



38th

In-Training Examination for Radiation Oncology Residents

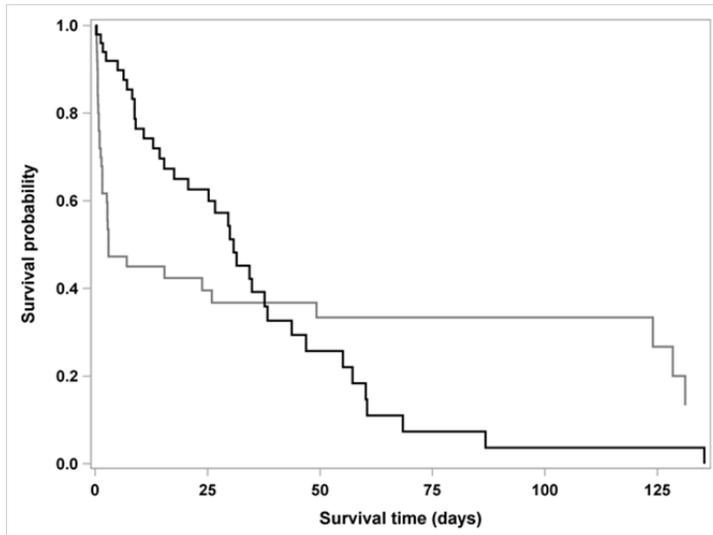
March 2021

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IMPORTANT NOTE: This document contains all the questions that were included on the 2021 examination in CONTENT DOMAIN ORDER. However, because the examination was delivered for the first time via computerized testing, the questions were in scrambled order for each resident who was administered the test (for security reasons). That is, all residents took the same test questions this year, but not in the same order.

1. In an analysis to compare the time to event outcomes for two different groups, based on the survival plot below what is the assumption violated if a Cox regression was used to analyze these data?



- A. Proportional hazards
- B. Data are normally distributed
- C. Noninformative censoring
- D. Survival times are independent between subjects

Key: A

Domain: 1.4

Citations: Klein, J. P., & Moeschberger, M. L. (2003). *Survival analysis: Techniques for censored and truncated data*. New York: Springer.

Allison, P. D., & SAS Institute. (1995). *Survival analysis using SAS: A practical guide*. Cary, NC: SAS Institute.

Rationale: A key assumption of Cox regression analysis is that the hazard ratio (ratio of hazard rates) is constant over time. This is termed the proportional hazard assumption. In the figure, the survival curves cross indicating that the ratio of the hazards between the two groups varies over time.

2. In clinical trials, what randomization procedure ensures that treatment groups are balanced among prognostic factors?
- A. Stratified randomization
 - B. Simple randomization
 - C. Block randomization
 - D. Unequal randomization

Key: A

Domain: 1.7

Citations: T. D. Cook and D. L. DeMets (eds). Introduction to Statistical Methods for Clinical Trials. Chapman and Hall/CRC Press, Boca Raton, Florida, 2008.

Rationale: Stratified randomization is the approach whereby treatments are randomly assigned within prognostic factors (e.g., biological sex) to ensure that these factors are balanced between the treatment groups.

3. Which research study design is used to determine the effectiveness of an intervention?
- A. Phase I clinical trial
 - B. Cohort study
 - C. Phase III clinical trial
 - D. Case control study

Key: C

Domain: 1.7

Citations: DeMets, D., Friedman, L., and Furberg, C. (2010). Fundamentals of Clinical Trials (4th ed.). Springer.

Rationale: This type of research study typically entails patients being randomly assigned to a new intervention and a control group and is aimed at determining the effectiveness of the intervention.

4. Which type of trial compares the benefits of a new intervention to control data from an earlier study?
- A. Concurrent control trial
 - B. Historical control trial
 - C. Randomized control trial
 - D. Phase I clinical trial

Key: B

Domain: 1.8

Citations: T. D. Cook and D. L. DeMets (eds). Introduction to Statistical Methods for Clinical Trials. Chapman and Hall/CRC Press, Boca Raton, Florida, 2008.

Rationale: In a historical control trial the new intervention is compared to previously collected data. These historical data can come from observational or clinical trial research studies.

5. A study used a paired design in which samples from each study participant were tested for the presence of a disease using the two different diagnostic tests. What is the appropriate statistical test to compare the sensitivity between the two tests?
- A. McNemar test
 - B. F-test
 - C. t-test
 - D. Wilcoxon rank-sum test

Key: A

Domain: 1.10

Citations: Agresti, A. (2007). An introduction to categorical data analysis. Hoboken, NJ: Wiley-Interscience.

Genders, T. S. S., Spronk, S., Stijnen, T., Steyerberg, E. W., Lesaffre, E., & Hunink, M. G. M. (2012). Methods for Calculating Sensitivity and Specificity of Clustered Data: A Tutorial. *Radiology*, 265(3), 910-916. doi:10.1148/radiol.12120509.

Rationale: In the example provided there are two diagnostic tests performed on samples from the same person. These paired nominal outcomes are clustered and the analysis needs to adjust correlation of the observations within clusters. The McNemar test is the only test listed that accounts for clustering for nominal outcomes.

6. What is the mode of this number set? 3, 5, 5, 4, 8

- A. 3
- B. 4
- C. 5
- D. 8

Key: C

Domain: 1.2

Citations: Pagano M, Gauvreau K. Principles of biostatistics. CRC Press; 2018.

Rationale: The mode of a set of values is the one that occurs most frequently.

7. What is the mean of the following number set? 3, 5, 5, 4, 8

- A. 3
- B. 4
- C. 5
- D. 8

Key: C

Domain: 1.2

Citations: Pagano M, Gauvreau K. Principles of biostatistics. CRC Press; 2018.

Rationale: Mean is calculated as the sum of all the numbers divided by the total number.

8. What is the median of this number set? 3, 5, 5, 4, 8

- A. 3
- B. 4
- C. 5
- D. 8

Key: C

Domain: 1.2

Citations: Pagano M, Gauvreau K. Principles of biostatistics. CRC Press; 2018.

Rationale: Median is the 50th percentile of a set of numbers.

9. What is a phase I trial used to determine?

- A. Sample size of a phase III trial
- B. Efficacy of an experimental drug
- C. The maximum tolerated dose
- D. The duration of a phase III trial

Key: C

Domain: 1.9

Citations: Yin G. Clinical trial design: Bayesian and frequentist adaptive methods. Vol 876: John Wiley & Sons; 2012.

Rationale: The main aim of a typical phase I oncology trial is to determine the maximum tolerated dose.

10. When using historical controls in a Phase III trial, what is the top priority to maintain trial integrity?

- A. Reduce the sample size of the phase III trial
- B. Reduce the duration of the phase III trial
- C. Remove the placebo arm
- D. Control the type I error

Key: D

Domain: 1.8

Citations: Viele K, Berry S, Neuenschwander B, et al. Use of historical control data for assessing treatment effects in clinical trials. *Pharmaceutical statistics*. 2014;13(1):41-54.

Rationale: Historical data may behave differently with the placebo data from a phase III trial; thus any possibility of inflated type I error may be controversial and jeopardize the trial outcome. Measures must be taken to control type I error.

11. What are the criteria for an ideal screening test that balances sensitivity and specificity?

- A. Low sensitivity and low specificity
- B. High sensitivity and low specificity
- C. Low sensitivity and high specificity
- D. High sensitivity and high specificity

Key: D

Domain: 1.5

Citations: <https://www.statisticshowto.com/sensitivity-vs-specificity-statistics/> .

<https://www.uspreventiveservicestaskforce.org/uspstf/document/RecommendationStatementFinal/lung-cancer-screening> .

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.

12. What is an advantage of a retrospective study?

- A. Controls are representative of the general population
- B. They determine both causation and association
- C. They are less expensive than prospective studies
- D. Abstractors are not blinded

Key: C

Domain: 1.1

Citations: <https://litfl.com/retrospective-studies-and-chart-reviews/> .

Rationale: Retrospective studies involve data analysis, based upon historic record review. Therefore, they are quicker and cheaper to perform than prospective studies.

13. What are the FDA's commonly recommended endpoints for approval for new cancer drugs?

- A. Time to progression and PFS
- B. DFS and event free survival
- C. Time to treatment failure
- D. A and B

Key: D

Domain: 1.3

Citations: <https://www.fda.gov/media/71195/download>

Rationale: The FDA has very specific criteria for assessing and analyzing the data from new (experimental) cancer agents.

14. Which of the following is TRUE about a Chi Square test for statistical significance?

- A. Indicates the strength of an association between two variables
- B. Indicates the direction of an association between two variables
- C. Provides absolute, conclusive proof of a relationship
- D. Needs to consider degrees of freedom

Key: D

Domain: 1.6

Citations: <https://web.csulb.edu/~msaintg/ppa696/696stsig.htm> .

Rationale: Chi Square tests require that one put the obtained values into context. The degrees of freedom refer to the size of contingency table upon which the Chi Square value has been calculated.

15. Which of the following is TRUE about clinical study designs?

- A. Phase I studies aim to identify MTD in animal studies
- B. Phase I trials usually include more people (more than a few dozen)
- C. Case series include a group of case reports of patients with a similar exposure, treatment, or disease
- D. Cohort study can be prospective only

Key: C

Domain: 1.1

Citations: <https://step1.medbullets.com/stats/101001/observational-studies>

Rationale: Phase I studies aim to identify MTD in human beings and include a small number of people. Cohort study can be either prospective or retrospective.

16. A 42-year-old female was incidentally found to have an infiltrative contrast enhancing asymptomatic 6 cm mass in the right rectus abdominus muscle. Biopsy reveals desmoid fibromatosis. What treatment should be initially recommended?

- A. Active surveillance
- B. Definitive radiation
- C. Sorafenib
- D. Surgical resection

Key: A

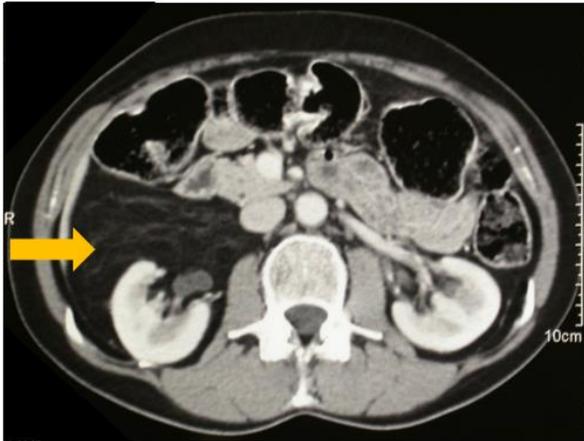
Domain: 2.4

Citations: Desmoid Tumor Working Group. The management of desmoid tumours: a joint global consensus-based guideline approach for adult and paediatric patients. *Eur J Cancer*. 2020; 127:96-107.

Salas S, Dufresne A, Bui B, et al: Prognostic factors influencing progression-free survival determined from a series of sporadic desmoid tumors: a wait-and-see policy according to tumor presentation. *J Clin Oncol* 29:3553-8, 2011.

Rationale: Biologic behavior of desmoid tumors varies. Some progress and can cause significant morbidity while others remain indolent or spontaneously regress. For patients with asymptomatic, stable tumors, an active surveillance strategy is recommended. For patients with progressing or symptomatic desmoid tumors, therapeutic options include systemic therapy, definitive radiation therapy, or surgery with initial treatment disposition determined by taking various patient and tumor characteristics into account.

17. What is the preferred timing and dose of RT when used in the treatment of this malignancy?



- A. Preoperative, 50 Gy
- B. Preoperative, 60 Gy
- C. Postoperative, 50 Gy
- D. Postoperative, 60 Gy

Key: A

Domain: 2.1

Citations: Baldini EH, et. al. Treatment guidelines for preoperative radiation therapy for retroperitoneal sarcoma: preliminary consensus of an international expert panel. *IJROBP* 92(3): 602-12; 2015.

Bishop AJ, et. al. Combined modality management of retroperitoneal sarcomas: a single institution series of 121 patients. *IJROBP* 93(1): 158-65, 2015.

Bonvalot S, et al. Preoperative radiotherapy plus surgery versus surgery alone for patients with primary retroperitoneal sarcoma (EORTC-62092: STRASS): a multicentre, open-label, randomised, phase 3 trial. *Lancet Oncol.* 2020 Sep 14: S1470-2045(20)30446-0. doi: 10.1016/S1470-2045(20)30446-0. Epub ahead of print. PMID: 32941794.

Rationale: When RT is incorporated into the management of retroperitoneal sarcomas, consensus guidelines have recommended using preoperative RT to 5000-5040 cGy. Postoperative RT is not recommended due to a high risk of complications. The recently published EORTC STRASS trial of preoperative RT + surgery versus surgery alone did not show a difference in 3-year abdominal recurrence-free survival between the 2 arms, 60% (95% CI: 51%-68%) for RT + surgery versus 59% (95% CI 50%-67%) for surgery alone (HR 1.01, log rank 0.95). A post hoc analysis by histopathologic subtype and grade suggested that there may be an improvement in abdominal recurrence-free survival with the addition of preoperative RT in liposarcoma and low-grade RPS.

18. What postoperative RT dose is recommended for a high grade malignant peripheral nerve sheath tumor of the upper extremity following R1 resection?

- A. 50 Gy
- B. 60 Gy
- C. 66 Gy
- D. 72 Gy

Key: C

Domain: 2.1

Citations: Delaney TF, Kepka L, Goldberg SI, et al. Radiation therapy for control of soft-tissue sarcomas resected with positive margins. *Int J Radiat Oncol Biol Phys* 2007; 67:1460-1469.

Zagars GK, Ballo MT. Significance of dose in postoperative radiotherapy for soft tissue sarcoma. *Int J Radiat Oncol Biol Phys* 2003; 56:473-481.

Rationale: Several reports have shown inferior local control for soft tissue sarcoma resected with positive microscopic margins. It is worthwhile to ask the surgeon if re-excision for negative margins is possible. For microscopic positive margins (R1 resection), a postoperative RT dose of 6600-6800 cGy is recommended. A higher dose of ≥ 7000 cGy is considered in the setting of gross residual disease (R2 resection).

19. What is the recommended preoperative GTV to CTV target volume expansion for an 8.5 cm high grade myxofibrosarcoma of the vastus lateralis muscle?

- A. 3 cm longitudinally and 1.5 cm radially including bone
- B. 3 cm circumferentially including peritumoral edema
- C. 4 cm longitudinally and 1.5 cm radially, anatomically constrained
- D. 5 cm longitudinally and 2.5 cm radially excluding subcutaneous tissue

Key: C

Domain: 2.1

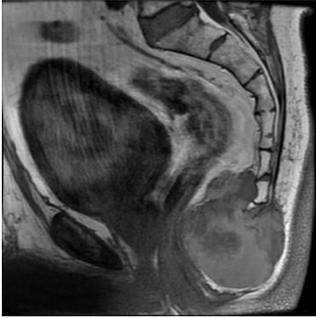
Citations: Haas RL, Delaney TF, O'Sullivan B, et. al. Radiotherapy for management of extremity soft tissue sarcomas: why, when, and where? *Int J Radiat Oncol Biol Phys* 2012; 84:572-580.

Wang D, Zhang Q, Eisenberg BL, et. al. Significant Reduction of Late Toxicities in Patients With Extremity Sarcoma Treated With Image-Guided Radiation Therapy to a Reduced Target Volume: Results of Radiation Therapy Oncology Group RTOG-0630 Trial. *J Clin Oncol.* 2015;33(20):2231-2238.

White LM, Wunder JS, Bell RS, et. al. Histologic assessment of peritumoral edema in soft tissue sarcoma. *Int J Radiat Oncol Biol Phys* 2005;61(5):1439-45

Rationale: Soft tissue sarcomas within muscle are more likely to spread longitudinally along the planes of muscle fibers rather than radially, which is why the longitudinal expansions are greater than the radial expansions. A study correlating peritumoral edema on preoperative MRI with presence of tumor cells in tissue at time of resection showed that for 10 of 15 resected soft tissue sarcomas, there were tumor cells ranging from 1 to 4 cm beyond the gross tumor (White et al). This is the rationale for the 4 cm longitudinal expansions (Haas et al). RTOG 0630 used a longitudinal margin of 3 cm with daily IGRT (Wang et al). The recommended CTV expansion for preoperative RT in the treatment of extremity soft tissue sarcoma is GTV + 3-4 cm longitudinally and 1.5 cm radially, anatomically constrained, with inclusion of peritumoral edema when feasible.

20. What is the MOST likely diagnosis of this midline mass arising from the sacrum and coccyx that is brachyury positive on biopsy?



- A. Chondrosarcoma
- B. Chordoma
- C. Ewing sarcoma
- D. Giant cell tumor of bone

Key: B

Domain: 2.2

Citations: Stacchiotti S, Sommer J; Chordoma Global Consensus Group. Building a global consensus approach to chordoma: a position paper from the medical and patient community. *Lancet Oncol.* 2015;16(2): e71-e83. doi:10.1016/S1470-2045(14)71190-8.

Whelan JS, Davis LE. Osteosarcoma, Chondrosarcoma, and Chordoma. *J Clin Oncol.* 2018;36(2):188-193. doi:10.1200/JCO.2017.75.1743.

NCCN Bone Cancer v1.2020.

Rationale: Chordomas are rare tumors arising from notochord remnants, most commonly occurring in the skull base and sacrum. Expression of brachyury in addition to clinicopathologic features confirms the diagnosis. Chordomas usually present with locally advanced disease, are treated with surgical resection and radiation, and have high rates of local recurrence that can result in significant morbidity.

21. What is the appropriate initial follow-up evaluation of a 47 year-old female who underwent surgical excision for LCIS?

- A. Annual screening mammogram
- B. Annual diagnostic mammogram
- C. Bi-annual screening mammogram
- D. Bi-annual diagnostic mammogram

Key: A

Domain: 3.2

Citations: NCCN Guidelines Version 1.2019, Breast Cancer Screening and Diagnosis.

Rationale: NCCN Guidelines recommend women with a history of LCIS undergo annual screening mammograms beginning at diagnosis of LCIS, but not prior to age 30, in addition to clinical encounters and breast awareness.

22. In the EORTC 10981-22023 AMAROS trial, what were the 5-year rates of clinical signs of lymphedema with axillary dissection vs. axillary RT?

- A. 5% vs. 3%
- B. 23% vs. 11%
- C. 13% vs. 22%
- D. 14% vs. 11%

Key: B

Domain: 3.15

Citations: Donker M, Tienhoven G V, Straver M E, et. al., Radiotherapy or surgery of the axilla after positive sentinel node in breast cancer (EORTC 10981-2203 AMAROS): a randomised, multicentre, open-label, phase 3 non-inferiority trial. *Lancet Oncology*. 2014 Nov;15(12):1303-10.

Rationale: Clinical signs of lymphedema in the ipsilateral arm were noted significantly more often after axillary lymph node dissection than after axillary radiotherapy at 1 year, 3 years and at 5 years.

23. Per the SSO-ASTRO-ASCO consensus guidelines, what is the recommended surgical margin for patients with DCIS treated with breast-conserving surgery and whole-breast RT?

- A. No ink on DCIS
- B. 2 mm
- C. 3 mm
- D. 5 mm

Key: B

Domain: 3.2

Citations: Morrow M, Van Zee K J, Solin L J, et. al. Society of Surgical Oncology-American Society for Radiation Oncology-American Society of Clinical Oncology Consensus Guideline on Margins for Breast-Conserving Surgery with Whole-Breast Irradiation in Ductal Carcinoma in Situ. *Ann Surg Oncol.* 2016 Nov;23(12):3801-10.

Rationale: A 2-mm margin minimizes the risk of IBTR compared with smaller negative margins. More widely clear margins do not significantly decrease IBTR compared with 2-mm margins.

24. What is the rate of supraclavicular recurrence in women with N1 breast cancer treated without nodal RT?

- A. < 3 %
- B. 4-6 %
- C. 7-8 %
- D. 9-10 %

Key: A

Domain: 3.12

Citations: Poortmans PM, Collette S, Korkove C, et. al. Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer. *NEJM.* 2015; 373:317-27.

Whelan TJ, Olivotto IA, Parulekar WR, et. al. Regional Nodal Irradiation in Early-Stage Breast Cancer. *NEJM.* 2015; 373:307-16.

Rationale: Both EORTC 22922 and the NCIC MA 20 demonstrated low rates of failure in the supraclavicular region in patients not receiving nodal radiation, 2% and < 1% respectively.

25. A 45 year-old woman undergoes wide local excision for a 3 cm, grade 3, invasive lobular carcinoma. On final pathology, the sentinel node is negative, and a single margin is close at < 1mm. Which is the MOST appropriate next step in local management?
- A. Re-excision of the close margin prior to RT
 - B. Accelerated partial breast RT
 - C. Whole breast RT using conventional fractionation
 - D. Hypofractionated whole breast RT with a boost

Key: D

Domain: 3.1

Citations: Moran MS, et. al. Society of Surgical Oncology - American Society for Radiation Oncology Consensus Guideline on Margins for Breast-Conserving Surgery with Whole-Breast Irradiation in Stages I and II Invasive Breast Cancer. *Journal of Clinical Oncology*. 2014; 32(14):8.

B.D. Smith, J.R. Bellon, R. Blitzblau, et al. Radiation therapy for the whole breast: executive summary of an American Society for Radiation Oncology (ASTRO) evidence-based guideline *Pract Radiat Oncol*, 8 (2018), pp. 145-152.

Rationale: Hypofractionated whole breast radiation therapy is standard of care for women undergoing radiation therapy to the breast, and boost is indicated based on her age, grade, and narrow margin. The accepted standard for margins for invasive breast cancer is no tumor on ink. Therefore, re-excision is not indicated. The patient's age, lobular histology, size, and status margin are all outside of the "suitable" criteria for accelerated partial breast radiation.

26. What is the lifetime risk of tubo-ovarian cancer in a woman who carries a pathogenic BRCA1 mutation?
- A. < 10%
 - B. 11 - 30%
 - C. 31 - 70%
 - D. > 70%

Key: C

Domain: 3.10

Citations: Kuchenbaecker KB, Hopper JL, Barnes DR, et. al. Risks of Breast, Ovarian, and Contralateral Breast Cancer for BRCA1 and BRCA2 Mutation Carriers. *JAMA*. 2017;317(23):2402-2416. doi:10.1001/jama.2017.7112.

Rationale: BRCA1 carriers have a higher cumulative risk of Ovarian Cancer than BRCA2 carriers. Though there is some variation within published series, the lifetime risk is best represented by the 30-70% category.

27. Following breast-conserving surgery, the use of the 21 gene recurrence score assay to guide decision making about adjuvant chemotherapy is validated in which of the following scenarios?

- A. T2N0 ER+ PR+ HER2+
- B. T1bN2 ER+ PR+ HER2-
- C. T2N0 ER+ PR+ HER2-
- D. T1cN0 ER- PR- HER2-

Key: C

Domain: 3.13

Citations: Harris LN, Ismaila N, McShane LM, et. al. Use of Biomarkers to Guide Decisions on Adjuvant Systemic Therapy for Women With Early-Stage Invasive Breast Cancer: American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol.* 2016;34(10):1134-1150.

Kalinsky K, Barlow WE, Meric-Bernstam F, et al. First results from a phase III randomized clinical trial of standard adjuvant endocrine therapy (ET) +/- chemotherapy (CT) in patients (pts) with 1-3 positive nodes, hormone receptor-positive (HR+) and HER2-negative (HER2-) breast cancer (BC) with recurrence score (RS) < 25: SWOG S1007 (RxPonder). San Antonio Breast Cancer Symposium 2020. Abstract GS3-00.

Rationale: The 21 gene recurrence score is validated for hormone receptor positive, her 2 negative, node negative breast cancer. Patients with ER-positive cancers that are node negative derive substantial benefit from chemotherapy if the 21-gene RS is high, whereas the benefits are limited for those with a low score. The 21 gene recurrence score is not used in triple negative or HER2 amplified tumors. Early data from the RxPonder trial suggest that chemotherapy can be safely omitted for post-menopausal women with N1a disease and 21 gene RS ≤ 25.

28. A patient with a 2.5 cm cNO breast cancer is determined to have a 2 mm deposit of tumor in a sentinel lymph node biopsy performed at breast conserving surgery. What outcome(s) is/are associated with completion axillary LND?

- A. Increases the risk of lymphedema without reducing axillary recurrence
- B. Reduces axillary recurrence, but does not improve OS
- C. Increases the risk of lymphedema and reduces axillary recurrence
- D. Would detect additional positive nodes in < 5% of women

Key: A

Domain: 3.14

Citations: V. Galimberti, B.F. Cole, S. Zurrida, et. al. IBCSG 23-01 randomised controlled trial comparing axillary dissection versus no axillary dissection in patients with sentinel node micrometastases *Lancet Oncol*, 14 (2013), pp. 297-305.

Rationale: Both the IBCSG 23-01 and ACOSOG Z-11 trials demonstrate an increased risk of lymphedema without difference in axillary recurrence for women with T1-2 clinically node negative breast cancer patients detected to have 1-2 positive nodes on sentinel node biopsy. In the IBCSG study, which specifically evaluated women with micrometastasis on SLN biopsy, 13% of women were found to have additional positive nodes at the time of ALND. In Z-11, 27% had additional node metastases. More axillary symptoms, including lymphedema were noted in both trials in the ALND group.

29. A 50 year-old patient presents with breast cancer involving axillary and infraclavicular lymph nodes and exhibits a pCR at mastectomy and sentinel node biopsy following neo-adjuvant chemotherapy. What is the current standard of care for adjuvant RT?

- A. No adjuvant RT is indicated for a pathologic complete response
- B. Adjuvant RT to the chest wall and regional nodes
- C. Adjuvant RT directed only to the undissected level 3 node
- D. Adjuvant RT directed only to the chest wall

Key: B

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Domain: 3.4

Citations: McGuire SE, Gonzalez-Angulo AM, Huang EH, Tucker SL, Kau SW, Yu TK, et. al. Postmastectomy radiation improves the outcome of patients with locally advanced breast cancer who achieve a pathologic complete response to neoadjuvant chemotherapy. *Int J Radiat Oncol Biol Phys.* 2007;68(4):1004–1009. doi: 10.1016/j.ijrobp.2007.01.023

Rationale: With initial level 1 and 3 lymph node involvement, the clinical N stage is N3b and the anatomic stage group is III. In this group, even in the setting of pCR, there is an overall advantage to radiation therapy. Women with cN1 disease with pN0 may be candidates for clinical trial enrollment for de-escalation of radiation (NSABP B-51). Standard post mastectomy radiation therapy fields would include the regional lymphatics as well as the chest wall.

30. In the setting of an in-breast recurrence, a second lumpectomy and partial breast RT results in which of the following at 5-years based on RTOG 1014?

- A. < 10% rate of local recurrence
- B. 25% rate of late grade 3 breast shrinkage and pain
- C. Increased regional recurrence compared to mastectomy
- D. Decreased OS compared to mastectomy

Key: A

Domain: 3.6

Citations: <https://jamanetwork.com/journals/jamaoncology/fullarticle/2755430>

Arthur DW, Winter KA, Kuerer KM, et al. Effectiveness of Breast-Conserving Surgery and 3-Dimensional Conformal Partial Breast Reirradiation for Recurrence of Breast Cancer in the Ipsilateral Breast. The NRG Oncology/RTOG 1014 Phase 2 Clinical Trial. *JAMA Oncol* 2020;6(1):75-82.

Rationale: RTOG 1014 was a single-arm prospective trial and the rate of late grade 3 adverse events was only 7%. The rate of local recurrence was low at exactly 5% at 5 years. There was no comparison to mastectomy in this trial.

31. Which shorter breast RT regimen is supported by a RCT showing equivalence or non-inferiority in local control to the comparative standard arm with at least 5 years of follow-up?

- A. 26 Gy in 5 Fx whole breast RT every day
- B. 38.5 Gy in 5 Fx whole breast RT once a week
- C. 35 Gy in 5 Fx partial breast RT every other day
- D. 38.5 Gy in 10 Fx partial breast RT twice a day

Key: A

Domain: 3.1

Citations: [https://linkinghub.elsevier.com/retrieve/pii/S0140-6736\(19\)32514-0](https://linkinghub.elsevier.com/retrieve/pii/S0140-6736(19)32514-0)

Vicini FA, Cecchini RS, White JR, et al. Long-term primary results of accelerated partial breast irradiation after breast-conserving surgery for early-stage breast cancer: a randomised, phase 3, equivalence trial. *Lancet* 2019; 394:2155-2164.

Rationale: The favored experimental arm of the UK FAST-Forward trial delivered 26 Gy in 5 fractions to the whole breast with equivalent in breast control. The UK Fast trial delivered 28.5 Gy in 5 fractions to the whole breast once a week. The Florence trial gave 30 Gy in 5 fractions partial breast RT every other day. The NSABP B-39 trial administered 38.5Gy in 10 fractions BID but did not reach equivalence in local control. Importantly, each of the other shorter breast regimens have been found to be both safe and effective on large randomized trials with at least 5 years of follow-up.

32. Which patient would gain the greatest benefit in local control from RT?

- A. 0.9 cm grade 3 DCIS s/p lumpectomy with negative margin
- B. 1.8 cm grade 2 DCIS s/p lumpectomy with negative margin
- C. 7 cm DCIS s/p mastectomy with negative margins
- D. 4.5 cm DCIS s/p mastectomy with a positive margin

Key: A

Domain: 3.2

Citations: <https://pubmed.ncbi.nlm.nih.gov/22975615/>

Childs SK, Chen Y-H, Duggan MM, et al. Impact of margin status on local recurrence after mastectomy for ductal carcinoma in situ. *Int J Radiat Oncol Biol Phys* 2013;85(4):948-952.

<https://www.ncbi.nlm.nih.gov/pubmed/26371148>

Solin LJ, Gray L, Hughes LL, et al. Surgical excision without radiation for ductal carcinoma in situ of the breast: 12-year results from the ECOG-ACRIN E5194 Study. *J Clin Oncol* 2015; 33:3938-3944.

Rationale: ECOG E5194 showed that grade 3 DCIS has local recurrence rate as high as 25%, even for small tumors <1cm. Post-mastectomy radiation for DCIS is generally not recommended due to <10% recurrence benefit, even for close or positive margins.

33. What were the 5-year local control results for the 1-week regimens of the FAST-Forward phase III RCT as compared to 3-week hypofractionated breast RT?

- A. Increased ipsilateral breast tumor relapse
- B. Increased locoregional relapse
- C. Non-inferior ipsilateral breast tumor relapse
- D. Non-inferior ipsilateral breast tumor relapse but increased locoregional relapse

Key: C

Domain: 3.1

Citations: Brunt AM et. al. Hypofractionated breast radiotherapy for 1 week versus 3 weeks (FAST-Forward): 5-year efficacy and late normal tissue effects results from a multicentre, non-inferiority, randomised, phase 3 trial. *The Lancet*, Volume 395, Issue 10237, 1613-162.

[https://doi.org/10.1016/S0140-6736\(20\)30932-6](https://doi.org/10.1016/S0140-6736(20)30932-6) .

