S. & Bahn, A.K. Epidemiology: An Introductory Text, (1974) Chapter 11.

77. Which treatment is MOST appropriate for a Stage IE retroorbital MALT lymphoma?

- (A) Systemic chemotherapy
- (B) 20 Gy involved site
- (C) **30 Gy involved site**
- (D) 45 Gy involved site

Rationale: From the NCCN guidelines: Orbital MALT lymphomas should receive between 24 – 30 Gy involved site.

References: NCCN Clinical Practice Guidelines in Oncology.

78. What percentage of data points is encompassed by 1 SD in a Gaussian distribution?

- (A) 50%
- (B) 68%**
- (C) 95%
- (D) 100%

References: Riffenburgh RH, Statistics in Medicine, p. 58-60.

79. A Cox regression analysis used to compare survival between two study groups:

- (A) assumes hazard ratios are approximately proportional.**
- (B) generates an odds ratio comparing survival.
- (C) yields the same result as a logistic regression analysis.
- (D) implemented with covariates that are dichotomous variables.

80. What would be the optimal stem cell source for a bone marrow transplant for a 6-year-old patient with very high risk relapsed leukemia in remission?

- (A) Autologous stem cells
- (B) Fraternal twin with 6/6 HLA match**
- (C) Identical twin with 6/6 HLA match
- (D) Unrelated donor with 10/10 HLA match

Rationale: A completely matched related donor is the ideal source for patients undergoing allogeneic transplant. An identical twin source is more likely to fail due to a reduced graft versus leukemia reaction. If a matched related donor is not available, then an unrelated complete matched donor is acceptable. The role of an autologous transplant is less clear.

References: Pizzo, Pediatric Oncology.

81. Compared to conventionally fractionated radiation (60 Gy) for unresectable stage I NSCLC, SBRT:

- (A) has no significant benefit in OS or local control.
- (B) is better in both local control and OS.**
- (C) is better in local control but not in OS.
- (D) is better in OS but not in local control OS.

Rationale: Conventionally fractionated radiation has worse local control and by retrospective reviews the comparison of overall survival is worse than most prospective or retrospective evaluations of overall survival, even in unresectable NSCLC.

References: Kong, Zhao, Hayman, Kong, Zhao, Hayman, (2006).

82. Which of the following radiation fractionations was the experimental arm in the phase III study by Turrisi (1999) for limited stage SCLC?

- (A) 37.5 Gy in 2.5 Gy fractions daily
- (B) 45 Gy in 1.5 Gy fractions twice daily**
- (C) 45 Gy in 1.8 Gy fractions daily
- (D) 66 Gy in 1.2 Gy fractions twice daily

Rationale: In both groups, the total dose of thoracic radiotherapy was 45 Gy for each patient. Patients receiving once-daily therapy received 1.8 Gy daily in 25 treatments over a period of five weeks. Accelerated twice-daily thoracic radiotherapy involved the administration administration of 1.5 Gy in 30 treatments over a period of three weeks. In both groups, thoracic radiotherapy began concurrently with the first cycle of chemotherapy. The target volume for thoracic radiotherapy, which was similar in both groups, included the gross tumor, as defined by the chest CT scan, and the bilateral mediastinal and ipsilateral hilar lymph nodes. Irradiation of uninvolved supraclavicular fossae was forbidden.

References: Turrisi AT et al., Twice-Daily Compared with Once-Daily Thoracic Radiotherapy in Limited Small-Cell Lung Cancer Treated Concurrently with Cisplatin and Etoposide, (1999) pp. 265-271.

83. The postoperative radiation volume for a Merkel cell carcinoma in the right temple includes:
- (A) surgical bed.
 - (B) surgical bed, right parotid.
 - (C) surgical bed, right parotid, and neck.**
 - (D) surgical bed, right parotid, and the skull base.

Rationale: Merkel cell carcinoma has a high risk for lymph node metastasis, and a high rate of local-regional recurrence after surgery. Postoperative radiation is indicated and has been shown to improved local-regional control. The target volume consists of the surgical bed with margin of 4 to 5 cm except when the lesion locates in vicinity of critical structures and draining lymphatics. The right temple lesion drains to right parotid and right level II, and subsequently downward to level III to IV. It is rare to drain to contralateral neck.

References: Veness MJ, Ang KK, Cutaneous Carcinoma, (2012) -In: Gunderson LLG, Tepper JE (eds). Clinical Radiation Oncology; p765, 767.

84. Post-operative irradiation is generally avoided for management of desmoid tumor (aggressive fibromatosis) at which of the following sites?

- (A) Trunk
- (B) Extremity
- (C) Head and Neck
- (D) Retroperitoneal**

Rationale: RT is not generally recommended for desmoid tumors that are retroperitoneal/intra-abdominal. RT is generally only recommended for desmoid tumors that are in the extremity, superficial trunk or head and neck areas.

References: NCCN Clinical Practice Guidelines in Oncology.

85. What is the definitive therapy for progressive/symptomatic deep thalamic pilocytic astrocytoma in a 10-year-old patient?

- (A) Surgical resection
- (B) Temozolomide chemotherapy
- (C) Platinum-based chemotherapy
- (D) 50.4 – 54 Gy with close margins**

Rationale: For completely unresectable pilocytic astrocytoma, radiotherapy is the treatment of choice in a 10 year old child. Chemotherapy may be considered for patients younger than that age, but radiotherapy is still considered the definitive therapy.

86. According to a prospective randomized trial (GORTEC 99-02), which of the following is TRUE regarding chemoradiation therapy for advanced head and neck cancer?

- (A) Induction chemotherapy has no benefit.
- (B) Concurrent chemotherapy is inferior to adjuvant therapy.
- (C) Accelerated radiation cannot compensate for absence of chemotherapy.**
- (D) Accelerated radiation is superior to conventional radiation when used with concurrent chemotherapy.

Rationale: Gortec 99-02 showed chemotherapy has a substantial treatment effect given concomitantly with radiotherapy and acceleration of radiotherapy cannot compensate for the absence of chemotherapy. The most favourable outcomes for conventional chemoradiotherapy, suggesting that acceleration of radiotherapy is probably not beneficial in concomitant chemoradiotherapy schedules. Induction chemotherapy was not part of the study.

References: Bourhis, J. et al., Concomitant chemoradiotherapy versus acceleration of radiotherapy with or without concomitant chemotherapy in locally advanced head and neck carcinoma (GORTEC 99-02): an open-label phase 3 randomised, (2012) pp. 145-53.

87. Which of the following treatment programs provides superior overall survival for patients with rhabdomyosarcoma arising in a previously irradiated field?

- (A) Surgery
- (B) Chemotherapy
- (C) Radiation therapy
- (D) Surgery + chemotherapy**

Rationale: Rhabdomyosarcoma arising in a previously irradiated area is best treated with chemotherapy and local therapy, either surgery or RT or both. The 3 year overall survival was 66% for patients receiving chemotherapy + local therapy, consisting of either surgery or RT or both. Overall survival for patients receiving single modality therapy (chemotherapy or surgery or RT only) was 29%.

References: Dang, N.D. et al., Rhabdomyosarcoma Arising in a Previously Irradiated Field: An Analysis of 43 Patients, (2013) pp. 598-603.

88. The MOST common age distribution (years) for primary bone tumors is:

- (A) 10-20.**
- (B) 25-35.
- (C) 40-50.
- (D) 55-65.

Rationale: 10-20 years is associated with the most rapid skeletal growth rate. In patients older than 60, >50% of patients arise from other conditions such as Paget's Disease or fibrous dysplasia.

References: Hansen-Roach, editors, Handbook of Evidence Based Radiation Oncology, (2010) p. 607.

89. Which of the following catalyzes strand exchange during homologous recombination repair of DNA double strand breaks?

- (A) Artemis
- (B) BRCA1
- (C) RAD51**
- (D) RAD52

Rationale: RAD51 is a human homologue of the RecA recombinase found in *E. coli* and mediates the invasion of the homologous strand of the sister chromatid. RAD52 provides protection against exonucleolytic degradation, while BRCA1 assists in the loading of RAD51. Artemis removes 3' and 5' overhangs during non-homologous end joining.

References: Hall, E.J., Radiobiology for the Radiologist, (2012) -Chapter 2, Figure 2.10

90. Compared with postoperative chemoradiation for resectable T3 or node positive rectal cancer, preoperative chemoradiation has:

- (A) less toxicity and greater local control.**
- (B) less toxicity and decreased local control.
- (C) greater toxicity and greater local control.
- (D) greater toxicity and decreased local control.

Rationale: In the German CAO/ARO/AIO-94 trial, preoperative chemoradiation was compared with postoperative chemoradiation in T3+ or node-positive disease. The preoperative group had a significant decrease in rates of local failure, acute toxicity, and chronic toxicity. There was no difference in overall survival.

References: Sauer et al., Preoperative vs. postoperative chemoradiotherapy for rectal cancer, (2004) pg. 1731-40.

91. According to the SEER database, the MOST common cause of death for women diagnosed with Stage I-IV breast cancer at age 75-84 years is:

- (A) stroke.
- (B) pneumonia.
- (C) breast cancer.**
- (D) heart disease.

Rationale: Causes of death: breast cancer 45%; heart disease 21%, CVA 5% and pneumonia 2.5%

References: Yancik, R. et al., Effect of Age and Comorbidity in Postmenopausal Breast Cancer Patients Aged 55 Years and Older, (2001).

92. What is the anatomic relationship of the level III axillary lymph nodes to the pectoralis minor muscle when contouring target structures for regional node irradiation in breast cancer?

- (A) **Medial**
- (B) Lateral
- (C) Anterior
- (D) Posterior

Rationale: Contouring of target structures in breast cancer is becoming increasingly important as the field moves away from fields based on bony landmarks to CT-based 3D conformal or intensity modulated radiation therapy. The location of the different levels of the axilla can be defined by their relative position to the pectoralis minor muscle. The level I axilla is lateral to the pectoralis minor muscle. The level II axilla is posterior to the pectoralis minor muscle. The level III axilla is medial to the pectoralis minor muscle. The Rotter's nodes are located between the pectoralis major and minor muscles (anterior to the pectoralis minor).

References: Madu et al., Definition of the Supraclavicular and, (2001) pp. 333–339.
rtog.org, Breast Cancer Atlas,
<http://www.rtog.org/CoreLab/ContouringAtlases/BreastCancerAtlas.aspx>.

93. Which of the following management options is MOST appropriate for a 53-year-old patient with WHO 3 nasopharyngeal carcinoma invading into the clivus with bilateral cervical lymphadenopathy?

- (A) Induction chemotherapy followed by IMRT
- (B) Combination of cetuximab and IMRT
- (C) IMRT followed by adjuvant chemotherapy
- (D) Concurrent chemotherapy and IMRT**

Rationale: Several international randomized clinical trials performed in patients with endemic, WHO Type II and III, nasopharyngeal carcinoma confirmed that concurrent Cisplatin-based chemotherapy improves survival compared to radiotherapy alone in locally advanced disease (1,2). Along with the results of the US Intergroup 0099 trial, these established concurrent chemoradiation as the standard of care. Meta-analyses of chemotherapy trials have demonstrated that the greatest improvement in survival is associated with concomitant chemotherapy with radiation, with no significant improvement associated with neoadjuvant or adjuvant chemotherapy. The anatomic location of the nasopharynx and its proximity to critical structures historically presented major challenges with conventional radiotherapy techniques to deliver adequate dose to tumor without excessive doses to critical structures. Both dosimetric and clinical studies have established that IMRT improves the therapeutic ratio, facilitating improved tumor coverage while reducing doses to the parotid glands, brainstem, temporal lobes and optic structures]. As with any conformal radiotherapy technique, meticulous attention to careful delineation of tumor volumes and areas of subclinical risk is essential. Modern chemoradiation series with IMRT demonstrate very high rates of locoregional control >90%, even in many patients with advanced T-stage primaries (4). In fact, distant relapse with rates ranging from 20-30% in these series appears to outweigh locoregional failure. No trial has been done to compare cetuximab with radiation to radiation alone.

References: Baujat B, Audry H, Bourhis J, et al, Chemotherapy in locally advanced nasopharyngeal carcinoma: an individual patient data meta-analysis of eight randomized trials and 1753 patients, (2006) pp. 47-56

Wee, J, Tan EH, Tai BC, et al, Randomized trial of radiotherapy versus concurrent chemoradiotherapy followed by adjuvant chemotherapy in patients with American Joint Committee on Cancer/International Union against cancer stage III, (2005) pp. 6730-6738

Lin, JC, Jan JS, Hsu CY, et al., Phase III study of concurrent chemoradiotherapy versus radiotherapy alone for advanced nasopharyngeal carcinoma: positive effect on overall and progression-free survival, (2003) pp. 631-637.

Lee, A., Nasopharyngeal Cancer: Advances in Radiotherapy, (2007) pp. S115-S117.

94. Which of the following is the MOST characteristic of lymphocyte predominant nodular Hodgkin lymphoma?

- (A) Cells express CD 20 and CD 45
- (B) Associated with poor outcome
- (C) Commonly affects people over age 40
- (D) Most commonly presents in infradiaphragmatic lymph nodes

Rationale: Disease commonly affects peripheral sites. Cell usually express CD 20 and CD 45 and are CD 15 and CD 30 negative.

References: Perez & Brady's Principles and Practice of Radiation Oncology.

95. According to the data from Darby et al (NEJM 2013), what is the risk of major coronary events before age 80 with radiation involving a 3 Gy mean heart dose for a 50-year-old woman with no preexisting cardiac risk factors if her risk is 4.5% without radiation?

- (A) 5.4%
- (B) 10.8%
- (C) 16.2%
- (D) 21.6%

Rationale: Darby et al reported a population-based case-control study of major coronary events in 2168 women who underwent radiotherapy for breast cancer between 1958 and 2001. The rate of major coronary events increased by 7.4% for each increase of 1 Gy in the mean radiation dose delivered to the heart (95% CI, 2.9 to 14.5; $P < 0.001$). A mean cardiac dose of 3 Gy would result in a relative increase of $7.4 \times 3 = 22.2\%$. This would result in this case in an absolute increase of about $4.5\% \times 0.2 = 0.9\%$.

References: Darby et al., Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer, (2013) pp. 987-98.

96. Which of the following would be the MOST appropriate initial management for a 12-month-old patient with bilateral International Classification group C retinoblastoma?

- (A) Systemic chemotherapy
- (B) Bilateral enucleation
- (C) Intra-ocular chemotherapy
- (D) Bilateral EBRT

Rationale: For babies with bilateral retinoblastoma and useful vision systemic chemotherapy is the most appropriate initial management. Group C includes eyes with discrete local disease with minimal subretinal/vitreous seeding. Enucleation could be considered for more advanced disease with no functional vision. External beam radiotherapy is currently used as salvage therapy after failure of other systemic or local management such as laser or cryotherapy. Subtenon or intra-arterial chemotherapy is being evaluated as alternatives and adjunctive therapy to systemic therapy.

References: International Classification for Retinoblastoma.

97. How would a tumor with a short cell cycle time, a low growth fraction and a high cell loss rate behave before and in response to radiation therapy?

- (A) **Grow slowly; regress rapidly**
- (B) Grow slowly; regress slowly
- (C) Grow rapidly; regress slowly
- (D) Grow rapidly; regress rapidly

Rationale: A tumor with a low growth fraction and high cell loss rate would grow slowly overall, despite containing a subpopulation of cells with short cell cycle times and that are proliferating rapidly. On the assumption that the radiation therapy would be preferentially toxic to the rapidly growing cells, and possibly, impair the ability of the survivors to repopulate rapidly, this would “unmask” the high rate of cell loss, causing the tumor to regress rapidly during and after treatment.

98. Which tumor is MOST likely to grow or change configuration during a course of fractionated radiation therapy?

- (A) **Craniopharyngioma**
- (B) Hemangioblastoma
- (C) Astrocytoma, WHO grade II
- (D) Breast cancer brain metastasis

Rationale: The cystic component of craniopharyngioma can enlarge during fractionated radiation treatment. It is possible that this can lead to underdosing of tumor. Some authors have suggested q2 week MRI during therapy.

References: Winkfield, K.M. et al., Surveillance of craniopharyngioma cyst growth in children treated with proton radiotherapy, (2009) 716-21.

99. On RTOG 9408 subgroup analysis of the intermediate risk prostate cancer patients, what was the percent improvement in 10 year overall survival associated with the radiotherapy + hormone arm compared to radiation alone?

- (A) 3
- (B) 7**
- (C) 11
- (D) 15

Rationale: RTOG 9408 is the largest phase III study to show a benefit with the administration of a short term course of hormone therapy with radiation therapy for patients with intermediate risk prostate cancer. It revealed an increase in the 10-year rate of overall survival from 54 to 61% (hazard ratio for death with radiotherapy alone, 1.23; 95% CI, 1.02 to 1.49) and a reduction in the 10-year disease-specific mortality from 10% to 3% (hazard ratio, 2.49; 95% CI, 1.50 to 4.11). There was no significant benefit noted in patients with low risk disease.

References: Jones CU, Hunt D, McGowan DG, et al., Radiotherapy and short-term androgen deprivation for localized prostate cancer, (2011) pp. 107-18.

100. According to the AJCC 7th edition staging manual for NSCLC, which of the following is classified as T4?

- (A) Chest wall invasion
- (B) Separate tumor nodule(s) in the same lobe
- (C) Separate tumor nodule(s) in a different ipsilateral lobe**
- (D) Involvement of the main bronchus, ≥ 2 cm distal to the carina

Rationale: Pertinent changes to the lung staging system from the 6th to 7th edition include (1) more discrete stratification of tumors by size and partitioning of larger (>7 cm) tumors into T3, (2) downstaging of multiple nodules to T3 (same lobe), T4 (same lung), and M1a (contralateral lobe), and (3) upstaging of malignant pleural effusion from T4 to M1a.

References: AJCC Cancer Staging Manual, (2010).

101. According to the CALOR trial, what is the 5-year DFS for patients with ER negative-local-regional breast cancer recurrence who receive chemotherapy?

- (A) 37%
- (B) 47%
- (C) 57%
- (D) 67%**

Rationale: Women who experienced a local-regional recurrence after initial therapy for breast cancer (either conservation therapy or mastectomy) were randomized to receive adjuvant chemotherapy after resection with completion mastectomy or resection of recurrent disease. Patients with ER- tumors had the greatest benefit. At a median 5 year follow up, patients with ER- tumors had a 67% DFS compared with 35% of ER- patients without chemotherapy. For patients with ER+ disease, the respective rates were 70% vs. 69%. Women with ER+ tumors received appropriate hormonal therapy, and there were very few recurrences in that group, regardless of whether they received chemotherapy. The majority of benefit was seen in ER-disease. This is the first randomized controlled trial that shows benefit of adjuvant chemotherapy works isolated local-regional recurrent disease.

References: Results of the CALOR trial, (2012).

102. Which change in the four R's of radiotherapy has been implicated in the success of SBRT for early-stage NSCLC?

- (A) Limited tumor reoxygenation
- (B) Inhibited tumor stem cell repopulation
- (C) Disrupted cell-cycle redistribution
- (D) Incomplete sublethal damage recovery**

Rationale: Most tumors are characterized by α/β ratios of at least 10 Gy, which makes them less sensitive to changes in dose fractionation than most late responding normal tissues (α/β ratios of approximately 3 Gy). Nevertheless, even tumors with high α/β ratios will still be affected by the large fraction sizes associated with SBRT due to incomplete repair of sublethal damage. The short overall treatment times with SBRT could also be advantageous in that subset of tumors that have the ability to undergo accelerated repopulation over a several-week course of fractionated radiation therapy. However, reoxygenation of hypoxic tumors could be limited during a short course of SBRT, which is a disadvantage of the technique and could lead to local relapse. The question of whether the large fraction sizes used in SBRT invoke a "new (radio)biology" is a matter of active research and debate.

References: Brown JM et al., Brown JM et al., (2013) pp. 1159-1160.
Brenner D et al., Brenner D et al., (2008) pp. 234-239.