Rationale: The FAST-Forward hypofractionated breast radiotherapy trial compared 40 Gy in 15 fractions, 27 Gy in 5 fractions over 1 wk, and 26 Gy in 5 fractions over 1 wk (n= 4096 pts). Primary endpoint was ipsilateral breast tumor relapse (IBTR). Normal tissue effects were assessed by both patients and clinicians and included photography. Two third of patients on trial were low risk (age \geq 50 and grade 1-2); the majority were treated with BCT with SLNBx; and were node negative. With a median follow up 71.5 months, non-inferior IBTR was demonstrated in the 1 wk courses vs 3 wks (5-year cumulative incidence of IBTR was 1.7% [95% CI 1.2–2.6] for the 27 Gy group, 1.4% [0.9–2.2] for the 26 Gy group, and 2.1% [1.4–3.1] for the 40 Gy group).

34. Which clinical finding is characteristic of locally advanced breast cancer?

- A. Bloody nipple discharge
- B. Mobile axillary lymph nodes
- C. Nipple retraction
- D. Palpable supraclavicular node

Key: D

Domain: 3.4

Citations: AJCC Cancer Staging Manual 8th edition.

Smith B. Breast Cancer: Postmastectomy Radiation, Locally Advanced Disease, and Inflammatory Breast Cancer. In: Gunderson and Tepper Clinical Radiation Oncology 4th edition. Philadelphia: Elsevier, 2016: 1329-1344.

Rationale: There is no single uniform accepted definition of locally advanced breast cancer (LABC) though typically LABC refers to patients with stage III unresectable breast cancer at presentation. Presence of supraclavicular adenopathy is cN3 disease, anatomic stage IIIC. Presence of bloody nipple discharge, mobile axillary lymph nodes (cN1), and nipple retraction can be seen in early stage breast cancer and do not necessarily preclude upfront resection.

35. Which is considered a high-penetrance breast cancer susceptibility gene?

- A. APC
- B. MSH2
- C. PALB2
- D. RET

Key: C

Domain: 3.10

Citations: NCCN Genetic/Familial High-Risk Assessment: Breast, Ovarian, and Pancreatic Guideline Version 1.2020.

Rationale: High-penetrance breast and/or ovarian cancer susceptibility genes include: BRCA1, BRCA2, CDH1, PALB2, PTEN, and TP53. APC is associated with familial adenomatous polyposis; MSH2 is associated with Lynch syndrome, RET is associated with multiple endocrine neoplasia type 2 (MEN2).

36. What is the TMN classification in a patient that presents with a 5 cm, grade 3 breast cancer with matted axillary lymph nodes, received neoadjuvant chemotherapy, and had a pCR at time of MRM?

- A. cT2N2aM0, pT0N0
- B. cT3N2aM0, pT0N0M0
- C. cT2N2aM0, ypT0N0
- D. cT3N2aM0, ypT0N0Mx

Key: C

Domain: 3.10

Citations: AJCC Cancer Staging Manual 8th edition.

Rationale: Her clinical stage is based on initial presentation: cT2 is tumor >2cm but ≤ 5cm; fixed or matted axillary lymph nodes are cN2a; pathologic complete response (pCR) to neoadjuvant chemotherapy is denoted using the “y” prefix and can be ypT0n0 or ypTisN0 per the AJCC guidelines. pM0 and pMx are not valid categories in the TNM system.

37. What heart and lung dose constraints are acceptable for PMRT planning?

- A. Mean heart dose of 4 Gy and ipsilateral lung V20 of 35%
- B. Mean heart dose of 6 Gy and total lung V20 of 35%
- C. Mean heart dose of 4 Gy and total lung V30 of 35%
- D. Mean heart dose of 6 Gy and ipsilateral lung V30 of 35%

Key: A

Domain: 3.12

Citations: RTOG 1304/NSABP B-51 and Alliance 11202 clinical trials.

Rationale: The RTOG 1304/NSABP-B51 and Alliance clinical trials provide target definitions and normal tissue dose constraints for use when treating the breast or chest wall with regional nodal irradiation. Mean heart dose < 4 Gy is ideal; < 5 Gy is acceptable. Ipsilateral lung V20 < 34% is ideal and <38% is acceptable.

38. What is the BEST treatment for a 55 year-old female who underwent breast-conserving surgery for a pT1cN1mi cM0 ER+ HER2- breast cancer and 21 gene recurrence score of 22?

- A. RT followed by endocrine therapy
- B. Chemotherapy followed by RT
- C. Chemotherapy followed by RT and endocrine therapy
- D. Endocrine therapy alone

Key: A

Domain: 3.1

Citations: TAILOR-X Trial: Adjuvant chemotherapy guided by a 21-gene expression assay in breast cancer. Sparano JA, Gray RJ, Makower DF, et al. NEJM 2018; 379:111-121.

Rationale: The patient is over the age of 50 and had an 21 gene recurrence score of <25 so no chemotherapy is recommended. She underwent BCS so adjuvant radiation is standard of care. Her tumor was ER+ so she needs adjuvant endocrine therapy.

39. Which is associated with the highest risk of locoregional recurrence after neoadjuvant chemotherapy in breast cancer?

- A. Clinically node negative with residual nodal disease after chemotherapy
- B. Complete response in the lymph nodes and the breast
- C. Complete response in the lymph nodes but not the breast
- D. Clinically node positive with residual nodal disease after chemotherapy

Key: D

Domain: 3.4

Citations: Mamounas EP Anderson SJ, Dignam JJ, et al. Predictors of locoregional recurrence after neoadjuvant chemotherapy: results from combined analysis of National Surgical Adjuvant Breast and Bowel Project B-18 and B-27. J Clin Oncol 2012; 30:3960-3966.

Rationale: In a combined analysis of NSABP B-18 and B-27, the independent risk factors associated with LRR were: clinically positive nodes, T3 disease (compared to T1-T2), young age, and pathologically positive nodes after chemotherapy.

40. Which characteristic is MOST typical of an inflammatory breast cancer?

- A. A discrete breast mass
- B. Slow disease progression
- C. Erythema over an otherwise normal breast
- D. Warmth and edema

Key: D

Domain: 3.5

Citations: Strauss JB, Morrow M, Small W Jr. Radiotherapy in Breast Cancer. Clinical Radiation Oncology: Indications, Techniques, and Results, ed 3, Wiley Blackwell, 2017.

Rationale: Inflammatory breast cancer is characterized by the rapid onset and spread of erythema, warmth, and edema throughout the breast. Often a discrete mass is not palpable because the breast is diffusely infiltrated with tumor.

41. For which brachytherapy APBI technique do randomized trial data support equivalent rates of LR with whole breast RT?

- A. Single Entry Devices (balloon- or strut-based)
- B. Multi-catheter interstitial
- C. IORT with electrons
- D. IORT with low energy photons

Key: B

Domain: 3.8

Citations: Strnad V, Ott OJ, Hildebrandt G, et al. 5-year results of accelerated partial breast irradiation using sole interstitial multicatheter brachytherapy versus whole-breast irradiation with boost after breast-conserving surgery for low-risk invasive and in-situ carcinoma of the female breast: a randomised, phase 3, non-inferiority trial. *Lancet* 2016; 387:229-238.

Veronesi U, Orecchia R, Maisonneuve P, et al. Intraoperative radiotherapy versus external radiotherapy for early breast cancer (ELIOT): a randomised controlled equivalence trial. *Lancet Oncol* 2013;14(13):1269-1277.

Vaidya JS, Wenz F, Bulsara M, et al. Risk-adapted targeted intraoperative radiotherapy versus whole-breast radiotherapy for breast cancer: 5-year results for local control and overall survival from the TARGIT-A randomised trial., *Lancet* 2014;383(9917):603-613.

Vicini FA, Cecchini RS, White JR, et al. Long-term primary results of accelerated partial breast irradiation after breast-conserving surgery for early-stage breast cancer: a randomised, phase 3, equivalence trial. *Lancet* 2019; 394:2155-2164.

Rationale: Both a small Hungarian trial and the larger GEC-ESTRO trial showed equivalence between multi-catheter interstitial brachytherapy and whole breast RT. By contrast, both IORT with electrons (ELIOT trial) and IORT with low energy photons (TARGIT-A) showed higher rate of IBTR in the IORT arms. No trial exists that has directly compared single entry devices to whole breast RT. The NSABP B-39 trial was not designed to compare the three APBI techniques, although external beam appeared superior on subset analysis.

42. For a 54 year-old woman with newly diagnosed metastatic ER- PR- HER2+ breast cancer and an ECOG of 0, what is the preferred first-line systemic therapy?

- A. Trastuzumab
- B. Trastuzumab and pertuzumab
- C. Trastuzumab and docetaxel
- D. Trastuzumab, pertuzumab, and docetaxel

Key: D

Domain: 3.3

Citations: Swain SM et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA): end-of-study results from a double-blind, randomised, placebo-controlled, phase 3 study. *Lancet Oncology*. 2020; 21(4):519-530.

Rationale: The Phase III CLEOPATRA study compared the efficacy and safety of trastuzumab and docetaxel +/- pertuzumab in patients with treatment-naïve HER2-positive metastatic breast cancer. The addition of pertuzumab to trastuzumab and docetaxel increased the 8-year overall survival rate from 23% (95% confidence interval 19-28%) to 37% (31-42%).

43. For which age group does the use of screening mammography avoid the most breast cancer deaths?

- A. 39 - 49
- B. 50 - 59
- C. 60 - 69
- D. 70 - 74

Key: C

Domain: 3.9

Citations: Nelson HD, Fu R, Cantor A, et. al. Effectiveness of Breast Cancer Screening: Systematic Review and Meta-analysis to Update the 2009 U.S. Preventive Services Task Force Recommendation. *Annals of Internal Medicine*. 2016; 164(4):244-55.

Rationale: A 2016 systematic review and meta-analysis on the use of mammography for breast cancer screening revealed that the number of breast cancer deaths prevented per 10,000 women screened over 10 years was 3 in those ages 39-49, 8 in those ages 50-59, 21 in those ages 60-69, and 13 in those ages 70-74.

44. In the 2014 Early Breast Cancer Trialists' Collaborative Group meta-analysis examining the effect of PMRT after MRM, what was the decrease in 20-year breast cancer mortality with the use of RT for those with node-positive breast cancer?

- A. 3%
- B. 8%
- C. 13%
- D. 18%

Key: B

Domain: 3.12

Citations: EBCTCG (Early Breast Cancer Trialists' Collaborative Group). Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials. *Lancet*. 2014; 383(9935):2127-35.

Rationale: The 2014 EBCTCG meta-analysis examined data from over 3000 women with pathologic node-positive breast cancer randomized to chest wall and regional nodal radiation or no radiation following mastectomy and axillary dissection. They found that the 20-year breast cancer mortality was 66.4% for node-positive patients receiving no radiation versus 58.3% for patients receiving radiation therapy.

45. The addition of memantine to WBRT in a placebo-controlled phase III trial yielded what outcome compared to placebo and WBRT?

- A. Better intracranial control
- B. Poorer intracranial control
- C. Better cognitive function
- D. Poorer cognitive function

Key: C

Domain: 4.2

Citations: Brown PD, Pugh S, Laack NN, et al. Memantine for the prevention of cognitive dysfunction in patients receiving whole-brain radiotherapy: A randomized, double-blind, placebo-controlled trial. *Neuro-oncol* 15:1429-1437, 2013.

Rationale: In a placebo-controlled phase III trial evaluating the role of memantine in patients receiving WBRT, Brown and colleagues reported that memantine use resulted in better preservation of cognitive function. This established memantine as standard of care for patients receiving WBRT with a better prognosis.

46. What was the impact of hippocampal avoidance WBRT plus memantine compared to conventional WBRT plus memantine in a phase III trial?

- A. No benefit over conventional WBRT
- B. Improved neurocognitive function but worse intracranial tumor control
- C. No benefit for neurocognitive function but improved patient-reported symptoms
- D. Improved neurocognitive function and improved patient-reported symptoms

Key: D

Domain: 4.2

Citations: Brown et. al. Hippocampal avoidance during whole-brain radiotherapy plus memantine for patients with brain metastases: Phase III Trial NRG Oncology CC001. JCO 38: 10; 2020.

Rationale: In NRG-CC001, neurocognitive failure was significantly lower in patients receiving HA-WBRT plus memantine versus WBRT plus memantine (HR 0.74, 95% CI 0.58-0.95, $p=0.02$) and patients reported less fatigue, less difficulty remembering things, and less difficulty speaking with overall fewer cognitive symptoms. There was no difference in OS, intracranial PFS, or toxicity.

47. What is the estimated rate of cavity recurrence at 12 months in patients not receiving postoperative RT following brain metastasis resection?

- A. 10 - 20%
- B. 30 - 40%
- C. 50 - 60%
- D. 70 - 80%

Key: C

Domain: 4.2

Citations: Mahajan et. al. Post-operative stereotactic radiosurgery versus observation for completely resected brain metastases: a single-centre, randomized, controlled, phase 3 trial. Lancet Oncol Aug 18(8): 2017

Rationale: Based on a randomized study evaluating the role of postop SRS vs. surveillance after brain metastasis resection, the 12-month freedom from local recurrence was 43% versus 72% in the SRS group (HR 0.46, 95% CI 0.24-0.88, $p=0.015$).

48. What is the BEST method for diagnosing primary intraocular lymphoma?

- A. CT head with and without contrast
- B. Ocular slit lamp exam
- C. Extra-ocular muscle movement exam
- D. PET/CT with FDG

Key: B

Domain: 4.12

Citations: Batchelor T and Loeffler J. Clinical presentation, pathologic features, and diagnosis of primary central nervous system lymphoma. <https://www.uptodate.com/contents/clinical-presentation-pathologic-features-and-diagnosis-of-primary-central-nervous-system-lymphoma> . Literature review current through: Jun 2020. | This topic last updated: Aug 23, 2019. Accessed July 2020.

AU Matsuo T, Yamaoka A, Shiraga F, Matsuo N. Two types of initial ocular manifestations in intraocular-central nervous system lymphoma. *SO Retina*. 1998;18(4):301.

Rationale: Primary intraocular lymphoma (PIOL) is a form of Primary Central Nervous System Lymphoma (PCNSL). Slit lamp examination is the diagnostic procedure of choice for evaluation of possible ocular disease in patients with suspected or confirmed PCNSL. Initial signs of primary ocular lymphoma include yellowish-white infiltrates at the subretinal pigment epithelium and/or vitreous opacity. PIOL tends to involve the posterior segment of the eye, including the vitreous, choroid, or retina.

49. In the Collaborative Ocular Melanoma Study (COMS), an eye plaque for ocular melanoma at the most common dose of 85 Gy is prescribed to which depth?

- A. 1 mm
- B. 5 mm
- C. 1 cm
- D. 10 cm

Key: B

Domain: 4.12

Citations: Chiu-Tsao ST1, Astrahan MA, Finger PT, et. al. Dosimetry of (125)I and (103)Pd COMS eye plaques for intraocular tumors: report of Task Group 129 by the AAPM and ABS. *Med Phys.* 39(10):6161-84. 2012 Oct.

Rationale: The American Association of Physicists in Medicine (AAPM) and American Brachytherapy Society (ABS) review indicates the most commonly used prescription dose for ocular melanoma eye plaques is 85 Gy at 5 mm depth or prescribed to the tumor apex when using (125)I and (103)Pd sources.

50. What is the MOST likely location for primary intraocular lymphoma?

- A. Posterior orbit including the vitreous, choroid, or retina
- B. Anterior orbit including lens, conjunctiva, or eye lids
- C. Lateral orbit including lateral rectus, lacrimal gland, or conjunctiva
- D. Medial orbit including the conjunctiva, superior oblique, or lens

Key: A

Domain: 4.12

Citations: Batchelor T and Loeffler J. Clinical presentation, pathologic features, and diagnosis of primary central nervous system lymphoma. Up-to-Date. <https://www.uptodate.com/contents/clinical-presentation-pathologic-features-and-diagnosis-of-primary-central-nervous-system-lymphoma> .

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51. What was the 3-year OS on RTOG 0424 for patients with high-risk low-grade glioma treated with concurrent and adjuvant temozolomide and RT?

- A. 43%
- B. 60%
- C. 73%
- D. 90%

Key: C

Domain: 4.5

Citations: Fisher et al. Phase 2 Study of a Temozolomide-Based Chemoradiation Therapy Regimen for High-Risk, Low-Grade Gliomas: Long-Term Results of Radiation Therapy. *Oncology Group 0424* vol 107, issue 4, p. 720-725, July 15, 2020. DOI: <https://doi.org/10.1016/j.ijrobp.2020.03.027> .

Rationale: For this single-arm, phase 2 study, patients with low-grade gliomas with ≥ 3 risk factors (age ≥ 40 years, astrocytoma, bihemispheric tumor, size ≥ 6 cm, or preoperative neurologic function status >1) received RT (54 Gy in 30 fractions) with TMZ and up to 12 cycles of post-RT TMZ. The 3-year OS was 73.5% (95% confidence interval, 65.8%-81.1%), numerically superior to the 3-year OS historical control of 54% ($P < .001$).

52. Which patient with a low-grade glioma would gain an OS benefit from treatment with RT followed by chemotherapy based on RTOG 9802?

- A. 18 year-old female with gross total resection
- B. 30 year-old female with gross total resection
- C. 60 year-old male with subtotal resection
- D. 30 year-old male with gross total resection

Key: C

Domain: 4.5

Citations: Buckner JC, Shaw EG et. al. Radiation plus Procarbazine, CCNU, and Vincristine in Low-Grade Glioma. N Engl J Med. 2016 Apr 7. 374(14):1344-55.

Rationale: RTOG 9802 randomized high risk low grade glioma patients, defined as either >40 years only or subtotal resection, to either radiation versus radiation followed by PCV. The updated analysis found both a progression free survival benefit and overall survival benefit.

53. Which histological variant of meningioma is classified as grade II?

- A. Anaplastic
- B. Papillary
- C. Chordoid
- D. Rhabdoid

Key: C

Domain: 4.3

Citations: Louis et. al. WHO Classification of Tumours of the Central Nervous System. Chapter 10 Meningiomas. Stylus Publishing, LLC. 2016. Revised 4th Edition.

Rationale: Grade III meningioma histologies include rhabdoid, papillary, and anaplastic. Grade II meningioma histologies include clear cell, chordoid, and atypical.

54. What is the upper limit of mitotic figures per 10 HPF (high power fields) in defining a grade I meningioma?

- A. 1
- B. 3
- C. 5
- D. 7

Key: B

Domain: 4.3

Citations: Louis et. al. WHO Classification of Tumours of the Central Nervous System. Chapter 10 Meningiomas. Stylus Publishing, LLC. 2016. Revised 4th Edition.

Rationale: Meningiomas are graded by mitotic figures among other features. Grade I (1) meningiomas have 3 or fewer mitotic figures per 10 HPF. Grade III (3) meningiomas have 20 or more mitotic figures per 10 HPF.

55. What is the recommended conventionally fractionated prescription dose range for non-functioning pituitary adenomas?

- A. 20 - 34 Gy
- B. 35 - 44 Gy
- C. 45 - 54 Gy
- D. 55 - 65 Gy

Key: C

Domain: 4.4

Citations: Gunderson and Tepper. Clinical Radiation Oncology. Chapter 26 - Pituitary Tumors. Churchill Livingstone. 2006.

Rationale: The dose range for fractionated radiation therapy for pituitary adenoma includes a minimum of 45 Gy to maximum of 54 Gy.

56. What imaging characteristic of glioma is MOST indicative of low grade histology?

- A. Intratumoral hemorrhage
- B. High relative cerebral blood volume
- C. Marked mass effect
- D. Lack of contrast enhancement

Key: D

Domain: 4.6 (or 4.13)

Citations: Lanfermann et. al. Cranial Neuroimaging and Clinical Neuroanatomy Atlas of MR Imaging and Computed Tomography. 4th Edition.

Rationale: Ring enhancement, marked mass effect, intratumoral necrosis and hemorrhage, restricted diffusion and high relative cerebral blood volume are associated with higher grade gliomas.

57. A histological WHO grade II diffuse astrocytic glioma is found to be IDH wild-type. Which molecular criteria would suggest this glioma will follow an aggressive clinical course like glioblastoma?

- A. 1p/19q codeletion
- B. TERT promoter mutation
- C. Lack of MGMT methylation
- D. SYT gene amplification

Key: B

Domain: 4.6

Citations: Brat et. al. cIMPACT-NOW update 3: recommended diagnostic criteria for Diffuse astrocytic glioma, IDH-wildtype, with molecular features of glioblastoma, WHO grade IV. *Acta Neuropathologica* (2018) 136:805-810.

Rationale: Per c-IMPACT-NOW, histologic grade II and III IDH-wildtype diffuse astrocytic gliomas which contain high-level EGFR amplification, the combination of whole chromosome 7 gain and whole chromosome 10 loss (+ 7/- 10), or TERT promoter mutations, correspond to WHO grade IV and should be referred to as diffuse astrocytic glioma, IDH-wildtype, with molecular features of glioblastoma, WHO grade IV.

58. In a randomized phase III trial, the addition of which agent to standard temozolomide chemoRT and adjuvant temozolomide for GBM with methylated MGMT promoter improved OS?

- A. Procarbazine
- B. Lomustine
- C. Bevacizumab
- D. Vincristine

Key: B

Domain: 4.6

Citations: Herrlinger et al. Lomustine-temozolomide combination therapy versus standard temozolomide therapy in patients with newly diagnosed glioblastoma with methylated MGMT promoter (CeTeG/NOA-09): a randomised, open-label, phase 3 trial. *Lancet* 2019; 393: 678–88

Rationale: In this phase 3 trial, patients with newly diagnosed glioblastoma with methylated MGMT promoter were randomized to standard temozolomide chemoradiotherapy (75 mg/m² per day concomitant to radiotherapy followed by six courses of temozolomide 150–200 mg/m² per day on the first 5 days of the 4-week course) or to up to six courses of lomustine (100 mg/m² on day 1) plus temozolomide (100–200 mg/m² per day on days 2–6 of the 6-week course) in addition to radiotherapy. Median overall survival was improved from 31.4 months (95% CI 27.7–47.1) with temozolomide to 48.1 months (32.6 months–not assessable) with lomustine-temozolomide (hazard ratio [HR] 0.60, 95% CI 0.35–1.03; p=0.0492 for log-rank analysis).

59. At what level does the thecal sac end in adults?

- A. L1/L2
- B. L3/L4
- C. S1/S2
- D. S4/S5

Key: C

Domain: 4.10

Citations: Bailey & Love's Essential Clinical Anatomy, J. S. P. Lumley, J. Craven, P. Abrahams, R. Tunstall, 1st edition, 2018. p. 419.

Rationale: The thecal sac ends at S1/S2, best seen on sagittal T2 MRI.

60. What function is associated with the occipital lobe of the brain?

- A. Vision
- B. Swallowing
- C. Personality
- D. Balance

Key: A

Domain: 4.10

Citations: Bailey & Love's Essential Clinical Anatomy, J. S. P. Lumley, J. Craven, P. Abrahams, R. Tunstall, 1st edition, 2018. p. 403.

Rationale: The occipital lobe is associated with vision. Brainstem is associated with swallowing, frontal lobe with personality, and cerebellum with balance.

61. What connects the lateral and third ventricles?

- A. Foramen of Monro
- B. Cerebral aqueduct
- C. Foramens of Luschka and Magendie
- D. Arachnoid granulations

Key: A

Domain: 4.10

Citations: Bailey & Love's Essential Clinical Anatomy, J. S. P. Lumley, J. Craven, P. Abrahams, R. Tunstall, 1st edition, 2018. p. 406.

Rationale: The foramen of Monro connects the lateral and third ventricles.

62. What is the MOST important component of treatment for primary CNS lymphoma?

- A. High-dose systemic methotrexate
- B. Cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP)
- C. Whole brain RT
- D. Rituximab

Key: A

Domain: 4.9

Citations: PMID 12637469; 15929034; 18757775; 18227422.

Rationale: High-dose intravenous methotrexate is the standard backbone of induction treatment for most patients with primary CNS lymphoma and has been shown to be more effective than either radiation alone or regimens that do not contain methotrexate.

63. What factor is associated with better prognosis in primary CNS lymphoma?

- A. Age younger than 30 years
- B. Elevated LDH level
- C. Involvement of cerebellum
- D. Performance status 0 or 1

Key: D

Domain: 4.9

Citations: PMID 12525518

Rationale: Age more than 60 years, performance status (PS) more than 1, elevated lactate dehydrogenase (LDH) serum level, high CSF protein concentration, and involvement of deep regions of the brain (periventricular regions, basal ganglia, brainstem, and/or cerebellum) have been found to be significantly and independently associated with a worse survival.

64. In the WHO 2016 classification of brain tumors, which molecular feature is required for the diagnosis of an oligodendroglioma?

- A. IDH wild type
- B. Combined 1p/19q loss
- C. TERT promoter mutation
- D. EGFR amplification

Key: B

Domain: 4.13

Citations: Louis DN, Ohgaki H, Wiestler OD, Cavenee WK (Eds). WHO Classification of Tumours of the Central Nervous System, 4th ed, IARC, Lyon 2016.

Rationale: The diagnosis of an oligodendroglioma now requires the presence of both an isocitrate dehydrogenase (IDH) mutation and combined 1p/19q loss.

65. Which laboratory test abnormality is MOST frequently associated with a rectal adenocarcinoma?

- A. CEA
- B. CA 19-9
- C. CA 125
- D. AFP

Key: A

Domain: 5.7

Citations: Palmqvist R, et. al. Prediagnostic levels of carcinoembryonic antigen and CA 242 in colorectal cancer: a matched case-control study. *Dis Colon Rectum*. 2003;46(11):1538.

Rationale: Carcinoembryonic antigen (CEA) is the classical tumor marker for colorectal cancer. CA 19-9 levels also have low specificity. CA 19-9 is frequently elevated in patients with pancreatic cancers as well various benign pancreaticobiliary disorders. CA 125, an ovarian cancer tumor marker. AFP can be elevated in patients with hepatocellular carcinoma and testicular germ cell tumors.

66. For patients with resectable non-metastatic rectal adenocarcinoma, what is an acceptable treatment regimen?

- A. Short course chemoRT (25 Gy in 5 Fx with concurrent 5-FU) followed by surgery within 1 week
- B. Short course RT (25 Gy in 5 Fx without concurrent 5-FU) followed by surgery within 1 week
- C. Long course chemoRT (50 Gy in 25 Fx with concurrent 5-FU) followed by surgery within 1 week
- D. Long course RT (50 Gy in 25 Fx without concurrent 5-FU) followed by surgery after 4-8 weeks

Key: B

Domain: 5.7

Citations: Johan Erlandsson, et. al. Optimal fractionation of preoperative radiotherapy and timing to surgery for rectal cancer (Stockholm III): a multicentre, randomised, non-blinded, phase 3, non-inferiority trial. *Lancet Oncol*. 2017 Mar;18(3):336-346. doi: 10.1016/S1470-2045(17)30086-4.

Rationale: In the Stockholm III trial (Erlandsson, *Lancet* 2017), patients with resectable non-metastatic rectal adenocarcinoma were randomly assigned to receive short course radiation therapy (25 Gy in 5 fractions) followed by surgery within 1 week OR short course radiation therapy (25 Gy in 5 fractions) followed by surgery after 4-8 weeks OR long course radiation therapy (50 Gy in 25 fractions) with surgery after 4–8 weeks.

67. What is the local failure rate at 10 years for patients with stage II-III rectal cancer who undergo neoadjuvant chemoRT (50.4 Gy in 28 Fx)?

- A. <5%
- B. 5 - 10%
- C. 11 - 15%
- D. 16 - 20%

Key: B

Domain: 5.7

Citations: Rolf Sauer, et. al. Preoperative versus postoperative chemoradiotherapy for locally advanced rectal cancer: results of the German CAO/ARO/AIO-94 randomized phase III trial after a median follow-up of 11 years. *J Clin Oncol.* 2012 Jun 1;30(16):1926-33. doi: 10.1200/JCO.2011.40.1836. PMID: 22529255.

Rationale: The 10-year cumulative incidence of local relapse was 7.1% in the pre-operative arm of the German Rectal Cancer Trial. Other trials have showed similar results, with local failure rates of 5-10% at 10 years.

68. Which chemotherapy regimen and radiation dose were administered for a 7 cm anal cancer tumor with a single 2 cm inguinal node in RTOG 05-29?

- A. 5-FU and Cisplatin, with a dose of 54 Gy to the primary tumor and 50.4 Gy to the involved node
- B. 5-FU and Cisplatin, with a dose of 50.4 Gy to the primary tumor and 45 Gy to the involved node
- C. 5-FU and Mitomycin C with a dose of 54 Gy to the primary tumor and 50.4 Gy to the involved node
- D. 5-FU and Mitomycin C with a dose of 50.4 Gy to the primary tumor and 45 Gy to the involved node

Key: C

Domain: 5.3

Citations: Kachnic LA, et al. RTOG 0529: a phase 2 evaluation of dose-painted intensity modulated radiation therapy in combination with 5-fluorouracil and mitomycin-C for the reduction of acute morbidity in carcinoma of the anal canal. *Int J Radiat Oncol Biol Phys.* 2013 May 1;86(1):27-33. doi: 10.1016/j.ijrobp.2012.09.023. Epub 2012 Nov 12. PMID: 23154075.

Rationale: In the RTOG 05-29 trial, two cycles of 5FU (1000 mg/m²/d as a 96-hour infusion, days 1-5 and 29-33) and MMC (10 mg/m² bolus, days 1 and 29) were administered concurrently with radiation therapy. T2-4N0-3M0 anal cancer patients received 5FU and MMC days 1 and 29 of DP-IMRT, prescribed per stage - T2N0: 42Gy elective nodal and 50.4Gy anal tumor planning target volumes (PTVs) in 28 fractions; T3-4N0-3: 45Gy elective nodal, 50.4Gy ≤ 3cm or 54Gy > 3cm metastatic nodal and 54Gy anal tumor PTVs in 30 fractions.

69. What was the RT prescription dose scheme for a patient with T2N0 anal cancer enrolled on RTOG 0529?

- A. 50.4 Gy to the primary tumor and 42 Gy to the elective lymph nodes
- B. 54 Gy to the primary tumor and 42 Gy to the elective lymph nodes
- C. 45 Gy to the primary tumor and 45 Gy to the elective lymph nodes
- D. 54 Gy to the primary tumor and 45 Gy to the elective lymph nodes

Key: A

Domain: 5.3

Citations: Kachnic LA, et. al. RTOG 0529: a phase 2 evaluation of dose-painted intensity modulated radiation therapy in combination with 5-fluorouracil and mitomycin-C for the reduction of acute morbidity in carcinoma of the anal canal. *Int J Radiat Oncol Biol Phys.* 2013 May 1;86(1):27-33. doi: 10.1016/j.ijrobp.2012.09.023. Epub 2012 Nov 12. PMID: 23154075.

Rationale: In the RTOG 05-29 study, patients with cT2N0 anal cancer received 50.4Gy to the primary tumor and 42 Gy to the elective lymph nodes in 28 fractions using dose-painted IMRT.

70. Which of the following is NOT used in calculating a patient's Child-Pugh Score?

- A. Ascites
- B. Bilirubin
- C. Creatinine
- D. Albumin

Key: C

Domain: 5.6

Citations: Child CG, Turcotte JG. Surgery and Portal Hypertension. *Major Probl Clin Surg.* 1964; 1:1-85. PMID 4950264.

Rationale: The Child-Pugh score consists of five clinical features and is used to assess the prognosis of chronic liver disease and cirrhosis. The five clinical features include: bilirubin, PT/INR, albumin, ascites, hepatic encephalopathy. Each item is graded from a scale of 1 (best) to 3 (worst) and the scores across all five features are then summed to create a total score from 5-15. The Child-Pugh score was originally developed in 1973 to predict surgical outcomes in patients presenting with bleeding esophageal varices. In addition to being used with the Model for End-Stage Liver Disease (MELD) to determine priority for liver transplantation, The Child Pugh Score can also risk stratify patients for liver SBRT.

71. Which of the following best defines non-classic radiation-induced liver disease (RILD)?

- A. Increase in ALBI grade by 1 or more points
- B. Increase in Child Pugh score from baseline by 2 or more points
- C. Progressive abdominal pain and weight loss
- D. Progressive fatigue, bruising and itching

Key: A & B **NOTE:** This item was double-keyed for scoring purposes upon post-exam statistical item analysis.

Domain: 5.6

Citations: Koay EJ, Owen D, Das P. Radiation-Induced Liver Disease and Modern Radiotherapy. *Semin Radiat Oncol.* 2018 Oct;28(4):321-331. PMID: 30309642.

Rationale: In the current era of more precise radiotherapy planning and avoidance of whole liver radiotherapy, non-classic RILD is much more common than classic RILD. Non-classic RILD manifests as markedly elevated serum transaminases (>5X upper limit of normal), and jaundice. The most commonly used criteria in cirrhotic patients is an increase in Child Pugh score greater than or equal to 2.

72. What is the approximate local control rate at 1 year for a 2 cm hepatocellular carcinoma treated with SBRT to BED > 100 Gy?

- A. 85 - 100%
- B. 70 - 84%
- C. 55 - 69%
- D. 40 - 54%

Key: A

Domain: 5.6

Citations: Bujold A, Massey CA, Kim JJ. Sequential Phase I and II Trials of Stereotactic Body Radiotherapy for Locally Advanced Hepatocellular Carcinoma. *J Clin Oncol.* 2013 May 1;31(13):1631-9. PMID: 23547075.

Rationale: Prospective clinical trials of liver SBRT have demonstrated high rates of local control, defined as no progression of disease per RECIST criteria, ranging from approximately 85% to 100% at 1-3 years (Mendez-Romero, 2006, Phase I/II; Kang, 2012, Phase II; Bujold, 2013, Phase I/II; Culleton, 2014, Phase I/II; Lasely, 2015, Phase I/II; Hong, 2016, Phase II). Progression elsewhere in the liver and distantly is common unfortunately, as is death from underlying liver dysfunction, which can be exacerbated by radiation therapy.

73. Which of the following would be the LEAST acceptable fractionation regimen for definitive radiation therapy for a 4 cm hepatocellular carcinoma, presuming all liver constraints can be met?

- A. 60 Gy in 3 Fx
- B. 67.5 Gy in 15 Fx
- C. 48 Gy in 3 Fx
- D. 40 Gy in 5 Fx

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

Domain: 5.6

Citations: Yeap BY, Wo JY, Hong TS. Multi-Institutional Phase II Study of High-Dose Hypofractionated Proton Beam Therapy in Patients With Localized, Unresectable Hepatocellular Carcinoma and Intrahepatic Cholangiocarcinoma. *J Clin Oncol.* 2016 Feb 10;34(5):460-8. PMID: 26668346.

Rationale: Multiple radiotherapy regimens are acceptable for definitive radiation therapy in HCC, with SBRT technically referring to treatment regimens consisting of 5 fractions or fewer. In general, 48 Gy in 3 fractions is considered one of the acceptable doses for patients with Child Pugh A liver function, while 40 Gy in 5 fractions may be more appropriate for those with B7 and B8 disease. In 2016, Hong et al published a Phase II study on proton beam radiotherapy for unresectable HCC or intrahepatic cholangiocarcinoma using 67.5 Gy RBE in 15 fractions. In contrast, doses of 54 Gy and higher in 3 fractions, or radiobiological equivalents, may be more suitable for treatment of metastatic lesions wherein underlying liver dysfunction is less of a concern.

74. What is the MINIMUM volume of uninvolved liver that must be spared from receiving a critical dose threshold in liver SBRT?

- A. 400 cc
- B. 700 cc
- C. 900 cc
- D. 1500 cc

Key: B

Domain: 5.6

Citations: Pan CC, Kavanaugh BD, Dawson LA. Radiation Associated Liver Injury. International Journal of Radiation, Biology and Physics. 2010 Mar 1;76(3 Suppl): S94-100. PMID 20171524.

Rationale: For liver SBRT, the fundamental premise is that to preserve adequate liver function, a minimum volume of normal liver must be spared from receiving a dose that might render it nonfunctional. This minimum “critical volume” was estimated from partial hepatectomy series to be 700 mL; the maximum dose allowed to this critical volume was estimated to be 15 Gy in three fractions (based on LQ conversion, $\alpha/\beta = 3$ Gy). When SBRT is given according to these constraints, the risk of radiation induced liver disease is very low.

75. A Phase III trial randomizing patients with unresectable hepatocellular carcinoma to atezolizumab plus bevacizumab versus sorafenib showed which of the following?
- A. The combination of atezolizumab and bevacizumab was associated with no difference in PFS or OS as compared to sorafenib
 - B. The combination of atezolizumab and bevacizumab was associated with improved PFS as compared to sorafenib, but no difference in OS
 - C. The combination of atezolizumab and bevacizumab was associated with worse OS and PFS as compared to sorafenib
 - D. The combination of atezolizumab and bevacizumab was associated with improved OS and PFS as compared to sorafenib

Key: D

Domain: 5.6

Citations: Finn RS, Qin S, Ikeda M, et al. Atezolizumab Plus Bevacizumab in Unresectable Hepatocellular Carcinoma. *NEJM*. 2020 May 14;382(20):1894-1905. PMID 32402160.

Rationale: In a phase 3 trial, patients with unresectable hepatocellular carcinoma who had not previously received systemic treatment were randomly assigned in a 2:1 ratio to receive either atezolizumab plus bevacizumab or sorafenib. Results showed that the hazard ratio for death with atezolizumab-bevacizumab as compared with sorafenib was 0.58 (95% confidence interval [CI], 0.42 to 0.79; $P < 0.001$). Overall survival at 12 months was 67.2% (95% CI, 61.3 to 73.1) with atezolizumab-bevacizumab and 54.6% (95% CI, 45.2 to 64.0) with sorafenib. Median progression-free survival was 6.8 months (95% CI, 5.7 to 8.3) and 4.3 months (95% CI, 4.0 to 5.6) in the respective groups (hazard ratio for disease progression or death, 0.59; 95% CI, 0.47 to 0.76; $P < 0.001$).

76. Which concurrent chemotherapy regimen is MOST appropriate for preoperative chemoRT to 50.4 Gy in a HER2+ T3N1 adenocarcinoma of the distal esophagus?
- A. Carboplatin, paclitaxel, and trastuzumab
 - B. Carboplatin and paclitaxel
 - C. Carboplatin, paclitaxel, and erlotinib
 - D. Carboplatin, paclitaxel, and capecitabine

Key: B

Domain: 5.1

Citations: Safran H et al. Trastuzumab with trimodality treatment for esophageal adenocarcinoma with HER2 overexpression: NRG Oncology/RTOG 1010. ASCO Annual Meeting abstract, 2020.

Rationale: The NRG/RTOG 1010 trial randomized HER2+ esophageal adenocarcinoma patients to receive standard preoperative chemoradiation with or without concurrent trastuzumab. The study demonstrated no benefit in disease-free survival with the addition of trastuzumab.

77. Which perioperative therapy for locally advanced adenocarcinoma of the GE junction is the LEAST appropriate?

- A. Preoperative chemoRT with carboplatin and paclitaxel
- B. Preoperative chemoRT with fluorouracil and cisplatin
- C. Perioperative chemotherapy with fluorouracil, leucovorin, oxaliplatin and docetaxel (FLOT)
- D. Preoperative chemotherapy with carboplatin and paclitaxel

Key: D

Domain: 5.1

Citations: Al-Batran S et al. Perioperative chemotherapy with fluorouracil plus leucovorin, oxaliplatin, and docetaxel versus fluorouracil or capecitabine plus cisplatin and epirubicin for locally advanced, resectable gastric or gastro-oesophageal junction adenocarcinoma (FLOT4): a randomised, phase 2/3 trial. *Lancet* 2019; 393: 1948-57.

Rationale: Preoperative carboplatin and paclitaxel alone have not been demonstrated to improve survival in esophageal cancer. Choices A) and B) have proven efficacious in the CROSS and RTOG 8501 trials respectively, and Choice C) has proven effective in the FLOT 4 trial when compared to perioperative ECF/ECX chemotherapy.

78. For esophageal cancer, which lymph node station is considered nonregional or distant?

- A. Lower paratracheal nodes (level 4)
- B. Celiac nodes (level 20)
- C. Pulmonary hilar nodes (level 10)
- D. Lower cervical/supraclavicular nodes (level 1)

Key: C

Domain: 5.1

Citations: Rice TW et. al. Cancer of the Esophagus and Esophagogastric Junction: An Eighth Edition Staging Primer. *Journal of Thoracic Oncology*, Vol. 12 (1): 36-42.

Rationale: In the 8th edition AJCC staging manual, regional nodes are found in the peri-esophageal tissue from the upper esophageal sphincter to the celiac artery. Pulmonary hilar nodes are regional nodes for lung cancer but would not be considered regional nodes for esophageal cancer.

79. What is an indication for postoperative chemoRT following total gastrectomy for localized node negative gastric adenocarcinoma?

- A. D1 lymph node dissection
- B. Negative surgical margins
- C. D2 lymph node dissection
- D. Diffuse-type adenocarcinoma

Key: A

Domain: 5.2

Citations: Smalley SR et. al. Updated analysis of SWOG-directed intergroup study 0116: a phase III trial of adjuvant radiochemotherapy versus observation after curative gastric cancer resection. J Clin Oncol 30 (19): 2327-2333.

Rationale: The Intergroup 0116 trial showed that postoperative chemoradiation improved survival compared to surgery alone in a population of patients who mostly received D0 or D1 lymph node dissections, which is now considered suboptimal compared to D2 dissection. Subsequent randomized trials have since suggested that postoperative chemoradiation does not improve survival compared to chemotherapy alone in patients who undergo margin-negative, D2 dissections. However, patients who receive <D2 dissection, or have a positive surgical margin, may still benefit from postoperative chemoRT.

80. Which intervention for resectable gastric cancer was evaluated in the CRITICS randomized trial?

- A. Postoperative chemoRT
- B. Preoperative chemoRT
- C. Preoperative chemotherapy
- D. D2 lymph node dissection

Key: A

Domain: 5.2

Citations: Cats A, et. al. Chemotherapy versus chemoradiotherapy after surgery and preoperative chemotherapy for resectable gastric cancer (CRITICS): an international, open-label, randomised phase 3 trial. Lancet Oncol 2018, 19:616-28.

Rationale: CRITICS randomized patients to receive perioperative chemotherapy alone, or preoperative chemotherapy with postoperative chemoradiotherapy. No benefit was found with postoperative chemoradiotherapy.

81. Which treatment would be LEAST appropriate for a cT3N1 gastric adenocarcinoma?

- A. Surgical resection with postoperative chemoRT
- B. Surgical resection with perioperative chemotherapy
- C. Surgical resection with preoperative chemoRT
- D. Definitive chemoRT

Key: D

Domain: 5.2

Citations: Ajani JA. Phase II trial of preoperative chemoradiation in patients with localized gastric adenocarcinoma (RTOG 9904): quality of combined modality therapy and pathologic respons. J Clin Oncol 24:3953-3958.

Rationale: A) and B) are both well-established treatment options based on the MacDonald (INT 0116) and MAGIC trials respectively. C) is a less well-established option but can be supported with the results of the RTOG 9904 study cited above. D) Definitive chemoradiation without surgery is not considered a standard or proven treatment options for gastric adenocarcinoma (as opposed to esophageal adenocarcinoma).

82. In the German rectal study, what chemotherapy was given concurrent with RT?

- A. Continuous venous infusion of 5-FU during weeks 1 through 5
- B. Bolus infusion of 5-FU during weeks 1 and 5
- C. Oral capecitabine
- D. Oral capecitabine with infusion of oxaliplatin

Key: B

Domain: 5.7

Citations: Sauer R, Becker H, Hohenberger W, et. al. Preoperative versus postoperative chemoradiotherapy for rectal cancer. N Engl J Med. 2004;351(17):1731-1740. doi:10.1056/NEJMoa040694.

Rationale: The preoperative treatment consisted of 5040 cGy, and fluorouracil, given in a 120-hour intravenous infusion at a dose of 1000 mg per square meter of body-surface area per day during the first and fifth weeks of radiotherapy. One month after surgery, four five-day cycles of fluorouracil (500 mg per square meter per day) were given with radiotherapy.

83. In the Stockholm III trial, what was the benefit of delay to surgery when using short course RT?

- A. Increased local control
- B. Decreased distant metastases
- C. Increased OS
- D. Decreased surgical complications

Key: D

Domain: 5.7

Citations: Erlandsson J, Holm T, Pettersson D, et al. Optimal fractionation of preoperative radiotherapy and timing to surgery for rectal cancer (Stockholm III): a multicentre, randomised, non-blinded, phase 3, non-inferiority trial. *Lancet Oncol.* 2017;18(3):336-346. doi:10.1016/S1470-2045(17)30086-4.

Rationale: Participants were randomly assigned to receive either 5 × 5 Gy radiation dose with surgery within 1 week (short-course radiotherapy) or after 4-8 weeks (short-course radiotherapy with delay) or 25 × 2 Gy radiation dose with surgery after 4-8 weeks (long-course radiotherapy with delay). There was a slightly higher risk of surgical complications in SC (36%) vs SC-Delay (28%) (p=0.03).

84. In the International Watch and Wait Database for rectal cancer, what were the rates of local regrowth at 2 years?

- A. <5 %
- B. 5 - 15%
- C. 20 - 30%
- D. 40 - 50%

Key: C

Domain: 5.7

Citations: van der Valk MJM, Hilling DE, Bastiaannet E, et al. Long-term outcomes of clinical complete responders after neoadjuvant treatment for rectal cancer in the International Watch & Wait Database (IWWD): an international multicentre registry study. *Lancet.* 2018;391(10139):2537-2545. doi:10.1016/S0140-6736(18)31078-X.

Rationale: In the International Watch & Wait Database for rectal cancer, the 2-year cumulative incidence of local regrowth was 25.2%. 88% of all local regrowth occurring in the first 2 years, usually in bowel wall, treated with TME (78%) and local excision (22%).

85. Which is a manifestation of chronic kidney injury as a result of RT?

- A. Anemia
- B. Polycythemia
- C. Leukopenia
- D. Leukocytosis

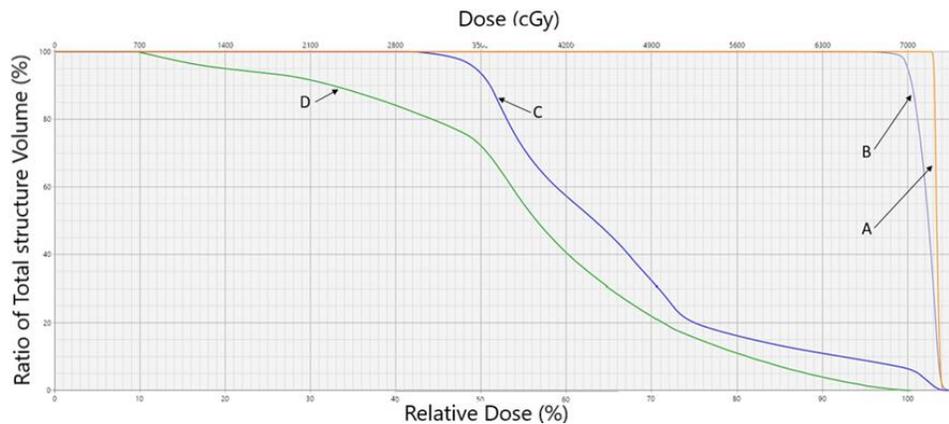
Key: A

Domain: 5.8

Citations: Dawson LA, Kavanagh BD, Paulino AC, et. al. Radiation-associated kidney injury. Int J Radiat Oncol Biol Phys. 2010; 76(3 Suppl):S108-S115. doi:10.1016/j.ijrobp.2009.02.089.

Rationale: Chronic injury (>18 months) is characterized by benign or malignant hypertension, elevated creatinine levels, anemia, and renal failure.

86. The following graph shows the DVH of a patient with prostate cancer being treated to a dose of 70 Gy in 28 Fx. Which curve is MOST likely the PTV?



- A. A
- B. B
- C. C
- D. D

Key: B

Domain: 6.1

Rationale: Choice B represents the most likely curve for the PTV.

87. The ORIOLE phase 2 randomized trial compared SBRT to observation in patients with oligometastatic prostate cancer. What outcome was increased in the SBRT arm?

- A. OS
- B. Grade 3 - 4 toxicity
- C. PFS
- D. ctDNA concentration

Key: C

Domain: 6.1

Citations: Phillips R, Yue Shi W, Deek M, et al. Outcomes of observation vs stereotactic ablative radiation for oligometastatic prostate cancer The ORIOLE Phase 2 randomized clinical trial. *JAMA Oncol* 2020; 26: 650- 9.

Rationale: Treating the sites of oligometastasis with SBRT lead to improved progression free survival and distant metastasis free survival.

88. What is the 5-year OS for MIBC treated with chemoRT?

- A. 15 - 20%
- B. 45 - 50%
- C. 60 - 65%
- D. 80 - 85%

Key: B

Domain: 6.4

Citations: James ND, Hussain SA, Hall E, et al. Radiotherapy with or without chemotherapy in muscle-invasive bladder cancer. *N Engl J Med* 2012; 366: 1477-88.

Rationale: In a Phase 3 randomized trial comparing chemoradiation to radiation alone, the group of patients receiving chemoradiation had a 5-year OS rate of 48%.

89. In otherwise healthy patients with MIBC receiving chemoRT, which is an appropriate radiosensitizing chemotherapy regimen?

- A. Cisplatin and pemetrexed
- B. Carboplatin and paclitaxel
- C. Cisplatin and etoposide
- D. 5-FU and mitomycin

Key: D

Domain: 6.4

Citations: James ND, Hussain SA, Hall E, et al. Radiotherapy with or without chemotherapy in muscle-invasive bladder cancer. *N Engl J Med* 2012; 366: 1477-88.

Rationale: A phase III randomized trial showing the efficacy of chemoradiation for bladder cancer used concurrent 5FU and mitomycin as a radiosensitizer.

90. What is a preferred surgical treatment paradigm for patients with resectable urothelial MIBC and good renal function?

- A. Neoadjuvant pembrolizumab followed by radical cystectomy
- B. Radical cystectomy followed by adjuvant cisplatin/gemcitabine
- C. Radical cystectomy followed by adjuvant pembrolizumab
- D. Neoadjuvant cisplatin/gemcitabine followed by radical cystectomy

Key: D

Domain: 6.2

Citations: Grossman et al. Neoadjuvant chemotherapy plus cystectomy compared with cystectomy alone for locally advanced bladder cancer. *N Engl J Med* 2003. PMID: 12944571.

Rationale: Neoadjuvant cisplatin-based chemotherapy is preferred and based on a higher level of evidence compared to adjuvant cisplatin-based chemotherapy. Immunotherapy does not yet have a defined role in the non-metastatic setting.

91. What is the 4-year local control rate after SBRT for primary renal cell carcinoma?

- A. 60 – 70%
- B. 71 - 80%
- C. 81 – 90%
- D. 91% - 100%

Key: D

Domain: 6.2

Citations: Siva et al. Pooled analysis of stereotactic ablative radiotherapy for primary renal cell carcinoma: A report from the International Radiosurgery Oncology Consortium for Kidney (IROCK). Cancer 2018. PMID: 29266183.

Rationale: In an international analysis of 223 patients, the 4-year rate of local control, cancer-specific survival, and progression-free survival were 97.8%, 91.9%, and 65.4%, respectively.

92. What is the predominant pattern of failure in patients with MIBC \geq pT3 status post radical cystectomy with negative margins?

- A. Inguinal lymph nodes
- B. Presacral nodes
- C. Cystectomy bed
- D. Iliac/obturator nodes

Key: D

Domain: 6.4

Citations: Baumann et al. Bladder Cancer Patterns of Pelvic Failure: Implications for Adjuvant Radiation Therapy. Int J Radiat Oncol Biol Phys 2016. PMID: 27026309.

Rationale: Recognition of patterns of failure is very important in designing radiotherapy fields. Based on a large series of patients who had undergone radical cystectomy for urothelial bladder cancer, Baumann et al. found that the predominant site of failure was the iliac/obturator nodes for patients with negative margins and for patients with positive margins, the predominant pattern of failure is the cystectomy bed and presacral nodes.

93. Which single feature would make a patient's prostate cancer Unfavorable Intermediate Risk Group?

- A. PSA > 10
- B. T2a
- C. Grade Group 2
- D. Grade Group 3

Key: D

Domain: 6.1

Citations: Zumsteg ZS, et. al. A new risk classification system for therapeutic decision making with intermediate-risk prostate cancer patients undergoing dose-escalated external-beam radiation therapy. *European urology*. 2013;64(6):895-902.

Rationale: In the widely used prostate risk stratification criteria adapted by the NCCN that originated from the Zumsteg et. al. 2013 publication showed GG3, >50% core positivity and >1 intermediate risk factors as the three populations that have worse prognosis in the intermediate risk category of prostate cancer.

94. What is the lowest risk-group of prostate cancer where a metastatic workup with a bone scan may be recommended?

- A. Low risk
- B. Favorable Intermediate
- C. Unfavorable Intermediate
- D. High risk

Key: C

Domain: 6.1

Citations: NCCN Guidelines May 2020.

Rationale: The probability of bone metastasis becomes relevant at unfavorable intermediate risk and higher risk groups of prostate cancer.

95. For stage I seminoma treated with orchiectomy alone and no adjuvant treatment, what are the 15-year relapse and salvage rates respectively?

- A. 20% and 100%
- B. 30% and 100%
- C. 20% and 80%
- D. 30% and 90%

Key: A

Domain: 6.3

Citations: Kollmannsberger, C., T. et. al. (2015). "Patterns of relapse in patients with clinical stage I testicular cancer managed with active surveillance." J Clin Oncol 33(1): 51-57.

Rationale: The risk-adapted management approach of testicular seminoma is based on low rates of 15 year relapse of about 20% and a very high rate of cure for those who relapse.

96. A 65 year-old male diagnosed with MIBC decided to proceed with bladder preservation as his treatment choice. Given no other comorbidities, normal tolerance doses and concurrent chemotherapy, what total bladder radiation dose in 1.8 - 2.0Gy/fx is appropriate?

- A. 50 Gy
- B. 55 Gy
- C. 64 Gy
- D. 74 Gy

Key: C

Domain: 6.4

Citations: Tester W et. al. Neoadjuvant combined modality program with selective organ preservation for invasive bladder cancer: results of Radiation Therapy Oncology Group phase II trial 8802. J Clin Oncol. 1996 Jan;14(1):119-26.

Rationale: 65Gy in conventional fractionation is the appropriate standard regimen for bladder preservation in the setting of concurrent chemotherapy.

97. A 68 year-old male presents with favorable intermediate risk prostate cancer and elects to receive low dose rate brachytherapy alone. Which is an appropriate isotope and dose prescription?

- A. ¹²⁵Iodine and 115 Gy
- B. ¹²⁵Iodine and 145 Gy
- C. ¹⁰³Palladium and 85 Gy
- D. ¹⁰³Palladium and 100 Gy

Key: B

Domain: 6.1

Citations: NCCN Guidelines. 1.2020- Prostate Cancer

Rationale: The appropriate low dose rate brachytherapy prescription for monotherapy is 145 Gy with Iodine-125 and 125 Gy with Palladium-103.

98. A 73 year-old male is diagnosed with prostate cancer and his staging workup reveals 6 bone metastases on his bone scan. Which of the following is considered a category 1 treatment recommendation per the NCCN?

- A. Abiraterone and prednisone with ADT
- B. RT to the prostate with ADT
- C. RT to the prostate and SBRT to the bone metastases with ADT
- D. Pembrolizumab with ADT

Key: A

Domain: 6.1

Citations: NCCN Guidelines. 2.2020- Prostate Cancer

Rationale: This patient presents with high volume metastatic disease. Two phase 3 studies have shown abiraterone with androgen deprivation therapy is associated with improved survival compared to androgen deprivation therapy alone. Per the NCCN, radiation therapy to the prostate should not be routinely performed in patients with high volume metastatic disease and this is based on two randomized trials, the HORRAD and STAMPEDE studies.

99. In a patient with bladder cancer, which is a CONTRAINDICATION to a bladder preservation strategy with definitive chemoRT?

- A. Any tumor with bilateral hydronephrosis
- B. T3 disease
- C. T2 disease
- D. 4 cm tumor in the right lateral wall

Key: A

Domain: 6.4

Citations: NCCN Guidelines Bladder Cancer v1.2020

Rationale: Definitive chemoradiation for bladder cancer is most successful for patients without tumor associated hydronephrosis and without extensive carcinoma in situ.

100. In a patient undergoing RT for stage IIB seminoma with gross nodal disease, what dose and treatment method are recommended?

- A. 20 Gy with AP/PA fields
- B. 20 Gy using IMRT
- C. 36 Gy with AP/PA fields
- D. 36 Gy using IMRT

Key: C

Domain: 6.3

Citations: Wilder RB, Buyyounouski MK, Efstathiou JA, Beard CJ. Radiotherapy treatment planning for testicular seminoma. *Int J Radiat Oncol Biol Phys.* 2012;83(4):e445-e452.

Rationale: The standard dose for IIB seminoma is 36 Gy. Mean dose to kidneys, liver and bowel are lower with CT based AP/PA three-dimensional conformal radiation therapy than intensity modulated radiation therapy. As a result, the risk of second cancers may be lower with an AP/PA beam arrangement than with intensity modulated radiation therapy.

101. What is the inferior border of the prostate bed RT volume with respect to the vesiculourethral anastomosis (VUA)?

- A. At the VUA
- B. 1-5 mm below the VUA
- C. 8-12 mm below the VUA
- D. 16-20 mm below the VUA

Key: C

Domain: 6.1

Citations: RTOG contouring atlas

Rationale: The prostate bed has the following boundaries:

- anterior: posterior edge of pubic bone, or posterior 1-2 cm of bladder wall (when above superior edge of pubic symphysis)
- posterior: anterior rectal wall, or mesorectal fascia (when above superior edge of pubic symphysis)
- lateral: levator ani muscles, obturator internal, sacrorectogenitopubic fascia
- inferior: 8-12 mm below the vesiculourethral anastomosis

102. For a patient with a bladder cancer invading into the muscularis propria, with one involved lymph node below the common iliacs, what is the stage according to the AJCC 8th edition?

- A. IIIA
- B. IIIB
- C. IVA
- D. IVB

Key: A

Domain: 6.4

Citations: AJCC Staging manual

Rationale: In the AJCC 8th edition staging, patients with N1 disease have Stage IIIA bladder cancer.

103. For penile cancer, which features are consistent with AJCC 8th ed Stage IV disease?

- A. Fixed lymph node / extracapsular extension
- B. Invasion of the cavernosum
- C. Bilateral inguinal lymph node
- D. Unilateral inguinal nodes

Key: A

Domain: 6.5

Citations: AJCC 8th ed staging manual

Rationale: In the AJCC 8th edition staging, patients with fixed lymph nodes or extranodal extension have N3 disease, and patients with N3 disease have Stage IV disease.

104. What percent of patients have tumor marker elevation at the time of relapse from seminoma?

- A. 1
- B. 15
- C. 30
- D. 45

Key: B

Domain: 6.3

Citations: Utility of serum tumor markers during surveillance for stage I seminoma. Vesprini, et al. Cancer 2012

Rationale: 527 men managed by surveillance in one institution [11]. At a median of 72 months, relapse occurred in 75 men (14 percent). Only 11 of these men (15 percent) had an elevated marker at the time of relapse. Elevated tumor markers (before the documentation of clinical or radiologic progression) were detected in only one man (1.3 percent). These findings support the guidelines from the American Society of Clinical Oncology (ASCO) and suggest not using markers to monitor for relapse in men with stage I seminoma.

105. What was the result of the MRC testicular tumor working group TE10 trial, which randomized men to paraaortic strip or paraaortic plus ipsilateral iliac LN RT following inguinal orchiectomy?
- A. Azoospermia was not affected by RT field size
 - B. 3-year relapse free survival was greater in the paraaortic strip RT arm
 - C. Side effects were decreased in the paraaortic strip RT arm
 - D. 5% of patients on each arm died due to seminoma

Key: C

Domain: 6.3

Citations: Fossa, et al. JCO 1999 Optimal planning target volume for stage I testicular seminoma

Rationale: The short-term side effects of RT were decreased, and the incidence of azoospermia was significantly decreased using paraaortic strip RT compared with a more extensive RT field (11 versus 35 percent). With a median follow-up of 4.5 years, there were nine relapses in each group (4 percent). There was only one death due to seminoma in the trial.

106. What is the MOST common site of insufficiency fracture after EBRT?
- A. Lumbar vertebrae
 - B. Sacrum
 - C. Pubis
 - D. Acetabulum

Key: B

Domain: 7.4

Citations: Sapienza LG, Salcedo MP, Ning S, Hjingran A, Klopp AH, et. al. Pelvic Insufficiency Fractures after External Beam Radiation Therapy for Gynecologic Cancers: A Meta-analysis and Meta-regression of 3929 Patients. Int J Radiat Oncol Biol Phys 106(3):475-484, 2020

Rationale: Bony fractures appear to be more common after external beam irradiation, compared to the general population. These findings, known as “insufficiency fractures”, can be asymptomatic. In a recent study, the most common fracture sites were sacroiliac joint (39.7%), body of the sacrum (33.9%), pubis (13%), lumbar vertebra (7%), iliac bone (2.8%), acetabulum (2.1%), and femoral head/neck (1.5%). The median time to fracture was 7.1 to 19 months after radiation therapy.

107. In the subset analysis of PORTEC-3 trial, patients with which histology MOST benefited from the addition of chemotherapy to RT?

- A. Endometrioid
- B. Carcinosarcoma
- C. Clear cell
- D. Serous

Key: D

Domain: 7.1

Citations: De Boer SM, Powell ME, Mileskin L, Katsaros D, et. al. Adjuvant Chemoradiotherapy versus radiotherapy alone in women with high-risk endometrial cancer (PORTEC-3): Patterns of Recurrence and Post-hoc Survival Analysis of a Randomised Phase 3 Trial. *Lancet Oncol* 20(9):1273-1285, 2019

Rationale: Chemotherapy is the mainstay of adjuvant treatment for advanced serous carcinomas. PORTEC-3 was a phase III study of radiotherapy alone vs. chemoradiation for advanced, resected endometrial cancers. When comparing serous cancers with all other histologies in a post-hoc exploratory subgroup analysis, women with serous cancers had significantly lower overall survival and failure-free survival than did those with other histologies, irrespective of treatment received. After adjusting for stratification factors, significant improvements in overall survival and failure-free survival were observed for serous cancers treated with chemoradiotherapy versus radiotherapy alone: 5-year overall survival was 71.4% (95% CI 60.1–84.7) with chemoradiotherapy versus 52.8% (40.6–68.6) with radiotherapy alone (HR 0.48 [95% CI 0.24–0.96]; $p=0.037$), and 5-year failure-free survival was 59.7% (95% CI 45.1–71.6) with chemotherapy versus 47.9% (33.9–60.6) with radiotherapy alone (HR 0.42 [95% CI 0.22–0.80]; $p=0.008$).