103. What treatment factor is MOST correlated to long-term cosmetic result after balloon-based accelerated partial breast irradiation?

- (A) Re-excision
- (B) Skin spacing**
- (C) Chemotherapy
- (D) Balloon fill size

Rationale: The American Society of Breast Surgeons (ASBS) MammoSite Registry has over 1,440 patients with early-stage breast cancer. At 36 and 72 months, the rate of excellent/good cosmesis was 93.3% and 90.4% respectively. Best outcomes were associated with larger skin spacing and smaller tumors (less than 2 cm).

References: Vicini et al., Factors Associated With Optimal Long-Term Cosmetic Results in Patients Treated With Accelerated Partial Breast Irradiation Using Balloon-Based Brachytherapy, (2012) pp. 512-518

104. Which of the following slowly- or non-proliferating normal tissues expresses radiation injury within days of the start of radiotherapy?

- (A) Salivary glands**
- (B) Gastric mucosa
- (C) Seminal vesicles
- (D) Spinal cord

Rationale: Rapidly proliferating tissues (such as mucosa) express radiation damage acutely, within days or weeks, while slow- or non-proliferating tissues (such as spinal cord) express damage after many months or years. Salivary glands, which are slowly proliferating tissues, are an exception in that they are highly sensitive to radiation and express injury, in the form of reduced salivary flow, within days. The loss of salivary gland function is progressive with increasing dose and time, and will culminate in xerostomia in many cases.

References: Avila et al., Avila et al., (2009) pp. 523-529.

105. In the ACOSOG Z0011 trial, what was the rate of regional recurrence in patients with breast cancer with a positive sentinel node biopsy treated by lumpectomy and tangential irradiation but no further axillary dissection?

- (A) 1%
- (B) 6%
- (C) 11%
- (D) 16%

Rationale: In the report of the trial by Giuliano et al in the Annals of Surgery 2010, regional recurrence was seen in 2 (0.5%) patients randomized to and treated with ALND compared with 4 (0.9%) patients randomized to and treated with SLND alone (not significant). All patients had tangential whole-breast irradiation without additional fields for regional nodal irradiation and 97% of patients had some form of adjuvant systemic therapy (46% endocrine therapy and 58% chemotherapy).

References: Giuliano et al., Locoregional Recurrence After Sentinel Lymph Node Dissection With or Without Axillary Dissection in Patients With Sentinel Lymph Node Metastases, (2010) pp. 426-433.

Giuliano et al., Axillary Dissection vs No Axillary Dissection in Women With Invasive Breast Cancer and Sentinel Node Metastasis: A Randomized Clinical Trial, (2011) pp. 569-575.

106. NRC regulations stipulate that a patient who has received a permanent radioactive implant may NOT be released from the hospital unless the total effective dose equivalent (mSv) to any other individual is less than:

- (A) 1.
- (B) 5.
- (C) 10.
- (D) 20.

Rationale: The NRC limit for release from the hospital requires that no other individual receive more than 5 mSv. For I-125, if the total implanted activity is 9 mCi or less, the patient may be released.

References: U.S.NCR, NRC: 10 CFR Part 35 - Medical Use of Byproduct Material, NUREG-1556: Consolidated Guidance About Material Licenses, Vol. 9, Rev. 1.

107. The meta-analysis for 10-year probability of local recurrence after breast-conserving therapy with a 1 mm surgical margin from “tumor on ink” is:

- (A) 6%.
- (B) 11%.
- (C) 16%.**
- (D) 21%.

Rationale: The 10 year local recurrence rate for margin width of 1 mm from “tumor on ink” was 15.8%. When the margin was 2 mm, the rate was 12.4% and at 3 mm was 8.8%. When a negative surgical margin was defined as 2 mm from “tumor on ink”, a positive margin recurrence rate was 12.4%, for close margin 9.5% and for negative margin 5.5%. When the negative margin was defined as 5mm or more from “tumor on ink”, the rate for a positive margin was 8.8%, 6.7% for close and 3.8% for negative margins.

References: Houssami et al., Meta-analysis of 10 year local recurrence rate for invasive carcinoma by margin width, (2010) pp. 3219-3232

108. In NSABP B-18, the complete pathologic response rate in the breast after neoadjuvant AC chemotherapy for breast cancer was:

- (A) 3%.
- (B) 5%.
- (C) 7%.
- (D) 9%**

Rationale: The pathologic complete response rate was 9%

References: Fisher, B., et al., Effect of preoperative chemotherapy on local-regional disease in women with operable breast cancer: findings from the NSABP B-18, (1997) pp. 2483-2493
Rastogi, P. et al., Preoperative chemotherapy updates of the NSABP B-18 and B-27, (2008) pp. 778-785.

109. Which of the following is a non-ionizing type of radiation?

- (A) 250 kVp X-rays
- (B) 250 nm photons**
- (C) 250 MeV protons
- (D) 250 MeV/amu carbon ions

Rationale: 250 nm photons have an energy of approximately 5 eV, in the ultraviolet UVC range, and thus are considered a non-ionizing form of radiation. The three other options are all forms of electromagnetic radiation with sufficient energy to ionize atoms.

References: Hall, E.J., Radiobiology for the Radiologist, (2012) Chapter 20, pp. 328-329.

110. Locally advanced carcinomas (stage T3-T4) of the prostatic urethra are BEST treated by which of the following treatment options?

- (A) Surgery alone
- (B) Surgery and adjuvant radiation therapy
- (C) Radiation therapy with concurrent chemotherapy
- (D) Neoadjuvant chemotherapy followed by surgery**

Rationale: These cancers are best treated with a combination of neoadjuvant chemotherapy (MVAC) with consolidative surgery or radiation therapy

References: DeVita et al., Cancer: Principles and Practice of Oncology, (2011).

111. Which histological staining technique is used to visualize senescent cells *in vitro*?

- (A) Ki-67
- (B) MPM-2
- (C) SA- β -galactosidase**
- (D) Hematoxylin and eosin

Rationale: Senescent cells develop a characteristic flattened and enlarged morphology (“fried eggs”), and can be identified more conclusively by staining with senescence-associated β -galactosidase (SA- β -gal) activity, which stains the perinuclear compartment blue. H&E staining is used to visualize the basic structure of tissue samples, KI-67 staining is used as a cell proliferation marker, and MPM-2 is a mitosis-related stain.

References: Ewald J.A., Desotelle J.A., Wilding G., Jarrard D.F., Therapy-induced senescence in cancer, (2010) 1536-1546.

112. How does the quality of cervical cancer brachytherapy impact local recurrence (LR) and DFS?

- (A) Symmetry of ovoids to tandem has no impact
- (B) Inappropriate placement of packing has a higher DFS
- (C) Displacement of ovoids from OS has increased risk of LR**
- (D) Tandem in midpelvis has decreased DFS and increased LR

Rationale: Patients with unacceptable symmetry of ovoids to the tandem had a significantly higher risk of LR than patients in the acceptable group. Patients with displacement of ovoids in relation to the cervical os had a significantly increased risk of LR and a lower DFS rate. Inappropriate placement of packing resulted in a lower DFS rate. The tandem in midpelvis did not impact these outcomes.

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).

113. Which of the following types of DNA damage is NOT caused by exposure to ionizing radiation or to alkylating agents?

- (A) Monoadducts
- (B) Single strand breaks
- (C) Interstrand crosslinks
- (D) Pyrimidine dimers**

Rationale: Ionizing radiation and alkylating agents share in common the generation of DNA monoadducts, single strand breaks and interstrand crosslinks. Cyclobutane dimers are formed by exposure to ultraviolet UVC radiation

References: Wilson PF and Bedford JS, Leibel and Philips Textbook of Radiation Oncology, (2010).

114. The effects of small aperture electron blocks (“cutouts”) on the d_{max} and the output, respectively, are to:

- (A) decrease, decrease.**
- (B) decrease, increase.
- (C) increase, increase.
- (D) increase, decrease.

Rationale: Small aperture electron blocks result in a loss of side scatter equilibrium, which reduces the output and causes d_{max} to shift toward the surface.

References: McDermott & Orton, The Physics and Technology of Radiation Therapy, (2010) Chapter 15.

115. What BEST describes the use of a breast boost with whole-breast hypofractionation for early stage breast cancer?

- (A) Should not be used outside of a clinical trial
- (B) When used, is normally given with 267 cGy per day
- (C) Normally given sequentially rather than concurrently**
- (D) Not used unless in the randomized hypofractionation trials

Rationale: Although not used in the Canadian whole breast hypofractionation study, a sequential boost at 2 Gy per day was allowed on the UK START hypofractionation trials. There are excellent 5-year results of concurrent boost in phase II clinical trials but it is not yet a nationally accepted standard compared to sequential boost. RTOG 1005 is a clinical trial of sequential or concurrent boost – the control arm uses a sequential boost at 2 Gy per day with either conventionally fractionated or hypofractionated whole breast radiation. The investigational arm for RTOG 1005 is a concurrent boost of 53 cGy per day added to the 267 per day x 15 fractions used in the UK START B trial.

References: The UK Standardisation of Breast Radiotherapy (START) Trial B of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial, (2008) pp. 1098-107 rtog.org, Clinical Trials,

<http://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?study=1005>.

Whelan et al. Long-Term Results of Hypofractionated Radiation Therapy for Breast Cancer, (2010) pp. 1098-107.

116. Which of the following is typically seen in classic radiation-induced liver disease?

- (A) Thrombocytopenia
- (B) Right upper quadrant pain
- (C) Elevated liver transaminases
- (D) Anicteric hepatomegaly**

Rationale: Classic RILD is defined as a triad of anicteric hepatosplenomegaly, ascites, and elevated alkaline phosphatase. Elevated transaminases or decline in liver function can occur in non-classic RILD. Pain and thrombocytopenia are not typically seen.

References: Pan, C.C. et al., Radiation-associated liver injury, (2010) pp. S94:100.

117. What is the MOST appropriate treatment after a subtotal resection of a temporal lobe 19q-deleted WHO grade 2 oligodendroglioma for a 50-year-old?

- (A) Close observation
- (B) Systemic chemotherapy alone
- (C) Partial brain radiotherapy alone**
- (D) Combined systemic chemotherapy and partial brain radiotherapy

Rationale: This patient has unfavorable features including age (> 40 years), incompletely resected tumor, and solitary 19q deletion. She also has symptomatic disease, rendering upfront radiotherapy necessary. The role of systemic chemotherapy alone or with radiotherapy is not well defined, so partial brain radiotherapy remains the standard treatment.

References: Scheie D, Meling TR, Cvancarova M, Skullerud K, Mørk S, Lote K, Eide TJ, Helseth E, Beiske K, Prognostic variables in oligodendroglial tumors: a single-institution study of 95 cases., (2011) pg. 1225-33

Pignatti F, van den Bent M, Curran D, Debruyne C, Sylvester R, Therasse P, Afra D, Cornu P, Bolla M, Vecht C, Karim, European Organization for Research and Treatment of Cancer Brain Tumor Cooperative Group; European Organization for Research and Treatment of Cancer Radiotherapy Cooperative Group. Prognostic factors, (2002) pg. 2076-84.

Karim AB, Maat B, Hatlevoll R, Menten J, Rutten EH, Thomas DG, Mascarenhas F, Horiot JC, Parvinen LM, van Reijn M, Jager JJ, Fabrini MG, van Alphen AM, Hamers HP, Gaspar L, Noordman E, Pierart M, v, A randomized trial on dose-response in radiation therapy of low-grade cerebral glioma: European Organization for Research and Treatment of Cancer (EORTC) Study 22844., (1996) pg. 549-56.

118. For a grade II astrocytoma, the rate in percent of transformation into a high grade glioma is approximately:

- (A) 10.
- (B) 30.
- (C) 70.**
- (D) 95.

Rationale: The rate of progression to a high grade glioma on the ‘Non-Believers’ trial was 72% with radiotherapy vs. 66% without radiotherapy (not-significant) (eg, radiotherapy does not increase the rate of transformation to high grade glioma).

References: van den Bent, M.J. et al., Long-term efficacy of early versus delayed radiotherapy for low-grade astrocytoma and oligodendroglioma in adults: the EORTC 22845 randomised trial, (2006) -

Karim, A.B. et al. Randomized trial on the efficacy of radiotherapy for cerebral low-grade glioma in the adult: European Organization for Research and Treatment of Cancer Study 22845 with the Medical Research Council st, (2002).

119. What should the radiation volume and dose for an 8-year-old with a sub-totally resected left parietal primitive neuroectodermal tumor be?

- (A) 16 Gy SRS to tumor bed and residual disease
- (B) 23.4 Gy CSI, tumor boost to 54 Gy
- (C) 36 Gy CSI, tumor boost to 54 Gy**
- (D) 59.4 Gy to tumor bed and residual disease

Rationale: Treatment for supratentorial PNET has historically been similar to high risk medulloblastoma even if completely resected. An incompletely resect tumor would place the patient in a high risk category and require full dose craniospinal RT followed by a local tumor boost.

References: Halperin, Pediatric Radiation Oncology.

120. High-risk AML is defined as having a:

- (A) Hgb < 10,000.
- (B) Hgb > 10,000.
- (C) WBC < 10,000.
- (D) WBC > 10,000.**

Rationale: High-risk AML is defined as WBC >10,000

References: NCCN Clinical Practice Guidelines in Oncology.

121. How does reducing the dose rate of low LET radiation affect the survival curve parameters α and β ?

- (A) α is increased and β is reduced.
- (B) α is reduced and β is increased.
- (C) α is reduced and β is unchanged.
- (D) α is unchanged and β is reduced.**

Rationale: The theoretical underpinning of the α/β survival model is the theory of dual radiation action, that postulates that lethal lesions result from the combination of two sublesions. In one case, both lesions result from the same energy absorption event, in this example, a single electron track. These single track events have linear kinetics and are proportional to dose (αD). In another case, each sublesion results from an independent track. These multi-track events produce curvature and are proportional to the square of the dose (βD^2).

By reducing the dose rate, α is unaffected since both sublesions originate from the same track. β , on the other hand; is reduced since each sublesion is formed from an independent track and as the dose rate is lowered, the probability that a specific sublesion might be repaired before a second sublesion that it can potentially combine with is formed is increased. This reduces the frequency of multi-track events and cell survival is increased.

References: Joiner M, van der Kogel A., Basic Clinical Radiobiology, (2009) Chapters 4 and 8.

122. Which of the following laboratory tests is MOST appropriate in the initial diagnostic workup of suspected multiple myeloma?

- (A) AFP
- (B) ESR
- (C) β -HCG
- (D) β -2 microglobulin**

Rationale: According to the NCCN guidelines 2013, B-2 microglobulin is most appropriate in the workup for multiple myeloma. ESR is used for Hodgkin; AFP and B-HCG for seminoma.

References: NCCN Clinical Practice Guidelines in Oncology.

123. Graves' disease of the eye represents which of the following?

- (A) Dyplasia
- (B) Neoplasia
- (C) Metaplasia
- (D) Inflammation**

Rationale: Graves, disease of the eye is an inflammatory disease of the extraocular eye muscles.

124. What is the dominant photon interaction in tissue for megavoltage photon treatments?

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

Rationale: This item requires basic knowledge of fundamental photon interactions.

References: Khan, Physics of Radiation Therapy, (2003) Chapter 5.

125. For a 15 MV photon beam ($d_{\max}=3.0$ cm), how does the PDD at 10 cm change when the patient is moved from 100 cm to 400 cm from the source?

- (A) 3% lower
- (B) 9% lower
- (C) 3% higher
- (D) 9% higher**

Rationale: The dose falloff in a PDD curve is a combination of beam attenuation and a reduction in beam intensity due to the inverse square effect. The contribution of attenuation to PDD is the same for identical depths regardless of distance from source. The effect of inverse square can be found by squaring the ratio of the depth of maximum dose to the depth for which PDD is being calculated. In this case, the 100 SSD inverse square effect is given by $(103/110)^2 = 0.88$, and the 400 SSD inverse square effect is given by $(403/410)^2 = 0.97$. The impact of inverse square is thus much less for the 400 cm setup by a factor of $(1-0.88/0.97) = 0.09$, or 9%.

References: Khan, Physics of Radiation Therapy, (2003).

126. Appropriate therapy for a 9-year-old patient with average risk medulloblastoma would include:

- (A) 18 Gy CSI, 36 Gy boost to primary.
- (B) 23.4 Gy CSI, 30.6 Gy boost to primary.**
- (C) 36 Gy CSI, 18 Gy boost to primary.
- (D) 54 Gy to primary.

Rationale: All PNETs of the central nervous system require craniospinal irradiation (CSI) due to their propensity for drop metastases and include: medulloblastoma, supratentorial PNET, atypical teratoid/rhabdoid tumor, and pineoblastoma. The recommended dose is 36 Gy. The one exception is children >3 years old with standard risk medulloblastoma, in which the dose is lowered to 23.4 Gy and concurrent vincristine is administered. Dose reduction for CSI in patients under 3 years-old is currently under investigation.

127. Which of the following is TRUE regarding the ECOG E4201 trial of locally advanced pancreatic cancer (Loehrer et al, JCO 2011)?

- (A) Radiation was administered with concurrent 5-FU.
- (B) Chemoradiation improved quality-of-life compared to chemotherapy alone.
- (C) Chemoradiation had similar grade 3 and 4 toxicity compared to chemotherapy alone.**
- (D) Patients were randomized to gemcitabine alone or with gemcitabine chemoradiation to 60 Gy.

Rationale: The ECOG trial was a randomized trial of gemcitabine alone versus gemcitabine and concurrent radiation to 50.4 Gy. Quality-of-life measures were similar between the 2 arms. Patients who received concurrent chemoradiation had similar grade 3 and 4 toxicity (77% vs 79%).

References: Loehrer et al., Gemcitabine alone versus gemcitabine plus radiotherapy in patients with locally advanced pancreatic cancer: an eastern cooperative oncology group trial, (2011) pp. 4105-12.

128. Which of the following is NOT a recommended management option for a woman diagnosed with LCIS after an excisional biopsy?

- (A) Tamoxifen
- (B) Close observation
- (C) Radiation therapy**
- (D) Bilateral mastectomy

Rationale: There is no role for unilateral or bilateral radiation therapy in women diagnosed with pure lobular carcinoma in situ.

References: Opong and King, Recommendations for women with lobular carcinoma in situ (LCIS), (2011) pp. 1051-1058.

129. According to the UNSCEAR 2001 report, what is the absolute hereditary risk (in percent/Gy) for the offspring of parents who were exposed over several years' time to low dose, low LET ionizing radiation?

- (A) 0.4 to 0.6**
- (B) 0.8 to 1.0
- (C) 1.2 to 1.4
- (D) 1.6 to 1.8

Rationale: The current best estimate of the genetic risk from chronic exposure to low LET, low dose irradiation is between 0.4% and 0.6% absolute risk per Gy for first generation (expressed as a percent of the spontaneous risk).

References: Hall, E.J., Radiobiology for the Radiologist, (2012) -Chapter 11

130. Which of the following increases the risk of a pterygia?

- (A) **Sun exposure**
- (B) Alcohol
- (C) Tobacco
- (D) Gorlin's syndrome

Rationale: Sun exposure is associated with the development of pterygia. Gorlin's syndrome is associated with the development of multiple basal cell carcinomas.

References: Threlfall TJ, English DR, Sun exposure and pterygium of the eye: a dose-response curve, (1999) pp. 280-7.

131. For a 3-year-old patient with stage III neuroblastoma, WHEN is primary site radiotherapy used with induction chemotherapy, second look surgery, and high dose chemotherapy with stem cell rescue?

- (A) No role
- (B) **After high dose chemotherapy with stem cell rescue**
- (C) Before high dose chemotherapy with stem cell rescue
- (D) Before second-look surgery

Rationale: At this time according to the COG established regimens, consolidative primary site radiotherapy is used after recovery from the tandem high dose chemotherapy with stem cell rescue. It is important to complete radiotherapy within 100 days to allow for recovery and further treatment with Anti- disialoganglioside GD2 antibody which appears to improved overall outcomes for patients with high risk disease.