108. If postoperative concurrent chemoradiation is given for endometrial cancer, what is the MOST common dose of cisplatin?

- A. 20 mg/m²
- B. 30 mg/m²
- C. 40 mg/m²
- D. 50 mg/m²

Key: D

Domain: 7.1

Citations: De Boer SM, Powell ME, Mileskin L, Katsaros D, et. al. Adjuvant Chemoradiotherapy versus radiotherapy alone in women with high-risk endometrial cancer (PORTEC-3): Patterns of Recurrence and Post-hoc Survival Analysis of a Randomised Phase 3 Trial. *Lancet Oncol* 20(9):1273-1285, 2019.

Rationale: The role of concurrent chemoradiation after hysterectomy for stage III-IV endometrial cancer remains under investigation. In the PORTEC-3 study, in the chemoradiotherapy group, women received two cycles of cisplatin 50 mg/m² administered intravenously in the first and fourth week of external-beam radiotherapy, followed by four cycles of carboplatin AUC5 and paclitaxel 175 mg/m² administered intravenously at 21-day intervals. This schedule has initially been evaluated in phase II RTOG studies.

109. Following lymphadenectomy for endometrial cancer, a focus of tumor cells measuring 0.3 mm is detected by immunohistochemistry in a paraaortic node. What is the AJCC stage?

- A. N0(i+)
- B. N1mi
- C. N1a
- D. N2mi

Key: D

Domain: 7.1

Citations: National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology, Uterine Neoplasms version 2.2020 – July 24, 2020.

Rationale: N2mi - Regional lymph node metastasis (greater than 0.2 mm but not greater than 2.0 mm in diameter) to para-aortic lymph nodes, with or without positive pelvic lymph nodes. This was updated in the latest, 8th edition of AJCC staging manual. FIGO staging rules for endometrial cancer have not yet been revised to match AJCC.

110. As demonstrated in the PORTEC-1 study, what is the absolute improvement in local control at 5 years with the addition of RT to stage I intermediate risk endometrial cancer patients?

- A. 0%
- B. 10%
- C. 20%
- D. 30%

Key: B

Domain: 7.1

Citations: Creutzberg CL, et. al. Surgery and postoperative radiotherapy versus surgery alone for patients with stage-1 endometrial carcinoma: multicentre randomized trial. PORTEC Study Group. Post Operative Radiation Therapy in Endometrial Carcinoma. *Lancet*. 2000; 355 (9213): 1404-11.

Rationale: The 5-year actuarial locoregional recurrence rates were 4% in the radiotherapy group and 14% in the control group ($p < 0.001$). There was no difference in OS.

111. What was the approximate rate of vaginal stenosis in the EMBRACE study after cervical cancer chemoRT resulting in rectovaginal reference point dose of 85 Gy?

- A. 10%
- B. 15%
- C. 25%
- D. 35%

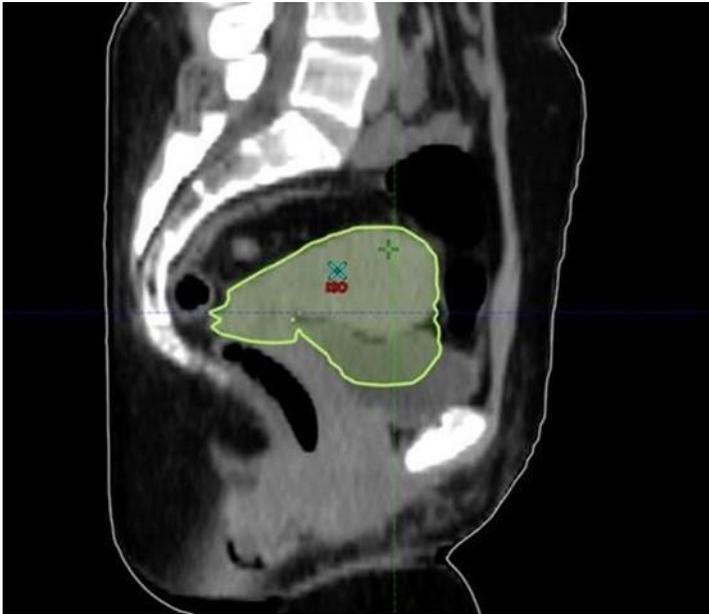
Key: D

Domain: 7.5

Citations: Kirchheiner K., Nout R.A., Lindegaard J.C. et. al. Dose-effect relationship and risk factors for vaginal stenosis after definitive radio (chemo)therapy with image-guided brachytherapy for locally advanced cervical cancer in the EMBRACE study. *Radiother Oncol*. 2016; 118: 160-166.

Rationale: A large study of 630 cervical cancers, treated with modern definitive brachytherapy ("the EMBRACE") found that the ICRU ectovaginal point dose significantly correlated with vaginal stenosis. With a median follow up of 24 months, the probability to develop symptomatic vaginal stenosis was 16% with a rectovaginal point of 55 Gy and 34% with 85 Gy. Other methods to evaluate vaginal dose constraints in cervical brachytherapy are under study.

112. What is the purpose of the structure outlined on this treatment planning image for cervical cancer?



- A. ITV of Uterus based on bladder filling
- B. ITV of Bowel based on bladder filling
- C. ITV of Sigmoid based on rectal filling
- D. GTV of Uterus based on bladder filling

Key: A

Domain: 7.5

Citations: Buchali A, Koswig S, Dinges S, et al. Impact of the filling status of the bladder and rectum on their integral dose distribution and the movement of the uterus in the treatment planning of gynecological cancer. *Radiother Oncol* 1999; 52:29-34.

Rationale: The structure in light green/outline highlights the movement of the uterus with an empty and full bladder. This is important in cervical cancer IMRT because the uterus can move depending on filling. This is an ITV of a uterus accommodating changes in bladder size. To initiate radiotherapy planning, additional expansion to account for posterior displacement would be necessary.

113. In cervical cancer, what is associated with open abdominal hysterectomies compared to minimally invasive approaches?

- A. Lower rates of DFS and OS
- B. Lower rates of DFS, but no OS difference
- C. Higher rates of DFS, but no OS difference
- D. Higher rates of DFS and OS

Key: D

Domain: 7.5

Citations: Ramirez PT, Frumovitz M, Pareja R, et. al. Minimally Invasive versus Abdominal Radical Hysterectomy for Cervical Cancer. *N Engl J Med* 2018; 379:1895-1904.

Rationale: The LACC randomized trial demonstrated that minimally invasive radical hysterectomy (laparoscopic or robot-assisted) was associated with lower disease-free survival and overall survival when compared to open radical hysterectomy in early stage cervical cancer patients.

114. According to the original GEC ESTRO working group recommendations from 2006 for cervical cancer brachytherapy, what parameter MUST be reported for the high-risk CTV?

- A. V90
- B. D90
- C. V95
- D. D95

Key: B

Domain: 7.8

Citations: Potter R, Haie-Meder C, Limbergen EV, et. al. Recommendations from gynaecological (GYN) GEC ESTRO working group (II): Concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy – 3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology.

Rationale: The GEC ESTRO working group guidelines recommended reporting the D90 for HR-CTV and IR-CTV as well as the D100 for GTV.

115. For cervical brachytherapy, what is the risk of fistulae development when the total rectal D2cc EQD2 of ≥ 75 Gy?

- A. <1%
- B. 2-5%
- C. 6-10%
- D. >10%

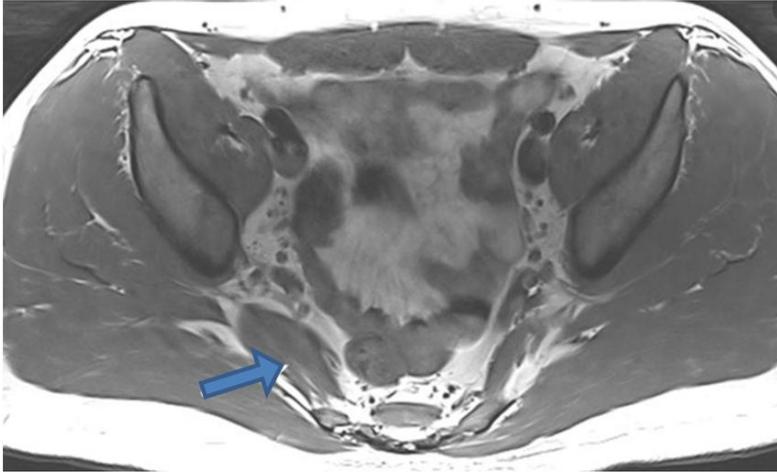
Key: D

Domain: 7.6

Citations: Mazon R, Fokdal LU, Kirchheiner K, et. al. Dose-volume effect relationships for late rectal morbidity in patients treated with chemoradiation and MRI-guided adaptive brachytherapy for locally advanced cervical cancer: results from the prospective multicenter EMBRACE study. *Radiother Oncol.* 2016; 120:412-19.

Rationales: A large DVH analysis has shown that rectal D2cc doses ≤ 75 Gy was associated with a 2.7% rate of fistula development vs 12.5% when D2cc is >75 Gy.

116. What muscle is indicated by the arrow?



- A. Iliacus
- B. Internal obturator
- C. Psoas
- D. Piriformis

Key: D

Domain: 7.5

Citations: Small W Jr, Mell LK, Anderson P, et al. Consensus guidelines for delineation of clinical target volume for intensity-modulated pelvic radiotherapy in postoperative treatment of endometrial and cervical cancer. *Int J Radiat Oncol Biol Phys.* 2008;71(2):428-434.

Rationale: The piriformis muscle originates from the sacrum and inserts on the greater trochanter. Classic contour guidelines for postoperative gynecologic cancers IMRT proposed to utilize it as a landmark to discontinue presacral lymph node coverage, in some situations when clearly visualized.

117. What genetic syndrome predisposes to a higher risk of endometrial cancer?

- A. Hereditary nonpolyposis colorectal cancer
- B. Ataxia-telangectasia
- C. Fanconi's Anemia
- D. Li-Fraumeni

Key: A

Domain: 7.1

Citations: Bonadona V, Bonaïti B, Olschwang S, et. al. Cancer risks associated with germline mutations in MLH1, MSH2, and MSH6 genes in lynch syndrome. JAMA. 2011;305(22):2304–10.

Rationale: Lynch Syndrome (hereditary nonpolyposis colorectal cancer) results from mismatch repair deficiency (MLH1, MSH2, MSH6, PMS2) and has an increased risk of colon, gastric, small bowel, urothelial and endometrial cancers. Other syndromes with increased risk include Cowden syndrome, PTEN mutation, and Peutz-Jeghers, STK11.

118. What is a benefit of IMRT over 3D-CRT after hysterectomy for gynecologic cancers?

- A. OS
- B. Local control
- C. Less acute GI side effects
- D. Improved patient throughput

Key: C

Domain: 7.4

Citations: Klopp et. al. 2018. Patient-Reported Toxicity During Pelvic Intensity-Modulated Radiation Therapy: NRG Oncology–RTOG 1203. J Clin Oncol. 2018 Aug 20; 36(24): 2538–2544.

Rationale: In RTOG 1203, patients with cervical and endometrial cancer who received pelvic radiation postoperatively were stratified by dose (45 or 50.4 Gy), use of chemotherapy (none or 5 cycles of weekly cisplatin at 40 mg/m²), and disease site, and then randomly assigned to standard 4-field radiation or IMRT. The primary endpoint was a change in acute gastrointestinal (GI) toxicity from baseline to 5 weeks measured by the bowel domain of Expanded Prostate Cancer Index Composite (EPIC). 20.4% of women on the standard RT arm took 4 or more antidiarrheal medications daily, as compared to 7.8% of women on the IMRT arm (P =0.04). At the 3-year update (abstract form), improvements in late GU toxicity are demonstrated while sustained difference GI toxicity is not apparent. Regarding the option D, IMRT is not expected to improve access to care due to higher demand on resources compared to the conventional 3D CRT.

119. What is the preferred postoperative treatment for IBG2 endometrioid adenocarcinoma of the endometrium with positive LVI?

- A. Pelvic EBRT
- B. Concurrent chemoRT
- C. Chemotherapy alone
- D. Re-resection of residual vaginal tissue

Key: A

Domain: 7.1

Citations: Randall et. al. Phase III Trial: Adjuvant Pelvic Radiation Therapy Versus Vaginal Brachytherapy Plus Paclitaxel/Carboplatin in High-Intermediate and High-Risk Early-Stage Endometrial Cancer. *J Clin Oncol.* 2019 Jul 20; 37(21): 1810–1818.

Rationale: GOG 249 enrolled 610 patients randomly assigned to the typical pelvic irradiation vs. the combination of chemotherapy and vaginal brachytherapy. Most patients had the G1-2 endometrioid histology with additional risk features. Standard EBRT resulted in lower nodal relapse rate, better acute toxicities, and lower patient-reported fatigue levels while maintaining the same OS and RFS as the experimental treatment.

120. Which brachytherapy apparatus is the LEAST suitable in newly diagnosed, medically inoperable endometrial cancer?

- A. Tandem and ring
- B. Multichannel vaginal cylinder
- C. Heyman packing
- D. Tandem and ovoids

Key: B

Domain: 7.6

Citations: Nguen, et al. High-dose-rate brachytherapy for Medically Inoperable Stage I Endometrial Cancer. *Gynecologic Oncology.* 71, 196–203 (1998).

Rationale: Curative-intent brachytherapy is the treatment of choice for uterine neoplasms that cannot be safely removed via hysterectomy. An appropriate apparatus must allow introduction of the radioactive sources into the endometrial cavity. Among implant types listed, only vaginal cylinders do not meet this goal.

121. What is an expected adverse reaction to cervical brachytherapy?

- A. Bacteremia
- B. Insufficiency fracture
- C. Lymphedema
- D. Hyperpigmentation

Key: A

Domain: 7.2

Citations: Gupta et. al. Acute complications following intracavitary high-dose-rate brachytherapy in uterine cancer. *J Contemp Brachytherapy*. 2014 Oct; 6(3): 276–281.

Rationale: Brachytherapy for intact cervical cancer is an example of an invasive medical procedure. As such, it is associated with a risk of infection including sepsis. Other syndromes listed may result from pelvic EBRT but are unlikely to be caused by brachytherapy.

122. What is a gray zone in MR-assisted cervical brachytherapy?

- A. High T2 signal in gross tumor
- B. Avoidance structure within the bladder wall
- C. Area at high risk for residual microscopic disease
- D. Avoidance structure within the rectal lumen

Key: C

Domain: 7.6

Citations: Prescribing, Recording, and Reporting Brachytherapy for Cancer of the Cervix. CRU, J. o. (2013). ICRU REPORT 89. Oxford University Press.

Rationale: MR is useful in defining target structures for cervical brachytherapy boost after EBRT. For cancers with lateral parametrial extensions, the concept of gray zones indicating residual pathologic tissue in the case of infiltrative extra-cervical growth has been introduced. In other words, gray zones represent areas with a high risk of residual disease. Such gray zones must be located in areas where gross disease was seen on MRI before the initial treatment. An effort should be made to deliver a sufficient brachytherapy dose to gray zones.

123. What is the MOST appropriate total EQD2 limit for D2cc of the urinary bladder in the treatment of intact cervical cancer?

- A. 55 Gy
- B. 80 Gy
- C. 85 Gy
- D. 90 Gy

Key: B

Domain: 7.4

Citations: Chino et. al. Radiation Therapy for Cervical Cancer: Executive Summary of an ASTRO Clinical Practice Guideline. *Pract Radiat Oncol.* 2020 Jul-Aug;10(4):220-234. doi: 10.1016/j.prro.2020.04.002.

Rationale: Women undergoing cervical implants are at risk for late, severe bladder toxicity. The first generation of high dose-rate brachytherapy data was interpreted as evidence for relatively high radiation tolerance of the bladder. However, current practice guidelines for brachytherapy suggest limiting total bladder dose to < 80 Gy.

124. Which of the DVH parameters is acceptable in postoperative cervical IMRT?

- A. Small bowel $D_{max} = 52.5$ Gy
- B. Femur $D_{max} = 55$ Gy
- C. Bladder V_{45} Gy = 75%
- D. Pelvic bone marrow D_{40} Gy = 60%

Key: A

Domain: 7.4

Citations: Klopp et. al. 2018. Patient-Reported Toxicity During Pelvic Intensity-Modulated Radiation Therapy: NRG Oncology–RTOG 1203. *J Clin Oncol.* 2018 Aug 20; 36(24): 2538–2544.

Rationale: When 50-50.4 Gy is prescribed for a resected cervical cancer, a small portion of bowel within the PTV expansion would be expected to receive prescribed dose + acceptable inhomogeneity. Volume of the bladder receiving high dose should be limited using intensity modulation techniques. The spinal cord dose can be kept below 45 Gy in all adjuvant scenarios, even if PTV is extended into the para-aortic region.

125. Which arrow points to an abnormality MOST likely to be caused by stage IIB cervical cancer?



- A. A
- B. B
- C. C
- D. D

Key: D

Domain: 7.5

Citations: Lagasse, et. al. Results and complications of operative staging in cervical cancer: Experience of the Gynecologic Oncology Group. *Gynecol Oncol.* 1980 Feb; 9(1):90-8. doi: 10.1016/0090-8258(80)90013-x.

Rationale: Metastatic lymphadenopathy is a common finding in locally advanced cervical cancer.

126. Which nodal levels are included in the CTV when treating a cT2N0 nasopharyngeal carcinoma confined to the nasopharynx?

- A. Bilateral retropharyngeal lymph nodes and cervical lymph node levels II, III, and Va
- B. Bilateral retropharyngeal lymph nodes and cervical lymph node levels IB, II, III
- C. Bilateral cervical lymph node levels IB, II, III, IV and Va
- D. Bilateral cervical lymph node levels IB, II and III

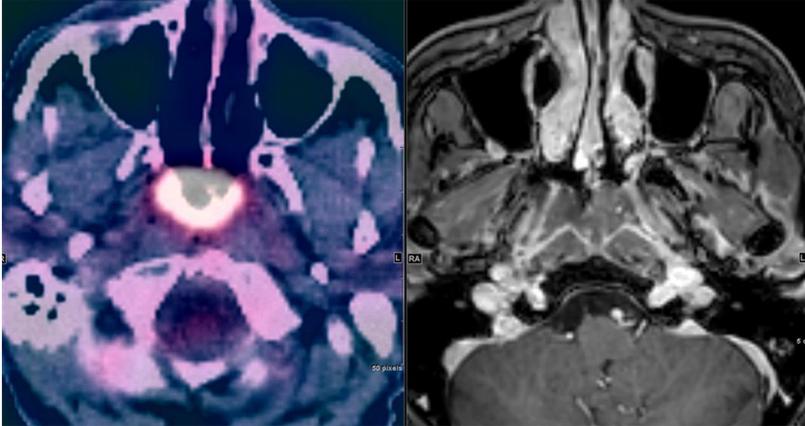
Key: A

Domain: 8.1

Citations: Lee AW, et. al. International guideline for the delineation of the clinical target volumes (CTV) for nasopharyngeal carcinoma. *Radiotherapy and Oncology* 126 (2018) 25-36.

Rationale: Current guidelines recommend elective coverage of bilateral retropharyngeal lymph nodes and cervical nodal levels II, III and Va for all patients. Level IB should be considered for tumor that extend to involve the nasal cavity or regions for which level IB is primary echelon lymph node drainage.

127. A patient presents with nasal congestion, epistaxis, and progressive bilateral cervical lymphadenopathy. Flexible endoscopy demonstrates a mass posterior to the nasal choanae, and biopsy confirms keratinizing squamous cell carcinoma, EBV negative. Axial PET-CT and T1-weighted MRI images are shown below. What is the most appropriate clinical stage for this patient?



- A. T2N0
- B. T1N1
- C. T1N2
- D. T2N1

Key: C

Domain: 8.1

Citations: AJCC Cancer Staging Manual Eighth Edition, 2017

Rationale: Based on the information provided in the MRI and PET-CT images, the examinee should recognize that the tumor involves the nasopharynx and is confined to the mucosa without parapharyngeal involvement which is T1. Given a history of bilateral cervical LAD, the N stage is N2. Among the choices provided, the best answer is T1N2 (AJCC VIII).

128. What is the recommended adjuvant therapy for a patient with a resected oral tongue cancer, pT2N1 cM0 with PNI, LVI, 5mm margin, and depth of invasion 7mm?

- A. RT to the primary site and bilateral neck level I-IV
- B. RT to the primary site and bilateral neck level I-III
- C. RT to the primary site
- D. ChemoRT to the primary site and bilateral neck level I-IV

Key: A

Domain: 8.2

Citations: Beyers, et al., "Frequency and therapeutic implication of 'skip metastasis' in the neck from squamous carcinoma of the oral tongue", *Head and Neck* 1996.

Rationale: LVI and PNI are indications for adjuvant treatment. In the absence of ECE (pN2a or N3b) and positive margins concurrent chemotherapy is not indicated. Oral tongue cancer has metastatic skip lesions to level IV ~15% of the time and depth of invasion >4 mm is high risk of lymph node involvement.

129. For resected oral cavity cancer with extranodal extension, the key benefit of adding concurrent cisplatin to postoperative RT is the reduction of:

- A. local-regional recurrence.
- B. metastatic disease.
- C. second primary cancers.
- D. radiation dose.

Key: A

Domain: 8.2

Citations: Cooper, et. al. Postoperative concurrent radiotherapy and chemotherapy for high-risk squamous-cell carcinoma of the head and neck. *NEJM*, 2004, 350(19):1937-1944.

Bernier, et. al. Postoperative irradiation with or without concomitant chemotherapy for locally advanced head and neck cancer. *NEJM*, 2004, 350(19):1945-1952.

Rationale: An improvement in local-regional control is the greatest benefit of adding postoperative chemotherapy to radiation for high-risk patients with positive margins or extranodal extension. The RTOG 9501 and EORTC 22931 trials both showed a significant improvement in local-regional control but with increased grade 3 or higher acute toxicity. Neither trial showed a significant improvement in distant metastases and only the EORTC 22931 trial showed a statistically significant improvement in overall survival.

130. How does smoking during treatment of oropharyngeal cancer affect OS in the risk stratified RTOG 0129 study?

- A. No impact on OS
- B. Decreased by ≈5%
- C. Decreased by ≈15%
- D. Decreased by ≈25%

Key: D

Domain: 8.3

Citations: Maura L. Gillison, et. al., Tobacco smoking and increased risk of death and progression for patients with p16-positive and p16-negative oropharyngeal cancer. *J Clin Oncol.* 2012 Jun 10; 30(17): 2102–2111. Published online 2012 May 7. doi: 10.1200/JCO.2011.38.4099. PMID: 22565003.

Rationale: In the RTOG 0129 data, patients that continued smoking during treatment had an OS decrease of approximately 25%. An absolute benefit in OS of 24.6% (95% CI, 5.9% to 43.3%) was observed at 5 years.

131. The ORATOR trial compared RT +/- chemotherapy to transoral robotic surgery and neck dissection with adjuvant treatment as indicated for oropharyngeal squamous cell carcinoma. What did this study show with regards to the primary endpoint, swallowing-related QOL scores 1 year after treatment?

- A. Surgery was superior
- B. Radiation was superior
- C. There was no difference
- D. The addition of chemotherapy worsened swallowing scores

Key: B

Domain: 8.3

Citations: Nichols et al. Radiotherapy versus transoral robotic surgery and neck dissection for oropharyngeal squamous cell carcinoma (ORATOR): an open-label, phase 2, randomised trial. *Lancet Oncol.* 2019 Oct; 20(10):1349-1359.

Rationale: Patients treated with radiotherapy showed superior swallowing-related quality of life (QOL) scores 1 year after treatment. QOL at 1 year was established using the MD Anderson Dysphagia Inventory (MDADI) score. MDADI total scores at 1 year were mean 86.9 (SD 11.4) in the radiotherapy group versus 80.1 (13.0) in the TORS plus neck dissection group (p=0.042).

132. What is the stage group for a 1 cm thyroid nodule that is fully contained in the lobe on ultrasound, biopsy shows anaplastic thyroid carcinoma, and PET CT indicates no other disease?

- A. IA
- B. II
- C. IIIA
- D. IVA

Key: D

Domain: 8.4

Citations: AJCC Cancer Staging Manual Eighth Edition, 2017

Rationale: The lowest stage grouping for anaplastic thyroid carcinoma is IVA.

133. Which treatment offers the highest chance of larynx preservation for locally advanced (T3/T4) larynx cancer?

- A. RT alone
- B. Induction chemotherapy followed by RT
- C. RT followed by chemotherapy
- D. Concurrent chemoRT

Key: D

Domain: 8.5

Citations: Forastiere AA, et al. Use of larynx-preservation strategies in the treatment of laryngeal cancer: american society of clinical oncology clinical practice guideline update. J Clin Oncol 36:1143-1169, 2017.

Forastiere AA, Zhang Q, Weber RS, 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. J Clin Oncol 31:845-852, 2013.

Rationale: RTOG 91-11 was a 3-arm trial comparing larynx preservation approaches: RT alone vs induction chemotherapy followed by RT vs concurrent chemoRT. Larynx preservation was highest in the concurrent chemoRT arm (10-yr 81.7%, HR 0.58; 95% CI, 0.37 to 0.89) compared to induction chemo followed by RT (10-yr 67.5%, p=0.0050) and over RT alone (10-yr 63.8%, p<0.001). The sequential approach of 1-3 cycles of induction chemotherapy for selection of patients for larynx preservation with chemoRT requires more data to be considered a standard option.

134. Twelve weeks after chemRT for a cT3N1 larynx cancer, a patient has a complete response on office examination and PET-CT with IV contrast. What is the MOST appropriate next step?
- A. Neck dissection
 - B. Repeat PET-CT in 4 weeks
 - C. Clinical monitoring
 - D. Exam under anesthesia

Key: C

Domain: 8.5

Citations: Forastiere, et. al. Use of larynx-preservation strategies in the treatment of laryngeal cancer: American Society of Clinical Oncology clinical practice guideline update. 2018, J Clin Oncol 26:1143-1169

Rationale: The 2018 ASCO Larynx Preservation Guideline Update emphasizes that patients with clinically involved lymph nodes that have a post-treatment complete response on imaging and examination, do not require elective neck dissection.

135. A patient presents with progressive hoarseness and odynophagia. CT of the neck is shown below. There is no lymphadenopathy or distant metastases. Which treatment would provide the optimal tumor control?



- A. RT to 70 Gy in 35 Fx
- B. Induction chemotherapy followed by RT to 70 Gy in 35 Fx
- C. Concurrent cisplatin-based chemoRT to 70 Gy in 35 Fx
- D. Total laryngectomy and adjuvant (chemo)RT based on pathologic findings

Key: D

Domain: 8.5

Citations: Forastiere, et. al. Use of larynx-preservation strategies in the treatment of laryngeal cancer: American Society of Clinical Oncology clinical practice guideline update. 2018, J Clin Oncol 26:1143-1169

Rationale: The purpose of this question is to identify optimal treatment of resectable clinical stage T4a larynx cancer. The patient has significant extrathyroidal extension with cortical breakthrough of the thyroid cartilage. Although controversial to some, the best level of evidence indicates optimal local control and survival with definitive surgical treatment.

136. What were the OS outcomes in the EORTC 24891 which randomized patients with locally advanced hypopharynx squamous cancer to surgical resection followed by RT versus a larynx preservation approach (3 cycles induction chemotherapy followed by RT in complete responders)?
- A. Better with larynx preservation approach
 - B. Worse with larynx preservation approach
 - C. Non-inferior with larynx preservation approach
 - D. Not the primary endpoint of the trial

Key: C

Domain: 8.6

Citations: Lefebvre J-L, et al. Laryngeal preservation with induction chemotherapy for hypopharyngeal squamous cell carcinoma: 10-year results of EORTC trial 24891. *Annals of Oncology* 23:2708-2714, 2012.

Rationale: End points of EORTC 24891 were overall survival, progression-free survival, and survival with a functional larynx. The larynx preservation approach with induction chemotherapy did not compromise disease control or survival and allowed more than half of the survivors to retain their larynx.

137. A 52 year-old non-smoker presents with a single right level II lymph node that measures 2.5 cm. His history, physical exam, and fiberoptic laryngoscopy are negative for a primary site. What are the next steps for work-up?
- A. FNA, HPV testing, contrast-enhanced CT, PET-CT, exam under anesthesia
 - B. Nodal excision, HPV testing, contrast-enhanced CT, exam under anesthesia, PET-CT
 - C. Core needle biopsy, HPV testing, contrast-enhanced CT, exam under anesthesia, PET-CT
 - D. FNA, HPV testing, MRI, exam under anesthesia, PET-CT

Key: A

Domain: 8.7

Citations: Maghami E, et al. Diagnosis and management of squamous cell carcinoma of unknown primary in the head and neck: ASCO Guideline. *J Clin Oncol* 38:2570-2596, 2020.

Rationale: PET-CT should always be done prior to examination under anesthesia, as PET may guide biopsies and PET after examination under anesthesia with biopsies may result in false positives.

138. Which salivary malignancy is MOST likely to be HER2+?

- A. Adenoid cystic carcinoma
- B. Hyalinizing clear cell carcinoma
- C. Low grade mucoepidermoid carcinoma
- D. Salivary ductal carcinoma

Key: D

Domain: 8.8

Citations: Glisson, et. al. HER2 expression in salivary gland carcinomas. *Clinical Cancer Research* 2004, 10 (944-946).

Limaye, et. al. Trastuzumab for the treatment of salivary duct carcinoma. *Oncologist*. 2013; 13(3):294-300.

Rationale: Salivary duct carcinoma is an aggressive high-grade salivary malignancy with a high rate of HER2 overexpression compared with other salivary malignancies. There is controversy regarding the potential use of HER2-directed therapy for recurrent or metastatic HER2-overexpressing salivary cancers.

139. A patient has an enlarging lesion in the left hard palate and nasal cavity. The patient endorses numbness of the medial portion of the left nasolabial fold indicating involvement of which nerve?

- A. Vidian nerve
- B. Greater and lesser palatine nerves
- C. Infraorbital nerve
- D. Mental nerve

Key: C

Domain: 8.9

Citations: Ko, et. al., A contouring guide for head and neck cancers with perineural invasion. *Pract Rad Onc* 2014; 247-258

Rationale: Adenoid cystic carcinoma is recognized for its propensity for perineural spread and is the most likely diagnosis for a younger nonsmoker with indolent tumor growth. Regardless, the purpose of the question is for the examinee to recognize upper lip innervation by the infraorbital nerve, an important clinical pearl in sinonasal tumors.

140. What is included in the postoperative radiation volume for a 5.1 cm Merkel cell carcinoma of the left temple after wide local excision of the primary?

- A. Surgical bed
- B. Surgical bed, left parotid
- C. Surgical bed, left parotid and neck
- D. Surgical bed and left neck

Key: C

Domain: 8.10

Citations: Verness and Howle Cutaneous Carcinoma, (2016) – IN Gundersoon LLG, Tepper JE 4th edition page 763.

Jouary et al. Adjuvant prophylactic regional radiotherapy versus observation in stage I Merkel cell carcinoma: a multicentric prospective randomized study. *Ann Oncol.* 2012 Apr;23(4):1074-80

Rationale: Skin on the temple drains to the parotid lymph nodes and then to level Ib-III. Adjuvant radiation of Merkel cell carcinoma would include the surgical bed and draining nodal regions.