References: Matthay KK, George RE, Yu AL, Promising therapeutic targets in neuroblastoma, (2012) pg. 2740-53.

132. For a brain metastasis treated with surgery or radiosurgery without whole brain irradiation, the rate of new brain metastases is:

- (A) 0-20%.
- (B) **40-60%.**
- (C) 60-80%.
- (D) 80-100%.

Rationale: The rate of new distant intracranial failure at 2 years improved from 42-48% without WBRT to 23-33% with the addition of 30Gy WBRT on the EORTC trial.

References: Kocher, M. et al., Adjuvant whole-brain radiotherapy versus observation after radiosurgery or surgical resection of one to three cerebral metastases: results of the EORTC 22952-26001 study, (2011).

133. ^{32}P is a good choice for the interstitial treatment of selected craniopharyngiomas because it:
- (A) has a low cost.
 - (B) is a beta emitter.**
 - (C) is organically bound.
 - (D) has a short half-life.

Rationale: The beta emitting property of ^{32}P allows treatment of the cystic component of a craniopharyngioma cyst wall to a high dose without exceeding the tolerance of nearby tissues. Because it is a beta emitter it cannot treat the solid component that these tumors may have. The half-life of 14 days makes it logistically feasible to delivery clinically. ^{90}Y has similar properties but has not been utilized in as many patients as ^{32}P .

References: Sadeghi M, Karimi E, Hosseini SH, Dosimetric comparison of ^{90}Y , ^{32}P , and ^{186}Re radiocolloids in craniopharyngioma treatments, (2009) pp. 5022-6.

134. What percent of CNS germ cell tumors in males occurs in the pineal area?
- (A) 15
 - (B) 30
 - (C) 45
 - (D) 60**

Rationale: According to a SEER analysis, 61% of CNS germ cell tumors occur in the pineal area in male.

References: Goodwin TL, Sainani K, Fisher PG, Incidence patterns of central nervous system germ cell tumors: a SEER Study, (2009) pg. 541-4.

135. What are the annual breast screening recommendations for a 40-year-old female treated at age 25 with mantle radiation for Hodgkin Disease?
- (A) Ultrasound
 - (B) Mammography
 - (C) MRI
 - (D) Mammography and MRI**

Rationale: From the NCCN guidelines: Panel recommends breast MRI in addition to mammography for women who received irradiation to the chest between the ages of 10 and 30.

References: NCCN Clinical Practice Guidelines in Oncology, American Cancer Society (ACS) Guidelines.

136. The spread pattern of fallopian tube carcinoma is similar to which of the following ovarian tumors?

- (A) Borderline
- (B) Endodermal sinus
- (C) Granulosa-theca cell
- (D) Malignant epithelial**

Rationale: Fallopian tube cancers spread to peritoneum, bowel, and omentum similar to the spread of malignant epithelial ovarian tumors.

References: Barkat, Markman and Randall, Principles of Gynecologic Oncology, (2009) p. 786.

137. Which of the following is an adverse prognostic factor in a patient with a WHO grade II oligodendroglioma?

- (A) Male sex
- (B) Contrast enhancement on MRI**
- (C) Patient age of 35 years
- (D) Seizure activity

Rationale: Male sex is not a prognostic factor. Patients with presence of seizures at presentation have better overall survival. Absence of contrast enhancement is favorable. An age of < 40 years is favorable.

References: Bauman G, Lote K, Larson D, Stalpers L, Leighton C, Fisher B, Wara W, MacDonald D, Stitt L, Cairncross JG, Pretreatment factors predict overall survival for patients with low-grade glioma: a recursive partitioning analysis., (1999) pg. 923-9.
El-Hateer H, Souhami L, Roberge D, Maestro RD, Leblanc R, Eldebawy E, Muanza T, Melançon D, Kavan P, Guiot MC, Low-grade oligodendroglioma: an indolent but incurable disease?, (2009) pg. 265-71.

138. Which of the following regimens was used in the TROG trial comparing postoperative radiation versus observation in high-risk melanoma patients?

- (A) 30 Gy at 3.0 Gy per fraction over 2 weeks
- (B) 30 Gy at 6.0 Gy per fraction over 2.5 weeks
- (C) 48 Gy at 2.4 Gy per fraction over 4 weeks**
- (D) 60 Gy at 2.5 Gy per fraction BID over 4 weeks

Rationale: A recent published Trans-Tasman Radiation Oncology (TROG) randomized trial showed that adjuvant radiotherapy significantly reduced lymph node recurrence in high-risk melanoma compared to observation. While radiation regimens of A, C and D have been used in clinical practice, in this study, 48 Gy at 2.4 Gy per fraction in 20 fractions was used.

References: Burmeister BH et al, Adjuvant radiotherapy versus observation alone for patients at risk of lymph-node field relapse after therapeutic lymphadenectomy for melanoma: a randomized trial, (2012) pp. 589-97.

139. Based on the Stephenson et al. nomogram, a patient with a PSA of 1.1 offered salvage radiation alone (without ADT) for prostate cancer would have an expected 6 year progression free probability of:

- (A) 10-20%.
- (B) 20-30%.**
- (C) 40-50%.
- (D) 50-60%.

Rationale: 6-year progression-free probability was 32% (95% CI, 28% to 35%). However, an estimated 48% (95% CI, 40% to 56%) who received SRT alone without ADT when the PSA was 0.50 ng/mL or less were disease free at 6 years compared with 40% (95% CI, 34% to 46%), 28% (95% CI, 20% to 35%), and 18% (95%, 14% to 22%) of those treated at PSA levels of 0.51 to 1.00, 1.01 to 1.50, and greater than 1.50 ng/mL, respectively.

References: Stephenson AJ, Scardino PT, Kattan MW, et al., Predicting the outcome of salvage radiation therapy for recurrent prostate cancer after radical prostatectomy, (2007) pp. 2035-2041.

140. Immunohistochemical staining is important to distinguish mesothelioma from which of the following types of lung cancer?

- (A) Adenocarcinoma**
- (B) Small cell carcinoma
- (C) Squamous cell carcinoma
- (D) Large cell neuroendocrine carcinoma

Rationale: Diagnosis of mesothelioma can be difficult. Immunohistochemical staining is important to distinguish mesothelioma from adenocarcinomas of lung origin or metastatic from other sites. Calretinin is commonly positive in mesothelioma, with a reported sensitivity of 95% and specificity of 87%.Thrombomodulin has the best specificity at 92% but is less sensitive at 68%.

References: Husain AN, Colby TV, Ordoñez NG, et al., Guidelines for pathologic diagnosis of malignant mesothelioma: a consensus statement from the International Mesothelioma Interest Group, (2009) pp. 1317-1331.

141. What is the MOST appropriate treatment for a 25-year-old male with a localized suprasellar mixed germinoma and yolk sac tumor?

- (A) Chemotherapy alone
- (B) CSI and tumor bed boost
- (C) Whole ventricular irradiation and tumor bed boost
- (D) Chemotherapy, CSI, and tumor bed boost**

Rationale: With a mixed germ cell tumor, the patient should be managed according to the non-germinomatous component.

References: Kretschmar C, Kleinberg L, Greenberg M, Burger P, Holmes E, Wharam M., Pre-radiation chemotherapy with response-based radiation therapy in children with central nervous system germ cell tumors: a report from the Children's Oncology Group., (2007) pg. 285-91.

142. To which organ is uveal melanoma MOST likely to metastasize?

- (A) Liver**
- (B) Lung
- (C) Bone
- (D) Lymph nodes

Rationale: Uveal melanoma metastasizes to the liver more often than skin melanomas. About 75% of patients with metastatic disease from uveal melanoma will have liver involvement.

References: Bakalian, S. et al., Molecular Pathways Mediating Liver Metastasis in Patients with Uveal Melanoma, (2008) pp. 951-956.

143. What is the incidence of BRAF mutations in choroidal melanoma?

- (A) < 5%**
- (B) 30%
- (C) 50%
- (D) >70%

Rationale: BRAF mutation in choroidal melanoma is seldom occurs. Newer drugs targeting this pathway are not likely to be of use to patients with these tumors.

References: Zuidervaart, W. et al., Gene expression profiling identifies tumour markers potentially playing a role in uveal melanoma development, pp. 1914-1919.

144. What is the 15-year risk for death from breast cancer for a woman with DCIS treated by breast-conserving surgery and radiation therapy?

- (A) **2-5%**
- (B) 8-10%
- (C) 13-15%
- (D) 18-20%

Rationale: In the long term outcome of the NSABP B-17 and B-24 trials, the 15-year cumulative incidence of breast cancer death was 3.1% for lumpectomy alone (B-17), 4.7% for lumpectomy and radiation (B-17), 2.7% for lumpectomy and radiation + placebo (B-24), and 2.3% for Lumpectomy and radiation + Tamoxifen (B-24).

References: Wapnir et al., Long-Term Outcomes of Invasive Ipsilateral Breast Tumor Recurrences After Lumpectomy in NSABP B-17 and B-24, (2011) pp. 478-488.

145. In a patient who presented with bitemporal hemianopsia, what is the radiation dose limiting structure following a sub-total resection of a craniopharyngioma?

- (A) Pituitary
- (B) Brainstem
- (C) **Optic chiasm**
- (D) Hypothalamus

Rationale: Similar to many benign CNS tumors, craniopharyngiomas can be controlled with moderate doses of radiosurgery (e.g. 12 Gy). Unfortunately the proximity to the optic chiasm may make delivering this full dose to the entire tumor difficult. An optimal radiosurgery plan would limit the maximal dose to the optic chiasm to 8-10 Gy. Complete treatment of the entire tumor has been associated with better local control so there may be a trade off in tumor control and toxicity if a single fraction of radiation is utilized. For this reason many centers prefer a fractionated approach rather than radiosurgery.

References: Niranjana, A. et al., Radiosurgery for craniopharyngioma, (2010) pp. 64-71.

146. Regarding spinal ependymomas:

- (A) they occur more commonly in children than adults.
- (B) conus and thecal sac ependymomas are commonly WHO grade I.**
- (C) they are associated with worse prognosis in comparison to intracranial ependymomas.
- (D) observation is recommended after an incompletely resected WHO grade I ependymoma of the conus.

Rationale: Spinal ependymoma carries a better prognosis compared to intracranial ependymoma. According to a systematic review from UCSF, the majority of ependymomas in the conus/ cauda equina are WHO grade I tumors. It occurs more commonly in adults. Even after gross total resection of a spinal myxopapillary ependymoma, postoperative can improve local control.

References: Oh MC, Kim JM, Kaur G, Safaee M, Sun MZ, Singh A, Aranda D, Molinaro AM, Parsa AT, Prognosis by tumor location in adults with spinal ependymomas., (2013) pg. 225-35, Pica A, Miller R, Villà S, Kadish SP, Anacak Y, Abusaris H, Ozyigit G, Baumert BG, Zaucha R, Haller G, Weber DC, The results of surgery, with or without radiotherapy, for primary spinal myxopapillary ependymoma: a retrospective study from the rare cancer network., (2009) pg. 1114-20.

147. What is the MOST appropriate management for a palpable single 3 cm inguinal node for an excised T1 penile squamous cell cancer, grade 1, negative surgical margins, and no LVI?

- (A) Fine needle aspiration of involved node**
- (B) Radiotherapy with concurrent chemotherapy
- (C) Inguinal lymph node dissection of involved side
- (D) Pelvic and inguinal lymph node dissections

Rationale: The extent of regional inguinal lymph node metastasis is one of the most important prognostic factors in men with penile squamous cell cancer. Palpable lymphadenopathy at time of diagnosis does not require an immediate inguinal lymph node dissection. Approximately 30-50% of palpable inguinal lymph nodes in the setting of penile cancer will be enlarged secondary to inflammation. Fine needle aspiration is the recommended initial step to determine if the lymph nodes are palpable and < 4cm.

References: NCCN Clinical Practice Guidelines in Oncology, Version 1.2013 – Penile Cancer.

148. Stage I/II melanoma has an approximate 5-year overall survival of:

- (A) 20%.
- (B) 50%.
- (C) 70%.
- (D) 90%.**

Rationale: Invasive melanoma up to 2 mm in depth carries an overall excellent prognosis with complete excision.

References: Balch C, et al., Final version of the American Joint Committee on Cancer staging system for cutaneous melanoma", (2001) pp. 3635-48.

149. Which of the following is an advantage of proton radiotherapy compared to photon therapy?

- (A) **Lower integral dose**
- (B) Minimal range uncertainty in soft tissue
- (C) Increased tumor cell kill
- (D) Higher RBE of ~1.5

Rationale: Proton beam radiation generally achieves satisfactory target coverage with 2-3 beams, and therefore does not produce a low dose bath as seen with standard photon therapy which requires more fields. Protons at clinically used energies have a low LET and a RBE of only 1.0-1.1.

References: Loeffler JS; Durante M., Charged particle therapy - optimization, challenges and future directions, (2013) pp. 411-424.

DeLaney TF, Proton therapy in the clinic, (2011) pp. 465-485.

150. Which of the following is a prognostic factor in natural killer/T-cell lymphoma?

- (A) **Increased Ki-67**
- (B) Increased hemoglobin
- (C) Decreased bilirubin
- (D) Decreased LDH

Rationale: Increased Ki-67 is a risk factor in NK/T-cell lymphoma. It is also a marker used in surveillance.

References: NCCN Clinical Practice Guidelines in Oncology.

151. In a patient with a history of hepatitis C, cirrhosis, and an elevated AFP, which is the BEST method for diagnosis of hepatocellular carcinoma?

- (A) AFP
- (B) Excisional biopsy
- (C) **Contrast-enhanced MRI scan**
- (D) Trans-abdominal ultrasound

Rationale: Intense arterial uptake followed by “washout” of contrast in the venous-delayed phases of a CT or MRI scan is considered diagnostic in a patient with cirrhosis. Biopsy is not necessary in these patients, and hepatocellular cancer may be difficult to diagnose pathologically. Additionally, there is a small risk of biopsy tract seeding. Trans-abdominal ultrasound is useful for screening, but not diagnostic. Alpha-fetoprotein alone is not diagnostic.

References: Taouli B, Krinsky GA., Diagnostic imaging of hepatocellular carcinoma in patients with cirrhosis before liver transplantation, (2006) pp. S1-7.

152. What is the single MOST important factor for local recurrence in women with DCIS treated with lumpectomy alone without radiation?

- (A) Age
- (B) Size
- (C) Grade**
- (D) Margin

Rationale: In a prospective trial of excision alone without radiation, the 5-year rate of ipsilateral breast events with low/intermediate grade was 6.1% versus 15.3% with high-grade.

References: Hughes et al., Local Excision Alone Without Irradiation for Ductal Carcinoma In Situ of the Breast: A Trial of the Eastern Cooperative Oncology Group, (2009) pp. 5319-5324.

153. Hurthle cell carcinoma is a variant of which of the following types of thyroid carcinomas?

- (A) Papillary
- (B) Follicular**
- (C) Medullary
- (D) Anaplastic

Rationale: When more than 75% of cells in follicular thyroid carcinoma exhibit Hurthle cell features, the tumor is classified as Hurthle cell carcinoma.

References: Hay ID, Petersen IA, Foote RL., Thyroid cancer, (2012) In: Gunderson LLG, Tepper JE (eds). Clinical Radiation Oncology. 3rd edition. 2012; Saunders. p 711.

154. In which of the following hepatocellular carcinoma (HCC) cases is radiotherapy MOST appropriately indicated?

- (A) A solitary 4 cm lesion invading the right portal vein**
- (B) A solitary 3 cm lesion without vascular involvement
- (C) Two lesions, each 1.5 cm, without vascular involvement
- (D) Bilateral lesions and a portahepatic lymph node metastasis

Rationale: Patient A is not a candidate for surgical resection or trans-arterial chemoembolization because of vascular involvement, but has localized disease. Patient D has metastatic disease, and should receive sorafenib. Patients B and C should be considered for surgical resection or liver transplantation.

References: Forner A, Reig ME, de Lope CR, Bruix J., Current strategy for staging and treatment: the BCLC update and future prospects, (2010) pp. 61-74.

155. What were the findings of RTOG 9811 for anal cancer?

- (A) **Improved overall survival in the mitomycin-C and 5-FU arm**
- (B) Reduced hematological toxicity in the mitomycin-C and 5-FU arm
- (C) Survival with cisplatin/5-FU + RT was similar to mitomycin/5-FU + RT
- (D) Real time QA detected a high number of contouring errors

Rationale: Mitomycin and 5FU are superior to cisplatin and 5FU in terms of survival as per RTOG 9811.

References: Gunderson, L.L et al., Long-term update of US GI intergroup RTOG 98-11 phase III trial for anal carcinoma: survival, relapse, and colostomy failure with concurrent chemoradiation involving fluorouracil/mitomycin versus fluo, (2012) pp. 4344-51.

156. What is the MOST appropriate hormone ablation therapy duration to be given with EBRT for a patient with no cardiac risk and stage T2b, Gleason 7 [3+4], PSA 14.0, prostate cancer?

- (A) **6 months**
- (B) 12 months
- (C) 28 months
- (D) Hormone ablation therapy is not needed

Rationale: D'Amico et al showed overall survival benefit for patients with intermediate-risk prostate cancer with the addition of 6 months of hormone ablation therapy to the radiation therapy.

References: D'Amico AV, Chen MH, Renshaw AA, Loffredo M, Kantoff PW., Androgen suppression and radiation vs radiation alone for prostate cancer: a randomized trial, (2008) pp. 289-95.

157. The key difference in the molecular pathways of radiation-induced apoptosis and mitotic catastrophe is that:

- (A) **apoptosis relies on p53 signaling pathways while mitotic catastrophe does not.**
- (B) mitotic catastrophe is triggered by DNA damage while apoptosis is not.
- (C) apoptosis causes caspase activation while mitotic catastrophe does not.
- (D) a defective G₂ checkpoint frequently accompanies apoptosis, but not mitotic catastrophe.

Rationale: The key difference between the two radiation induced cell death pathways is that apoptosis signals through p53 while mitotic catastrophe is p53 independent. Both can lead to caspase activation and both are cellular responses to DNA damage. A defective G2 checkpoint frequently accompanies mitotic catastrophe, but not apoptosis.

References: Eriksson D, Stigbrand T, Radiation-induced cell death mechanisms, (2010) pp. 363-372.

Fragkos M, Beard P, Mitotic catastrophe occurs in the absence of apoptosis in p53-null cells with a defective G1 checkpoint, doi:10.1371/journal.pone.0022946.

158. What is the tolerance of the whole liver to conventionally fractionated radiation?

- (A) 20 Gy
- (B) 30 Gy**
- (C) 40 Gy
- (D) 50 Gy

Rationale: 30 Gy is the tolerance of the whole liver. Partial volumes of the liver can tolerate extremely high doses.

References: Pan, C.C. et al., Radiation-associated liver injury, (2010) pp. S94:100.

159. What are portal images compared to when verifying patient setup?

- (A) Scout images
- (B) DRRs**
- (C) PTV contours
- (D) Surface rendering

Rationale: Basic knowledge of different image types and reconstructions used for patient setup verification is required. Surface renderings and autoradiographs are not used to compare to port films during setup verification, and BEVs cannot be generated from scout images.

References: Khan, Physics of Radiation Therapy, (2003) Chapter 25.

160. Which receptors do Reed-Sternberg cells express?

- (A) CD 15 and CD 20
- (B) CD 15 and CD 30**
- (C) CD 20 and CD 45
- (D) CD 30 and CD 45

Rationale: Reed-Sternberg cell usually account for <1% of Hodgkin lymphoma cells; they are CD 15 and CD30 positive and CD20 and Cd45 negative.

References: Perez & Brady's Principles and Practice of Radiation Oncology.

161. After complete resection for locally advanced rectal cancer, the MOST common site for local recurrence is the:

- (A) perineum.
- (B) inguinal nodes.
- (C) presacral space.**
- (D) pelvic sidewalls.

Rationale: In published series of patients who previously underwent low anterior resection or abdominoperineal resection for rectal cancer without adjuvant radiotherapy, the most common site of recurrence is the posterior central pelvis (presacral space).

References: Hruby G. et al., Sites of local recurrence after surgery, with or without chemotherapy, for rectal cancer: implications for radiotherapy field design, (2003) pg. 138-143.

162. Which of the following is TRUE of the ESPAC-1 trial regarding adjuvant therapy for pancreatic cancer?

- (A) The observation arm had the worst survival.
- (B) Local failure was the most common site of recurrence.**
- (C) The radiation dose was 50.4 Gy given at 1.8 Gy/fraction.
- (D) Patients were randomized to observation, 5-FU alone, gemcitabine, or chemoradiation.

Rationale: The ESPAC-1 trial was a 4 arm study of 1) observation, 2) 5-fluorouracil alone, 3) 5-fluorouracil/radiation therapy, or 4) 5-fluorouracil/radiation therapy followed by 5-fluorouracil chemotherapy. The radiation dose was 40 Gy at 2 Gy/fraction given as a split course with a 2-week break after 20 Gy. The chemoradiation only arm had the worst survival (13.9 months) compared with observation (16.9 months), 5-fluorouracil alone (21.6 months), and 5-fluorouracil/radiation therapy followed by 5-fluorouracil chemotherapy (19.9 months). Of known recurrence, 35% were local, 34% were distant, and 27% had a component of both local and distant.

References: Neoptolemos et al., A randomized trial of chemoradiotherapy and chemotherapy after resection of pancreatic cancer, (2004) pp. 1200-10.

163. Based on the INT 0116, what is the recommended adjuvant therapy for a resected gastric cancer?

- (A) Chemoradiation to 45 Gy and adjuvant FOLFOX
- (B) Chemoradiation to 45 Gy and adjuvant 5-FU/leucovorin**
- (C) Chemoradiation to 50.4 Gy and adjuvant FOLFOX
- (D) Chemoradiation to 50.4 Gy and adjuvant 5-FU/leucovorin

Rationale: INT 0116 compared surgery alone to surgery followed by adjuvant 5FU/LV and chemoradiation to a dose of 45 Gy with concurrent 5-FU/LV.

References: MacDonald et al., Chemoradiotherapy after Surgery compared with Surgery alone for Adenocarcinoma of the Stomach, (2001) pp. 725-730.

164. Concerning prospective randomized trials to evaluate treatment of painful bony metastases:
- (A) pain response rates are lower when the initial pain scores are lower.
 - (B) there is dose response relationship for palliation of bone metastases.
 - (C) retreatment rates are higher after 8 Gy treatment by a factor of 2-3.**
 - (D) single dose 8 Gy treatment provides less pain relief than treatment regimens of 30 Gy in 10 fractions.

Rationale: Retreatment rates are higher after 8Gy fractionation therapy compared with longer schedules. 8 Gy fraction therapy provides similar pain relief to longer treatment regimens. Response rates are better when the initial pain scores are lower. There is no consistent dose-response relationship for palliation of bone metastases.

References: Wm. Hartsell and S. Yajnik, Palliation of Bone Metastases, (2013) p. 1788, Perez & Brady's Principles and Practice of Radiation Oncology.

165. The MOST common site of an extramedullary plasmacytoma is:

- (A) gastric.
- (B) head and neck.**
- (C) respiratory.
- (D) hepatic.

Rationale: The head and neck region is the most common site of an extramedullary plasmacytoma.

References: Gunderson, L.L & Tepper, J.E., Clinical radiation oncology, (2000) p. 1193.

166. What is the next appropriate management step for a T3N0 anal squamous cell carcinoma with significant shrinkage during chemoradiation, but with a persistent palpable mass on DRE at 4 weeks post-treatment?

- (A) Additional radiation boost
- (B) Biopsy of the residual anal cancer
- (C) Continue to monitor every 4-8 weeks**
- (D) Send for surgical evaluation for APR

Rationale: It is recommended to continue close follow-up of anal cancer patients after completion of chemoradiation. Should the tumor regress, the patient can continue to be monitored. If the tumor is not regressing or there is any growth of the tumor, biopsy should be performed and possible APR depending on the biopsy results. Additional radiation therapy would not be warranted 2 months after the primary course of treatment completed.

References: NCCN Clinical Practice Guidelines in Oncology.

167. In the ARTIST study, chemoradiation was associated with an improved DFS among gastric cancer patients with:

- (A) N0 disease.
- (B) N1 disease.**
- (C) R0 resection.
- (D) R1 resection.

Rationale: The ARTIST (Adjuvant Chemoradiation Therapy in Stomach Cancer) trial was the first phase III to investigate the role of postoperative chemoradiotherapy therapy in patients with curatively resected gastric cancer with D2 lymph node dissection. This trial was designed to compare postoperative treatment with capecitabine plus cisplatin (XP) versus XP plus radiotherapy with capecitabine (XP/XRT/XP). Overall, the addition of XRT to XP chemotherapy did not significantly prolong disease-free survival. However, in the subgroup of patients with pathologic lymph node metastasis at the time of surgery, patients randomly assigned to the XP/XRT/XP arm experienced superior DFS when compared with those who received XP alone (P =0.0365).

References: Lee et al., Lee et al., (2012) pp. 368-273.

168. For I-125, after 10 months what percentage of activity remains?

- (A) 1
- (B) 3**
- (C) 5
- (D) 7

Rationale: I-125 has a half life of approximately 59.4 days, or approximately 60 days. Ten months of decay represents approximately 5 half lives, so the activity of the source will be $(1/2)^5=0.031$, or 3.1%.

References: Khan, Physics of Radiation Therapy, (2003) -

169. What was the 5-year pelvic control rate for FIGO Stage I vaginal cancers treated with definitive radiation, as reported by Frank et al. (MD Anderson)?

- (A) 79%
- (B) 86%**
- (C) 89%
- (D) 92%

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., pp. 138-47.

170. Based on the CROSS study, what is the pathologic complete response rate (%) for patients with squamous cell carcinoma of the esophagus treated with neoadjuvant chemoradiation?

- (A) 8
- (B) 23
- (C) 35
- (D) 49**

Rationale: A pathologic complete response was seen in 18 of 37 (49%) of patients with squamous cell carcinomas.

References: Van Hagen et al., Preoperative Chemoradiotherapy, (2012) pp. 2074-2084.

171. What is the biologic rationale for hypofractional radiotherapy for prostate cancer?

- (A) Low α/β**
- (B) Tumor hypoxia
- (C) Tumor microenvironment
- (D) Rapid repopulation of cancer

Rationale: Low alpha/beta ratio of prostate cancer makes it sensitive to high radiation dose per fraction with SBRT

References: Brenner DJ, Hall EJ., Fractionation and protraction for radiotherapy of prostate carcinoma, (1999) p. 1095-1101.

172. Which lymph node station is LEAST likely to be involved for an adenocarcinoma of the distal gastric antrum?

- (A) Celiac
- (B) Subpyloric
- (C) Splenic hilum**
- (D) Greater curvature

Rationale: For patients with distal gastric tumors, the risk of splenic lymph node involvement is <10%.

References: Smalley et al., Gastric Surgical Adjuvant Radiotherapy Consensus Report: Rationale and Treatment Implementation, (2002) pp. 283-93.

173. What is the five year estimated OS percent for children and adolescents diagnosed with Hodgkin lymphoma?

- (A) 60-70
- (B) 70-80
- (C) 80-90
- (D) >90**

References: Children's Oncology Group's 2013 Blueprint for Research: Hodgkin lymphoma, (2013) Vol 60; pp. 972-978.

174. Which of the following field borders would NOT be appropriate for preoperative radiation of cT4N0 rectal cancer (with direct extension into the prostate gland)?

- (A) Inferior border 4cm distal to the tumor
- (B) Superior border at the L5-S1 interspace
- (C) Posterior border 1.5cm behind the sacrum
- (D) Anterior border behind the pubic symphysis**

Rationale: For T4 disease with invasion of anterior structures, the anterior border of the radiation field should be anterior to the pubic symphysis in order to cover the external iliac lymph nodes.

References: Minsky B et al, Rectal cancer, (2012).

175. Which of the following isotopes has a half-life of 17 days?

- (A) I-125
- (B) Cs-131
- (C) Ir-192
- (D) Pd-103**

Rationale: Prostate Brachytherapy is routinely completed with either LDR or HDR brachytherapy based on radioisotope characteristics. The long half-life of Cs-137 makes it inappropriate for this purpose and Ir-192 is best suited for temporary implant with HDR. Both I-125 and Pd-103 are common LDR permanent implant isotopes based on the short half-life of approximately 60 days and 17 days respectively.

References: Nori D, Merimsky O, Osian AD, Heffernan M, Cortes E, Turner JW, Palladium-103: a new radioactive source in the treatment of unresectable carcinoma of the pancreas: a phase I-II study, (1996) pp. 300-5.

176. Which single agent chemotherapy has been shown to be effective for stage I testicular seminoma?

- (A) Bleomycin
- (B) Etoposide
- (C) Ifosfamide
- (D) Carboplatin**

Rationale: Carboplatin has been shown to be the single agent chemotherapy effective for Stage I seminoma.

177. For a 1.45 cm^3 target volume treated with SRS, the prescription isodose volume is 1.80 cm^3 and the half prescription isodose volume is 5.7 cm^3 . What is the volume (in cm^3) of normal tissue receiving at LEAST 50% of the prescription dose?

- (A) 1.24
- (B) 3.90
- (C) 4.25**
- (D) 5.70

Rationale: The PIV_{half} encompasses both the normal tissues and tumor. Since the tumor volume is not classified as normal tissue, the resulting normal tissue receiving at least the 50% of the prescription dose is $5.7 \text{ cm}^3 - 1.45 \text{ cm}^3 = 4.25 \text{ cm}^3$.

References: Paddick I, Lippitz B, A simple dose gradient measurement tool to complement the conformity index, (2006) pp. 194-201.

178. A rounded shoulder on a target volume cumulative DVH represents:

- (A) hot spots within a target volume.
- (B) an area of lower dose in the target volume.**
- (C) an area of uniform dose in the target volume.
- (D) sharp dose gradient at a target/normal tissue interface.

Rationale: This item requires knowledge of the DVH display of dose distribution. An ideal DVH shape for a target structure would be a straight vertical line at the prescription dose value indicating 100% of the target volume received the target dose. A DVH is a 2D (volume and dose) presentation of dose 3D dose distribution; there is no way to tell where in a particular structure the dose is cold or hot. A tail on a target DVH would represent a hot spot in the target volume.

References: Khan, Physics of Radiation Therapy, (2003) Chapter 19.

179. For standard 3D conformal radiotherapy, the lasers must accurately indicate the position of isocenter within:

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

Rationale: QA standards for radiotherapy facilities are defined in AAPM Task Group 142. For standard 3D conformal (non-IMRT) treatments, TG-142 states that laser accuracy of 2 mm is sufficient. For IMRT treatment delivery or SRS/SBRT, lasers should be aligned to indicate the position of isocenter to within 1 mm.

References: Klein et al., AAPM Task Group 142: Quality Assurance of Medical Accelerators, (2009).

180. Which of the following is NOT a potential long term complication of TBI?

- (A) Cataracts
- (B) Second malignancies
- (C) Late-onset renal failure
- (D) Low testosterone levels in men**

Rationale: Total body irradiation (TBI) can cause cataracts, second malignancies, late-onset cardiovascular and renal disease, and infertility in both men and woman. However, the dose range used for TBI is not high enough to cause hypogonadism in men.

References: Tichelli A, et al., Late complications after hematopoietic stem cell transplantation, (2009) pp. 583-601.

181. Oncotype DX analysis is appropriate for all of the following cases, EXCEPT:

- (A) T1N0 invasive ductal, ER+/PR+/Her2+.
- (B) T1N0 invasive ductal, ER-, PR-, Her2-.**
- (C) T1N1 invasive ductal, ER+, PR-, Her2-.
- (D) T1N0 invasive lobular, ER+, PR-, Her2+.

Rationale: Oncotype DX was a gene recurrence analysis validated initially on ER+ node negative breast cancer patients from NSABP B-14. This study evaluated the benefit of adjuvant tamoxifen in patients with ER+, node negative disease. Similar findings were validated with node positive, ER+ breast cancer patients from the data bases of ECOG 2197 and SWOG 8814. In these studies, the patients were treated with chemotherapy and tamoxifen. Limited retrospective study of Oncotype DX applied specifically to lymph node negative, ER + lobular histology patients confirms usefulness of this tool.

References: Goldstein, et al., Prognostic utility of the 21 gene assay compared with Adjuvant! in hormone receptor positive operable breast cancer patients with 0-3 positive nodes treated with adjuvant chemohormonal therapy: (2007).

Paik, S. et al., A multigene assay to predict recurrence of tamoxifen-treated, node –negative breast cancer, (2004) pp. 2817-2826.

Albain, E. et.al., Prognostic and predictive value of the 21 gene recurrence score assay in postmenopausal, node +, ER+ breast cancer (S8814, INTO100). [Abstract 100], (2007).

Deneve, J.L. et al., Results of Oncotype DX in early stage invasive lobular carcinoma, (2011).

182. The Internal Margin (IM) used in treatment planning related to other planning volumes accounts for:

- (A) 1-2 mm margin around PTV for internal motion.
- (B) microscopic disease extension from the GTV.
- (C) uncertainty in initially positioning.
- (D) variation in size, shape and position of CTV in relation to anatomy.**

Rationale: The CTV to PTV margin is composed of both a Setup Margin (SM) and IM. The SM accounts for uncertainty in the patient-beam positioning. Microscopic disease extension from GTV is accounted for in the CTV. No additional planning margins are placed on the PTV.

References: ICRU 50: Prescribing, Recording and Reporting Photon Beam Therapy, (1993).

183. Which structures should be included in the initial pelvic radiation field of a male patient receiving radiation therapy for bladder preservation?

- (A) Bladder, external iliac, and internal iliac lymph nodes
- (B) Bladder, prostate, external iliac, and internal iliac lymph nodes**
- (C) Bladder, prostate, external, internal, and common iliac lymph nodes
- (D) Bladder, prostate, external, internal, common iliac, and lower para-aortic lymph nodes

Rationale: The initial pelvic radiation field should encompass the bladder, prostate (and the prostatic urethra), internal and external iliac lymph nodes.

References: Perez & Brady's Principles and Practice of Radiation Oncology.

184. What is the tolerance dose (Gy) of the distal vagina?

- (A) 45-50
- (B) 60-70**
- (C) 80-90
- (D) 120-150

Rationale: The distal and mid vagina are substantially more sensitive to radiation compared to the upper vagina. As such the location of the tumor must be taken into consideration during radiation treatment planning.

References: Erickson-Wittman et al., Biologic and Physical Aspects of Radiation Oncology in Principles and Practice of Gynecologic Oncology, (2009).

185. Regarding Langerhans cell histiocytosis:

- (A) the course of the disease is often unpredictable.**
- (B) patients with multi-organ disease do not benefit from chemotherapy.
- (C) multiple organ involvement is most common in children over 10 years of age.
- (D) children with involvement of a single bone require chemotherapy and radiation.

Rationale: Localized disease may be effectively treated with only surgery or radiation.

References: Badalian-Very, G. et al., Recent advances in the understanding of Langerhans cell histiocytosis, (2011) -DOI: 10.1111/j.1365-2141.2011.08915.x.

186. Ipilimumab is a targeted agent that acts synergistically with radiotherapy by:
- (A) sensitizing tumor cells to radiotherapy by inhibiting DNA repair pathways.
 - (B) sensitizing tumor cells to radiotherapy by inhibiting cytotoxic T cell lymphocytes.
 - (C) increasing the immune response to tumor antigens released after radiotherapy.**
 - (D) increasing radiotherapy effectiveness by improving tumor oxygenation.

Rationale: Ipilimumab (Yervoy) is a monoclonal antibody that works by enhancing T-cell activity by modifying the Cytotoxic T-Lymphocyte Antigen 4 (CTLA-4) inhibitory receptor. The activated T-cells increase the immune response to antigen-presenting tumor cells. Radiotherapy can increase the immune response even further by releasing tumor cell-associated antigens into the microenvironment.

References: Postow MA, et al., Immunologic correlates of the abscopal effect in a patient with melanoma, (2012) pp. 925-931.

187. What was the key finding of RTOG 0617, a phase III trial exploring high dose (74 Gy) chemoradiation vs. standard dose (60 Gy) chemoradiation (+/- cetuximab) for patients with locally advanced NSCLC?

- (A) Local control was superior for the 74 Gy arm
- (B) OS was superior for the 60 Gy arm**
- (C) OS was superior for the 74 Gy arm
- (D) Equivalent treatment related toxicities in both arms

Rationale: In this pivotal trial, patients were randomly assigned to high dose (74 Gy) radiation vs. standard dose (60 Gy) chemoradiation, and then secondarily randomized to +/- cetuximab. Early results showed a paradoxical improvement in local control and overall survival for the 60 Gy arm. Chemotherapy was weekly carbo/taxol. No benefit was seen with the addition of cetuximab.

References: Bradley et al., N/A (4), (2012).

188. Over the last 50 years, public health concerns related to heritable effects of radiation have:

- (A) decreased, while those related to carcinogenesis have increased.**
- (B) decreased, while those related to carcinogenesis have remained the same.
- (C) increased, while those related to carcinogenesis have decreased.
- (D) remained unchanged, while those related to carcinogenesis have increased.

Rationale: Data from Drosophila experiments during the first half of the 20th century indicated a fairly high risk for radiation-induced mutations. These risk estimates were reduced over time as mutagenesis data in rodents became available. At the same time, the perception of risk for radiation carcinogenesis increased, especially in light of long-term data from the Japanese A-bomb survivors.

References: Hall, E.J., Radiobiology for the Radiologist, (2012) Chapters 10 and 11.

189. Which protein is involved in the G2 phase cell cycle checkpoint, but NOT in the G1 phase cell cycle checkpoint?

- (A) pRb
- (B) p21
- (C) Cdk1**
- (D) RAD50

Rationale: The Cdk1 (“cyclin dependent kinase 1”) protein, along with its partner Cyclin B, form a complex that phosphorylates target proteins and ultimately results in cell cycle progression from G2 phase into mitosis. G2 arrest occurs when the activity of the Cdk1/Cyclin B complex is inhibited, typically by upstream inhibition of the Cdc25C phosphatase. Of the remaining answer options, all are involved in the G1 or S phase checkpoints only, or else participate in multiple checkpoint pathways (e.g., p21).

References: Hall, E.J., Radiobiology for the Radiologist, (2012) Chapter 22, Figure 22.2.

190. Which of the following proteins is a well-characterized therapeutic target based on its ability to promote tumor angiogenesis?

- (A) VEGF receptor 1
- (B) VEGF receptor 2**
- (C) EGF receptor 1
- (D) EGF receptor 2

Rationale: The VEGF receptor 2 mediates many of the known cellular responses to VEGF, most notably, angiogenesis. The VEGF receptor 1 protein is produced by a wide variety of cell types, but is less well studied. It is thought to be involved with modulating VEGF receptor 2 signaling and can also act as a “decoy receptor” by sequestering VEGF from VEGF receptor 2 binding. The EGF receptors 1 and 2 are known to modulate other cellular phenotypes, including migration, adhesion and proliferation

References: Cébe-Suarez S, Zehnder-Fjällman A, Ballmer-Hofer K., The role of VEGF receptors in angiogenesis complex partnerships, (2006).

Holmes K, Roberts OL, Thomas AM, Cross MJ., Vascular endothelial growth factor receptor-2: structure, function, intracellular signaling and therapeutic inhibition, (2007) pp. 2003-2012.

191. Which radiologic staging studies would you recommend for a stage T1c, Gleason 6, PSA 4.5 prostate cancer?

- (A) Bone scan
- (B) CT scan of the abdomen and pelvis
- (C) No additional staging studies are necessary**
- (D) MRI scan of the pelvis with an endorectal coil

Rationale: According to the NCCN guidelines, patients with low-risk prostate cancer do not need additional staging studies.