141. Cranial nerve IX exits the skull base through which opening?

- A. Foramen spinosum
- B. Foramen ovale
- C. Jugular foramen
- D. Foramen lacerum

Key: C

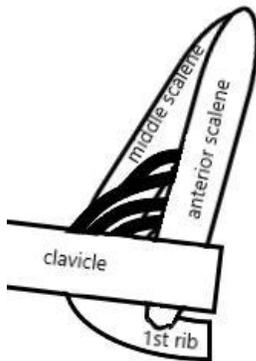
Domain: 8.11

Citations: Mourad, et al. Clinical validation and applications for CT-based atlas for contouring the lower cranial nerves for head and neck cancer radiation therapy. *Oral Oncol.* 2013 Sep;49(9):956-963.

Ko et al. A contouring guide for head and neck cancers with perineural invasion. *Pract Radiat Oncol.* Nov-Dec 2014; 4(6):e247-58.

Rationale: The following skull base foramina are shown with the respective nerves that exit them: cavernous sinus – CN III, CN IV, V1, V2, CN VI; foramen rotundum – CN V2; foramen ovale – CN V3; jugular foramen – CN IX, X, XI; foramen lacerum – greater and deep petrosal nerves to form nerve of pterygoid canal, internal carotid artery with venous and sympathetic plexus.

142. The inferior end of the middle scalene muscle inserts onto which bone?



- A. Sternum
- B. Clavicle
- C. 1st rib
- D. Scapula

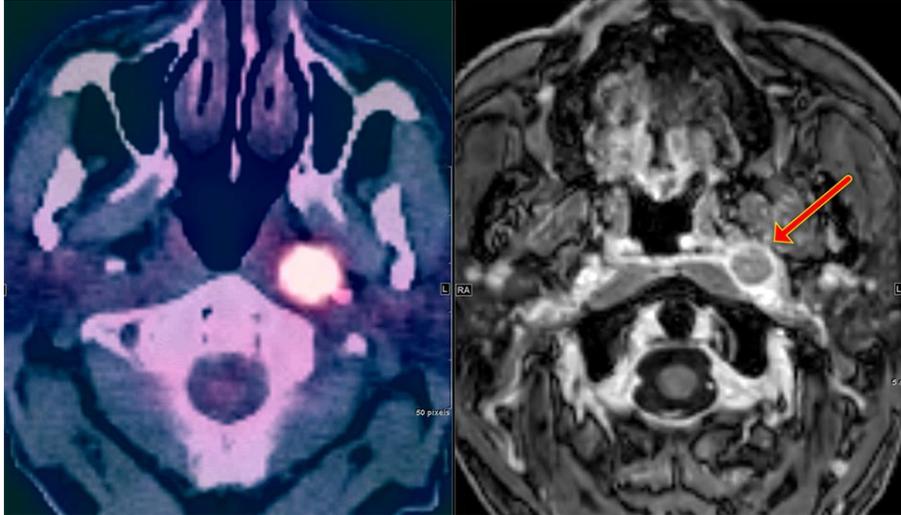
Key: C

Domain: 8.11

Citations: Hall, et al. Development and validation of a standardized method for contouring the brachial plexus: preliminary dosimetric analysis among patients treated with IMRT for head-and-neck cancer. *Int J Radiat Oncol Biol Phys.* 2008 Dec 1;72(5):1362-7.

Rationale: The anterior and middle scalene muscles arise from the transverse processes of cervical vertebrae and insert on the first rib. The brachial plexus passes between the anterior and middle scalene and then over the 1st rib behind the clavicle.

143. What is the level of the pathologic lymph node indicated on PET-CT and MRI?



- A. IV
- B. V
- C. VI
- D. VII

Key: D

Domain: 8.11

Citations: Gregoire V, et. al. Delineation of the neck node levels for head and neck tumors: a 2013 update. DAHANCA, EORTC, HKNPCSG, NCIC CTG, NCRI, RTOG, TROG consensus guidelines. *Radiotherapy and Oncology* 2014; 110: 172-181.

Rationale: The MRI and PET-CT clearly show a lymph node in the lateral retropharyngeal space, medial to the internal carotid. This is categorized as a level VIIa node.

144. A patient presents with a right lateral oral tongue SCC, 1.5 cm in size, 8mm depth of invasion, and ipsilateral adenopathy in level Ib (2 cm) and IIa (2.5cm). There is overt extranodal extension of the 1b node. Metastatic work-up is negative. What is the clinical stage?

- A. T1N2bM0, Stage IVa
- B. T2N2bM0, Stage IVa
- C. T1N2aM0, Stage IVa
- D. T2N3bM0, Stage IVb

Key: D

Domain: 8.12

Citations: AJCC Cancer Staging Manual Eighth Edition, 2017

Rationale: In the 8th Edition, depth of invasion in oral cavity cancer now influences T stage. A primary tumor that is ≤ 2 cm with a depth of invasion of >5 mm is now T2. A single ipsilateral lymph node larger than 3cm but not larger than 6cm is N2a, multiple ipsilateral lymph nodes <6 cm without overt extranodal extension is N2b, any node(s) with clinically overt ENE is N3b.

145. A patient with p16-positive squamous cell carcinoma of a cervical lymph node with no identified primary on comprehensive workup is staged according to which staging rules?

- A. Nasopharynx
- B. Oropharynx (p16-) and hypopharynx
- C. HPV-mediated (p16+) oropharyngeal cancer
- D. Cervical lymph nodes and unknown primary tumors of the head and neck

Key: C

Domain: 8.12

Citations: AJCC Cancer Staging Manual Eighth Edition, 2017

Rationale: Patients with HPV-mediated p16+ cervical lymph nodes of unknown primary site are staged according to the HPV-mediated (p16+) oropharyngeal cancer staging system. Staging of patients who present with an occult primary tumor and EBV-unrelated and HPV-unrelated metastatic cervical adenopathy are staged using the staging system for Cervical Lymph Nodes and Unknown Primary tumors of the Head and Neck.

146. In two randomized trials comparing concurrent cisplatin + RT versus cetuximab + RT in low risk HPV+ oropharynx cancer patients, what was the outcome with using cetuximab + RT?

- A. Decreased acute toxicity
- B. Increased compliance
- C. Decreased overall survival
- D. Increased locoregional control

Key: C

Domain: 8.13

Citations: Gillison ML, et. al. Radiotherapy plus cetuximab or cisplatin in human papillomavirus-positive oropharyngeal cancer (NRG Oncology RTOG 1016): a randomized, multicenter, non-inferiority trial. *Lancet* 393:40-50-, 2019.

Mehanna H, et. al. Radiotherapy plus cisplatin or cetuximab in low-risk human papilloma-virus-positive oropharyngeal cancer (De-ESCALaTE HPV): an open-label randomized controlled phase 3 trial.

Rationale: Both RTOG 1016 and De-ESCALaTE HPV showed that cetuximab + RT did not reduce toxicity, but instead showed significant detriment in terms of locoregional control and overall survival.

147. Which systemic agent is used in the treatment of nasopharyngeal cancer but is not commonly used for other squamous cell carcinomas of the head and neck?

- A. Carboplatin
- B. Hydroxyurea
- C. Gemcitabine
- D. Pembrolizumab

Key: C

Domain: 8.13

Citations: Zhang et al. Gemcitabine and cisplatin induction chemotherapy in nasopharyngeal carcinoma. *N Engl J Med*. 2019 Sep 19;381(12):1124-1135.

Zhang et al. Gemcitabine plus cisplatin versus fluorouracil plus cisplatin in recurrent or metastatic nasopharyngeal carcinoma: a multicentre, randomised, open-label, phase 3 trial. *Lancet*. 2016 Oct 15;388(10054):1883-1892.

Rationale: Gemcitabine in combination with cisplatin has shown benefit in randomized controlled trials for the treatment of nasopharyngeal carcinoma as induction therapy and in the setting of recurrent and metastatic disease. The other systemic agents listed may be used in other head and neck squamous cell carcinomas while gemcitabine is not.

148. What is the rate of transformation of oral dysplasia to invasive cancer?

- A. 10%
- B. 30%
- C. 50%
- D. 70%

Key: A

Domain: 8.14

Citations: Mehanna et al. Treatment and follow-up of oral dysplasia - a systematic review and meta-analysis. *Head Neck*. 2009 Dec;31(12):1600-9.

Warnakulasuriya and Ariyawardana, Malignant transformation of oral leukoplakia: a systematic review of observational studies. *J Oral Pathol Med*. 2016 Mar;45(3):155-66.

Rationale: A variety of studies range widely, but most indicate malignant transformation rates of below 10%, and meta-analysis puts overall rates around 10%.

149. Which of the following best represents expected optic neuropathy rates following conventionally fractionated irradiation of the optic nerve and chiasm?

- A. 5% at 55 Gy
- B. <3% at 55 Gy and 25% at 60 Gy
- C. <3% at 55 Gy and 7% at 60 Gy
- D. 50% at 60 Gy

Key: C

Domain: 8.15

Citations: Marks, et. al., *Int. J. Radiation Oncology Biol. Phys.*, Vol. 76, No. 3, Supplement, pp. S10–S19, 2010.

Rationale: The QUANTEC dose-volume limit summary lists optic neuropathy rates of <3% for 55 Gy, 3-7% for 55-60 Gy, and 7-20% for 60 Gy.

150. For conventionally fractionated RT, what is the mean dose limit to the cochlea to minimize the risk for sensorineural hearing loss?

- A. 25 Gy
- B. 30 Gy
- C. 45 Gy
- D. 60 Gy

Key: C

Domain: 8.15

Citations: Honore HB, Bentzen SM, Moller K, et. al. Sensori-neural hearing loss after radiotherapy for nasopharyngeal carcinoma: Individualized risk estimation. *Radiother Oncol* 2002; 65:9–16.

Rationale: Quantec recommendations are for dose to the cochlea to be less of equal to 45Gy to minimize sensorineural hearing loss.

151. What is the recommended management of limited stage SCLC?

- A. Consolidation durvalumab after chemoRT
- B. Surveillance MRI in lieu of PCI
- C. 66 Gy in 33 Fx is recommended over BID fractionation
- D. Adjuvant chemotherapy after lobectomy for stage I disease

Key: D

Domain: 9.1

Citations: NCCN Guidelines, Small Cell Lung Cancer, version 1.2021

Rationale: Choice D is the correct answer because SCLC is inherently a systemic disease, even at the earliest stages, and therefore even with effective local therapy like surgery in a resectable patient, adjuvant chemotherapy +/- PCI should be considered for all patients. Choice A is incorrect since durvalumab (or atezolizumab) is given with chemotherapy in extensive stage SCLC, and not a standard of care in limited stage SCLC. Consolidation durvalumab is given after chemoradiation for stage III NSCLC. Choice B is incorrect since PCI is still recommended for limited stage SCLC but based on Takahashi et al phase II RCT, consideration can be made to do MRI surveillance in lieu of PCI for extensive stage SCLC after chemotherapy. Choice C is incorrect since the CONVERT trial still considered 45 Gy in 30 fractions at 1.5 Gy BID (Turrisi regimen) as the standard since there is no difference in outcomes between the Turrisi regimen and the experimental arm of 66 Gy in 33 fractions when the primary hypothesis was that there would be benefit of the 66 Gy arm. However, there was no improved toxicity in the 66 Gy arm and no improvement in overall survival.

152. What is a treatment option for a patient with stage IA SCLC?

- A. Platinum-etoposide doublet chemotherapy alone
- B. SBRT followed by chemotherapy
- C. SBRT alone
- D. 45 Gy in 30 Fx BID RT alone

Key: B

Domain: 9.1

Citations: Simone CB 2nd et al. Radiation Therapy for Small Cell Lung Cancer: An ASTRO Clinical Practice Guideline. *Pract Radiat Oncol.* May-Jun 2020;10(3):158-173. PMID: 32222430.

Rationale: In the recent ASTRO SCLC guidelines either SBRT or conventional fractionation is recommended. Adding RT to chemotherapy is likely to improve survival rates compared to chemotherapy alone for LS-SCLC, hence option A is incorrect. For patients receiving SBRT, chemotherapy should be delivered to patients in whom it is medically tolerated. This was a strong recommendation supported by moderate evidence, hence option B is correct, with SBRT started and completed before initiation of chemotherapy or delivered between early cycles of chemotherapy. Standard fractionation is an option but is not evidence-based in the absence of radiosensitizing chemotherapy.

153. Based on the Impower133 and CASPIAN trials, the addition of which drugs, respectively, when combined with chemotherapy can improve OS as first-line treatment of extensive stage SCLC?

- A. Durvalumab and nivolumab
- B. Atezolizumab and durvalumab
- C. Nivolumab and ipilimumab
- D. Atezolizumab and ipilimumab

Key: B

Domain: 9.1

Citations: Horn et al. First-Line Atezolizumab plus Chemotherapy in Extensive-Stage Small-Cell Lung Cancer *N Engl J Med* 2018 Dec 6;379(23):2220-2229. PMID: 30280641.

Paz-Ares et al. Durvalumab plus platinum-etoposide versus platinum-etoposide in first-line treatment of extensive-stage small-cell lung cancer (CASPIAN): a randomised, controlled, open-label, phase 3 trial. *Lancet* 2019 Nov 23;394(10212):1929-1939. PMID: 31590988.

Rationale: The IMpower133 and CASPIAN phase III randomized clinical trials demonstrated a median overall survival benefit of 2 to 3 months with the addition of the PDL-1 inhibitors atezolizumab and durvalumab, respectively, when added to the standard chemotherapy doublet of platinum-etoposide.

154. What were the rates of \geq grade 3 esophagitis noted in the two arms of the CONVERT phase III randomized trial comparing concurrent once-daily chemoRT (66 Gy in 2 Gy Fx) versus twice-daily (45 Gy in 1.5 Gy Fx) for limited-stage SCLC?

- A. 40% for daily, 20% for BID
- B. 20% for both daily and BID
- C. 20% for daily, 40% for BID
- D. 40% for both daily and BID

Key: B

Domain: 9.1

Citations: Faivre-Finn C. et al. Concurrent once-daily versus twice-daily chemoradiotherapy in patients with limited-stage small-cell lung cancer (CONVERT): an open-label, phase 3, randomised, superiority trial. *Lancet Oncol.* 2017;18(8):1116-1125. PMID: 28642008.

Rationale: The CONVERT trial was designed to examine superiority of once-daily vs. twice daily RT, and at a median follow-up of 45 months, median overall survival was 30 months (95% CI 24–34) in the twice-daily group versus 25 months (21–31) in the once-daily group (HR in the once daily group 1.18 [95% CI 0.95–1.45]; $p=0.14$). Survival and toxicity did not differ except grade 4 neutropenia was higher with BID (49%) vs. daily RT (38%, $p=0.05$). Grade 3-4 esophagitis was 19% for both BID and daily RT groups ($p=0.70$), and grade 3-4 radiation pneumonitis was 3% for BID and 2% for daily RT ($p=0.70$).

155. What was the single fraction lung SBRT dose in the RTOG 0915 randomized phase II trial?

- A. 18 Gy
- B. 24 Gy
- C. 34 Gy
- D. 38 Gy

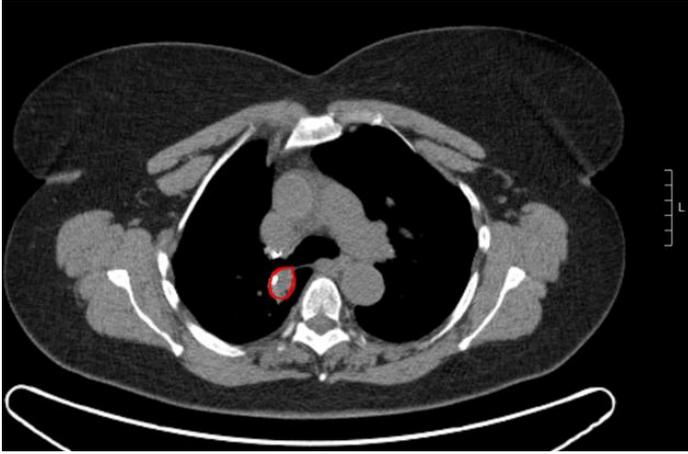
Key: C

Domain: 9.3

Citations: Videtic et. al. Long-term follow-up on NRG Oncology RTOG 0915 (NCCTG N0927): A randomized phase II study comparing 2 stereotactic body radiation therapy schedules for medically inoperable patients with stage I peripheral non-small cell lung cancer. *Int J Radiat Oncol Biol Phys.* 2019 April 01; 103(5): 1077–1084. PMID: 30513377.

Rationale: RTOG 0915 compared 34 Gy in 1 fraction to the standard dose of 48 Gy in 4 fractions for patients with peripheral stage I NSCLC. The primary endpoint was toxicity rates. Rates of grade 3 and higher toxicity, and primary tumor control rates at 5 years were similar by arm. A larger trial will be necessary to detect any survival differences.

156. A patient with prior wedge-resection for an early stage NSCLC presents 2 years later with an enlarging lesion as seen in the image, with SUV of 9.8 on PET-CT, biopsy confirmed to be recurrent NSCLC. What would be a preferred fractionation to treat this lesion with RT alone?



- A. 30 Gy in 1 Fx SBRT
- B. 50-54 Gy in 3 Fx SBRT
- C. 60-70 Gy in 8-15 Fx hypofractionated RT
- D. 60-70 Gy in 30-35 Fx conventionally fractionated RT

Key: C

Domain: 9.3

Citations: Videtic GMM, et al. Stereotactic body radiation therapy for early-stage non-small cell lung cancer: Executive Summary of an ASTRO Evidence-Based Guideline
Pract Radiat Oncol. Sep-Oct 2017;7(5):295-301. PMID: 28596092.

Rationale: The demonstrated lesion is in direct contact with right mainstem bronchus. Tumors that directly abut proximal bronchial tree (or luminal mediastinal structures) are often labeled as “Ultracentral” tumors which are at a higher risk of serious complications with standard dose SBRT in 1-3 fractions. While such patients were included in the RTOG 0813 trial, they formed a small proportion of the patients. Most studies recommend use of more protracted regimens of 8-15 fractions. Conventionally fractionated RT alone is not a preferred option for these tumors.

157. What is the AJCC staging for a patient with biopsy proven lung adenocarcinoma with a 2.9 cm nodule in the right upper lobe, subaortic node involvement, and no other evidence of disease?

- A. IIA
- B. IIIB
- C. IIIC
- D. IVA

Key: B

Domain: 9.4

Citations: Amin MB, ed. AJCC Cancer Staging Manual, 8th Edition Switzerland: Springer, 2017.

Rationale: Patient would be staged as cT1c (2.1-3cm) with contralateral mediastinal lymph node involvement (N3) with no distant metastasis (M0). The prognostic stage group is IIIB.

158. What is the benefit of the addition of local consolidative therapy in patients with oligometastatic (3 or fewer sites) NSCLC?

- A. No significant difference in PFS or OS
- B. Both PFS and OS improved
- C. Only PFS improved
- D. Only OS improved

Key: B

Domain: 9.4

Citations: Gomez et. al. Local Consolidative Therapy Vs. Maintenance Therapy or Observation for Patients with Oligometastatic Non–Small-Cell Lung Cancer: Long-Term Results of a Multi-Institutional, Phase II, Randomized Study. J Clin Oncol 2019 Jun 20; 37(18): 1558-1565. PMID: 31067138.

Rationale: With a median follow-up time of 38.8 months, patients receiving local consolidative therapy had an improved median progression-free survival (23.1 months vs 14.2 months) and an improved overall survival (41.2 months vs 17 months).

159. A 65-year old smoker was found to have an asymptomatic mediastinal mass on screening low dose CT imaging that was biopsy proven to be an adenocarcinoma. Imaging showed numerous hepatic metastases and no brain metastasis. What is the recommended next step in management?

- A. Start osimertinib
- B. Request PD-L1 and mutation testing
- C. Start palliative thoracic RT
- D. Start platinum doublet chemotherapy

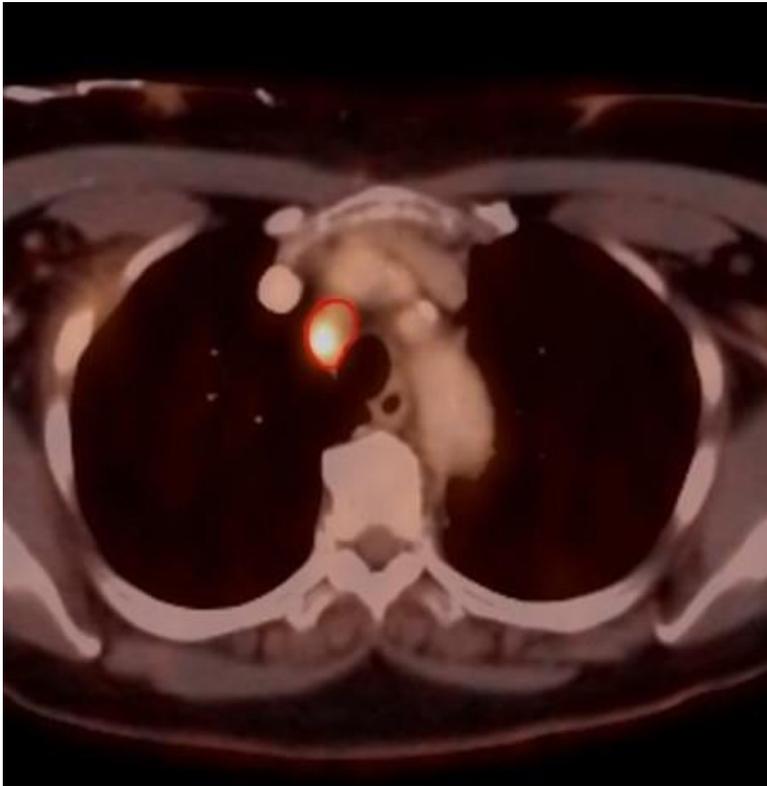
Key: B

Domain: 9.4

Citations: NCCN Guidelines, Small Cell Lung Cancer, version 2.2021

Rationale: Choice B is the correct answer since PD-L1 testing and mutation testing should be considered first in an asymptomatic good performance status patient to determine first line therapies. If there are no actionable mutations, immunotherapy based therapy (+/- chemotherapy) should be considered guided by PD-L1 testing results. Choice A is incorrect since osimertinib should not be started without knowing the EGFR mutation status, especially in a smoker with squamous cell carcinoma, since the possibility of an EGFR mutation is very small. Choice C is incorrect since this patient is asymptomatic and the tumor mass was found incidentally, and therefore palliative radiation should not be considered as the first treatment to be initiated. Choice D is incorrect since the patient likely has good performance status and would be a candidate for either targeted therapy or immunotherapy-based therapies, all of which will be guided by the biomarker testing. Systemic therapy with doublet chemotherapy should not be started without that information.

160. A patient with prior right sided SBRT for early stage NSCLC presents with a PET-CT finding of an FDG avid lymph node below the aortic arch on the right side of the trachea. What is the nodal station for this lymph node as shown below?



- A. 4R
- B. 5
- C. 7
- D. 10R

Key: A

Domain: 9.4

Citations: C F Mountain and C M Dresler. Regional lymph node classification for lung cancer staging. Chest. 1997 Jun;111(6):1718-23. PMID: 9187199.

Rationale: This lymph node is located at right lower paratracheal nodal station or level 4R. 10R will be right hilar, 7 will be subcarinal and 5 will be subaortic (AP window node).

161. Which clinical scenario will be acceptable when planning hippocampal avoidance WBRT in a patient with multiple brain metastases?
- A. Leptomeningeal disease
 - B. Metastases ≥ 5 mm from the hippocampi
 - C. Significant hydrocephalous
 - D. Symptomatic uncal herniation

Key: B

Domain: 9.5

Citations: Brown PD et. al. Hippocampal Avoidance During Whole-Brain Radiotherapy Plus Memantine for Patients with Brain Metastases: Phase III Trial NRG Oncology CC001. J Clin Oncol. 2020 Apr 1;38(10):1019-1029. PMID: 32058845.

Rationale: NRG CC001 study evaluated the role of hippocampal avoidance WBRT to help minimize neurocognitive toxicity of WBRT. Eligibility criteria excluded patients with LMD, patients within 5 mm of the hippocampi or radiographic evidence of hydrocephalus or other architectural distortion of the ventricular system, including placement of external ventricular drain or ventriculo-peritoneal shunt. These exclusions should be kept in mind when planning hippocampal avoidance WBRT.

162. What dose constraint is acceptable in thoracic RT in the following clinical scenarios?
- A. Limited stage SCLC receiving 45 Gy at 1.5 Gy BID: Spinal cord $D_{max} \leq 45$ Gy
 - B. Mesothelioma after extrapleural pneumonectomy receiving adjuvant RT: Mean lung dose ≤ 18 Gy
 - C. Stage III NSCLC receiving chemoRT to 66 Gy in 33 fractions: Total lung $V20 \leq 35\%$
 - D. Early stage NSCLC receiving SBRT to 50 Gy in 4 fractions: Chest wall $V30 \leq 120$ cc

Key: C

Domain: 9.7

Citations: NCCN Guidelines, Non-Small Cell Lung Cancer, version 3.2021.

NCCN Guidelines, Small Cell Lung Cancer, version 2.2021.

NCCN Guidelines, Malignant Pleural Mesothelioma, version 2.2021.

Rationale: Choice C is correct because total lung dose constraint of $V20 \leq 35\%$ -40% is the standard dose constraints for conventionally fractionated chemoradiation. Choice A is incorrect since the spinal cord D_{max} constraint for 45 Gy in 1.5 Gy BID is 36 Gy (41 Gy is acceptable using modern IMRT techniques). Choice B is incorrect because the dose constraints for the remaining lung is mean dose < 8.5 Gy. Choice D is incorrect since the chest wall constraints for SABR 50 Gy in 4 fractions is $V30 \leq 30$ cc (upwards of 50-70 cc is also acceptable with 5 fraction regimens).

163. What potential toxicity is MOST likely to be fatal in patients with ultracentral NSCLC treated with SBRT?

- A. Radiation pneumonitis
- B. Radiation esophagitis
- C. Myocardial infarction
- D. Pulmonary hemorrhage

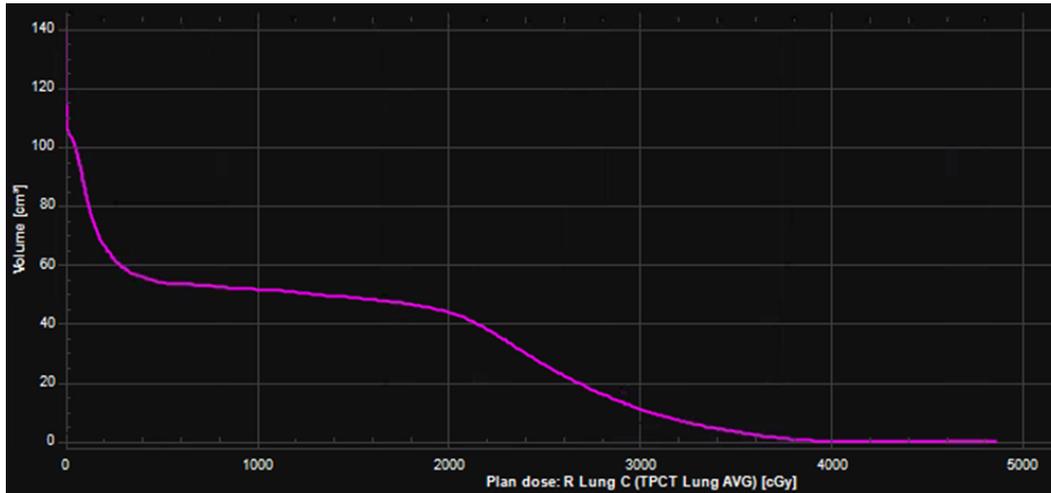
Key: D

Domain: 9.7

Citations: Tekatli et. al. Outcomes of Hypofractionated High-Dose Radiotherapy in Poor-Risk Patients with “Ultracentral” Non–Small Cell Lung Cancer. *J Thoracic Oncol* 2016 Jul;11(7): 1081-1089. PMID: 27013408.

Rationale: Tekatli et. al. treated 47 patients unfit for surgery with ultracentral NSCLC with 60 Gy in 12 fractions. Median overall survival was 15.9 months. No isolated local recurrences were observed. Grade 3 or higher toxicity was recorded in 38% of patients, with 21% scored as having a “possible” (n = 2) or “likely” (n = 8) treatment-related death between 5.2 and 18.2 months after treatment. Fatal pulmonary hemorrhage was the most likely cause of grade 5 toxicity and was observed in 15% of patients.

164. In a 5 fraction lung SBRT treatment, which of the following organs would meet acceptable dose constraints if this were the DVH of that organ?



- A. Spinal cord
- B. Skin
- C. Great vessels
- D. Brachial Plexus

Key: C

Domain: 9.7

Citations: NCCN Clinical Practice Guidelines for Non-Small Cell Lung Cancer, version 3.2021.

Rationale: NCCN Guidelines suggest limiting Spinal Cord, Plexus and Skin to < 30, 32 and 32 Gy respectively when using a 5 fraction regimen. Great Vessels can receive up to 105% of PTV prescription. This DVH shows about 10% of volume above 30 Gy, hence the likely OAR is great vessel.

165. Which is the MOST appropriate first-line systemic therapy for metastatic squamous cell carcinoma of the lung with PD-L1 positivity of 10%?

- A. Carboplatin-pemetrexed-pembrolizumab
- B. Pembrolizumab alone
- C. Carboplatin-paclitaxel-pembrolizumab
- D. Atezolizumab-bevacizumab

Key: C

Domain: 9.6

Citations: Paz-Ares L, et. al. Pembrolizumab plus Chemotherapy for Squamous Non-Small-Cell Lung Cancer. *N Engl J Med.* 2018 Nov 22;379(21):2040-2051. PMID: 30280635.

Rationale: Pemetrexed is a favored chemotherapy in non-squamous (adeno) NSCLC but appears to have less efficacy in squamous cell carcinoma. Pembro alone is reserved for patient with PD-L1 >50%. Combining pembrolizumab plus chemo was demonstrated to be superior in Keynote 407 in squamous cell carcinoma; hence option C is correct. Bevacizumab is contraindicated in lung squamous cell carcinoma given increased hemoptysis risk in this setting.

166. What drug is used as first line therapy for patients with metastatic ALK rearrangement positive NSCLC?

- A. Afatinib
- B. Osimertinib
- C. Alectinib
- D. Gefitinib

Key: C

Domain: 9.6

Citations: NCCN Clinical Practice Guidelines for Non-Small Cell Lung Cancer, version 3.2021.

Rationale: Afatinib, Osimertinib and Gefitinib are all used for treatment of EGFR mutation positive metastatic NSCLC. Alectinib is used in the management of ALK rearrangement positive metastatic NSCLC.

167. Which findings would be MOST consistent with a newly diagnosed thymoma?

- A. Ptosis, miosis, and anhidrosis
- B. Hyponatremia
- C. Hypercalcemia
- D. Muscle weakness with activity

Key: D

Domain: 9.8

Citations: NCCN guidelines Thymomas and Thymic Carcinomas. Version 1.2021.

Rationale: Choice D is correct since this is a classic sign of myasthenia gravis, which occurs in up to 50% of thymoma patients and manifests as easy fatigability with walking. Choice A is incorrect, and although ptosis is one presenting sign of myasthenia gravis, miosis and anhidrosis are not associated with myasthenia gravis. This trio of signs are known as Pancoast syndrome due to lung apex tumors. Choice B is incorrect since SIADH resulting in hyponatremia is often associated with small cell lung cancer. Choice C is incorrect since hypercalcemia of malignancy is often associated with squamous cell carcinoma of the lung.