References: NCCN Clinical Practice Guidelines in Oncology.

192. Which of the following options would be MOST appropriate after TURBT for a high grade stage 1 transitional cell cancer of the bladder?

- (A) Observation
- (B) Intravesicular BCG**
- (C) Intravesicular mitomycin C
- (D) Cisplatin and radiation to 63 Gy

Rationale: The risk of recurrence in this setting would likely be greater than 50% thus observation would not be preferred routinely. While mitomycin C is useful in reducing risk of recurrence in low grade Ta tumors, higher grade or invasive T1 disease has a lower risk of recurrence with BCG over mitomycin C. The role for non-muscle invasive cancer to be treated with chemotherapy and radiation is not standard of care.

References: Sylvester RJ, Oosterlinck W, van der Meijden AP., A single immediate postoperative instillation of chemotherapy decreases the risk of recurrence in patients with stage Ta T1 bladder cancer: a meta-analysis of published results of randomized clinical, (2004) pp. 2186-90.

193. Regarding the HIF-1 transcription factor:

- (A) HIF-1 α down-regulates genes associated with cell motility, invasion, and metastasis.
- (B) HIF-1 α must be stabilized by hydroxylation before it can act as a transcription factor.
- (C) HIF-1 β must be transported from the cytoplasm to the nucleus.
- (D) reoxygenation induces its activity, causing production of pro-angiogenic cytokines.**

Rationale: In addition to its role as an oxygen sensor and regulator of angiogenesis, HIF-1 has also been implicated in tumor radioresistance. HIF-1 is activated in response to other cellular stressors besides hypoxia, including an excess of reactive oxygen species as would be produced by tumor reoxygenation that occurs after irradiation. This, in turn, leads to the activation of angiogenic cytokines that help protect tumor vasculature – vascular endothelial cells in particular – from radiation injury.

References: Dewhirst MW, Cao Y and Moeller B, Cycling hypoxia and free radicals regulate angiogenesis and radiotherapy response, (2008) pp. 425-437.

Semenza, G.L., Defining the role of hypoxia-inducible factor 1 in cancer biology and therapeutics, (2010) pp. 625-634.

194. In RTOG 9408, for patients with non-bulky localized prostate cancer and an initial PSA \leq 20 ng per mL or less, the addition of short-term androgen deprivation was associated with:

- (A) **increased overall survival.**
- (B) decreased treatment toxicity.
- (C) no difference in biochemical failure.
- (D) no difference in disease-specific mortality.

Rationale: With a median follow-up period of 9.1 years, RTOG 94-08 showed that the 10-year rate of overall survival was 62% among patients receiving radiotherapy plus short-term androgen deprivation as compared with 57% among patients receiving radiotherapy alone.

References: Jones CU, Hunt D, McGowan DG, et al., Radiotherapy and short-term androgen deprivation for localized prostate cancer, (2011) p. 107-118.

195. What is the Grade 2 hematologic toxicity associated with a V40 for bone marrow $>37\%$ for cervical cancer treated with postoperative IMRT with concurrent Cisplatin?

- (A) 15%
- (B) 30%
- (C) 50%
- (D) **75%**

Rationale: IMRT has the potential to spare bone marrow over conventional radiation. RTOG 0418 is a prospective study to test the feasibility of delivering postoperative IMRT for cervical and endometrial cancer. Patients were treated to 50.4 Gy to the pelvic lymphatics and vagina. Endometrial cancer patients (43) received IMRT alone whereas the cervical cancer patients (40) received concurrent Cisplatin chemotherapy. Among cervical cancer patients with a V40 $> 37\%$, 75% had grade 2 or higher hematologic toxicity compared with 40% of patients with a V40 $\leq 37\%$ (p=.025).

References: Klopp, et al, Hematologic Toxicity in RTOG 0418: A Phase 2 Study of Postoperative IMRT for Gynecologic Cancer, (2013) pp. 83-90.

196. The risk of NSCLC in a smoker working in the asbestos industry increases by what factor?

- (A) 5 X
- (B) 10 X
- (C) 30 X
- (D) 60 X

Rationale: The risk of developing mesothelioma was described as 10% over the lifetime of an asbestos worker, with up to 70% of all mesothelioma cases involving documented asbestos exposure. Concomitant smoking enhances the risk of malignancy in an asbestos worker, with a 60-fold increased risk of developing non-small cell lung cancer. The chance of dying of a malignancy (mesothelioma or lung cancer) versus a nonmalignant cause is 50% in an individual exposed to asbestos compared to 18% in an individual not exposed. Asbestos workers are at highest risk, but family members can also be at risk via exposure to fibers brought home on the clothing of the primary individual.

References: Selikoff IJ, Hammond EC, Seidman H., Latency of asbestos disease among insulation workers in the United States and Canada, (1980) pp. 2736-2740.

197. Approximately 60 % of male urethra tumors occur in the:

- (A) fossa novicularis.
- (B) pendulous urethra.
- (C) prostatic urethra.
- (D) **bulbomembranous urethra.**

Rationale: Location rates are 59 % Bulbomembranous urethra, 34% penile urethra, 7% Prostatic Urethra.

References: Srinivas B, Khan SA, Male urethral cancer: A review, (1988) pp. 61-65.

198. When γ -rays ionize water, the immediate products are:

- (A) e^-_{aq} .
- (B) $OH^- + H^\bullet$.
- (C) $H_2O^+ + e^-$.
- (D) $H_3O^+ + OH^\bullet$.

Rationale: Gamma photons ionize water by removing an electron from the molecule. This leaves a water ion radical (H_2O^+) plus a fast electron (an ion pair). The water ion radical rapidly reacts with other water molecules to produce a hydronium ion (H_3O^+) and a hydroxyl radical (OH^\bullet). The electron released in the first reaction can bind to a water molecule forming an aqueous electron (e^-_{aq}). This in turn can react with additional water molecules to form hydrogen radicals (H^\bullet) and hydroxyl ions (OH^-).

References: Hall, E.J., Radiobiology for the Radiologist, (2012) Chapter 1.

199. Linear energy transfer (LET) is defined as the:

- (A) total amount of energy deposited per unit track length.
- (B) average amount of energy deposited per unit track length.**
- (C) average number of tracks needed to deposit a unit of energy.
- (D) specific energy of a charged particle depositing energy over a unit track length.

Rationale: The track average LET is calculated by dividing the particle's total track into equal length increments, and determining the average energy deposition in each increment. Please note that this is an average amount of energy deposited per unit track length; in reality, particular track length increments do not necessarily all receive exactly the same energy deposition. Specific energy refers to the energy of an incident charged particle, and not to the amount of energy deposited.

References: Hall, E.J., Radiobiology for the Radiologist, (2012) Chapter 7.

200. What is the FIGO stage of a fallopian tube cancer with pelvic extension?

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

Rationale: FIGO Stage II is a fallopian cancer that involves one or both tubes and has pelvic extension to uterus and/or ovaries (IIA), to other pelvic structures (IIB), pelvic extension with +washings/malignant ascites.

References: Staging Manual, NCCN Clinical Practice Guidelines in Oncology.

201. Compared with all molecular subtypes, which of the following statements is TRUE regarding triple negative breast cancer?

- (A) Higher risk of relapse after 5 years
- (B) Higher risk of LRR after mastectomy**
- (C) Higher probability of positive axillary lymph nodes
- (D) Higher probability of stage IV disease at diagnosis

Rationale: The Carolina Breast Cancer Study shows rates of positive axillary nodes for TNBC to be 41%, compared with 56% for HR-/Her2+, 34% for HR+, Her2- and 47% for HR+,Her2+ disease. Respective rates of Stage IV disease are 5%, 6%, 2% and 1%. Most risk for relapse occurs before 5 years with TNBC. Other subtypes continue to relapse far beyond 5 years. There is a higher rate of LRR for TNBC with BCT and mastectomy. TNBC is not a contraindication for breast conservation therapy. Noted is that TNBC is associated with a higher rate of BRCA1 mutation.

References: Abdulkarim, B.S. et al., Increase Risk of Locoregional Recurrence for Women with T1T2N0 Triple Negative Breast Cancer treated with Modified Radical Mastectomy without Radiation compared with Breast Conservation Therapy.

Dominici, L.S., et al., Implications of Constructed Biologic Subtype and its Relationship to Locoregional Recurrence Following Mastectomy, (2012) RB82.

Carey, L., et al., Race, Breast Cancer Subtypes, and Survival in the Carolina Breast Cancer Study, (2006) pp. 2492-2502.

Adkins, F.C.et.al., Triple Negative Breast Cancer is Not a Contraindication for Breast Conservation Therapy, (2011) pp. 3164-73.

202. The key finding of the EORTC trial (Kocher et al.) showed that whole brain radiotherapy after SRS or surgery for brain metastases improved:

- (A) local control.**
- (B) quality of life.
- (C) overall survival.
- (D) functional independence.

Rationale: The addition of WBRT, as compared to observation, following surgery or radiosurgery, did not improve overall survival, functionally independent survival or quality of life. Local control of the initial site is improved. Quality of life scores were better in the observation than in the WBRT arms.

References: Soffiatti R et al., A European Organisation for Research and Treatment of Cancer phase III trial of adjuvant whole-brain radiotherapy versus observation in patients with one to three brain metastases from solid tumors af, (2013) pp. 65-72.

Kocher, M. et al., Adjuvant whole-brain radiotherapy versus observation after radiosurgery or surgical resection of one to three cerebral metastases: results of the EORTC 22952-26001 study, (2011) pp. 134-41.

203. What dose (Gy) of prophylactic testicular irradiation should be used for a 10-year-old boy with newly diagnosed standard risk ALL?

- (A) 0
- (B) 12
- (C) 18
- (D) 24

Rationale: With the advent of high dose systemic therapy, prophylactic testicular radiation is no longer recommended. 24 Gy consolidative radiation is incorporated in patients who have experienced a testicular failure as part of the definitive treatment.

References: Halperin, Pediatric Radiation Oncology.

204. Which study compares incident cases in a group to a random group of normal participants?

- (A) Case control
- (B) Randomized control
- (C) Case-series
- (D) **Case-cohort**

Rationale: In a case-cohort study, all incident cases in a cohort are compared to a random cohort of normal participants. A case control study is an observational study in which two existing groups differing in outcome are identified and compared on the basis of some possible causal attributes. A randomized control study is designed to compare treatment groups with control groups. Case-series study tracks patients with a given phenotype over time.

References: Brasky TM et al, No title, (2013).

205. Postoperative radiation for ureteral cancer with a positive margin improves local control by what percentage versus observation?

- (A) 5
- (B) 25
- (C) **50**
- (D) 75

Rationale: Though an infrequent malignancy, wide surgical resection margins are difficult to achieve and local recurrence risk can be improved with post-operative radiation with or without systemic chemotherapy.

References: Cozad, Cozad, (1992) pp. 743-5.

206. A patient had an initial sodium of 120 and a subsequent of 126. Has the patient become less hyponatremic?

- (A) No
- (B) Yes
- (C) Insufficient information: need SD**
- (D) Insufficient information: need median

Rationale: In order to answer this question you need to know the analytical variation of the lab's sodium analysis. If the standard deviation for this sodium control is 0.5 mmol/L, three times 0.5 mmol/L is 1.5 mmol/L. Since the observed change (6 mmol/L) is greater than 1.5 mmol/L, you can be 95% confident that the patient's sodium has increased to a degree which can be detected analytically.

References: Clinical Laboratory Statistics, <http://ucsdlabmed.wikidot.com/chapter-1>.

207. Which statement about the use of heat shock protein 90 (Hsp90) small molecule inhibitors as radiation sensitizers is TRUE?

- (A) Different Hsp90 inhibitors are uniform in their biological effects.
- (B) More than 40 Phase I-III clinical trials with Hsp90 inhibitors have been completed to date, and others are ongoing.**
- (C) Loss of Hsp90 chaperone function would not cause degradation of large, multi-unit proteins or multi-protein complexes.
- (D) A cocktail of different Hsp90 inhibitors would be required to effectively target multiple oncogenic kinases and transcription factors.

Rationale: More than 40 Phase I-III clinical trials have already been completed using Hsp90 inhibitors in combination with radiation and/or chemotherapy. Additional clinical trials are ongoing. Heat shock protein 90 (Hsp90) is a molecular chaperone upregulated in response to cellular stress, and is among the most abundant proteins expressed in cells. The functions of Hsp90 include assisting in protein folding, transport, stabilization and degradation (through the ubiquitin–proteasome pathway) in response to stress (e.g., heat shock, exposure to DNA damaging agents, etc.). Hsp90 stabilizes a number of oncoproteins involved in tumor survival and growth, including many signal transduction kinases and some transcription factors. Thus, inhibition of Hsp90 could lead to the simultaneous depletion of a multiple oncoproteins, which makes the development of Hsp90 inhibitors particularly attractive.

All of the clinical Hsp90 inhibitors studied to date are specific in their target, i.e. they bind exclusively to Hsp90 and two related heat shock proteins. However, Hsp90 inhibitors are markedly pleiotropic, causing degradation of over 200 client proteins and impacting critical multiprotein complexes.

References: Kabakov, A.E., Kudryavtsev, V.A., Gabai, V.L., Hsp90 inhibitors as promising agents for radiotherapy, (2010) pp. 241-247.

208. Which of the following imaging studies is MOST helpful in detecting seminal vesicle invasion in prostate cancer?

- (A) CT scan with contrast
- (B) FDG PET
- (C) MRI with T2 imaging**
- (D) Capromab pendetide SPECT

Rationale: While all four studies may be used for staging, only MRI will provide the level of soft tissue contrast required to see disease extending beyond the gland. MRI is playing an important role in prostate planning and even image guidance with the advent of parametric sequences as well, and may potentially evolve as the primary image of choice for prostate treatments.

References: McKenna DA et al., Prostate cancer: role of pretreatment MR in predicting outcome after external-beam radiation therapy--initial experience, (2008) pp. 141-6.

209. Approximately what percentage of penile cancer is positive for HPV DNA?

- (A) 50
- (B) 65
- (C) 80**
- (D) 90**

Rationale: In a large population-based case-control study “HPV DNA was detected in 79.8% of tumor specimens, and 69.1% of tumors were HPV16-positive. The proportion of HPV DNA-positive tumors did not vary by any risk factors evaluated. Many risk factors were common for both in situ and invasive disease. However, 3 factors that did not increase the risk for in situ cancer proved significant risk factors for invasive penile cancer: lack of circumcision during childhood, phimosis and cigarette smoking.”

References: J.R. Daling, M.M. Madeleine, L.G. Johnson et al., Penile cancer: importance of circumcision, human papillomavirus and smoking for in situ and invasive disease, (2005) pp. 606-616.

210. When treating PALN in cervical cancer with conventional fractionation the TD5/5 for the duodenum should be:

- (A) 50 Gy.
- (B) 55 Gy.
- (C) 60 Gy.
- (D) 65 Gy.

Rationale: Emami estimated that the TD5/5 for 1/3 of the bowel is 50 Gy; 3/3 is 40 Gy. TD 50/5 for 1/3 is 60 Gy and 3/3 is 50 Gy. Stanic and Mayadev recommended that the maximum dose to the small bowel should be kept less than 55 Gy and agreed with the TD 5/5 as reported by Emami.

References: Emami et al, Tolerance of normal tissue to therapeutic irradiation, (1991) pp. 109-122.

Stanic and Mayadev, Tolerance of Small Bowel to Therapeutic Irradiation A Focus on Late Toxicity in Patients Receiving Para-Aortic Nodal Irradiation for Gynecologic Malignancies, (2013) pp. 592-597.

211. What percent of women with a deleterious mutation in BRCA-1 will develop ovarian cancer by the age of 70?

- (A) 15 - 20
- (B) 25 - 30
- (C) 35 - 45
- (D) 50 - 75

Rationale: About 50 to 65% of women with BRCA 1 mutation will develop breast cancer by age 70 and 35 to 46% will develop ovarian cancer by the age of 70.

212. What is the expected 2-year overall cumulative incidence of both symptomatic and asymptomatic pelvic insufficiency fractures after definitive radiation for early stage cervical cancer?

- (A) 10%
- (B) 25%
- (C) 35%
- (D) 40%

Rationale: The 2 year pelvic insufficiency fracture cumulative occurrence rate was 36.9%. Patients with advanced age and low body weight may be at increased risk.

References: Tokumaru, et al., Insufficiency Fractures After Radiation Therapy for Uterine Cervical Cancer: An Analysis of Subjects in a Prospective Multi-Institutional Trial, and Cooperative Study of the Japan Radiation Oncology G, (2012).

213. What is the TNM stage of a cancer of the female urethra that extends to the vagina and has a 3 cm single LN?

- (A) T2N1M0
- (B) T2N2M0
- (C) T3N1M0
- (D) T3N2M0**

Rationale: A T3 cancer extends to the vagina and N2 spread due to size of LN.

References: AJCC Cancer Staging Manual, (2010).

214. Which of the following is NOT a sub-site of the supraglottic larynx?

- (A) Epiglottis
- (B) False vocal cords
- (C) Aryepiglottic fold
- (D) Pharyngoepiglottic fold**

Rationale: The pharyngoepiglottic fold is not part of the supraglottic larynx.

References: AJCC Cancer Staging Manual, (2010).

215. Acute lymphoblastic leukemia with a translocation of chromosomes 9:22:

- (A) confirms a non-ALL diagnosis.
- (B) has no prognostic significance.
- (C) is associated with a better survival.
- (D) is associated with a worse survival.**

Rationale: The translocation of 9:22 (Philadelphia chromosome) is a hallmark of CML, but it can also occur in patients with 5% of pediatric ALL patients with only a 20-30% long term control with conventional chemotherapy only. Ph+ ALL is an indication for allogeneic stem cell transplant at first remission, but tyrosine kinase inhibitors such as Imatinib may be as effective.

References: Halperin, Pediatric Radiation Oncology.

Oliansky DM et al., Role of cytotoxic therapy with hematopoietic stem cell transplantation in the treatment of pediatric acute lymphoblastic leukemia: update of the 2005 evidence-based review. Biol Blood Marrow Transplan, (2011) pp. 505-22.

216. When calibrating a linac using the TG-51 protocol, MU is defined as 1 cGy to what medium?

- (A) **Water**
- (B) Air
- (C) Lucite
- (D) Anthropomorphic phantom

Rationale: Knowledge of the definition of MU and linac calibration is necessary. According to TG-51 protocol, linacs are calibrated such that 1 MU delivers 1 cGy in water at a specific distance from the source, field size, and depth (referred to in the protocol as ‘reference conditions’).

References: Almond et al., AAPM Report 24 (TG-51): Protocol for clinical dosimetry of high-energy photon and electron beams, (1999).

217. Exposure to diagnostic X-rays in utero increases the relative risk of leukemia and solid cancers by a factor of approximately:

- (A) 1.0.
- (B) **1.5.**
- (C) 3.5.
- (D) 5.0.

Rationale: In its 1990 publication on low dose radiation effects, the BEIR committee recommended a lifetime excess relative cancer risk of about 1.5 for persons exposed to diagnostic X-rays in utero. This is due to the greater sensitivity of embryos and fetuses to radiation-induced effects.

References: Committee on the Biological Effects of Ionizing Radiation, National Research Council, Health Effects of Exposure to Low Levels of Ionizing Radiation, (1990).

218. Which of the following systems is the MOST secure option for backup of data from a treatment planning system?

- (A) A second hard drive on the treatment planning server
- (B) **A redundant archival facility that is located offsite**
- (C) An external hard drive stored in the Physicist's office
- (D) A USB flash drive that is kept next to the treatment planning station for quick access.

Rationale: The most secure way to archive data is through the use of a dedicated off-site facility.

References: Fraass et al., Task Group 53 report on quality assurance for clinical radiotherapy treatment planning, (1998) Vol. 25, No. 10.

219. A histologic criteria for a WHO grade II atypical meningioma is:

- (A) Rhabdoid features.
- (B) 0 to 3 mitotic figures per 10 HPF.
- (C) 4 to 19 mitotic figures per 10 HPF.**
- (D) 20 or more mitotic figures per 10 HPF.

Rationale: Greater than 20 mitotic figures per 10 HPF or rhabdoid features are among the criteria for a grade III (anaplastic/malignant) meningioma.

References: World Health Organization (WHO), 2007 WHO Classification of Brain Tumors, (2007).

220. Clinical outcomes for radiotherapy patients with persistently hypoxic tumors are typically worse because hypoxia:

- (A) selects for tumor cells with more aggressive phenotypes.**
- (B) stimulates compensatory tumor cell repopulation.
- (C) prevents the formation of toxic reactive oxygen species.
- (D) activates pro-apoptotic signaling pathways in tumor cells.

Rationale: Tumor hypoxia develops secondary to abnormalities in tumor vasculature and the tendency for tumors to outgrow their own blood supply. Hypoxia does activate pro-apoptotic signaling pathways in normal cells, however tumor cells, due to genomic instability, typically have lost these pathways. Hypoxia per se does not stimulate tumor cell proliferation, although reoxygenation of previously hypoxic cells can. What hypoxia (in particular, cycles of hypoxia and reoxygenation) does do however is cause genomic instability, which in turn tends to select for tumor cells that are already resistant to apoptotic cell death, are more invasive and more metastatic.

References: Brown JM, Wilson WR, Exploiting tumor hypoxia in cancer treatment, (2004) pp. 437-447.

221. According to the updated QUANTEC, what mean dose (Gy) to the whole lung with 3D-CRT would result in a 5% risk of symptomatic pneumonitis?

- (A) 7**
- (B) 13
- (C) 20
- (D) 24

Rationale: The risk of symptomatic radiation pneumonitis increases with the dose of radiation. Mean dose 7 Gy to whole lung would have 5% risk, 13 Gy 10%, 20 Gy 20% and 24 Gy 30%. To limit V20 < 30% would have the risk less than 20% risk.

References: Marks, L.B. et al., Use of Normal Tissue Complication Probability Models in the Clinic, (2010) pp. S10-S19.

222. Which of the following was a finding of the GYNECO 02 study that compared hysterectomy with no hysterectomy in patients that had a clinical and radiological complete response after chemoradiation for Stage IB2 and II cervical cancer?

- (A) Local failure rate was high without hysterectomy
- (B) 1/3 had residual disease in the hysterectomy specimen**
- (C) Hysterectomy improved survival in patients with residual disease
- (D) MRI and clinical exam are an accurate measure of response after CRT

Rationale: The trial was conducted by the Federation Nationale des Centres de Lutte Contre le Cancer in France. The main endpoint of the study was the 3 year event free survival rate. Unfortunately the trial closed because of poor accrual. Although the study was underpowered it is important because of some of the interesting results that were observed. The first important finding is that nearly one third of the patients undergoing hysterectomy (10 of 31) with a clinical and imaging complete response were found to have residual disease in the surgical specimen. Five had active tumor (3 < 1 cm and 2 > 1cm) the remainder had microscopic residual. This was interpreted as the lack of accuracy of MRI combined with clinical exam. Most of the recurrences were nodal rather than paracentral.

References: Morice, et al., Results of the GYNECO 02 Study, an FNCLCC Phase III Trial Comparing Hysterectomy with No Hysterectomy in Patients with a (Clinical and Radiological) Complete Response After Chemoradiation Therapy for, (2012) pp. 64-71.

223. Which of the following sign or symptom is associated with thymomas?

- (A) B symptoms
- (B) Abnormal CBC**
- (C) Proximal muscle weakness that improves with activity
- (D) Syndrome of Inappropriate Antidiuretic Hormone (SIADH)

Rationale: Low blood count due to Pure Red Cell Aplasia is a common paraneoplastic disorder associated with thymomas (5-15%). SIADH or Lambert Eaton Syndrome (proximal muscle weakness that improves with activity) is not associated with thymomas. B symptom is often associated with lymphomas.

224. Which of the following is appropriate for generating a preliminary hypothesis for the cause of a particular disease?

- (A) Cohort study
- (B) Clinical trial
- (C) Case-control study**
- (D) Cross-sectional study

Rationale: A case-control study is an observational study that begins with patient cases who have the outcome or disease being investigated and control subjects who do not have the outcome or disease. It then looks backward to identify possible precursors or risk factors.

References: Dawson B and Trapp RG, Basic and Clinical Biostatistics, (2004) p. 333 and 404.

225. A T-3 cancer of the endometrium invades the:

- (A) bladder.
- (B) rectum.
- (C) parametrium.**
- (D) deep myometrium.

Rationale: The most recent staging criteria gives T3 designation to tumors that involve the serosa, adnexa, vaginal or parametria.

References: AJCC Cancer Staging Manual, (2010) 7th edition.

226. Withers' skin colony assay requires that a "moat" of necrosis surround an "island" of keratinocytes to be irradiated because the:

- (A) moat prevents the migration of cells from outside the radiation field into the island.**
- (B) dying cells in the moat provide a feeder layer for the surviving cells in the island.
- (C) dying cells in the island are absorbed into the moat, leaving more room for survivors to repopulate.
- (D) cytokines released by the dying cells in the moat stimulate repopulation of the surviving cells in the island.

Rationale: In order for the skin colony assay to properly assess clonogenic survival of irradiated epithelial cells, it is necessary to minimize artifacts that could interfere with the measurement of inherent radiosensitivity. Migration and proliferation of clonogenic cells from outside the radiation field would artificially increase the surviving fraction of cells in the irradiated island. To prevent this from happening, a moat of necrosis is used to isolate the island.

References: Hall, E.J., Radiobiology for the Radiologist, (2012) Chapters 3 and 20.

227. About what percent of limited stage SCLC by conventional staging may be upstaged by FDG-PET?

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

Rationale: FDG-PET correctly upstaged 8.3% of patients to extensive-stage disease (initially diagnosed with limited disease small-cell lung cancer based on conventional staging). PET identified unsuspected regional nodal metastasis in six (25%) of 24 patients, and the radiation therapy plan was significantly altered to include the PET-positive/CT-negative nodes within the high-dose region in each of these patients. PET correctly identified tumor in each small-cell lung cancer mass (primary or nodal) that was suspected on computed tomography (CT) imaging, thus giving a lesion-based sensitivity relative to CT of 100%. FDG-PET has high sensitivity for small-cell lung cancer and appears to be of value for initial staging and treatment planning of patients with presumed limited-stage disease.

FDG-PET scan detected additional lesions in patients diagnosed as having limited-stage small-cell lung cancer by conventional staging procedures. The therapeutic strategies were changed in 8% of patients based on the results of FDG-PET. FDG-PET scan is recommended as an initial staging tool for patients with this disease.

References: Bradley, J.D. et al., Positron emission tomography in limited-stage small-cell lung cancer: a prospective study, (2004) pp. 3248-3254.

Niho, S. et al., Detection of unsuspected distant metastases and/or regional nodes by FDG-PET [corrected] scan in apparent limited-disease small-cell lung cancer, (2007) pp. 328-33.

228. The yield of PET/CT scan in detecting a primary cancer for patients presenting with cervical lymph node metastasis of unknown origin has been shown to be approximately:

- (A) 5%.
- (B) 15%.
- (C) 30%.
- (D) 50%.

Rationale: A prospective study of 18FDG-PET in the detection and management of patients with lymph node metastases to the neck from an unknown primary tumor from the DAHANCA-13 group showed a detection rate of approximately 30%.

References: Johansen, J. et al., Prospective study of 18FDG-PET in the detection and management of patients with lymph node metastases to the neck from an unknown primary tumor. Results from the DAHANCA-13 study, (2008) pp. 471-8.

229. For a course of spinal cord irradiation with 35 Gy in 2.5 Gy fractions 2 years prior, a 50% recovery of spinal cord tolerance is assumed. For re-irradiation, which dose fractionation scheme would be the safest? (Assume a cumulative, maximally tolerated dose of 25 x 2 Gy per fraction to 50 Gy, and an α/β ratio of 3 Gy.)

- (A) 21 Gy in 3 daily fractions
- (B) 27 Gy in 9 daily fractions
- (C) 30 Gy in 15 daily fractions**
- (D) 36 Gy in 24 twice daily fractions

Rationale: Fifteen fractions of 2 Gy QD to a total dose of 30 Gy would be the safest option in this case. First, calculate the equivalent dose in 2 Gy fractions (EQD2, based on an α/β ratio of 3 Gy), for the original treatment course of 35 Gy using 2.5 Gy per fraction. The $EQD2/3 = 38.5$ Gy. Then, assuming 50% tolerance dose recovery, the retreatment dose should not exceed 50 Gy - 19.25 Gy = 30.75 Gy (in 2 Gy fractions). Answer option C is the closest, that is, 30 Gy in 15 fractions of 2 Gy.

References: Bentzen et al., Bentzen et al., (2012) pp. 266-268.

Nieder et al., Nieder et al., (2006) pp. 1446-1449.

Hall, E.J., Radiobiology for the Radiologist, (2012) Chapters 23 and 25.

230. According to ACOSOG Z1071, the false negative rate of sentinel node biopsy among patients receiving neoadjuvant chemotherapy with node positive breast cancer is:

- (A) 6.6%.
- (B) 9.6%.
- (C) 12.6%.**
- (D) 15.6%.

Rationale: The study includes patients with T0-T4, N1-N2 disease. The false negative rate is 12.6%. There is a 95% probability that the false negative rate lies in the range of 9.4 – 16.7%

References: San Antonio Breast Cancer Symposium, (2012).

231. For which of the following squamous cell carcinoma of the skin is primary surgery preferred over radiation?

- (A) A 2 cm lesion on the vertex scalp**
- (B) When involving more than 1/3 of lower lip
- (C) When involving oral commissures
- (D) A 1.5 cm lesion in the medial canthus

Rationale: Surgery and radiation would offer similar tumor control in skin squamous cell carcinoma. Patient selection for treatment modality is important. When functional and cosmetic outcomes are affected by surgery, radiation is preferred.

References: Veness MJ, Ang KK, Cutaneous Carcinoma, (2012) -In: Gunderson LLG, Tepper JE (eds). Clinical Radiation Oncology. 3rd edition. 2012; Saunders. p763.

232. Approximately what percent of Merkel cell cancer is due to the polyomavirus?

- (A) 40
- (B) 60
- (C) 80**
- (D) 100

Rationale: The fact that multiple independent laboratories have detected Merkel cell polyomavirus genomic sequences in tumor DNA in 75–80% of Merkel cell carcinoma specimens, together with the demonstration that viral DNA is clonally distributed in Merkel cell carcinoma and is present in primary tumors as well as paired metastases, provides evidence that Merkel cell polyomavirus has a function in Merkel cell carcinoma oncogenesis.

References: Duncavage, D.J., Zehnbaauer, B.A., Pfeifer, J.D., Prevalence of Merkel cell polyomavirus in Merkel cell carcinoma, (2009) pp. 516-521.

233. Tumor cells develop multi-drug resistance to chemotherapeutics by:

- (A) silencing genes associated with drug metabolism.
- (B) upregulating genes that code for DNA repair proteins.
- (C) overexpressing P-glycoprotein on their outer cell membranes.**
- (D) increasing hepatic detoxification and clearance of the chemotherapy drug(s).

Rationale: Tumor cells develop multi-drug resistance to chemotherapeutics by upregulating the MDR1 gene that codes for the energy-dependent, integral membrane transporter P-glycoprotein. The role of P-glycoprotein is to increase the efflux of chemotherapy drugs out of the cell, in particular, drugs derived from natural products (e.g., plant toxins).

References: Pastan I, Gottesman M, Multiple-drug resistance in human cancer, (1987) pp. 1388-1393.

Borst P, Jonkers J, Rottenberg S, What makes tumors multidrug resistant? (2007) pp. 2782-2787.

234. The region of interest in a beam profile for defining flatness is specified using which descriptor of the field width?

- (A) Nominal
- (B) Central 50%
- (C) Central 80%**
- (D) Central 90%

Rationale: Beam flatness is defined as the middle 80% of the radiation field, with an acceptable variation between minimum and maximum dose within that range of 3%. While 80% is smaller than the flat portion of most beam profiles, the limited range is selected to avoid the region containing the “horns”. The horns are peripheral hotspots, resulting from the shape of the flattening filter, that decrease in magnitude as profile depth increases due to beam hardening effects.

References: Khan, Physics of Radiation Therapy, (2003).

235. Regarding the recently updated results of RTOG 91-11, which of the following is TRUE regarding the endpoint of 10-year laryngectomy-free survival?

- (A) **No difference between sequential versus concurrent chemoradiation**
- (B) Favored sequential chemoradiation versus concurrent chemoradiation
- (C) Favored concurrent chemoradiation versus sequential chemoradiation
- (D) No difference between radiation alone versus concurrent chemoradiation

Rationale: The recently updated findings showed no difference in 10-year laryngectomy-free survival between the two chemoradiation arms, which were improved compared to the radiation alone arm.

References: Forastiere AA et al., Long-term results of RTOG 91-11: a comparison of three nonsurgical treatment strategies to preserve the larynx in patients with locally advanced larynx cancer, (2013) pp. 845-52.

236. Which of the following is the appropriate treatment for management of the neck in definitive radiotherapy for a T2N0M0 nasopharyngeal carcinoma?

- (A) Primary site radiation only
- (B) **The level V and retropharyngeal nodes should be included**
- (C) Ipsilateral nodal radiation if the primary is well-lateralized
- (D) Concurrent chemotherapy without supraclavicular irradiation

Rationale: Nasopharyngeal carcinoma is associated with a very high rate of nodal dissemination. At presentation, 60 to 90% of patients have nodal metastases and as many as 50% have bilateral involvement. Thus, treatment of the bilateral neck is the standard of care for nasopharyngeal carcinoma, even in patients that are clinically and radiographically node negative (1). There is characteristically a relatively high rate of retropharyngeal as well as posterior cervical nodal involvement compared to other sites in the head and neck (2). Imaging-based studies have estimated the incidence of retropharyngeal nodal metastases as 63% (3). These most commonly involve the lateral retropharyngeal nodes, occur at the level of C1 with steadily decreasing incidence caudally to the level of C3, occur in association with cervical lymphadenopathy, and are often bilateral.

References: Ang KK, Garden AS, Radiotherapy for head and neck cancers : indications and techniques, (2006) pp. 76-82.

Wang XS, Hu CS, Ying HM, et al., Patterns of retropharyngeal node metastasis in nasopharyngeal carcinoma, (2009) pp. 194-201.

Lindberg R, Distribution of cervical lymph node metastases from squamous cell carcinoma of the upper respiratory and digestive tracts, (1972) pp. 1446-1449.

237. What was the complete pathologic response in GOG 201 a Phase 2 study of concurrent weekly cisplatin and radiation in advanced carcinoma of the vulva?

- (A) 30%
- (B) 40%
- (C) **50%**
- (D) 60%

Rationale: This chemoradiation therapy study demonstrated a high complete pathologic response in patients with locally advanced vulva carcinoma who otherwise would have required major surgery.

References: Moore DH, Ali S, Koh WJ et al., A phase II trial of radiation therapy and weekly cisplatin chemotherapy for the treatment of locally-advanced squamous cell carcinoma of the vulva: A GOG study, (2012) pp. 529-33.

238. Ultrasound imaging is commonly used in radiation therapy for:

- (A) **localization of prostate for IGRT.**
- (B) breast simulation in larger patients.
- (C) post-treatment assessment of lung lesions.
- (D) pre-treatment localization for pediatric patients.

Rationale: US is commonly used to identify the relative positions of the prostate, bladder and rectum prior to IGRT treatment. US is not used for simulation or pediatric patients or lung lesions.

References: Khan, F.M. & Gerbi, B.J., Physics of Treatment planning, (2012) Chapter 2.

239. When should gemcitabine be administered to achieve its maximum radiosensitizing effect?

- (A) At the conclusion of radiotherapy
- (B) Simultaneous with each radiation dose
- (C) Within a few hours after each radiation dose
- (D) **Within a few hours before each radiation dose**

Rationale: Based on both laboratory and clinical studies, there is no evidence of gemcitabine radiosensitization when irradiation occurred prior to drug exposure; the greatest sensitizer enhancement ratio was observed when gemcitabine was administered for 24 h before irradiation. Gemcitabine is an analog of cytarabine (cytosine arabinoside) which acts both as a cytotoxin against human cancers, particularly pancreatic and non-small cell lung cancer, as well as a potent radiosensitizer.

References: Spalding, A.C., Lawrence, T.S., New and emerging radiosensitizers and radioprotectors, (2006) pp. 444-456.

Shewach, D.S., Lawrence, T.S., Antimetabolite radiosensitizers, (2007) pp. 4043-4050.

240. What is the expected 3-year survival rate for a 55-year-old patient with a 20-pack-year history of smoking who has a T3N2bM0, p16+ base of tongue squamous carcinoma?

- (A) 30%
- (B) 50%
- (C) 70%**
- (D) 90%

Rationale: This patient has a p16 positive squamous carcinoma of the oropharynx, which is a favorable prognostic factor (1,2). However, his heavy smoking history is a negative prognostic factor and per the analysis of Ang et al, he would be in the intermediate-risk group with a 3-year rate of overall survival of 70.8% (95% CI, 60.7 to 80.8) (1). There is a strong agreement between tumor HPV status as determined by in situ hybridization and expression of biomarker p16. Tumor p16 status is a well-established prognostic factor in oropharyngeal cancers (1,2).

References: Ang KK, Harris J, Wheeler R, et al., Human Papillomavirus and Survival of Patients with Oropharyngeal Cancer, (2010) pp. 24-35.

Fakhry C, Westra WH, Li S, et al., Improved Survival of Patients With Human Papillomavirus – Positive Head and Neck Squamous Cell Carcinoma in a Prospective Clinical Trial, (2008) pp. 261-269.

241. The MOST appropriate postoperative treatment for a 30-year-old female with stage T4aN1aM0 papillary thyroid carcinoma is:

- (A) observation.
- (B) radioactive iodine.**
- (C) EBRT.
- (D) radioactive iodine and EBRT.

Rationale: Patients younger than 45 years with papillary thyroid cancer have better prognosis. Their tumors take up iodine well, and in general, radioactive iodine after surgery is sufficient for those with high risk of local regional failure. External beam radiation may be recommended for patients older than age 45 if residual diseases are concerned.

References: Hay ID, Petersen IA, Foote RL., Thyroid cancer, (2012) In: Gunderson LLG, Tepper JE (eds). Clinical Radiation Oncology. 3rd edition. 2012; Saunders. p717.

Hay ID, Petersen IA, Foote RL, Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer, (2009) pp. 1167-1214.

242. Which of the following DNA damage assays is used to detect the presence of single strand breaks?

- (A) **Alkaline elution**
- (B) Comet assay
- (C) Neutral elution
- (D) Pulsed-field gel electrophoresis

Rationale: DNA filter elution assays are useful in studies of DNA strand break production and rejoining caused by exposure to a wide variety of toxins and carcinogens, including ionizing radiation. The method involves forcing DNA fragments through small-pored membranes; the more fragmented the DNA (i.e., contains more strand breaks), the quicker it will pass through the membrane. The assay can be performed using a neutral or alkaline pH buffer solution, with the latter optimized to detect DNA single strand breaks.

References: Whitaker SJ, Powell SN, McMillan TJ, Molecular assays of radiation-induced DNA damage, (1991) pp. 922-928.

243. Ear pain due to laryngeal cancer is conducted by which of the following nerves?

- (A) Vidian
- (B) Galen
- (C) Jacobson
- (D) **Arnold**

Rationale: The auricular branch of the vagus nerve (CN X) is often termed the Alderman's nerve or Arnold's nerve

244. A TRUE null hypothesis has been rejected. Which of the following errors has been committed?

- (A) **Type I error**
- (B) Type II error
- (C) Stochastic error
- (D) Mean square error (MSE)

Rationale: A type I Error occurs when a true null hypothesis has been rejected (false positive), while a Type II error is the failure to reject a false null hypothesis (false negative). A stochastic error is the error that is random from one measurement to another. Mean square error (MSE) is a risk function used to measure the average of the squared of the errors.