168. What would be the appropriate adjuvant therapy for a patient with a 5 x 8 cm type A thymoma resected with negative margins without capsular invasion?

- A. Observation
- B. Adjuvant radiation
- C. Adjuvant chemotherapy
- D. Adjuvant radiation and chemotherapy

Key: A

Domain: 9.8

Citations: Kondo K, Monden Y. Therapy for thymic epithelial tumors: a clinical study of 1,320 patients from Japan. *Ann Thorac Surg.* 2003;76(3):878-885. PMID: 12963221.

NCCN guidelines Thymomas and Thymic Carcinomas. Version 1.2021

Rationale: A patient with completely resected R0 type A thymoma without capsular invasion would have Masaoka stage I and AJCC 8th edition T1N0M0 stage group I tumor. Recommended therapy would be surveillance imaging without adjuvant chemotherapy or radiation.

169. What surgery was performed for patients with malignant pleural mesothelioma treated with involved hemithoracic IMRT on the Phase II IMPRINT trial?

- A. Biopsy
- B. Lobectomy
- C. Pleurectomy-decortication
- D. Extra-pleural pneumonectomy

Key: C

Domain: 9.9

Citations: Rimner, et. al. Phase II Study of Hemithoracic Intensity-Modulated Pleural Radiation Therapy (IMPRINT) As Part of Lung-Sparing Multimodality Therapy in Patients with Malignant Pleural Mesothelioma *J Clin Oncol.* 2016 Aug 10; 34(23): 2761–2768. PMID: 27325859.

Rationale: The primary endpoint of the IMPRINT trial was the incidence of grade 3 or greater radiation pneumonitis of hemithoracic IMRT to 50.4 Gy in 28 fractions after chemotherapy and pleurectomy-decortication for patients with malignant pleural mesothelioma. Of the 27 patients that received IMRT, six patients experienced grade 2 RP, and two patients experienced grade 3 RP; all recovered after corticosteroid initiation. No grade 4 or 5 radiation-related toxicities were observed. The median progression-free survival and overall survival (OS) were 12.4 and 23.7 months, respectively; the 2-year OS was 59% in patients with resectable tumors and was 25% in patients with unresectable tumors.

170. Which histologic subtypes has the WORST prognosis in mesothelioma?

- A. Adenoid cystic
- B. Epithelioid
- C. Biphasic
- D. Sarcomatoid

Key: D

Domain: 9.9

Citations: Milano MT, Zhang H. Malignant pleural mesothelioma: a population-based study of survival. *J Thorac Oncol.* 2010;5(11):1841-1848. PMID: 20975379.

NCCN Guidelines, Malignant Pleural Mesothelioma, version 2.2021

Rationale: Based on US population based SEER data, for all patients, median survival in months was 11.1 for epithelioid, 7.2 for biphasic, and 4.5 for sarcomatoid / fibrous subtypes. Adenoid cystic is a rare histologic subtype of epithelioid mesothelioma.

171. What is the size cut-off in axial dimensions to define bulky disease as used in recent DLBCL clinical trials (e.g. RICOVER-60, UNFOLDER)?

- A. ≥ 5 cm
- B. ≥ 7.5 cm
- C. ≥ 10 cm
- D. ≥ 12 cm

Key: B

Domain: 10.1

Citations: Pfreundschuh M et al. Lancet Oncology. 2008. Feb. 9(2):105-16.

NCCN Guidelines® 2020.

Rationale: The definition of bulky disease has evolved from use of X-ray based definitions of maximum “Mass to Thoracic Ratio” $>33\%$ to CT scan based definition of the above ratio at T5-6 vertebral level of >0.35 , or nodal mass with maximal dimension >10 cm. Recent clinical trials use a cut-off of ≥ 7.5 cm which was also adapted in the latest versions of NCCN guidelines. This size is also important in helping to select patients which may benefit with the addition of consolidative radiotherapy after R-CHOP chemotherapy.

172. What dose is considered the standard of care based on findings from the FORT randomized phase 3 non-inferiority trial for indolent follicular and marginal zone lymphoma?

- A. 4 Gy in 2 Fx
- B. 10 Gy in 5 Fx
- C. 24 Gy in 12 Fx
- D. 36 Gy in 18 Fx

Key: C

Domain: 10.2

Citations: Hoskin PJ et al.; 4 Gy vs 24 Gy radiotherapy for patients with indolent lymphoma (FORT): a randomized phase 3 non-inferiority trial. 2014. Lancet Oncology. 15(4); 457-63.

Rationale: This trial help establish the use of 24 Gy in 12 fractions as a standard for follicular lymphoma with 4 Gy in single fraction as a reasonable alternative. The complete response was 68% in the 24 Gy arm vs 49% in the 4 Gy arm across all patients. After median follow-up of 26 months, the HR for time to local progression was 3.42 (95% CI: 2.10-5.57, $p < 0.001$) in favor of the 24 Gy group. There was no difference in overall survival.

173. Which of the following is included in the International Myeloma Working Group diagnostic criteria for solitary plasmacytoma?

- A. Presence of CRAB (hypercalcemia, renal insufficiency, anemia, bone lesions)
- B. Bone marrow involvement < 10%
- C. Normal skeletal survey (except for primary site of disease)
- D. PET scan showing hyperactive lesions

Key: C

Domain: 10.5

Citations: Tsang RW, et al. Radiotherapy Therapy for Solitary Plasmacytoma and Multiple Myeloma: Guidelines From The International Lymphoma Radiation Oncology Group. *Int J. Rad. Oncol. Biol & Phys.* 2018. 15;101(4):794-808.

Rajkumar SV, Dimopoulos MA, Palumbo A, et al. International Myeloma Working Group updated criteria for the diagnosis of multiple myeloma. *Lancet Oncol* 2014;15: e538-e548.

Rationale: All others (CRAB, PET scan showing multiple lesions, and bone marrow involvement) would not make it solitary plasmacytoma. Bone marrow less than 10% would be called solitary plasmacytoma with minimal marrow involvement. Thus, the best answer is C.

174. What was the main finding in the randomized trial that compared of 1-5 Fx vs. 10-20 Fx for multiple myeloma?

- A. Most patients experienced pain relief, although complete pain response occurs in <10% of the patients
- B. Most patients experienced pain relief, with nearly all patients achieving complete pain response
- C. Bone recalcification was expected for >90% of patients
- D. Longer dose fractionation had higher rate of motor function improvements in patients with cord compression

Key: D

Domain: 10.5

Citations: Rades D, Hoskin PJ, Stalpers LJ, et. al. Short-course radiotherapy is not optimal for spinal cord compression due to myeloma. *Int J Radiat Oncol Biol Phys.* 2006;64:1452-1457.

Rationale: A randomized trial of 1-5 vs. 10-20 fractions demonstrated that longer course regimens achieved higher rates of motor function improvement at 6 (67% vs. 43%; P=.043) and 12 months (76% vs. 40%; P=.003).

175. According to the German Hodgkin Study Group, what is the clinical stage of a Hodgkin lymphoma patient with involvement of the ipsilateral cervical and supraclavicular nodal regions?

- A. I
- B. II
- C. III
- D. IV

Key: A

Domain: 10.6

Citations: Brockelmann PJ, Goergen H, Fuchs M, et al. Impact of centralized diagnostic review on quality of initial staging in Hodgkin lymphoma: experience of the German Hodgkin Study Group 2015;171(4):547-56.

Rationale: According to the German Hodgkin Study Group, the left cervical and supraclavicular lymph node regions are considered to be one lymph node region.

176. What was the MOST common Deauville score on interval PET after ABVD in the UK NCRI RAPID trial for patients with Hodgkin lymphoma?

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

Key: A

Domain: 10.6

Citations: Radford J, Illidge T, Counsell N, et al. Results of a trial of PET-directed therapy for early-stage Hodgkin's lymphoma. NEJM 2015;372(17):1598-607.

Rationale: 52.7% of patients achieved a Deauville score of 1 after ABVD, which was the most common score.

177. In the HD10 trial, what was the finding of dose deintensification using less chemotherapy and lower RT with regards to PFS and OS?

- A. Improved PFS and no change in OS
- B. Decreased PFS and no change in OS
- C. No detriment to PFS and OS
- D. No detriment to PFS and improved OS

Key: C

Domain: 10.6

Citations: Sasse S, Brockelmann PJ, Goergen H, et. al. Long-term follow-up of contemporary treatment in early-stage Hodgkin's lymphoma: Updated analyses of the German Hodgkin Study Group HD7, HD8, HD10, and HD11 trials. 2017;35(18):1999-2007.

Rationale: The long-term outcomes from the GHSG HD10 trial showed that excellent outcomes persisted among the de-intensified arm of ABVD x 2 + 20 Gy with no significant difference versus the other arms. 10-year progression free survival was 87.2% and 10-year overall survival was 94.1%.

178. What is the principle toxicity of concern when using low dose rates during TBI for acute leukemia?

- A. Myocarditis
- B. Enteritis
- C. Hepatitis
- D. Pneumonitis

Key: D

Domain: 10.7

Citations: Gao RW, Weisdorf DJ, DeFor TE, et al. Influence of total body irradiation dose rate on idiopathic pneumonia syndrome in acute leukemia patients undergoing allogeneic hematopoietic cell transplantation. IJROBP 2910;103(1):180-189.

Rationale: TBI delivered with low dose rate is intended to reduce the risk of pneumonitis.

179. What is the recommended dose for definitive RT for a stage I MALT of the left parotid gland?

- A. 24 Gy
- B. 36 Gy
- C. 45 Gy
- D. 50.4 Gy

Key: A

Domain: 10.3

Citations: NCCN Guidelines- Non-Hodgkin Lymphoma Version 2020, NCCN Clinical Practice Guidelines in Oncology.

Rationale: 24 Gy is the recommended dose for MALT of left parotid gland. Other doses would be too high. MALT is radiosensitive, and low doses of RT can achieve excellent long-term control.

180. What is the minimum RT dose for a patient with Stage I NK/T-cell Lymphoma?

- A. 24 Gy
- B. 36 Gy
- C. 40 Gy
- D. 50.4 Gy

Key: D

Domain: 10.4

Citations: NCCN Guidelines- Non-Hodgkin Lymphoma Version 2020, NCCN Clinical Practice Guidelines in Oncology.

Rationale: Dose response over 50.4Gy has been demonstrated in many studies.

181. What parameter provides prognostic information for patients with follicular lymphoma (FLIPI index)?

- A. Extranodal site
- B. ESR
- C. Age \geq 60 years
- D. "B" symptoms

Key: C

Domain: 10.4

Citations: NCCN Guidelines- Non-Hodgkin Lymphoma Version 2020, NCCN Clinical Practice Guidelines in Oncology.

Rationale: All other choices are prognostic factors for early-stage classical HL, not FL. Age \geq 60 years is part of the FLIPI for follicular lymphoma.

182. Which translocation or chromosomal aberration is associated with a failure of antibiotic therapy for H. pylori eradication in gastric MALT?

- A. t(10;14)
- B. t(11;18)
- C. Chromosomal hyperdiploidy
- D. t(9;22)

Key: B

Domain: 10.3 (confirm)

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

Rationale: The presence of translocation t(11:18) is a feature associated with poor response to H.pylori eradication for gastric MALT. All others are not related to gastric MALT.

183. What is the risk of progression of solitary bone plasmacytoma to multiple myeloma in 10 years?

- A. <10%
- B. 10 - 30%
- C. 31 - 50%
- D. 60 - 90%

Key: D

Domain: 10.4

Citations: Ozsahin M, Tsang RW, Poortmans P, et al. Outcomes and patterns of failure in solitary plasmacytoma: A multicenter Rare Cancer Network study of 258 patients. *Int J Radiat Oncol Biol Phys* 2006; 64:210-217.

Rationale: Many patients (> 50%) with solitary bone plasmacytoma will develop multiple myeloma in 10 years. Thus, the correct answer is D.

184. What is the minimum recommended RT dose to treat a patient with a 2 cm solitary bone plasmacytoma of the left femur?

- A. 35 Gy
- B. 45 Gy
- C. 50.4 Gy
- D. 54 Gy

Key: A

Domain: 10.4

Citations: Radiation therapy for Solitary Plasmacytoma and Multiple Myeloma: Guidelines from the International Lymphoma Radiation Oncology Group (ILROG). *Int J Radiat Oncol Biol Phys*. June 2018.

Rationale: Per ILROG guidelines, the recommended dose is 35-40 Gy for solitary plasmacytoma that is less than 5 cm.

185. What is the BEST estimate of the increased risk of secondary solid cancer after allogeneic SCT conditioned with myeloablative TBI among pediatric patients age <10 years of age at the time of transplant?

- A. 15-fold increase
- B. 35-fold increase
- C. 55-fold increase
- D. 75-fold increase

Key: C

Domain: 10.8

Citations: J. Douglas Rizzo, et. al. Solid cancers after allogeneic hematopoietic cell transplantation, *Blood* (2009) 113 (5): 1175–1183.

Rationale: In a large multi-institutional cohort of over 28,000 allogeneic transplant recipients the risk of developing a solid malignancy was examined. Using a competing risk analysis, the cumulative incidence of developing a solid cancer was 1% at 10 years, 2.2% at 15 years and 3.3 % at 20 years. For all transplant patients studied, the development of an invasive second cancer was twice the rate expected. The risk of invasive solid cancer development was strongly related to the age of the transplant recipient as well as exposure to RT. Most patients in the study received doses of 10 Gy or more. Pediatric patients < 10 years of age had a 55-fold increase risk of developing a solid cancer, however for patients 30 years or older, no increased risk was observed.

186. Which TBI regimen would be expected to have the same risk of secondary solid cancer as a chemotherapy alone conditioning regimen?

- A. 2 Gy in 1 Fx
- B. 4 Gy in 1 Fx
- C. 12 Gy in 6 Fx
- D. 14.4 Gy in 12 Fx

Key: A

Domain: 10.8

Citations: R E Curtis 1, P A Rowlings, et.al. Solid cancers after bone marrow transplantation. *N Engl J Med.* 1997 Mar 27;336(13):897-904.

K. Scott Baker, et. al. Total body irradiation dose and risk of subsequent neoplasms following allogeneic hematopoietic cell transplantation. *Blood* (2019) 133 (26): 2790–2799.

Rationale: Early studies examining the risk of secondary solid cancers have suggested an increased risk of malignancies among patients treated with higher RT doses (Curtis RE et al NEJM 1997). Recent regimens have utilized chemotherapy alone or low TBI doses for allogeneic stem cell transplant in an effort to reduce treatment related morbidity and mortality. Among a cohort of just under 5,000, 1-year allogeneic HCT survivors with a median follow up of 12.5 years, myeloablative chemotherapy alone was associated with a two-fold higher risk of secondary cancer compared to the general population (Baker et al). The secondary malignancy risk for low-dose TBI (2-4.5 Gy) was comparable to chemotherapy alone regimens. The risk was the greatest for survivors that received high-dose unfractionated (6-12 Gy) or very high dose fractionated TBI (14.4 – 17.5 Gy). Fractionated TBI to 6-12 Gy was also associated with an increased risk of second cancer as compared to chemotherapy alone conditioning.

187. Blocking of which organ during TBI improves OS after allogeneic SCT?

- A. Kidney
- B. Liver
- C. Testes
- D. Lung

Key: D

Domain: 10.8

Citations: Esiashvili N, et al. Higher Reported Lung Dose Received During Total Body Irradiation for Allogeneic Hematopoietic Stem Cell Transplantation in Children With Acute Lymphoblastic Leukemia Is Associated With Inferior Survival: A Report from the Children's Oncology Group. *Int J Radiat Oncol Biol Phys.* 2019 Jul 1;104(3):513-521. doi: 10.1016/j.ijrobp.2019.02.034. Epub 2019 Feb 23. PMID: 30807822.

Savani BN, et. al. Prediction and prevention of transplant-related mortality from pulmonary causes after total body irradiation and allogeneic stem cell transplantation. *Biol Blood Marrow Transplant.* 2005 Mar;11(3):223-30. doi: 10.1016/j.bbmt.2004.12.328. PMID: 15744241.

Rationale: Pulmonary toxicity can occur as an acute or late complication of TBI. Many studies have shown that the dose rate of RT delivery, the TBI fraction size as well as the total dose administered to the lung influences the severity of pulmonary toxicity after RT. Inferior overall survival has been seen in several studies. Reduction in lung dose can be accomplished with lung shielding to keep the total dose to the lung lower than 8-10 Gy.

188. What is the optimal treatment approach to maximize disease control in a patient with favorable risk, non-bulky Hodgkin lymphoma?

- A. ABVD alone
- B. ABVD + consolidative RT
- C. Brentuximab vedotin + AVD
- D. ABVD + high dose chemotherapy

Key: B

Domain: 10.6

Citations: Fuchs M, et al. Positron Emission Tomography-Guided Treatment in EarlyStage Favorable Hodgkin Lymphoma: Final Results of the International, Randomized Phase III HD16 Trial by the German Hodgkin Study Group. *J Clin Oncol.* 2019;JCO1900964.

Andre MPE, Girinsky T, Federico M, et al. Early Positron Emission Tomography ResponseAdapted Treatment in Stage I and II Hodgkin Lymphoma: Final Results of the Randomized EORTC/LYSA/FIL H10 Trial. *J Clin Oncol.* 2017;35(16):1786-1794.

Radford J, Illidge T, Counsell N, et al. Results of a trial of PET-directed therapy for early-stage Hodgkin's lymphoma. *N Engl J Med.* 2015;372(17):1598-1607.

Straus DJ et. al. Brentuximab vedotin with chemotherapy for stage III/IV classical Hodgkin lymphoma: 3-year update of the ECHELON-1 study., *Blood* 2020 Mar 5;135(10):735-742. PMID: 31945149.

Rationale: To date, three randomized trials, UK Rapid, EORTC H10F and GHSG HD16 have demonstrated that among non-bulky favorable risk stage I/II HL patients, progression free survival is improved with combined modality therapy (ABVD followed by consolidative RT) as compared to ABVD alone. Extended follow up for these studies is lacking, therefore the impact of modern RT on secondary malignancy and cardiac morbidity is unknown. However, if the priority of frontline therapy is optimized disease control, combined modality therapy is the preferred treatment based on published randomized data. Brentuximab (A) is a novel antibody-drug conjugate targeting CD30. Recently the phase 3 ECHELON-1 study has demonstrated superior PFS for A+AVD as compared to ABVD as initial therapy for patients with advanced stage III/IV classical HL (and not limited stage HL) (Straus et al).

189. Which factor is associated with hypothyroidism after combined modality therapy for HL?
- A. V25 of the thyroid
 - B. Age at the time of RT
 - C. ABVD chemotherapy
 - D. Large thyroid gland

Key: A

Domain: 10.10

Citations: Pinnix CC, Cella L et. al. Predictors of Hypothyroidism in Hodgkin Lymphoma Survivors After Intensity Modulated Versus 3-Dimensional Radiation Therapy. *Int J Radiat Oncol Biol Phys* 2018; 101; 3:530-540.

Cella L, Conson M, Caterino M, et. al. Thyroid V30 predicts radiation induced hypothyroidism in patients treated with sequential chemoradiotherapy for Hodgkin's Lymphoma. *Int J Radiat Oncol Biol Phys* 2012; 82:1802-1808.

Bethge W et al, Thyroid toxicity of treatment for Hodgkin Disease. *Ann Hematol* 2000; 79:114-118.

Ivan R. Vogelius PhD, et. al. Risk factors for radiation-induced hypothyroidism A literature-based meta-analysis. *Cancer* Vol 117, issue 23, pages 5250-5260, 2011.

Rationale: Several dosimetric factors have been associated with the development of RT related hypothyroidism after treatment for HL. Among patients treated with 3D conformal and IMRT both V25 (cutoff of 63.5%) and V30 (cutoff of 62%) are influential (Cella et al, Pinnix et al). Age does not appear to influence the risk of RT induced hypothyroidism (Vogelius et al). Patients treated with ABVD alone have negligible risk of hypothyroidism (Bethge et al). Patients with small thyroid glands (less and 11.2 ml) are at greater risk of RT related hypothyroidism and likely require stricter criteria (Pinnix et al).

190. Which of the FDA approved radioimmuno-labeled agents has a beta and gamma emission?

- A. Ibritumomab tiuxetan
- B. Tositumomab
- C. ^{223}Ra dichloride
- D. Lintuzumab

Key: B

Domain: 10.1

Citations: Taskar-Pandit, Neeta. PMID 31451417. "Targeted Radioimmunotherapy and Theranostics with Alpha Emitters". J Med Imaging Radiat Sci. 2019. Dec; 504(4 suppl 1):S41-44.

Rationale: Tositumomab is labeled with I-131, which has both beta and gamma emission. The gamma emissions allows for imaging, and the longer half-life of 8 days allows for delayed imaging as well as multiple imaging time points after injection for dosimetry calculations. Therefore, I-131 is often used for RIT with antibodies. Xofigo is an alpha emitter used to treat bone disease. Lintuzumab is an antibody used to treat AML and was abandoned when phase IIb failed to show increased survival.

191. In addition to the primary tumor and operative bed, what else should be included in the recommended treatment volume for high-risk neuroblastoma?
- A. Prophylactic regional lymph node RT, and MIBG-avid metastases identified at diagnosis
 - B. Prophylactic regional lymph node RT, and persistent MIBG-avid metastases following induction chemotherapy
 - C. Persistent MIBG-avid metastases following consolidation chemotherapy
 - D. Persistent MIBG-avid metastases following induction chemotherapy

Key: D

Domain: 11.3

Citations: Braunstein SE, London WB, Kreissman SG, et. al. Role of the extent of prophylactic regional lymph node radiotherapy on survival in high-risk neuroblastoma: A report from the COG A3973 study. *Pediatr Blood Cancer*. 2019; 66(7):e27736. doi:10.1002/pbc.27736. PMID: 30968542.

Rationale: The post-induction chemotherapy, pre-surgical volume is the most appropriate starting point for defining the Gross Tumor Volume (GTV) in preparation for external beam radiotherapy following transplant. Elective coverage beyond the recommended Clinical Target Volume (CTV) expansion on the targeted disease extent is not recommended as it has not been shown to improve outcomes (PMID: 30968542). The number and extent of metastases identified in most cases of stage 4 high-risk neuroblastoma precludes radiotherapy to all sites of metastatic disease at diagnosis, and this has not been shown to improve outcomes. Historic studies used total-body irradiation as a component of conditioning prior to autologous stem cell transplant, but this approach was abandoned. Modern trial results demonstrate comparable event-free survival with alternative conditioning regimens [Carbo, Etoposide, Melphalan (CEM) or Busulfan, Melphalan (BuMel)] relative to historic studies and a more favorable late-effects profile (PMID: 16427213). Although TBI has no role in high-risk neuroblastoma anymore, analyses of patients treated with and without TBI have shown a reduced likelihood of relapse in metastatic sites identified at diagnosis (PMID: 28068235). Therefore, investigators have begun pursuing radionuclide/unsealed source-based approaches with therapeutic metaiodobenzylguanidine (I-131 as opposed to I-121 MIBG). This approach was first explored in relapse studies (PMID: 22700000, PMID: 21495159, PMID: 17369569) and is now being investigated in the front-line setting during induction chemotherapy as a part of ANBL1531 (NCT03126916).

192. In which clinical scenario can RT be omitted for the primary site in a patient with non-metastatic rhabdomyosarcoma following a margin negative resection?

- A. Alveolar rhabdomyosarcoma without a FOXO1-translocation following GTR at diagnosis
- B. Embryonal rhabdomyosarcoma with GTR following chemotherapy
- C. Alveolar rhabdomyosarcoma with a FOXO1-translocation following GTR at diagnosis
- D. Embryonal rhabdomyosarcoma following GTR at diagnosis

Key: D

Domain: 11.5

Citations: Wolden SL, Anderson JR, Crist WM, et al. Indications for radiotherapy and chemotherapy after complete resection in rhabdomyosarcoma: A report from the Intergroup Rhabdomyosarcoma Studies I to III. *J Clin Oncol.* 1999;17(11):3468-3475. doi:10.1200/JCO.1999.17.11.3468. PMID: 10550144.

Rationale: Analysis of patients with group 1 alveolar RMS from prior Children's Oncology Group protocols has demonstrated that routine use of adjuvant radiotherapy is required (PMID: 32124549). Therefore, adjuvant radiotherapy following resection (group 1, 2, or 3) for alveolar rhabdomyosarcoma (RMS) is always required independent of translocation (FOXO1) status. Alveolar RMS may be FOXO1-negative (approximately 20% of the time) and has clinical behavior and molecular characteristics comparable to those of embryonal RMS (PMID: 20351326). As a result, ARST1431 is evaluating whether the omission of radiotherapy in patients with group 1 translocation-negative alveolar RMS is possible when the resection is performed at diagnosis. Omitting radiotherapy following initial chemotherapy has been evaluated in both low- (select patients/sites in ARST0331) and intermediate-(D9803) risk RMS and has been found to result in inferior local control (PMID: 21298768, PMID: 25418440). Although omitting radiotherapy is not permitted following delayed primary excision, dose-de-escalation is acceptable if a gross-total or margin-negative resection is completed. ARST1431 is evaluating whether radiotherapy dose de-escalation following chemotherapy is possible when a complete radiographic response is obtained, and surgery is omitted (NCT02567435). Although response-based dose reduction has been utilized in low-risk orbital group 3 primaries, it has resulted in inferior local control, so use of <50.4 Gy should be discouraged (PMID: 28548706), especially in the context of reduced-dose cyclophosphamide. Concerns regarding cyclophosphamide dosing and its contribution to inferior local control were also been observed in ARST0531 (PMID: 31174239, PMID: 31174230).

193. What is the appropriate treatment for a pediatric patient whose disease relapsed at a limited number of sites less than 12 months following treatment for classic Hodgkin lymphoma?

- A. 2nd-line chemotherapy → PET/CT (Deauville 4-5) → Observation
- B. 2nd-line chemotherapy → PET/CT (Deauville 1-4) → ASCT +/- RT
- C. 2nd-line chemotherapy → Chemo-refractory → RT → PET/CT (Deauville 1-4) → ASCT +/- RT
- D. 2nd-line chemotherapy → PET/CT (Deauville 1-4) → ASCT → +/- RT → + Brentuximab

Key: D

Domain: 11.2

Citations: Moskowitz CH, Nademanee A, Masszi T, et al. Brentuximab vedotin as consolidation therapy after autologous stem-cell transplantation in patients with Hodgkin's lymphoma at risk of relapse or progression (AETHERA): a randomised, double-blind, placebo-controlled, phase 3 trial [published correction appears in Lancet. 2015 Aug 8;386(9993):532] [published correction appears in Lancet. 2015 Aug 8;386(9993):532]. Lancet. 2015;385(9980):1853-1862. doi:10.1016/S0140-6736(15)60165-9. PMID: 25796459.

Rationale: Initial response to 2nd-line chemotherapy should drive subsequent treatment options in relapsed/refractory Hodgkin lymphoma (PMID: 20564743). Patients with Deauville 4-5 disease following 2nd-line chemotherapy response evaluation with PET/CT have progressive disease (PMID: 25113771) and should not be observed following 2nd-line chemotherapy, especially in the setting of a short-interval relapse (<12 months) (PMID: 20564743). Instead these patients should proceed to an alternative systemic therapy with consolidation of progressive sites with radiotherapy (PMID: 31005229, PMID: 22398312, PMID: 15632410) if the number of sites is practical. Patients who experience a short-interval relapse (<12 mo) whose disease has a favorable response to 2nd-line chemotherapy on PET/CT should proceed to autologous stem cell transplant (ASCT) followed by consolidative radiotherapy (PMID: 32273588, PMID: 31005229) and brentuximab. The AETHERA trial demonstrated that patients with unfavorable risk factors prior to ASCT experienced a substantial improvement in median progression free survival with the addition of brentuximab maintenance (42.9 vs. 24.1 months (p=0.0013) (PMID: 25796459). Patients whose disease is treatment refractory following initiation of 2nd-line chemotherapy and is, thus, progressive should be strongly considered for consolidative radiotherapy to progressive sites of disease, assuming the disease extent is amenable. The response rate to radiotherapy in the relapse setting is high and should be strongly considered in the setting of chemo-refractory disease. Options B and C are wrong because they omit brentuximab following transplant, despite high-risk features (<12 month relapse and, in the case of option C, chemo-refractory disease). Patients who experience multiple relapses should be considered for immune checkpoint blockade (PMID: 25482239). AHOD1721 recommends the incorporation of consolidative involved-site radiotherapy to doses of 30-36 Gy into salvage programs composed of nivolumab, brentuximab, and bendamustine with or without transplant pending risk and response status (NCT02927769).

194. Young children with anaplastic rhabdomyosarcoma have a high rate of germline alterations in _____ and should be considered for _____.

- A. MYOD1; omission of RT because they have a more favorable prognosis
- B. MYCN; dose-escalated RT because they have a higher rate of local failure
- C. TP53; screening for cancer predisposition syndromes
- D. FOXO1; dose-escalated RT because they have a higher rate of local failure

Key: C

Domain: 11.5

Citations: Hettmer S, Archer NM, Somers GR, et al. Anaplastic rhabdomyosarcoma in TP53 germline mutation carriers [published correction appears in *Cancer*. 2014 Jun 15;120(12):1910]. *Cancer*. 2014;120(7):1068-1075. doi:10.1002/cncr.28507. PMID: 24382691.

Villani A, Shore A, Wasserman JD, et al. Biochemical and imaging surveillance in germline TP53 mutation carriers with Li-Fraumeni syndrome: 11 year follow-up of a prospective observational study. *Lancet Oncol*. 2016;17(9):1295-1305. doi:10.1016/S1470-2045(16)30249-2. PMID: 27501770.

Kratz CP, Achatz MI, Brugières L, et al. Cancer Screening Recommendations for Individuals with Li-Fraumeni Syndrome. *Clin Cancer Res*. 2017; 23(11):e38-e45. doi:10.1158/1078-0432.CCR-17-0408. PMID: 28572266.

Rationale: MYOD1 mutations are typically somatic alterations, are associated with spindle cell or sclerosing rhabdomyosarcoma, and have an aggressive clinical behavior (unfavorable prognosis)(PMID: 27562493, PMID: 30181563). MYCN is amplified in ~25% of alveolar rhabdomyosarcoma tumors (not germline) and has not been directly connected to young children who have anaplastic RMS (PMID: 22065083). PAX3- and PAX7- FOXO1 fusions are found in 80% of alveolar rhabdomyosarcoma tumors (not germline) and are associated with a more aggressive clinical course (PMID: 12039929). Translocation status of FOXO1 has not been shown to be related to anaplastic histology. Germline TP53 alterations are frequent (73%) in young children with anaplastic rhabdomyosarcoma, and nearly all patients screen positive using Chompret criteria (PMID: 16921036). Patients with focal or diffuse anaplasia have inferior failure-free (63% vs. 77% at 5 years) and overall (68% vs. 82% at 5 years) survival (PMID: 18985676). Young patients with anaplastic RMS should be screened using the Chompret criteria (PMID: 26014290) and referred to clinical genetics for appropriate testing. Those found to have Li Fraumeni syndrome should be surveilled for subsequent cancers (PMID: 28572266).

195. An 8-year-old child has classic medulloblastoma status post GTR with no radiographic evidence of metastatic disease and no tumor cells in the CSF. What is the recommended RT dose and volume?
- A. 59.4 Gy to the resection cavity + margin
 - B. 54 Gy to the resection cavity + margin
 - C. 23.4 Gy CSI, then 30.6 Gy boost to the resection cavity + margin
 - D. 36 Gy CSI, then 18 Gy boost to the posterior fossa

Key: C

Domain: 11.8

Citations: Packer R J, et. al. Neuro Oncol 2013;15:97-103. Survival and secondary tumors in children with medulloblastoma receiving radiotherapy and adjuvant chemotherapy: results of Children's Oncology Group trial A9961

Rationale: As established by Packer et al., the current standard treatment for average (standard) risk medulloblastoma is 23.4 Gy CSI with a focal boost to a total of 54-55.8 Gy. Patients receive concurrent vincristine and adjuvant PCV chemotherapy. COG ACNS0331 demonstrated that the boost may target the involved field (resection cavity + margin), rather than the entire posterior fossa.

196. A 5 year-old child has medulloblastoma. The surgeon reports that a GTR has been performed. What study should be performed to confirm that all disease has been resected?
- A. CT scan intraoperatively
 - B. CT scan within 1-3 days postoperatively
 - C. MRI scan within 1-3 days postoperatively
 - D. MRI scan within 1-3 weeks postoperatively

Key: C

Domain: 11.8

Citations: Pediatric Radiation Oncology. Merchant, Thomas E., Kortmann Rolf-Dieter (Eds.). Springer. 2018.

Rationale: An MRI scan of the brain should be performed within 24-72 hours postoperatively to evaluate the degree of resection. If the MRI is performed later, blood products may complicate the interpretation of the images.

197. A 12-year-old child presents with headaches and an MRI reveals a pineal mass. AFP is markedly elevated in the serum and CSF. These findings are consistent with which diagnosis?

- A. Intracranial pure germinoma
- B. Intracranial non-germinomatous germ cell tumor
- C. Ependymoma
- D. Pineoblastoma

Key: B

Domain: 11.8

Citations: Pediatric Neuro-oncology. Katrin Scheinemann and Eric Bouffet (Eds). Springer. 2015.

Rationale: The most common locations for intracranial germ cell tumors are the pineal and suprasellar regions. An elevated AFP level in the serum and/or CSF is consistent with a non-germinomatous germ cell tumor.

198. What is the typical initial treatment of a 4 year-old child with a posterior fossa ependymoma?

- A. Chemotherapy
- B. Maximal safe resection
- C. Craniospinal irradiation
- D. Focal RT to the tumor

Key: B

Domain: 11.8

Citations: Merchant et al. Conformal Radiotherapy After Surgery for Paediatric Ependymoma: A Prospective Study. Lancet Oncol. 2009 Mar;10(3):258-66.

Rationale: The standard treatment of posterior fossa ependymoma involves maximal safe resection, followed by conformal radiation therapy.

199. A 16 year-old has localized Ewing sarcoma of the sacrum and is receiving standard chemotherapy and definitive RT for local control. What dose should be given to the gross disease?

- A. 40 Gy
- B. 50.4 Gy
- C. 55.8 Gy
- D. 72 Gy

Key: C

Domain: 11.6

Citations: Womer, et. al. Randomized Controlled Trial of Interval-Compressed Chemotherapy for the Treatment of Localized Ewing Sarcoma: A Report From the Children's Oncology Group. JCO. 2012 Nov 20;30(33):4148-4154.

Rationale: The standard definitive radiation therapy dose for non-vertebral Ewing sarcoma is 55.8 Gy (45 Gy to the initial volume, followed by a 10.8 Gy boost to the pre-chemotherapy bone/post-chemotherapy soft tissue volume).

200. Which late effect is expected after a single dose 6 Gy of radiation?

- A. Sterility after radiation to the testes
- B. Necrosis after radiation to the brain
- C. Pericarditis after radiation to the heart
- D. Myelopathy after radiation to the spinal cord

Key: A

Domain: 11.9

Citations: Pediatric Radiation Oncology. Louis S. Constine, Nancy J. Tarbell, and Edward C. Halperin (Ed). Wolters Kluwer. 2016.

Rationale: The TD₅ and TD₅₀ for sterility are 1 Gy and 2 Gy to the testes, respectively. The other listed complications may be seen after higher doses.

201. Which factor is typically considered a CONTRAINDICATION to CSI for medulloblastoma?

- A. Anaplastic histology
- B. Complete surgical resection
- C. Diagnosis as an infant
- D. Lack of malignant cells in the CSF

Key: C

Domain: 11.8

Citations: Rutkowski et al. Treatment of Early Childhood Medulloblastoma by Postoperative Chemotherapy Alone. *NEJM* 2005 Mar 10;352(10):978-86.

Rationale: Craniospinal irradiation is typically avoided in infants because it causes significant neurotoxicity. To delay or eliminate the need for craniospinal irradiation, these patients are typically treated with intensive chemotherapy.

202. Which diagnosis has the poorest survival outcomes in children?

- A. Diffuse intrinsic pontine glioma
- B. Intracranial germinoma
- C. Juvenile pilocytic astrocytoma
- D. Medulloblastoma

Key: A

Domain: 11.8

Citations: Pediatric Radiation Oncology. Louis S. Constine, Nancy J. Tarbell, and Edward C. Halperin (Ed). Wolters Kluwer. 2016.

Rationale: Patients with diffuse intrinsic pontine glioma have a poor prognosis. Median survival is typically 8-12 months. The other listed diagnoses are associated with significantly more favorable outcomes.

203. A child with high risk neuroblastoma undergoes conventional therapy and at the time of RT has a 2 cc of residual disease at the primary site. In addition to receiving 21.6 Gy in 12 Fx to the extent of disease at the time of surgery, what boost dose should be prescribed to the residual disease?
- A. 0 Gy
 - B. 10.8 Gy in 6 Fx
 - C. 14.4 Gy in 8 Fx
 - D. 21.6 Gy in 12 Fx

Key: A

Domain: 11.3

Citations: Liu. Prospective Evaluation of Radiation Dose Escalation in Patients With High-Risk Neuroblastoma and Gross Residual Disease After Surgery: A Report From the Children's Oncology Group ANBL0532 Study. 2020, pp 1527-7755.

Rationale: Children's Oncology Group study ANBL found that boosting residual disease (with 14.4 Gy) did not improve local control compared to prior studies without boosts beyond 21.6 Gy

204. A 2-year-old with poorly differentiated high-risk neuroblastoma is treated according to Children's Oncology Group trial ANBL0532. What is the patient's approximate 3-year DFS if she received tandem autologous stem cell transplants as part of her course?
- A. 25%
 - B. 45%
 - C. 65%
 - D. 85%

Key: C

Domain: 11.3

Citations: Park. Effect of Tandem Autologous Stem Cell Transplant vs Single Transplant on Event-Free Survival in Patients With High-Risk Neuroblastoma. JAMA, 2019.

Rationale: The Children's Oncology Group Study ANBL0532 showed patients had a 3 year DFS of 62% with tandem transplant compared to 48% with single transplant, establishing tandem transplant as the new standard of care for most patients with high risk neuroblastoma.

205. Which imaging study is a necessary component of the workup for a pediatric patient with high risk neuroblastoma?

- A. Bone scan
- B. SPECT MRI
- C. Gallium scan
- D. MIBG scan

Key: D

Domain: 11.3

Citations: Brodeur, et. al. Neuroblastoma, in Principles and Practices of Pediatric Oncology. Wolters Kluwer. 7th Ed. 2016. p. 772.

Rationale: MIBG scans help identify metastases of neuroblastoma. In addition, I-Metaiodobenzylguanidine (MIBG) can be used for therapeutic purposes in neuroblastoma.

206. A patient has a 5 cm embryonal rhabdomyosarcoma and undergoes a biopsy and then induction chemotherapy with a subsequent radiographic complete response. What is the patient's Group?

- A. I
- B. IIA
- C. IIC
- D. III

Key: D

Domain: 11.5

Citations: Wexler. Rhabdomyosarcoma, in Principles and Practice of Pediatric Oncology. Wolters Kluwer. 7th Ed. 2016. p. 798.

Rationale: Stage refers to the extent of disease after surgical procedures before induction chemotherapy has started. It is not affected by the response to chemotherapy. Group I patients have had a gross total resection with negative margins, Group IIA patients have had a gross total resection with microscopic margins, Group IIC Group IIA patients have had a gross total resection with microscopic margins and positive resected draining lymph nodes, and Group III patients have residual gross disease at the time starting induction chemotherapy.

207. What is the MOST conventional dose and fractionation for a 7 year-old patient undergoing whole lung irradiation for lung metastases in rhabdomyosarcoma?

- A. 10.5 Gy in 7 Fx
- B. 10.8 Gy in 6 Fx
- C. 15 Gy in 10 Fx
- D. 12 Gy in 8 Fx

Key: C

Domain: 11.5

Citations: Wexler. Rhabdomyosarcoma, in Principles and Practice of Pediatric Oncology. Wolters Kluwer. 7th Ed. 2016. p. 798.

Rationale: When treating patients with rhabdomyosarcoma with lung metastases, the conventional fractionation is 15 Gy in 10 fractions. Twelve Gy in 8 fraction is the most common dose and fractionation for Wilms tumor lung metastases.

208. Among pediatric patients with rhabdomyosarcoma treated on Children's Oncology Group Studies, the SECOND MOST important prognostic factor (after metastases at time of staging) was:

- A. age.
- B. FOXO1 translocation status.
- C. histologic subtype.
- D. tumor size.

Key: B

Domain: 11.5

Citations: Hibbits. Refinement of risk stratification for childhood rhabdomyosarcoma using FOXO1 fusion status in addition to established clinical outcome predictors: A report from the Children's Oncology Group. Cancer Medicine. 2019. p. 6437.

Rationale: FOXO1 translocations involve the PAX3 gene on chromosome 2 or the PAX7 gene on chromosome 1 and the FOXO1 gene on chromosome 13 to generate PAX3-FOXO1 or PAX7-FOXO1 fusion genes, which encode fusion proteins with oncogenic activity. This study found it was the second most important factor in predicting clinical outcome.

209. What is the MOST common histologic subtype of classical Hodgkin lymphoma in pediatric patients in the US?

- A. Lymphocyte-depleted
- B. Nodular sclerosing
- C. Mixed cellularity
- D. Lymphocyte rich

Key: B

Domain: 11.2

Citations: Metzger. Hodgkin Lymphoma, in Principles and Practice of Pediatric Oncology. Wolters Kluwer, 7th Ed., 2016. p. 568.

Rationale: Nodular sclerosing subtype comprises 40-70% of the classic histology type of Hodgkin Lymphoma.

210. According to the Children's Oncology Group protocols, what is the recommended dose and fractionation when adjuvant RT is given for Hodgkin lymphoma and boosts are not needed?

- A. 15 Gy in 10 Fx
- B. 20 Gy in 10 Fx
- C. 21 Gy in 14 Fx
- D. 30 Gy in 15 Fx

Key: C

Domain: 11.2

Citations: Friedman. Dose-Intensive Response-Based Chemotherapy and Radiation Therapy for Children and Adolescents With Newly Diagnosed Intermediate-Risk Hodgkin Lymphoma: A Report From the Children's Oncology Group Study AHOD0031. JCO, 2014, pp. 3651-8.

Kelly. Response-adapted therapy for the treatment of children with newly diagnosed high risk Hodgkin lymphoma (AHOD0831): a report from the Children's Oncology Group. Br J Haematol, 2019, pp. 39-48.

Rationale: 21 Gy in 14 fractions has been the adjuvant radiation dose on recent COG trials. AHOD1431 is examining the role of a boost to a total of 30 Gy in 20 fractions in patients with metabolically-active residual disease.

211. The early phases of fibrogenesis after irradiation can be characterized by an upregulation of pro-inflammatory cytokines such as tumor-necrosis factor- α (TNF α) and interleukins 1 (IL1); and what other cytokine?

- A. IL2
- B. IL6
- C. IL10
- D. IL15

Key: B

Domain: 12.6

Citations: Bentzen, Preventing or reducing late side effects of radiation therapy: radiobiology meets molecular pathology. *Nat Rev Cancer*. 2006 Sep;6(9):702-13.

Rationale: Mechanistically, the early phases of fibrogenesis after irradiation can be seen as a wound-healing response characterized by an almost immediate upregulation of pro-inflammatory cytokines such as tumor-necrosis factor- α (TNF α), interleukins 1 and 6 (IL1 and IL6) and many growth factors in the irradiated tissue. Chemokines are released and these recruit inflammatory cells from the surrounding tissue into the irradiated volume. IL10 is potent anti-inflammatory cytokine. IL15 is involved in activation of immune cells.

212. Which DNA repair protein functions to promote DNA strand invasion and the search for homology during DNA DSB repair?

- A. DNA-PK
- B. Artemis
- C. Rad51
- D. MDC1

Key: C

Domain: 12.13

Citations: Lobrich and Jeggo. The impact of a negligent G2/M checkpoint on genomic instability and cancer induction. *Nat Rev Cancer*. 2007 Nov;7(11):861-9.

Povirk, et al. Processing of 3'-phosphoglycolate-terminated DNA double strand breaks by Artemis nucleas. *J. Biol. Chem.* 282 (6): 3547-58.

Rationale: Exposure of cells to ionizing radiation or radiomimetic drugs generates DNA double-strand breaks that are processed either by homologous recombination repair (HRR), or by canonical, DNA-PKcs-dependent non-homologous end-joining (C-NHEJ). RAD51 plays a major role in homologous recombination of DNA strand break repair. In this process, an ATP dependent DNA strand exchange takes place in which a template strand invades base-paired strands of homologous DNA molecules. RAD51 is involved in the search for homology and strand pairing stages of the process. Artemis is an endonuclease, a protein deficient in a human radiosensitivity syndrome associated with severe immunodeficiency (RS-SCID), in the processing of subsets of DSBs by HRR or C-NHEJ. It is thought that within HRR or C-NHEJ. DNA-PK is a key protein in NHEJ and MCD1 protein is a regulator of the Intra-S phase and the G2/M cell cycle checkpoints and recruits repair proteins to the site of DNA damage.

213. What protein inhibits Cyclin B/CDK1 interaction and inhibits the G2 to M transition after radiation damage?

- A. Mdm2
- B. Wee1
- C. P21^{CIP1}
- D. P27^{KIP1}

Key: B

Domain: 12.13

Citations: Bouwman and Jonkers. The effects of deregulated DNA damage signalling on cancer chemotherapy response and resistance. *Nat Rev Cancer*. 2012 Sep; 12(9):587-98.

Lorns, et al. Integrated functional, gene expression and genomic analysis for the identification of cancer targets. *PLoS One*. 2009; 4(4):e5120.

Rationale: Wee1 is a nuclear kinase belonging to the Ser/Thr family of protein kinases. Wee1 has a molecular mass of 96 kDa and it is a key regulator of cell cycle progression. It influences cell size by inhibiting the entry into mitosis, through inhibiting Cdk1. Wee1 is a tyrosine kinase that is known to be overexpressed in many cancer types such as luminal and HER2-positive breast cancer subtypes, hepatocellular carcinomas, and glioblastomas (Lorns et al., 2009). It regulates the G2-M transition by phosphorylating CDK2 to inactivate the CDK2/cyclin B complex to terminate the cell cycle. The G2 checkpoint is critical for premitotic DNA repair. P21 and P27 are proteins involved in regulating the G1/S phase transition; mdm2 is a protein involved with regulating activation of p53 and the G1/S transition.

214. Combining hyperthermia with radiation is considered a way of targeting cells in which phase of the cell cycle?

- A. G1
- B. S
- C. G2
- D. G0

Key: B

Domain: 12.23

Citations: Roti Roti. Cellular responses to hyperthermia (40-46 degrees C): cell killing and molecular events. *Int J Hyperthermia*. 2008;24(1):3–15.

Kampinga and Dikomey. Hyperthermic radiosensitization: mode of action and clinical relevance. *Int J Radiat Biol*. 2001;77(4):399-408.

Dewey, et. al. Cellular responses to combinations of hyperthermia and radiation. *Radiology* 123:463-474, May 1977.

Rationale: The two principal rationales for applying hyperthermia in cancer therapy are that: (a) the S phase, which is relatively radiation resistant, are most sensitive phase to hyperthermia, and can be selectively radiosensitized by combining hyperthermia with x-irradiation; the cycling tumor cells in S phase which would normally survive an x-ray dose could thus be killed by subjecting these cells to hyperthermia. For heat shock during S phase, however, the damage in the chromatin is reflected as chromatid aberrations in all the chromosomes. These aberrations apparently induce cell lethality, just as do x-ray-induced chromosomal aberrations.

215. What chemotherapeutic agent leads to DNA chain termination when it becomes incorporated into newly synthesized DNA as the cell replicates?

- A. Gemcitabine
- B. Mitomycin C
- C. Doxorubicin
- D. Bleomycin

Key: A

Domain: 12.22

Citations: Verweij and Pinedo. Mitomycin C: mechanism of action, usefulness and limitations. *Anticancer Drugs*. 1990 Oct;1(1):5-13.

Paz, et. al. A new mechanism of action for the anticancer drug mitomycin C: mechanism-based inhibition of thioredoxin reductase. *Chem Res Toxicol*. 2012 Jul 16; 25(7):1502-11.

Radiobiology for the Radiologist, Hall and Giaccia 6th Edition. Chapter 27, pages 440-452.

Rationale: Mitomycin C (MMC) is a chemotherapeutic drug that requires an enzymatic bioreduction to exert its biological effects and then leads to Alkylation of DNA is the most favored mechanism of action for MMC, but other modes of action, such as redox cycling and inhibition of rRNA, may also contribute to the biological action of the drug. Plicamycin - RNA synthesis inhibitor. Bleomycin induces strand breaks in DNA. Doxorubicin in an intercalating agent that interacts with DNA by intercalation and inhibition of macromolecular biosynthesis to inhibit the progression of topoisomerase II, an enzyme which relaxes supercoils in DNA for transcription. Gemcitabine is a nucleoside analog, once gemcitabine has entered the cell is becomes phosphorylated and can masquerade as deoxycytidine triphosphate and is incorporated into new DNA strands being synthesized as the cell replicates which leads to “masked chain termination.”

216. What hypoxic cell sensitizer undergoes redox recycling or decomposes to toxic product and has shown efficacy in head and neck cancer?

- A. Methotrexate
- B. Camptothecin
- C. Cetuximab
- D. Nimorazole

Key: D

Domain: 12.22

Citations: Overgaard et al. A randomized double-blind phase III study of nimorazole as a hypoxic radiosensitizer of primary radiotherapy in supraglottic larynx and pharynx carcinoma. Results of the Danish Head and Neck Cancer Study (DAHANCA) Protocol 5-85. *Radiother Oncol.* 1998 Feb;46(2):135-46.

Radiobiology for the Radiologist, Hall and Giaccia 6th Edition. Chapter 25, pages 422-426.

Rationale: Nimorazole as a hypoxic radiosensitizer of primary radiotherapy in supraglottic larynx and pharynx carcinoma. Results of the Danish Head and Neck Cancer Study (DAHANCA) Protocol 5–85. (*Radiother Oncol.* 1998; 46:135–146) showed efficacy in hypoxic tumors. Cetuximab is an inhibitor of EGFR (ErbB family) has have shown to be effective in Head and Neck cancer: Camptothecin is a TOP I inhibitors (poison) involved in cleavage of DNA strands. Methotrexate is a Folic acid analog.

217. Which radiation injury can be evaluated by the crypt stem cell survival assay?

- A. Sebaceous gland injury
- B. Intestinal injury
- C. Serous acini cell injury
- D. Eccrine gland injury

Key: B

Domain: 12.6

Citations: Withers HR, Elkind MM. Microcolony survival assay for cells of mouse intestinal mucosa exposed to radiation. *Int J Radiat Biol.* 1970; 17:261–7.

Venkateswaran K, et. al. Mitigation of radiation-induced gastro-intestinal injury by the polyphenolic acetate 7,8-diacetoxy-4-methylthiocoumarin in mice. *Sci Rep.* 2019; 9:14134.

Rationale: The crypt stem cell survival assay (or microcolony assay) as developed by Withers and Elkind in 1970 is a gold standard to assess the surviving fraction of epithelial stem cells in the small intestine after exposure to high (≥ 8 Gy) doses of ionizing radiation. The number of surviving crypt stem cells correlates with radiation-induced structural damage in the intestinal wall.

218. What apoptosis-related protein promotes the induction of radiation-induced cell death?

- A. Akt
- B. Bax
- C. Bcl2
- D. mTOR

Key: B

Domain: 12.13

Citations: McGill G, Fisher DE. Apoptosis in tumorigenesis and cancer therapy. *Front Biosci.* 1997; 2:d353-79.

Eriksson D, Stigbrand T. Radiation-induced cell death mechanisms. *Tumour Biol.* 2010 Aug;31(4):363-72.

Yao M, et. al. Sensitization of prostate cancer to radiation therapy: Molecules and pathways to target. *Radiother Oncol.* 2018; 128:283-300.

Rationale: Bax is a pro-apoptotic protein involved in the induction of radiation-induced cell death. Akt, Bcl2 and mTOR promote cell survival.

219. What cellular event activates the ATM protein upon exposure to ionizing radiation?

- A. Cell death
- B. DNA double strand break formation
- C. Mitochondrial respiration
- D. Ribosomal assembly

Key: B

Domain: 12.13

Citations: Paull TT. Mechanisms of ATM activation. *Annual Review of Biochemistry.* 2015;84:711-738.

Bakkenist C. J., Kastan M. B. DNA damage activates ATM through intermolecular autophosphorylation and dimer dissociation (2003) *Nature* 421, 499–506.

Rationale: ATM [Ataxia Telangiectasia Mutated], one of the first proteins activated in response to DNA double strand breaks, coordinates several downstream signaling pathway to help the cell respond to the DNA damage.

220. The LD50/30 in an animal radiation model is 5 Gy. When animals are treated with a radiation protector, the LD50/30 is 10 Gy. What is the dose reduction factor of the radiation protector?

- A. -5
- B. 0.5
- C. 2
- D. 5

Key: C

Domain: 12.22

Citations: Tabeie F, Tabatabaei SM, Mahmoud-Pashazadeh A, Assadi M. Radioprotective effect of beta D-glucan and vitamin E on gamma irradiated mice. *J Clin Diagn Res.* 2017;11:TC08-TC11.

Landes RD, Lensing SY, Kodell RL, Hauer-Jensen M. Practical advice on calculating confidence intervals for radioprotection effects and reducing animal numbers in radiation countermeasure experiments. *Radiat Res.* 2013; 180:567-74.

Rationale: The LD50/30 value is the radiation dose that leads to 50% survival 30 days after irradiation. The dose reduction factor can be calculated as the LD50/30 in the presence of the radiation protector divided by the LD50/30 value at baseline. Therefore, with the information given, the dose reduction factor is $10 \text{ Gy}/5 \text{ Gy} = 2$.

221. What is the biological mechanism by which a superoxide dismutase mimetic protects against radiation injury?

- A. By scavenging reactive oxygen species
- B. By reducing the absorbed radiation dose
- C. By promoting DNA repair
- D. By inhibiting inflammation

Key: A

Domain: 12.22

Citations: Batinic-Haberle I, Tovmasyan A, Spasojevic I. Mn porphyrin-based redox-active drugs: differential effects as cancer therapeutics and protectors of normal tissue against oxidative injury. *Antioxid Redox Signal.* 2018; 29:1691-1724.

Rationale: Superoxide dismutase (SOD) mimetics reduce cellular oxidative stress, in part by acting as an SOD enzyme and scavenging reactive oxygen species.

222. During RT, a change in what microenvironmental condition can improve tumor control?

- A. Decreased tumor oxygen levels
- B. Decreased blood flow
- C. Increased tumor glucose levels
- D. Increased tumor temperature

Key: D

Domain: 12.23

Citations: Zagar TM, et. al. Hyperthermia combined with radiation therapy for superficial breast cancer and chest wall recurrence: a review of the randomised data. *Int J Hyperthermia*. 2010;26:612-7.

Seifert G, et. al. Regional hyperthermia combined with chemotherapy in paediatric, adolescent and young adult patients: current and future perspectives. *Radiat Oncol*. 2016 Apr 30; 11:65.

Rationale: Locally increased temperatures during radiation therapy (hyperthermia) radiosensitizes many solid tumors. On the other hand, decreasing tumor oxygen levels during therapy or decreasing radiation dose rate may reduce the radiation injury in tumors. Lastly, many tumors are glycolytic, and increased available glucose may promote their growth.

223. Which property of cancer stem cells impact tumor control probability (TCP)?

- A. Most prevalent cell type
- B. Unlimited proliferative capacity
- C. More radiosensitive than other cell types
- D. Confer a protective effect on adjacent cells

Key: B

Domain: 12.18

Citations: Reid PA, Wilson P, Li Y, Marcu LG, Bezak E. Current understanding of cancer stem cells: Review of their radiobiology and role in head and neck cancers. *Head Neck*. 2017;39(9):1920-1932. doi:10.1002/hed.24848 (PMID: 28644558).

Radiobiology for the Radiologist, Hall and Giaccia 8th Edition. Chapter 3, "Cell survival curves "pages 89-121; Chapter 27 Chemotherapeutic Agents from the Perspective of the Radiation Biologist pp856.

Rationale: Mathematical models of TCP are based on a fundamental assumption that tumors contain a population of stem cells that have unlimited proliferative potential that, therefore, must be killed in order to achieve sustained tumor control. Escape of even one stem cell can result in re-population due to this unlimited proliferative capacity.

224. What clinical intervention can reduce the therapeutic ratio of a radiation treatment?

- A. Use of a radioprotector that accumulates preferentially in highly vascularized tissues
- B. Use of a radioprotector that requires oxygen for conversion from pro-drug to its active form
- C. Addition of a selective EGFR-targeted therapy, such as cetuximab
- D. Addition of a cytotoxic alkylating chemotherapeutic agent, such as cyclophosphamide

Key: D

Domain: 12.18

Citations: Emadi A, Jones RJ, Brodsky RA. Cyclophosphamide and cancer: golden anniversary. *Nat Rev Clin Oncol.* 2009;6(11):638-647. doi:10.1038/nrclinonc.2009.146 (PMID: 19786984).

Rationale: Alkylating agents are cytotoxic, targeting DNA, and tend to be cell-type non-specific. Such an agent would likely result in increased toxicity as well as increased tumor control. The other three responses take advantage of differences between the tumor and normal tissues with respect to molecular biology and/or microenvironment.

225. Why is prostate adenocarcinoma well-suited to hypofractionated RT?

- A. Relative to other tumor types, prostate cancer has a high proliferation rate resulting in a large fractionation effect
- B. Prostate tumors tend to be hypoxic, and hypofractionation increases reoxygenation compared to conventional fractionation
- C. Prostate cancer tends to have a low capacity for repair between fractions, so fewer fractions helps to minimize repair over the course of treatment
- D. The alpha/beta ratio of prostate cancer is low, resulting in a large fractionation effect relative to other tumor types

Key: D

Domain: 12.19

Citations: Vogelius IR, Bentzen SM. Meta-analysis of the alpha/beta ratio for prostate cancer in the presence of an overall time factor: bad news, good news, or no news?. *Int J Radiat Oncol Biol Phys.* 2013;85(1):89-94. doi:10.1016/j.ijrobp.2012.03.004 (PMID: 22652106).

Ritter M. Rationale, conduct, and outcome using hypofractionated radiotherapy in prostate cancer. *Semin Radiat Oncol.* 2008;18(4):249-256. doi:10.1016/j.semradonc.2008.04.007 (PMID: 18725112).

Rationale: The majority of prostate tumors are slowly proliferating, resulting in estimated alpha beta ratios of 1-3Gy; lower than other tumor types in which the alpha beta ratios are estimated to be ~8Gy or higher. These characteristics support hypofractionation to achieve higher doses that have been shown to improve tumor control with minimal increase in normal tissue toxicity.

226. How does increasing the number of fractions delivered to a late-responding tissue such as the kidney alter the isoeffective total dose curve?

- A. Increases more rapidly than in an early responding tissue
- B. Increases more slowly than in an early responding tissue
- C. Unaffected by number of fractions
- D. Total dose decreases

Key: A

Domain: 12.19

Citations: Radiobiology for the Radiologist, Hall and Giaccia 8th Edition. Chapter 23, Time, dose and fractionation in radiotherapy. pp 328-354 FIGURE 23.7 p758.

Joiner, M.C. and van der Kogel, A. Basic Clinical Radiobiology Fourth Edition. 2009. Taylor & Francis.

Rationale: A late responding tissue like the kidney has a low alpha/beta ratio, resulting in a sharper bend in the survival curve (corresponding to a more rapid increase in isoeffective total dose) compared with an early responding tissue in which the alpha/beta ratio would be higher, resulting in a more gradual bend in the survival curve.

227. Which is a mechanism through which hypoxia has been shown to confer resistance to chemotherapy?

- A. Activation of mTOR signaling
- B. Induction of cell cycle arrest
- C. Reduction in cellular adenosine levels
- D. Reduction in autophagy

Key: B

Domain: 12.21

Citations: Butturini E, Carcereri de Prati A, Boriero D, Mariotto S. Tumor Dormancy and Interplay with Hypoxic Tumor Microenvironment. *Int J Mol Sci.* 2019;20(17):4305. Published 2019 Sep 3. doi:10.3390/ijms20174305 (PMID: 31484342).

Hammond EM, Denko NC, Dorie MJ, Abraham RT, Giaccia AJ. Hypoxia links ATR and p53 through replication arrest. *Mol Cell Biol.* 2002;22(6):1834-1843. doi:10.1128/mcb.22.6.1834-1843.2002 (PMID: 11865061).

Rationale: Hypoxia within the tumor microenvironment is associated with cell cycle arrest, allowing the cells to survive in a dormant state and escape the cytotoxic effects chemotherapy.

228. What is the primary mechanism through which taxanes sensitize cells to RT?

- A. They promote reoxygenation of the tumor microenvironment
- B. They result in cell cycle arrest at the G₂/M phase
- C. They promote apoptosis
- D. They inhibit angiogenesis

Key: B

Domain: 12.21

Citations: Abal M, Andreu JM, Barasoain I. Taxanes: microtubule and centrosome targets, and cell cycle dependent mechanisms of action. *Curr Cancer Drug Targets*. 2003;3(3):193-203. doi:10.2174/1568009033481967 (PMID: 12769688).

Milas L, Milas MM, Mason KA. Combination of taxanes with radiation: preclinical studies. *Semin Radiat Oncol*. 1999;9(suppl 1):12–26.

Radiobiology for the Radiologist, Hall and Giaccia 8th Edition. Chapter 27, Chemotherapeutic agents from the perspective of radiation oncology p859.

Rationale: Taxanes' primary mode of action is to inhibit microtubule formation, thus arresting cells in G₂/M phase of the cell cycle, which is the most radiosensitive phase. Taxanes bind to microtubules and, by enhancing their stability and preventing disassembly, adversely affect their function. They act as mitotic inhibitors, blocking cells in the G₂/M phase of the cell cycle.

229. Expression of what cell surface marker acts as a “brake” on the immune system and prevents immune cell recognition of tumor?