245. In preparation for a bone marrow transplant, when conventional total body irradiation (TBI) is used to treat acute leukemia, the dose rate at midplane is closest to:

- (A) 0.01 Gy / min.
- (B) **0.10 Gy / min.**
- (C) 1.00 Gy / min.
- (D) 10.0 Gy / min.

Rationale: Most TBI protocols require the dose rate at mid-plane to be 0.10 – 0.15 Gy / min the dose rate is decreased at extended distance.

References: Perez Textbook, Chapter 73; p. 2144.

246. The MOST common cause of hyperviscosity in multiple myelom is a result of an increase in which of the following?

- (A) IgA
- (B) IgG
- (C) **IgM**
- (D) Light chains

Rationale: The M components in multiple myeloma are most often responsible for circulatory problems and hyperviscosity.

References: DeVita et al, DeVita et al, (1993) p. 2473.

247. All of the following factors define the treatment selection for a squamous cell carcinoma of the oropharynx, EXCEPT:

- (A) N-stage.
- (B) T-stage.
- (C) HPV status.**
- (D) primary location.

Rationale: T1-2N0 disease may be treated with local modality such surgery or radiation alone. T3-4 disease or N2+ disease should be managed by chemotherapy and radiation. Ipsilateral disease such as disease confined to tonsillar fossa without nodal disease may be treated with ipsilateral radiotherapy. Though, HPV positivity is prognostic, but at present time, itself would not alter the management of oropharyngeal carcinoma.

248. Which is influenced by the prevalence of disease in the population that is being tested?

- (A) Sensitivity
- (B) Specificity
- (C) True positive and negative test
- (D) **Positive and negative predictive values**

Rationale: If we test in a high prevalence setting, it is more likely that subjects who test positive truly have disease than if the test is performed in a population with low prevalence. It is illustrated in below two examples, the total population is 100 subjects and there are same sensitivity and specificity but different prevalence of disease.

Example 1: Prevalence of disease= $(10+5)/100=15\%$.

		Disease Status	
		Present	Absent
Test Result	Positive	10	40
	Negative	5	45

Sensitivity= $10/(10+5)=66.7\%$;

Specificity= $45/(40+45)=52.9\%$;

Positive predictive values= $10/(10+40)=20\%$;

Negative predictive values= $45/(5+45)=90\%$.

Example 2: Prevalence of disease= $(20+10)/100=30\%$.

		Disease Status	
		Present	Absent
Test Result	Positive	20	33
	Negative	10	37

Sensitivity= $20/(20+10)=66.7\%$;

Specificity= $37/(33+37)=52.9\%$;

Positive predictive values= $20/(20+33)=38\%$;

Negative predictive values= $37/(10+37)=79\%$.

Using the same test in a population with higher prevalence increases positive predictive value.

Conversely, increased prevalence results in decreased negative predictive value.

References: <https://onlinecourses.science.psu.edu/stat507/node/71>.

249. What is the MOST likely diagnosis for a 2-year-old patient who presents with an upper abdominal mass and periorbital bruising?

- (A) Wilms tumor
- (B) Askins tumor
- (C) Neuroblastoma**
- (D) Rhabdomyosarcoma

Rationale: Neuroblastoma has many classic clinical finding including raccoon eyes (periorbital ecchymosis), blueberry muffin spots (subcutaneous metastasis which blanch due to release of vasoconstrictive tumor by-products), large abdominal mass, opsoclonus myoclonus (dancing eyes and myoclonic jerks), Pepper syndrome, and paralysis due to paraspinal ganglia involvement.

References: Halperin, Pediatric Radiation Oncology.

250. In a Petri dish where 1,000 human fibroblasts were plated and irradiated with 4 Gy of γ -rays, 5 colonies developed. In an unirradiated dish, 100 cells were plated and 10 colonies developed. What is the surviving fraction of the irradiated cells?

- (A) 0.001
- (B) 0.005
- (C) 0.05**
- (D) 0.1

Rationale: Surviving fraction = [(number colonies counted) \div (the number of cells plated) x (plating efficiency)], where the plating efficiency = (number colonies counted) \div (the number of cells plated) for the unirradiated cells.

References: Hall, E.J., Radiobiology for the Radiologist, (2012) Chapter 3.

251. What is the appropriate T stage for a 3.5 cm base of tongue cancer extending to the lingual surface of the epiglottis?

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

Rationale: This patient has a locally-advanced squamous carcinoma of the tongue base as described by the physical exam findings and this is well supported by radiological evidence provided. The genioglossus is an extrinsic tongue muscle and its involvement is staged as a T4, per AJCC [1]. T2 tumors are < 4 cm in greatest dimension. No further information/investigation is necessary to clinically stage this patient. In most cases a CT of the neck is adequate, although an MRI is recommended for difficult cases due to the higher soft tissue resolution.

References: AJCC Cancer Staging Manual, (2010).

252. The OER is HIGHEST for cells irradiated with:

- (A) neutrons.
- (B) electrons.**
- (C) carbon ions.
- (D) alpha particles.

Rationale: The more severe, less repairable DNA damage caused by exposure to high LET radiation does not depend on oxygen free radicals to further augment the injury, as is the case for low LET radiation. Therefore, the OER is high for low LET radiations like electrons or X-rays, and lower (or equal to 1.0) for high LET radiations like carbon ions, neutrons or alpha particles.

References: Hall, E.J., Radiobiology for the Radiologist, (2012) Chapter 7.

253. In regards to thymomas:

- (A) 80% of patients have myasthenia gravis.
- (B) they are not sensitive to platinum-based chemotherapy.
- (C) maximum surgical resection should be performed in tumors with pericardial invasion.**
- (D) surgical resection often reverses the symptoms of thymoma-related myasthenia gravis.

Rationale: D is not correct because surgery does not reverse MG related symptoms right away, and requires continued active therapies. C is correct because for tumors with pericardial invasion, stage III pts benefit from surgery, either alone or with induction therapy and adjuvant radiotherapy. B is incorrect because thymomas are sensitive to platinum based chemotherapy and often employed as neoadjuvant therapy before attempted resection. Choice A is wrong because only about 50% of thymoma pts have MG.

254. According to the randomized study (Turrisi, 1999) for limited stage SCLC, in comparison to once-daily radiation, twice-daily radiation had:

- (A) **the 5-year OS of 26%.**
- (B) a similar grade 3 esophagitis.
- (C) improved DFS, but not OS.
- (D) improved local control, but not OS.

Rationale: Twice-daily treatment beginning with the first cycle of chemotherapy significantly improved survival as compared with concurrent once-daily radiotherapy. Concurrent radiation treatment began with the first cycle of cisplatin/etoposide chemotherapy. Grade 3 esophagitis was significantly more frequent with twice-daily thoracic radiotherapy, occurring in 27 percent of patients, as compared with 11 percent in the once-daily group. The survival rates for patients receiving once-daily radiotherapy were 41 percent at two years and 16 percent at five years. For patients receiving twice-daily radiotherapy, the survival rates were 47 percent at two years and 26 percent at five years.

References: Turrisi AT et al., Twice-Daily Compared with Once-Daily Thoracic Radiotherapy in Limited Small-Cell Lung Cancer Treated Concurrently with Cisplatin and Etoposide, (1999) pp. 265-271.

255. When calculating the transmission factor of the primary barrier for Ir-192 HDR suite, what value of the Use Factor (U) should be utilized in the shielding calculation?

- (A) 0.25
- (B) 0.50
- (C) 0.75
- (D) **1.00**

Rationale: The use factor is the fraction of the primary-beam workload that is directed toward a given primary barrier. Since the Ir-192 source effectively emits isotropically at large distances, the use factor should be 1 since all of the walls will be irradiated by the primary beam.

References: NCRP Report No. 151, Sec. 1.6.

256. What additional accuracy requirement is needed for sliding window IMRT as opposed to step and shoot IMRT?

- (A) Leaf speed
- (B) Leaf position
- (C) Collimator speed
- (D) Collimator angle position

Rationale: Knowledge of the difference between sliding window and step and shoot IMRT delivery is required for this item. The collimator does not rotate during delivery; therefore its speed accuracy is not relevant. Leaf position and collimator position accuracy are required for both types of delivery, and therefore are not additional requirements specific for sliding window.

References: Ezzell et al., AAPM Report 82: Guidance document on delivery, treatment planning, and clinical implementation of IMRT, (2003).
Khan, Treatment Planning in Radiation Oncology, Chapter 20.

257. Which of the following is the BEST estimate for the median survival (months) for patients with newly diagnosed resectable pancreatic cancer?

- (A) 12
- (B) 22
- (C) 30
- (D) 36

Rationale: The median survival across most randomized trials shows a median survival of 20-24 months.

References: Regine et al., Fluorouracil vs. Gemcitabine Chemotherapy Before and After Fluorouracil- based Chemoradiation Following resection of Pancreatic Adenocarcinoma: A Randomized Controlled Trial, (2008) -pp. 1019-26

Neoptolemos et al., A randomized trial of chemoradiotherapy and chemotherapy after resection of pancreatic cancer, (2004) pp. 1200-10.

Oettle et al., Adjuvant chemotherapy with gemcitabine vs observation in patients undergoing curative-intent resection of pancreatic cancer: a randomized controlled trial, (2007) pp. 267-77.

Neoptolemos et al., Adjuvant chemotherapy with fluorouracil plus folinic acid vs gemcitabine following pancreatic cancer resection: a randomized controlled trial, (2010) pp. 1073-81.

258. How does increasing electron beam energy from 6 MeV to 12 MeV affect surface dose and bremsstrahlung tail, respectively?

- (A) Decrease, decrease
- (B) Decrease, increase
- (C) Increase, decrease
- (D) Increase, increase**

Rationale: This question requires understanding of the components of an electron PDD and their dependence on energy. Increasing the electron energy reduces lateral scatter, limiting the number of electrons scattering into d_{max} and contributing additional dose relative to the surface. Increasing energy also increases the efficiency of bremsstrahlung production.

References: Khan, Physics of Radiation Therapy, (2003).

259. Which of the following statements is the MOST applicable in the management of patients with stage IAE gastric mucosa-associated lymphoid tumor (MALT)?

- (A) For H. pylori negative disease, total gastrectomy followed by close observation gives the highest cure rate.
- (B) For H. Pylori negative disease, radiotherapy is the first-line therapy.**
- (C) Anti-H. Pylori therapy, regardless of H.Pylori status, gives the highest cure rate.
- (D) H. Pylori positive gastric MALT with t (14:18) translocation maximizes response to R-CHOP chemotherapy.

Rationale: Anti-H. Pylori therapy is the most effective for H. Pylori positive cases. Radiotherapy is one of the most effective modalities in treating gastric MALT for H. Pylori negative cases or for persistent disease. T(14:18) translocation status is predictive of poor response to anti H. Pylori therapy and radiotherapy may be indicated as first line therapy.

References: Tsang, R.W. et al., Localized mucosa-associated lymphoid tissue lymphoma treated with radiation therapy has excellent clinical outcome, (2003) p. 4157-64.

260. What accounts for the higher surviving fraction when delaying the subculture of quiescent cells *in vitro* after a large, single dose of X-rays compared to cells cultured immediately after irradiation?

- (A) Base excision repair
- (B) Sublethal damage recovery
- (C) Nucleotide excision repair
- (D) Potentially lethal damage recovery**

Rationale: Operationally, potentially lethal damage recovery (PLDR) is defined as the increase in cell survival after a single dose of low LET radiation noted when plating for colony formation is delayed for several hours – leaving cells in a quiescent state in the interim – compared to cells plated immediately after irradiation. PLDR is one manifestation of the repair of DNA double strand breaks; the extent to which this recovery occurs depends on the post-irradiation environmental conditions, that is, conditions which favor PLDR are those that discourage cell proliferation (e.g., due to quiescence, presence of inhibitory drugs, etc.), and vice versa. In a simplistic sense, this can be viewed as a “competition” between continued cell proliferation and DNA repair, processes that normally don’t occur simultaneously.

References: Hall, E.J., Radiobiology for the Radiologist, (2012) Chapter 5.

261. Which of the following protein(s) is involved in ionizing radiation-induced autophagy?

- (A) Bcl-2
- (B) Caspases
- (C) Cytochrome c
- (D) Protein kinases**

Rationale: Protein kinases are involved in mediating both ionizing radiation-induced apoptotic and autophagic cell death. Bcl-2, cytochrome c, and caspases are only associated with apoptotic cell death.

References: Wilson PF and Bedford JS, Leibel and Philips Textbook of Radiation Oncology, (2010) Chapter 1.

262. Which of the following is a poor prognostic factor in favorable histology Wilms tumor?

- (A) 1p/19q co-deletion
- (B) EGFR amplification
- (C) Deletion in the Chromosome 22q**
- (D) Loss of heterozygosity in 1p/16q

Rationale: LOH 1p/16q is used as part of the risk stratification in multiple ongoing COG trials.

References: J Clin Oncol, (2005) -23(29); pp. 7312-21.

263. What was the key finding of INT 0160, a phase II trial exploring neoadjuvant chemoradiation followed by surgical resection for patients with superior sulcus NSCLC?

- (A) Local failure was the most common site of disease progression.
- (B) Most patients were unable to complete neoadjuvant chemoradiation.
- (C) Patients with T3 tumors had double the OS of those with T4 tumors.
- (D) Five-year OS for patients with a complete resection was 54%.**

Rationale: In this trial, a very select group of patients with superior sulcus NSCLC (T3-4, N0-1) underwent induction chemoradiation with cisplatin and etoposide concurrent with 45 Gy radiation. Five-year overall survival for the entire group was 44% and 54% for those who underwent a complete resection, which is nearly double that reported for those with N2 disease treated with definitive chemoradiotherapy or neoadjuvant chemoradiotherapy.

References: Rush et al., N/A (5), (2007).

264. Testing for EGFR mutations and ALK rearrangement is recommended for which of the following lung cancers?

- (A) Small cell carcinoma
- (B) Squamous cell carcinoma
- (C) Adenocarcinoma**
- (D) Neuroendocrine carcinoma

Rationale: Several biomarkers have been shown to be prognostic and predictive. Among these biomarkers, the evidence is strongest for EGFR, ERCC1, KRAS and ALK. Testing EGFR mutation and ALK gen rearrangements is recommended for patients with adenocarcinoma so that patients with these genetic abnormalities can receive effective targeted therapy such as erlotinib and crizotinib.

265. A permanently implanted I-125 seed gives an initial dose rate of 0.46 Gy/day. What is the total dose delivered over the lifetime of the seed (Gy)?

- (A) 30
- (B) 40**
- (C) 50
- (D) 60

Rationale: The total cumulative dose from a permanent seed implant is given by the initial dose rate times the average (mean) life of the isotope, or $D_c = T_{ave} D_0$. The mean life of an isotope is defined as $T_{ave} = 1.44 * T_{1/2}$. So, in this case, $D_c = 1.44 * T_{1/2} * D_0 = (1.44) * (60 \text{ days}) * (0.46 \text{ Gy/day}) = 40.0 \text{ Gy}$.

References: Khan, Physics of Radiation Therapy, (2003).

266. Which of the following is associated with clear cell renal cell carcinoma?

- (A) Lynch syndrome
- (B) Gorlin syndrome
- (C) Ataxia-Telangiectasia
- (D) Von Hippel-Lindau disease**

Rationale: Von Hippel-Lindau disease is an autosomal dominant syndrome that gives predisposes individuals to the development of highly vascularized tumors. The main manifestations include clear-cell renal cell carcinomas, central nervous system and retinal haemangioblastomas, endolymphatic sac tumors, pheochromocytomas and pancreatic neuroendocrine tumors. Von Hippel-Lindau disease is caused by mutations in the VHL tumor-suppressor gene.

References: Richard S, Gardie B, Couvé S, Gad S. Von Hippel-Lindau, How a rare disease illuminates cancer biology, (2013) pp. 26-37.

267. In a patient with limited stage SCLC with a complete response after chemotherapy and thoracic irradiation, PCI:

- (A) has no benefit.
- (B) increases 3-year OS by about 5%.**
- (C) improves DFS, but not OS.
- (D) has unacceptable risk of complications.

Rationale: PCI given to patients with small-cell lung cancer in complete remission decreases the risk of brain metastasis threefold without a significant increase in complications. PCI improves both overall survival and disease-free survival among patients with small-cell lung cancer in complete remission. PCI is associated with a 5.4 percent increase in the rate of survival at three years (15.3 percent in the control group vs. 20.7 percent in the treatment group).

References: Arriagada R, et al., Prophylactic Cranial Irradiation for Patients With Small-Cell Lung Cancer in Complete Remission, (1995) pp. 183-190.

Auperin A, et al., Prophylactic cranial irradiation for patients with small-cell lung cancer in complete remission. Prophylactic Cranial Irradiation Overview Collaborative Group, (1999) pp. 476-84.

268. Regarding early stage NSCLC:

- (A) the local control after lobectomy is better than SBRT.
- (B) there is a survival advantage of lobectomy over wedge resection.
- (C) there is a survival advantage seen for adjuvant chemotherapy in stage I.
- (D) there is no benefit of brachytherapy added to sublobar resection.**

Rationale: A is not correct since LACE shows only survival advantage for stage II-III resected NSCLC; B is not correct since local control is nearly equivalent between lobectomy (95%) and SBRT (98%-RTOG 0236); C is not correct because LCCSG921 only demonstrated better local control in lobectomy but not survival; Choice D is correct since ACOZOG Z4032 trial shows no local control or survival benefit of brachytherapy added to surgery.

References: Timmerman et al., Timmerman et al., (2010).
Fernando et al., Fernando et al., (2013).
Ginsberg and Rubinstein, Ginsberg and Rubinstein, (1995).
Pignon et al., Pignon et al., (2008).

269. Which of the following is MOST predictive for occult lymph node metastasis from squamous cell carcinoma of the floor of mouth?

- (A) Size
- (B) Grade
- (C) Location
- (D) Depth of invasion**

Rationale: Tumor thickness is the most important prognostic factor in regards to the risk of nodal spread and elective treatment of a clinically-negative neck is recommended when the tumor thickness exceeds 2 mm since the risk of occult disease is greater than 15%. Above listed studies along others demonstrated that the disease-related death was less common when oral tumors were thin (2 mm or less), regardless of the tumor stage. The increasing tumor thickness, rather than tumor stage had the best correlation with the disease control and survival.

References: Mohit-Tabatabai MA, Sobel HJ, Rush BH, et al., Relation of thickness of floor of mouth stage I and II cancer to regional metastasis, (1986) pp. 351-353.
Shaha AR, Spiro RH, Shah JP et al., Squamous carcinoma of the floor of the mouth, (1984) pp. 455-459.
Shah JP, Surgical approaches to the oral cavity primary and neck, (2007) pp. S15-18.

270. Which of the following human genetic diseases is characterized by an increased level of sister chromatid exchanges?

- (A) **Bloom syndrome**
- (B) Cockayne syndrome
- (C) Xeroderma pigmentosum
- (D) Nijmegen breakage syndrome

Rationale: The mutated gene responsible for Bloom Syndrome is a RecQ helicase that is involved in homologous recombination repair, specifically by repairing damage at stalled replication forks. This defect leads to exchanges with undamaged templates in either homologous chromosomes or sister chromatids. The genes involved in Xeroderma Pigmentosum and Cockayne Syndrome assist with excision repair while that of Nijmegen Breakage Syndrome works with non-homologous end joining.

References: Hall, E.J., Radiobiology for the Radiologist, (2012) -Chapter 18, Section on “Heritable syndromes that affect radiosensitivity, genomic instability and cancer”.
Friedberg, E.C., Walker, G.C., Siede, W., DNA Repair and Mutagenesis, (1995) Chapter 14.

271. What is the whole lung irradiation dose for a 2.5-year-old patient with a Wilms tumor with pulmonary metastases?

- (A) 12 Gy at 3 Gy per fraction
- (B) **12 Gy at 1.5 Gy per fraction**
- (C) 15 Gy at 1.5 Gy per fraction
- (D) 15 Gy at 3 Gy per fraction

Rationale: These are the current, off-protocol guidelines for patients with multiple lung metastases requiring total lung irradiation for Wilms tumor.

272. What was a finding of INT 0139, a phase III trial comparing neoadjuvant chemoradiation followed by surgical resection to definitive chemoradiation for patients with locally advanced NSCLC?

- (A) Both study arms received carboplatin and paclitaxel.
- (B) Most treatment related deaths occurred in lobectomy patients.
- (C) The majority of treatment-related deaths occurred during chemoradiation in both study arms.
- (D) Lobectomy after neoadjuvant chemoradiation had improved OS compared with definitive chemoradiation.**

Rationale: In this pivotal trial, only patients with stage IIIA (N2) NSCLC were eligible. Progression-free survival was superior for neoadjuvant chemoradiotherapy (median 12.8 vs. 10.5 mo, $p=0.017$), though overall survival was not. In an unplanned analysis, overall survival was improved for neoadjuvant chemoradiotherapy for patients who underwent lobectomy but not pneumonectomy. High rates of treatment related deaths occurred in patients undergoing pneumonectomy.

References: Albain et al., N/A (3), (2009).

273. Less than 40 Gy delivered to lymphatic drainage areas likely containing subclinical (microscopic) carcinoma:

- (A) does not reduce the nodal failure rate and will increase normal tissue toxicity.
- (B) does not reduce the nodal failure rate, even when adding concurrent chemotherapy.
- (C) will reduce the nodal failure rate, but not as much as total doses > 45 Gy.**
- (D) does not reduce the nodal failure rate, even with addition of neoadjuvant chemotherapy.

Rationale: A total dose of 45-50 Gy is commonly used for the treatment of subclinical disease and usually reduces the incidence of nodal failure by more than 90%. Using less than 45 Gy is still effective, but associated with a lower probability of control of nodal disease. The addition of chemotherapy before or during radiation therapy may increase nodal control, but still not as much as increasing the radiation dose instead. In addition, a possible drawback of adding chemotherapy is that it may trigger accelerated tumor stem cell repopulation.

References: Withers and Suwinski, Withers and Suwinski, (1998) pp. 224-228.

Kepka et al., Kepka et al., (2009) pp. 1391-1396.

Willers and Held, Willers and Held, (2006) pp. 1-24.

274. All of the following statements regarding extensive stage SCLC are CORRECT, EXCEPT:

- (A) **median survival time is around 20 months.**
- (B) a complete response rate is estimated at 10-20%.
- (C) overall response rate to chemotherapy is 40-70%.
- (D) recurrence is the rule, even following an excellent response to initial chemotherapy.

Rationale: Overall response rate to multi-agent chemotherapy is 40-70% and complete response rate is estimated at 10-20%. Recurrence of disease is the rule, even following an excellent response to initial chemotherapy. Median survival time is around 9 to 10 months. The most common metastatic sites at diagnosis are bone (19% to 38%), liver (17% to 34%), adrenal glands (10% to 17%), and brain (0% to 14%).

References: Abrams, J. et al., Staging, prognostic factors, and special considerations in small cell lung cancer, (1988) pp. 261-277.

Hanna N, et al., Randomized Phase III Trial Comparing Irinotecan/Cisplatin With Etoposide/Cisplatin in Patients With Previously Untreated Extensive-Stage Disease Small-Cell Lung Cancer, (2006) pp. 2038-2043.

275. A 55-year-old man presents with stage IIB bulky diffuse large B-cell non-Hodgkin lymphoma involving neck and mediastinum. Which therapy option gives the HIGHEST chance of DFS?

- (A) R-CHOP chemotherapy for 4 cycles
- (B) Extended field radiation therapy delivering the dose of 45 Gy
- (C) **R-CHOP chemotherapy for 6 cycles followed by involved-field radiation therapy to 36 Gy**
- (D) CHOP chemotherapy for 6 cycles followed by involved-field radiation treatment to 45 Gy

Rationale: This patient presents with aggressive NHL, will have the best disease-free survival by receiving combination of R-CHOP and involved-field radiation.

References: Phan, J. et al., Benefit of consolidative radiation therapy in patients with diffuse large B-cell lymphoma treated with R-CHOP chemotherapy, (2010) p. 4170-6
Miller et al., SWOG 8736.

276. Which of the following criteria is considered intermediate risk for recurrence in uterine cancer (GOG 99)?

- (A) Tumor size
- (B) Tumor grade**
- (C) Extension to the cervical glands
- (D) Middle third myometrial invasion

Rationale: GOG 99 randomized early stage, intermediate risk patients to observation or adjuvant pelvic radiation after surgery. Criterion used was age, moderate to poor tumor grade, lymph vascular space invasion and outer third myometrial invasion. Benefit was shown for patients with high intermediate risk disease: age >70 with 1 or more risk factors or age >50 with 2 or more risk factors.

References: Keys, H.M., Keys, H.M., (2004).

277. A typical PCI radiation fractionation for a child with ALL is:

- (A) 6 Gy / 3 fxs.
- (B) 18 Gy / 9 fxs.**
- (C) 25 Gy / 10 fxs.
- (D) 37.5 Gy / 15 fxs.

Rationale: Most protocols require 18 Gy. Some pediatric protocols use 12 Gy.

References: Perez Textbook, Chapter 73; p. 2134.

278. Concerning the CALGB 9633 study assessing the benefit of adjuvant chemotherapy for patients with resected T2N0 NSCLC, there was a benefit for:

- (A) all subgroups.
- (B) patients with visceral pleural invasion.
- (C) patients with tumors ≥ 4 cm.**
- (D) patients with incompletely resected tumors.

Rationale: There was no difference in any outcomes overall, but only in unplanned subset analysis showing survival benefit of ≥ 4 cm tumors.

References: Strauss et al, Strauss et al, (2008).

279. 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.

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

References: Staging Manual.

280. Rituximab targets which CD receptor?

- (A) 14
- (B) 16
- (C) 18
- (D) 20**

Rationale: Rituximab is an antibody that targets the CD 20 receptor. The other answers are erroneous.

References: Siegal T. J Clin Neurosci. 2014 May; 21(5):709-715. doi:10.1016/j.jocn.2014.02.002.

281. What dose is BEST for a patient with bulky Stage IIB Hodgkin Lymphoma following chemotherapy with a negative PET?

- (A) 12 Gy
- (B) 24 Gy
- (C) 36 Gy**
- (D) 45 Gy

Rationale: From the NCCN guidelines: Following chemotherapy, bulky disease sites should receive 30 – 36 Gy.

References: NCCN Clinical Practice Guidelines in Oncology.

282. What is the MOST appropriate treatment of diffuse superficial TCC of the bladder, which has recurred after TURBT and intravesical BCG?

- (A) Radical cystectomy**
- (B) Systemic chemotherapy
- (C) Intravesical chemotherapy
- (D) Radiation therapy and chemotherapy

Rationale: Radical cystectomy is the treatment of choice for diffuse superficial bladder tumor, especially in the setting of failed conservative management. Chemotherapy, whether given intravesically or systemically, will not be a curative treatment. Radiation therapy is not usually recommended for diffuse tumors.

References: Perez & Brady's Principles and Practice of Radiation Oncology.

283. Extramedullary plasmacytomas are associated with what form of multiple myeloma?

- (A) Limited
- (B) Indolent
- (C) Extensive
- (D) Aggressive**

Rationale: Extramedullary plasmacytomas are associated with more aggressive myeloma.

References: DeVita et al, DeVita et al, (1993) p. 2473.

284. What is the stage for a patient with a 6 cm non-parameningeal head and neck rhabdomyosarcoma, clinically involved regional lymph nodes but no metastases?

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

Rationale: Based on the TNM pre-treatment staging classification. Halperin, et al. book. Stage 1 includes Orbit, head/neck non-parameningeal, GU non-bladder/prostate, biliary tract primary sites with all size tumors, N0/N1/Nx, M0 patients.

285. What is the maximum dose constraint in Gy for the spinal cord when SBRT is given in 3 fractions for an early stage lung cancer?

- (A) 14
- (B) 18**
- (C) 26
- (D) 30

Rationale: Based on constraints used in recent and ongoing RTOG SBRT trials (0618, 0813, and 0915). Less than 14 Gy for single fraction, 18 Gy for 3 fractions, 26 Gy for 4 fractions and 30 Gy for 5 fractions of SBRT.

References: NCCN Clinical Practice Guidelines in Oncology.

286. Solitary osseous plasmacytomas are BEST treated with which of the following modalities?

- (A) Radiation < 45 Gy
- (B) Radiation < 45 Gy**
- (C) Chemotherapy < 8 AUC
- (D) Chemotherapy < 8 AUC

Rationale: Solitary plasmacytomas are best treated with involved-field radiation ≥ 45 Gy.

References: NCCN Clinical Practice Guidelines in Oncology.

287. Lung cancer screening should be recommended for which of the following individuals?

- (A) 45-year-old current smoker with 20-pack-year history of smoking
- (B) 50-year-old non-smoker with strong family history of lung cancer
- (C) 75-year-old with 35-pack-year history of smoking, but quit 20 years ago
- (D) 65-year-old with 30-pack-year history of smoking, but quit 10 years ago**

Rationale: The risk factors are age 55 to 74 years, 30 or more pack-year history of smoking tobacco, and if former smoker, have quit within 15 years.

References: NCCN Clinical Practice Guidelines in Oncology.

288. Which of the following are included in post-Rituximab Follicular Lymphoma International Prognostic Indicators?

- (A) Age, bone marrow involvement, LDH, PS, tumor size
- (B) Age, bone marrow involvement, extranodal involvement, LDH, tumor size
- (C) Age, $\beta 2$ microglobulin, bone marrow involvement, hemoglobin level, tumor size**
- (D) Age, bone marrow involvement, extranodal involvement, hemoglobin level, tumor size

Rationale: The following factors are found to be predictive of outcome in patients with follicular lymphoma: Tumor size, age, $\beta 2$ microglobulin, hemoglobin level, bone marrow involvement.

References: Federico, M. et al., Follicular lymphoma international prognostic index 2: a new prognostic index for follicular lymphoma developed by the international follicular lymphoma prognostic factor project, (2009) p. 4555-62.

289. Which volume and dose is BEST for a 65-year-old man with Stage IIA, nonbulky, diffuse large B-Cell lymphoma with a partial response based on PET to 3 cycles of R-CHOP chemotherapy but no additional chemotherapy recommended?

- (A) 36 Gy involved site
- (B) 45 Gy involved site**
- (C) 36 Gy extended field
- (D) 45 Gy extended field

Rationale: From the NCCN guidelines: Following a partial response to chemotherapy, involved site radiation should be delivered to a dose between 40 – 50 Gy.

References: NCCN Clinical Practice Guidelines in Oncology.

290. Which of the following statements about autophagy is TRUE?

- (A) Transgenic mice bearing bi-allelic deletions of autophagy-related genes are cancer prone.
- (B) It has no influence on radiation or chemosensitivity.
- (C) **It plays a tumor-suppressive role in normal cells by safeguarding them against metabolic stress.**
- (D) Mutations in the autophagy-associated gene *BECN1* are noted in 5-10% in breast cancers.

Rationale: In normal cells, autophagy serves as a tumor suppressor by protecting cells from metabolic stress that might otherwise lead to genomic instability. This is accomplished through the controlled degradation of mitochondria and aggregated proteins. Bi-allelic deletion of autophagy-related genes is embryonic lethal in transgenic mice, although mono-allelic loss does lead to cancer proneness. Mutations in one autophagy-associated gene, *BECN1*, are found in 40-75% of human breast, ovarian and prostate tumors, and are associated with aggressive tumors and poor prognosis. Genetic knockdown of autophagy-related proteins increases the effectiveness of radiation or chemotherapy in most cases, although there are exceptions.

References: Choi AMK, Ryter SW, Levine B., Autophagy in human health and disease, (2013) pp. 651-652.

Levine B, Kroemer G., Autophagy in the pathogenesis of diseases, (2008) pp. 27-42.

291. What is the MOST appropriate treatment for a 45-year-old non-smoker with a T3N0M0 p16+ base of tongue squamous cell carcinoma?

- (A) Radiotherapy alone
- (B) Composite resection and neck dissection
- (C) Concurrent chemotherapy and radiotherapy**
- (D) Induction chemotherapy followed by radiotherapy

Rationale: T-staging for oropharyngeal tumors is based upon size and degree of invasion. This patient has a clinical stage T3N0M0 tongue base SCC with a very favorable prognosis. Although the mass is well circumscribed and exophytic, epiglottic involvement upstages it from T2 to T3 (1). Data from prospective studies (2) showed that the prognosis is excellent with over 90% 3-year survival in this subset of cases i.e. nonsmoker with p16 positive oropharyngeal SCC, even with stage III and IV disease. While treatment de-intensification is a valid consideration, it is being studied in prospective clinical trials, and is currently not a standard option (3). Outside of a clinical trial, concurrent chemotherapy and radiotherapy is an accepted standard of care and is superior to conventionally fractionated radiotherapy alone (4). There is no level 1 evidence to support induction chemotherapy followed by concurrent chemo radiotherapy in this setting and the additional toxicity is not justifiable, especially given her excellent prognosis. Chemotherapy by itself is not a curative treatment for head and neck squamous cell carcinomas and does not merit consideration with the given information. Base of tongue resection has high morbidity. Surgery alone is not generally considered adequate for T3 base of tongue disease.

References: AJCC Cancer Staging Manual, (2010).

clinicaltrials.gov, Radiation Therapy With Cisplatin or Cetuximab in Treating Patients With Oropharyngeal Cancer, (2011) -<http://clinicaltrials.gov/ct2/show/NCT01302834>.

Ang KK, Harris J, Wheeler R, et al., Human Papillomavirus and Survival of Patients with Oropharyngeal Cancer, (2010) pp. 24-35.

Denis F, Garaud P, Bardet E, et al., Final Results of the 94-01 French Head and Neck Oncology and Radiotherapy Group Randomized Trial Comparing Radiotherapy Alone With Concomitant Radiochemotherapy in Advanced-Stage Oropharynx Carcinoma, (2004) pp. 69-76.

292. The MOST common site for neuroblastoma is the:

- (A) adrenal gland.**
- (B) posterior fossa.
- (C) sympathetic ganglia.
- (D) organ of Zuckerkandl.

Rationale: Neuroblastoma originates from neural crest cells, most often in the adrenal gland; though in very young children, it does have a predilection to occur in the paravertebral sympathetic ganglia. The organ of Zuckerkandl can be a primary site and may have a better prognosis. Neuroblastoma can involve the CNS as a secondary site, but is rarely the primary site.

References: Halperin, Pediatric Radiation Oncology.

293. Appropriate dose ranges for radiation with or without chemotherapy for NK/T-cell lymphoma in Gy are:

- (A) 20-24.
- (B) 25-30.
- (C) 31-40.
- (D) > 40.**

Rationale: With chemotherapy, radiation doses are 40-50 Gy while radiation alone doses are >50 Gy.

References: NCCN Clinical Practice Guidelines in Oncology.

294. For a WHO grade I meningioma, the expected 10 year local control following SRS is:

- (A) < 60%.
- (B) 70%.
- (C) 80%.
- (D) > 90%.**

Rationale: Local control ranges from 90% to 100% following fractionated radiotherapy or stereotactic radiosurgery. Pollack et al reported a 10 year local control of 99% following radiosurgery.

References: Pollock, B.E. et al., Single-fraction radiosurgery for presumed intracranial meningiomas: efficacy and complications from a 22-year experience, (2012) -pp. 1414-8.

295. What was the risk of vaginal recurrence at 5 years with intermediate-high risk endometrial cancer following postoperative pelvic radiation in PORTEC-2 (Nout)?

- (A) 0.6%
- (B) 1.5%
- (C) 1.9%**
- (D) 3.3%

Rationale: In PORTEC-2 patients with high-intermediate risk endometrial carcinoma were randomized to receive to pelvic radiation or vaginal brachytherapy after surgery. The vaginal recurrence risk was 1.9% and 1.5%, for pelvic radiation and brachytherapy, respectively.

References: Nout, R.A. et al., Vaginal brachytherapy versus pelvic external beam radiotherapy for patients with endometrial cancer of high-intermediate risk (PORTEC-2): an open-label, non-inferiority, randomised trial, (2010) pp. 816-23.

296. Prenatal death is MOST likely to occur if the embryo or fetus is exposed to ionizing radiation during what period after conception?

- (A) 0-2 weeks
- (B) 3-12 weeks
- (C) 13-23 weeks
- (D) 24-36 weeks

Rationale: Prenatal death is most likely to occur if the embryo is exposed to ionizing radiation within the first 8 days after conception.

References: Hall, E.J., Radiobiology for the Radiologist, (2012) Chapter 12.

297. The mechanism by which cells undergo radiation-induced senescence involves cells:

- (A) dying during or soon after an aberrant mitosis.
- (B) permanently arresting in one phase of the cell cycle.**
- (C) dying spontaneously within several hours of irradiation.
- (D) becoming genomically unstable and prone to neoplastic transformation.

Rationale: Senescence is a condition of permanent cell cycle arrest that cannot be reversed by the addition of growth factors. It can occur naturally (as part of the normal aging process for example) as well as be induced by genotoxic or oncogenic stress. The remaining answer options are characteristics of apoptosis (A) and mitotic catastrophe (B). Senescence is one way a cell can avoid becoming genomically unstable and prone to transformation.

References: Eriksson D, Stigbrand T, Radiation-induced cell death mechanisms, (2010) pp. 363-372.

Campisi J, d'Adda di Fagagna F, Cellular senescence: when bad things happen to good cells, (2007) pp. 729-740.

298. Which of the following characteristics BEST describes the site of origin and classification of an osteosarcoma?

- (A) Diaphysis of long bones, blastic tumor
- (B) Diaphysis of long bones, primitive neuroectodermal tumor
- (C) Metaphysis of long bones, blastic tumor**
- (D) Metaphysis of long bones, primitive neuroectodermal tumor

Rationale: Osteosarcomas occur in greater frequency in African American males, at the growth plate of long bones. Other characteristics for Ewing's sarcoma include a greater percentage of cases presenting in the axial skeleton, the t11:22 translocation.

299. In a 2012 JAMA publication comparing morbidity (SEER) using IMRT, proton therapy, or 3DCRT for localized prostate cancer, what is the important finding?

- (A) **IMRT was associated with less GI morbidity compared with proton therapy.**
- (B) 3DCRT was associated with fewer hip fractures compared with IMRT.
- (C) Proton therapy was associated with less erectile dysfunction compared with IMRT.
- (D) 3DCRT was associated with less GI morbidity compared with proton therapy.

Rationale: This study using SEER database showed that the use of IMRT was associated with less GI side effects compared with both 3DCRT and proton therapy. IMRT was associated with fewer hip fractures but more erectile dysfunction compared with 3DCRT

References: Sheets NC, Goldin GH, Meyer AM, et al., Intensity-modulated radiation therapy, proton therapy or conformal radiation therapy and morbidity and disease control in localized prostate cancer, (2012) p. 1611-1620

300. An appropriate dose (Gy) of radiotherapy for a grade II astrocytoma is:

- (A) 36.
- (B) **50.4.**
- (C) 59.4.
- (D) 64.8.

Rationale: A data-based dose range for low grade gliomas exists for 45 – 54 Gy. Higher doses (59.4Gy or 64.8Gy) do not improve outcomes and are associated with greater toxicity.

References: Karim, A.B. et al., A randomized trial on dose-response in radiation therapy of low-grade cerebral glioma: European Organization for Research and Treatment of Cancer (EORTC) Study 22844, (1996).

Shaw, E. et al., Prospective randomized trial of low- versus high-dose radiation therapy in adults with supratentorial low-grade glioma: initial report of a North Central Cancer Treatment Group/Radiation Therapy Oncol, (2002).

Karim, A.B. et al., Randomized trial on the efficacy of radiotherapy for cerebral low-grade glioma in the adult: European Organization for Research and Treatment of Cancer Study 22845 with the Medical Research Council st, (2002).