- A. CD20
- B. PD-L1
- C. HER2
- D. EGFR

Key: B

Domain: 12.11

Citations: <https://www.ncbi.nlm.nih.gov/gene?Db=gene&Cmd=ShowDetailView&TermToSearch=29126>

Kalbasi A, Ribas A. Tumour-intrinsic resistance to immune checkpoint blockade. *Nat Rev Immunol.* 2020 Jan;20(1):25-39.

Pardoll DM. The blockade of immune checkpoints in cancer immunotherapy. *Nat Rev Cancer.* 2012 Mar 22;12(4):252-64.

Rationale: EGFR is a growth factor receptor. Programmed death ligand 1 (PD-L1) is a cell membrane protein that binds to programmed cell death protein 1 (PD-1) on the effector T cells and transduces immunosuppressive signals. It is now clear that the expression of the PD-L1 protein on the tumor cell surface is critical for tumor cells to escape immunosuppression. PD-L1 protein is the functional unit involved in immunotherapy response. PD-L1 is a transmembrane protein that plays a major role in suppressing the immune system. CD-20 is a B-cell marker. HER2/neu is a growth factor receptor.

230. What makes cancer stem cells important targets of anti-cancer treatment?

- A. Prevent the development of new secondary cancers
- B. Reduces late toxicities of radiation therapy
- C. Elevate the repair normal tissue damage
- D. They exhibit therapeutic resistance

Key: D

Domain: 12.11

Citations: Peacock and Watkins, Cancer stem cells and the ontogeny of lung cancer Clin Oncol. 2008 Jun 10;26(17):2883-9.

Pajonk F, Vlashi E, McBride WH. Radiation resistance of cancer stem cells: the 4 R's of radiobiology revisited. Stem Cells. 2010 Apr;28(4):639-48.

Rationale: Cancer stem cells are pluripotent cells with high replicative potential, resistance to therapy, and ability to repopulate an entire tumor through differentiation. They are thought to be responsible for metastases and may be increased in sites of metastatic disease.

231. What is the percentage of worldwide cancers estimated to be caused by infections?

- A. 1%
- B. 5%
- C. 20%
- D. 50%

Key: C

Domain: 12.11

Citations: <https://www.cancer.org/cancer/cancer-causes/infectious-agents/infections-that-can-lead-to-cancer/intro.html>

Rationale: Worldwide, infections are linked to about 15-20% of cancers.

232. What was a principal conclusion from studies that measured radiation effects on the developing embryo?

- A. Irradiation results in macrocephaly
- B. Congenital malformations are only seen after 20 weeks gestation
- C. The effects are dependent on the gestational age of the embryo
- D. Children are heavier and taller than expected

Key: C

Domain: 12.26

Citations: Health Risks from Exposure to Low Levels of Ionizing Radiation: BEIR VII Phase 2, 2006.

Radiobiology for the Radiologist, Hall and Giaccia 8th Edition. Chapter 12, Effects of Radiation on the Embryo and Fetus. pp 328-354.

M Otake and W J Schull Radiation-related brain damage and growth retardation among the prenatally exposed atomic bomb survivors Int J Radiat Biol. 1998 Aug;74(2):159-71.

Rationale: The effects of radiation to the embryo and fetus depend upon the stage of gestation, the dose, and the dose rate. Congenital malformations are seen with radiation in the early (2-6 weeks) phases of development. Severe mental retardation is nearly 4 times more common if the radiation is received between 8 and 15 weeks than if it is received later. Children exposed in utero are shorter, lighter, and have a smaller head diameter than those not exposed to radiation.

233. What agent has been approved as a radiation protector in the event of a radiation emergency?

- A. Amifostine
- B. Sargramostim
- C. Cisplatin
- D. Pembrolizumab

Key: B

Domain: 12.27

Citations: <https://www.fda.gov/drugs/bioterrorism-and-drug-preparedness/radiation-emergencies>

Rationale: Cisplatin is a chemotherapy agent that induces DNA cross linkages; amifostine is used to reduce the side effects of chemotherapy and radiation; pembrolizumab is a antibody therapeutic targeting the immune response to cancer – it has no documented role in radiation protection; none of these compound is approved for use in a radiation emergency. Sargramostim is indicated to increase survival in patients exposed to myelosuppressive doses of radiation.

234. How do the BAD, BID and BIK function in the mechanism of apoptosis cell death?

- A. Anti-apoptotic BCL-2 proteins
- B. Inhibitor of apoptosis proteins
- C. Pro-apoptotic BCL-2 proteins
- D. Apoptotic protease activating factor 1 (APAF1) proteins

Key: C

Domain: 12.5

Citations: RC Taylor, SP Cullen, SJ Martin, Apoptosis: controlled demolition at the cellular level. *Nat. Rev. Mol. Cell Biol.* 9: 231-241 (2008).

Eriksson and Stigbrand. Radiation-induced cell death mechanisms. *Tumour Biol.* 2010 Aug;31(4):363-72.

Hotchkiss RS, Strasser A, McDunn JE, Swanson PE. Cell death. *N Engl J Med.* 2009 Oct 15;361(16):1570-83.

Rationale: BAD, BID and BIK are members of the BCL-2 family of apoptotic proteins that have only a single BH3 domain. These proteins induce oligomerization of BAK family members producing pores in the mitochondrial outer membrane, an important step in the intrinsic apoptotic pathway.

235. What assay is used to detect the death of cells by autophagy?

- A. X-gal cleavage
- B. Western blots of LC3-II
- C. Annexin V assay
- D. Propidium Iodine uptake

Key: B

Domain: 12.5

Citations: S Barth, D Glick and KF MacLeod, Autophagy: assays and artifacts. *J. Pathol.* 221: 117-124 (2010).

Radiobiology for the Radiologist, Hall and Giaccia 8th Edition. Chapter 3, Cell survival curves. pp 101.

Rationale: Modifications of the LC3 protein to LC3-II and its incorporation into the autophagosome are important steps in initiating autophagy.

236. For high dose rate low LET radiations, what does the αD term of the linear quadratic model describe?

- A. It describes the formation of a lethal lesion that results from the interaction of two proximate sublesions formed by the same charged particle track
- B. It describes the formation of a lethal lesion that results from the interaction of two proximate sublesions formed by two independent charged particle tracks
- C. It describes the formation of a lethal DNA double strand break produced by two proximate single strand breaks produced by a single charged particle track
- D. It describes the formation of a lethal DNA double stand break produced by the misrepair of two proximate damaged bases produced by a single charged particle track

Key: A

Domain: 12.7

Citations: AM Kellerer and HH Rossi, The theory of dual radiation action. *Curr. Top. Radiat. Res. Q.* 8:85-158 (1972).

SJ McMahon The linear quadratic model: usage, interpretation and challenges *Phys Med Biol*, 2018 Dec 19; 64(1):01TR01.

Rationale: The linear quadratic model of cell survival derives from Kellerer and Rossi's Theory of Dual Radiation Action. This model postulates a linear-quadratic dose response resulting from the interaction of spatially and temporally proximate pairs of "sublesions" to form lethal lesions that kill the cell. In some cases, both sublesions are formed by the same charged particle track. This forms the linear (αD) portion of the curve. The quadratic (βD^2) portion results when the interacting sublesions are produced by separate and independent particle tracks.

237. Increasing the dose rate from 0.5 cGy per minute to 1000 cGy per minute will produce what changes in alpha/beta linear quadratic model survival curve parameters?

- A. Alpha will increase while beta decreases
- B. Alpha will increase while beta increases
- C. Alpha will remain the same while beta increases
- D. Alpha will decrease while beta increases

Key: C

Domain: 12.7

Citations: AM Kellerer and HH Rossi, The theory of dual radiation action. *Curr. Top. Radiat. Res. Q.* 8:85-158 (1972).

Radiobiology for the Radiologist, Hall and Giaccia 8th Edition. Chapter 5, Fractionated Radiation and the Dose-Rate Effect Cell survival curves. pp 105-110.

Rationale: The alpha-beta survival model is based on the Theory of Dual Radiation Action. This postulates that two proximate sublesions interact to form a lethal lesion which in turn kills the cell. The linear-quadratic ($\alpha D + \beta D^2$) model for high dose rate low LET radiations has two significant components αD which is linear and results when both sublesions are produced by the same charged particle track. Since are essential formed simultaneously this component is independent of dose rate. The sublesions resulting in the quadratic portion (βD^2) of the curve are produced by two independent particle tracks. Here there is a potential for temporal spacing between the two track traversals such that in some cases the first sublesion might be repaired before the second is formed at a later time preventing any interaction. Therefore, increasing the dose rate will have no impact on α but will increase β as the temporal spacing of sublesions formation is reduced increasing the probability of lethal lesion induction via track interaction.

238. Which assumption(s) does the absolute risk model for radiation carcinogenesis make?
- A. Radiation risk increases at all ages, as cancer risk increases with age
 - B. Radiation induced cancer risk is a function of dose and the time since exposure
 - C. Radiation cancer risk is a function of the square of the dose, gender, and age at exposure
 - D. Radiation produces an increase in cancer risk over that occurring naturally

Key: D

Domain: 12.24

Citations: Hall and Giaccia, Radiobiology for the Radiologist, 8th Edition, 2019, Chapter 10 Radiation carcinogenesis pp262.

Rationale: The absolute risk model assumes any increase in carcinogenic risk will be simply added upon the risk of cancer induction in the absence of radiation exposure. The relative risk model takes age into account as the risk for many cancers increases with age. The time dependent relative risk model treats cancer risk as a function of dose, the square of the dose, age at exposure, and time since exposure.

239. In the DNA damage response, what does γ H2AX phosphorylation indicate?

- A. Failure of repair complex recruitment
- B. Activation of ATM
- C. Double strand break resolution
- D. Resumption of DNA synthesis

Key: B

Domain: 12.3

Citations: ATM phosphorylates histone H2AX in response to DNA double-strand breaks. Burma S, Chen BP, Murphy M, Kurimasa A, Chen DJ. *J Biol Chem*. 2001 Nov 9;276(45):42462-7. doi: 10.1074/jbc.C100466200. Epub 2001 Sep 24.

Bonner WM, Redon CE, Dickey JS, et al. γ H2AX and cancer. *Nat Rev Cancer*. 2008; 8:957–967.

Hall and Giaccia, *Radiobiology for the Radiologist*, 8th Edition, 2019, Chapter 2 Molecular Mechanisms of DNA and Chromosome Damage and Repair pp 54-89.

Rationale: γ H2AX is the phosphorylated form of histone H2AX, and is a phosphorylation target of ATM kinase. After breaks are detected, ATM is activated, H2AX is phosphorylated, and then repair complex proteins are recruited to repair the damage. H2AX is a histone protein, which is rapidly phosphorylated in response to damage to form γ H2AX. Staining for the unmodified histone (H2AX) gives a pan nuclear stain or unchanging band on a western blot while γ H2AX is rapidly induced on a western blot in response to stress and can be seen to form discrete nuclear foci in damaged cells.

240. Collision of a replication fork with a single strand break induces which cell cycle checkpoint?

- A. G1/S
- B. Intra-S phase
- C. G2
- D. M phase

Key: B

Domain: 12.3

Citations: Wu L, Luo K, Lou Z, Chen J. MDC1 regulates intra-S-phase checkpoint by targeting NBS1 to DNA double-strand breaks. *Proc Natl Acad Sci U S A*. 2008 Aug 12;105(32):11200-5. doi: 10.1073/pnas.0802885105. Epub 2008 Aug 4.

Rationale: DNA synthesis occurs in S phase. If a replication fork encounters a single strand break, unwinding of the DNA creates a double strand break, which will activate ATR and an intra-S phase arrest to allow for repair.

241. Which type of chromosomal aberration is MOST LIKELY to be lethal to a cancer cell?

- A. Loss of the p arm of a chromosome
- B. A balanced translocation
- C. Creation of a dicentric
- D. Chromosome deletions

Key: C

Domain: 12.4

Citations: Loucas BD, Durante M, Bailey SM, Cornforth MN. Chromosome damage in human cells by γ rays, α particles and heavy ions: track interactions in basic dose-response relationships. *Radiat Res*. 2013 Jan;179(1):9-20. doi: 10.1667/RR3089.1. Epub 2012 Nov 30.

Hall and Giaccia, *Radiobiology for the Radiologist*, 8th Edition, 2019, Chapter 2 Molecular Mechanisms of DNA and Chromosome Damage and Repair pp 54-89.

Rationale: Cancer cells often contain chromosome rearrangements, duplications and deletions. Dicentrics however, cannot be properly replicated and will lead most likely to replicative death. The three lethal aberrations are the dicentric; the ring, which are chromosome aberrations; and the anaphase bridge, which is a chromatid aberration. All three represent gross distortions and are clearly visible. The dicentric involves an interchange between two separate chromosomes.

242. Which type of radiation is MOST LIKELY to cause complex chromosomal damage?

- A. Gamma
- B. UV
- C. Proton
- D. Carbon ion

Key: D

Domain: 12.4

Citations: Chromosome damage in human cells by γ rays, α particles and heavy ions: track interactions in basic dose-response relationships. Loucas BD, Durante M, Bailey SM, Cornforth MN. Radiat Res. 2013 Jan;179(1):9-20. doi: 10.1667/RR3089.1. Epub 2012 Nov 30.

Hall and Giaccia, Radiobiology for the Radiologist, 8th Edition, 2019, Chapter 2 Molecular Mechanisms of DNA and Chromosome Damage and Repair pp 54-89

Rationale: High LET radiation causes more complex damage than low LET radiation because of higher levels of localized energy deposition. UV radiation is non-ionizing and causes pyrimidine dimers.

243. Why are normal tissues generally considered to be more radioresistant than tumors?

- A. Cells are in the S phase
- B. Cells are in the M phase
- C. Non-dividing cells in G0 phase
- D. Proliferating cells in G1 phase

Key: C

Domain: 12.12

Citations: Fabbri, MR. et. al. Molecular and epigenetic regulatory mechanisms of normal stem cell radiosensitivity. Cell Death Discovery volume 4, Article number: 117 (2018).

Hall and Giaccia, Radiobiology for the Radiologist, 8th Edition, 2019, Chapter 22 Cell, Tissue, and Tumor Kinetics p716.

Rationale: Most "normal" cells remain in a non-mitotic G0 phase, which is radioresistant because cells (non-hematopoietic) tend to die by mitotic catastrophe during cell division. The radiosensitivity of a population of cells varies with the distribution of cells through the cycle. In general, cells are most resistant in late S phase; slowly growing cells with a long cycle, however, may have a second resistant phase in the early G1 phase, which may be termed G0 if the cells are out of cycle. Thus, two quite different cell populations may be radioresistant.

244. How could the effectiveness of a densely ionizing charged particle with an LET of 1000 keV/ μm be increased to increase cell killing?
- A. Fractionate the dose
 - B. Decrease the LET to 100 keV/ μm
 - C. Decrease the dose rate
 - D. Decrease oxygenation of the tissue to 3mm Hg

Key: B

Domain: 12.8

Citations: Hall and Giaccia, Radiobiology for the Radiologist, 8th Edition, 2019, Chapter 7 Linear Energy Transfer and Relative Biologic Effectiveness FIGURE 7.9 p197-209.

Rationale: An LET of 1000 keV/ μm is past optimal LET for DNA damage and thus maximal RBE (occurring at $\sim 100\text{keV}/\mu\text{m}$), and so decreasing the LET of the ion would increase RBE. Moreover, RBE for densely ionizing charged particles is little affected by dose rate in general; decreasing dose rate would not increase RBE. 3 mm Hg is 0.5% oxygen, and at that concentration the relative radiation sensitivity is \sim midway between aerobic and hypoxic conditions so decreasing oxygenation would lower radiosensitivity and thus not increase RBE. Fractionation, would not increase RBE.

245. What effect would REDUCING tumor hypoxia have on cellular radiosensitivity to X rays?
- A. Decrease the OER
 - B. Increase HIF1 α activity
 - C. Lower free radical-induced DNA damage
 - D. Lower D0 parameter of cell survival curve

Key: D

Domain: 12.9

Citations: Hall and Giaccia, Radiobiology for the Radiologist, 8th Edition, 2019, Chapter 6 Oxygen Effect and Reoxygenation p167-189.

Rationale: The goal of lowering tumor hypoxia would be to lower the OER of x rays so that cell kill occurs at a lower dose, thus achieving a lower D0. Increasing HIF1 α activity would indicate increased hypoxia, not lower, and in that condition radiosensitivity would not be improved; lowering free radical induced DNA damage would not occur by lowering tumor hypoxia (increasing oxygen concentration) nor would it improve radiosensitivity.

246. What does the oxygen enhancement ratio describe?

- A. Increased cell killing in oxygen at isoeffect
- B. Increased cell killing in oxygen at the same dose
- C. Reduced level of tumor oxygenation
- D. Reduced level of HIF1 activation

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

Domain: 12.9

Citations: Hall and Giaccia, Radiobiology for the Radiologist, 8th Edition, 2019, Chapter 6 Oxygen Effect and Reoxygenation p167-189.

Rationale: The OER is a ratio of cell kill in aerated environments relative to hypoxic environments, so that for low LET X rays at low doses, the OER is 2.5 representing 2.5X more killing in aerated vs hypoxic conditions. 0.5% oxygen conditions represent the conditions at which the relative radiation sensitivity is midway between aerobic and hypoxic conditions, and the plateau of cell killing occurs at near 30mm Hg (5% oxygen). The S phase is a relatively resistant portion of the cell cycle, especially vs G1 or G2/M.

247. What explains the increase in cell survival observed when successive 2 Gy fractions are delivered 6 hours apart rather than 1 hour apart?

- A. Increased repair of sublethal damage
- B. Induction of hypoxia via HIF1 activity
- C. Decreased radical-induced DNA damage
- D. Reassortment of cells from resistant cell cycle phase

Key: A

Domain: 12.10

Citations: Hall and Giaccia, Radiobiology for the Radiologist, 8th Edition, 2019, Chapter 5 Fractionated Radiation and the Dose-Rate Effect pp142-168.

Rationale: The fluctuation of survival times observed during the course of a split dose experiment is due to reassortment of cycling cells in to portions of the cell cycle having different radiosensitivities. So an increase in survival time that occurs during the course of a split dose experiments is a result of reassortment into a more radiation resistant phase of the cell cycle, such as S, which has a higher capacity for sublethal damage repair. Hif1 activity would indicate a decrease in hypoxic conditions, which would lower cell survival, as would an increase in free radical induced DNA damage (typically occurs in more oxic conditions).

248. What biological characteristic describes sublethal damage repair (SLDR) and cell survival?

- A. The α component of LQ model of cell kill
- B. Repair of damage in the G2/M portion of the cell cycle
- C. A linear survival curve with no shoulder
- D. Repair is complete 6 hours after irradiation

Key: D

Domain: 12. 10

Citations: Hall and Giaccia, Radiobiology for the Radiologist, 8th Edition, 2019, Chapter 5 Fractionated Radiation and the Dose-Rate Effect pp142-168.

Rationale: SLDR is generally complete by 1-2 hours in culture. The β component of cell kill, and therefore the shoulder portion of the cell survival curve, best represents repair capacity; the α component best describes cell death as being an exponential function of dose (within limited repair). SLDR capacity is greatest during the dividing portions of the cell cycle, such as S phase.

249. Which is an advantage of carbon ions versus protons?

- A. Increased normal tissue sparing
- B. Higher LET
- C. Spread out Bragg peak
- D. Higher OER

Key: B

Domain: 12.20

Citations: Hall and Giaccia, Radiobiology for the Radiologist, 8th Edition, 2019, Chapter 7 Linear Energy Transfer and Relative Biologic Effectiveness p197-215.

Rationale: A radiobiologic advantage of carbon ions relative to protons is a greater LET, which results in increased cell kill. However, because of the high LET and RBE at the Bragg peak, repair capacity of normal tissues is reduced. As a result, sparing of normal tissues with fractionation is lower. For both protons and carbon ions, clinicians can take advantage of a spread-out Bragg peak for tumor treatment. Protons have very similar OER to conventional X-rays, whereas carbon ions have a lower OER than both protons and X rays.

250. Which radiolysis product of water is responsible for approximately two thirds of DNA damage caused by the indirect action of ionizing radiation?

- A. H_2O_2
- B. e_{aq}^-
- C. H_2O^+
- D. OH^\bullet

Key: D

Domain: 12.1

Citations: Mitchell JB, Russo A, Kuppusamy P, et al., Radiation, Radicals, and Images. Ann N Y Acad Sci 899:28-43, 2000.

Hall and Giaccia, Radiobiology for the Radiologist, 8th Edition, 2019, Chapter 1 Physics and Chemistry of Radiation Absorption pp38-55.

Rationale: Approximately 2/3 of the damage caused by the indirect action of radiation is attributed to the hydroxyl radical, OH^\bullet . Very little damage is caused by the hydrated electron, e_{aq}^- , hydrogen peroxide, H_2O_2 , produces predominantly single-strand breaks and excited water, H_2O^+ , is short-lived and leads to the production of OH^\bullet . Direct and indirect actions of radiation. In direct action, a secondary electron resulting from absorption of an x-ray photon interacts with the DNA to produce an effect. In indirect action, the secondary electron interacts with, for example, a water molecule to produce a hydroxyl radical (OH^\bullet), which in turn produces the damage to the DNA. The DNA helix has a diameter of about 20 Å (2 nm). It is estimated that free radicals produced in a cylinder with a diameter double that of the DNA helix can affect the DNA.

251. Which interactions of ionizing radiation with biological tissues is MOST important in PET?

- A. Photoelectric effect
- B. Pair production
- C. Compton scattering
- D. Photodisintegration

Key: B

Domain: 12.1

Citations: Walters Kluwer. Radiobiology for the Radiologist, Chapter 1 pp 2-10. Eds. Hall and Giaccia, 8th Ed.

Rationale: Pair production requires a photon energy of 1.02 MeV which is the energy required to produce an electron (511 keV) and positron (511 KeV) pair. The positron combines with an electron producing two 511 keV photons that are emitted at 180o to each other and are detected in a PET scanner. The photoelectric effect occurs when a a low energy photon interacts with the electron in the atom and removes it from its shell and the incident photon is completely absorbed in the process. The effect is dependent on atomic number of the absorber and is of fundamental importance in x-ray imaging. Compton scattering occurs due to the interaction of the x-ray or gamma photon with free electrons or loosely bound outer shell electrons. The resultant incident photon gets scattered and imparts energy to the electron (recoil electron) and is the predominant effect for therapeutic radiation. Photodisintegration occurs when a high energy photon is absorbed by a nucleus resulting in immediate disintegration of the nucleus.

252. Which cellular assay would be appropriate to use for quantitative measurement of DNA double strand breaks immediately after exposure to ionizing radiation?

- A. Neutral comet assay
- B. Alkaline elution
- C. Western blotting
- D. Incorporation of bromodeoxyuridine

Key: A

Domain: 12.2

Citations: Fairbairn DW, et. al. The comet assay: a comprehensive review. *Mutat Res.* 1995;339(1):37-59.

Hall and Giaccia, *Radiobiology for the Radiologist*, 8th Edition, 2019, Chapter 2 Molecular Mechanisms of DNA and Chromosome Damage and Repair pp 54-89.

Rationale: The neutral comet assay is used to measure DNA double-strand breaks. Alkaline elution is used to measure single-strand breaks and some base damages. Alkaline conditions separate the two DNA strands so single strand breaks are measured in each strand. Western blotting is for detection of proteins, and bromodeoxyuridine incorporation is used as a radiosensitizer or for cell kinetic analysis.

253. What genomic mechanism does NOT result in the activation of a proto-oncogene?

- A. Chromosome translocation
- B. Methylation of the promoter region
- C. Point mutation altering the function
- D. Retroviral activation

Key: B

Domain: 12.14

Citations: Pierotti MA, Sozzi G, Croce CM. Mechanisms of oncogene activation. In: Kufe DW, Pollock RE, Weichselbaum RR, et al., editors. *Holland-Frei Cancer Medicine*. 6th edition. Hamilton (ON): BC Decker; 2003.

Hall and Giaccia, *Radiobiology for the Radiologist*, 8th Edition, 2019, Chapter 18 Cancer Biology pp535-593.

Rationale: Methylation is a process that results in “silencing” of the gene by making it inaccessible to transcription factors. Chromosome translocation is a common process that activates proto-oncogenes such as C-MYC. Point mutations are responsible for the activation of proto-oncogenes such as RAS. Oncogenes were first discovered due to their incorporation into retroviruses.

254. What cellular process is considered a “hallmark of cancer”?

- A. Promotion of growth suppressors
- B. Immunogenesis
- C. Disabling replicative immortality
- D. Inducing angiogenesis

Key: D

Domain: 12.14

Citations: Hanahan, D. and Weinberg, R.A. Hallmarks of cancer: The next generation. *Cell* 144: 646-674, 2011.

Hall and Giaccia, *Radiobiology for the Radiologist*, 8th Edition, 2019, Chapter 18 Cancer Biology pp535-593.

Rationale: It is widely accepted that cancer cells require unlimited replicative potential in order to generate macroscopic tumors in contrast to the behavior of the cells in most normal cell lineages which are able to pass through only a limited number of successive cell growth-and-division cycles. Angiogenesis is the recruitment of new blood vessels to regions of chronically low blood supply and is essential for the progression of solid tumors to malignancy. Increasing evidence supports the hypothesis that tumor angiogenesis is controlled by an “angiogenic switch,” a physiologic mechanism involving a dynamic balance of angiogenic factors that include both inhibitors and inducers. Numerous angiogenic factors have been identified, including specific endothelial cell growth factors (e.g., vascular endothelial growth factor, or VEGF), cytokines and inflammatory agents (e.g., tumor necrosis factor α , or TNF- α , and interleukin-8, or IL-8), fragments of circulatory system proteins (e.g., angiostatin and endostatin), and ECM components (e.g., thrombospondins, or TSPs). Presumably, this diversity of angiogenic factors reflects a strict requirement for controlling angiogenesis under normal physiologic conditions and in response to oncogenic events by modulating the expression of both angiogenic inducers and inhibitors.

255. Which of the following is NOT a tumor suppressor gene?

- A. p16
- B. RB
- C. SRC
- D. PTEN

Key: C

Domain: 12.14

Citations: Irby, R., Yeatman, T. Role of Src expression and activation in human cancer. *Oncogene* 19, 5636–5642 (2000).

Hall and Giaccia, *Radiobiology for the Radiologist*, 8th Edition, 2019, Chapter 18 Cancer Biology pp535-593.

Rationale: Cell immortalization can be viewed as a competing process that requires both the activation of dominant activating oncogenes to induce proliferation and the loss of recessive tumor suppressor genes that induce a cell cycle arrest in response to this constitutive activating signal. Tumor suppressor genes act as negative growth regulator, such as PTEN, p16 and Rb which are involved in restricting growth and cell cycle regulation. The product of the human SRC gene, c-Src, has been found to be over-expressed and highly activated in a wide variety of human cancers and has an influence on the development of the metastatic phenotype. It was one of the first proto-oncogenes discovered as a retroviral gene (v-src) responsible for the development of tumors in chickens. p16 is a tumor suppressor gene associated with familial melanoma, RB is a tumor suppressor whose inactivation is associated with retinoblastoma and PTEN is a tumor suppressor gene which inhibits PI3K signaling and its loss of function is common in prostate cancer.

256. After performing a 4D CT study, what reconstructed CT image set best identifies the ITV of a hypodense lesion in the liver?

- A. Average CT
- B. 50% phase CT
- C. Maximum Intensity Projection (MIP) CT
- D. Minimum Intensity Projection (MinIP) CT

Key: D

Domain: 13.3

Citations: Dieterich, et. al, *Practical Radiation Oncology Physics*, 1st Ed., 2016.

Rationale: Because the lesion is hypodense within the liver, the MinIP will best represent the ITV of the lesion. The average CT will blur the edges of the lesion and will make it difficult to clearly delineate. The 50% phase will solely show the lesion in one phase of motion, and the MIP will erroneously show the lesion much smaller than it actually is.

257. When a therapeutic electron beam interacts with tissue, how do the electrons predominantly lose their energy?

- A. Inelastic collisions with atomic electrons
- B. Inelastic collisions with nuclei
- C. Elastic collisions with atomic electrons
- D. Elastic collisions with nuclei

Key: A

Domain: 13.3

Citations: Khan, The Physics of Radiation Therapy, 5th Ed, 2014.

Rationale: In low atomic number media such as water or tissues, electrons lose energy predominantly through ionizing events (inelastic collisions) with atomic electrons.

258. Which ionization chamber minimizes cavity perturbation effects in a radiation field?

- A. Parallel-plate chamber
- B. Farmer chamber
- C. Vented thimble chamber
- D. Unvented thimble chamber

Key: A

Domain: 13.6

Citations: Khan, The Physics of Radiation Therapy, 5th Ed, 2014.

Rationale: The small electrode spacing in a parallel-plate chamber minimizes cavity perturbations in a radiation field. Farmer and thimble shaped chambers typically produce significant perturbations in the radiation field that require corrections.

259. What depth, in water, is the beam flatness typically specified for a clinical photon beam?

- A. d_{\max}
- B. 5 cm
- C. 10 cm
- D. 15 cm

Key: C

Domain: 13.6

Citations: Khan, The Physics of Radiation Therapy, 5th Ed, 2014.

Rationale: For a clinical photon beam, the beam flatness is typically specified at 10 cm depth in water for all photon beam energies. The depth is important as the flattening filter shape is designed to ensure a flat beam profile at 10 cm.

260. An Ir-192 HDR source is exchanged while a patient is undergoing a three-fraction vaginal cylinder course. If the first fraction was delivered in 375 seconds with a source strength of 5.8Ci, what is the expected treatment time for the second fraction if the new source strength is 9.9Ci?

- A. 220 seconds
- B. 290 seconds
- C. 375 seconds
- D. 450 seconds

Key: A

Domain: 13.11

Citations: Khan, The Physics of Radiation Therapy, 5th Ed, 2014.

Rationale: The treatment time is inversely proportional to the source strength if the dose is kept constant. If the source strength increased, the treatment time will decrease accordingly by the same proportion.

261. Generally, respiratory motion management techniques are recommended if the target motion, in any given direction, is larger than:

- A. 3 mm.
- B. 5 mm.
- C. 10 mm.
- D. 15 mm.

Key: B

Domain: 13.11

Citations: Keall PJ, et al. TG 76 – Management of Respiratory Motion in Radiation Oncology. Med Phys. 2006;33(10).

Rationale: To ensure the dose is accurately delivered, AAPM Task Group 76 recommends that a 5mm motion limit criterion should be used as this level of motion can cause significant imaging artifacts and systematic errors during imaging procedures.

262. Compared to x-ray based IMRT/VMAT treatment plans, why is the high dose conformity of proton therapy to the target volume generally worse?

- A. Need to use higher energy (100-200 MeV) protons
- B. Enhanced biological effects of higher LET
- C. Proton range uncertainty
- D. Dosimetric contributions of neutrons

Key: C

Domain: 13.17

Citations: Dieterich, et. al, Practical Radiation Oncology Physics, 1st Ed., 2016.

Rationale: For the same target, the high dose conformity is generally worse for proton therapy delivery primarily due to the proton range uncertainty.

263. What is the activity on the 100th day for an Ir-192 source ($T_{1/2} = 78.4$ days) with an initial activity of 10 Ci?

- A. 2.8 Ci
- B. 4.1 Ci
- C. 5.1 Ci
- D. 7.8 Ci

Key: B

Domain: 13.1

Citations: McDermott, P. N. & Orton, C. G. (2018). The physics & technology of radiation therapy (2nd ed., pp. 3-14-3- 18). Madison, WI: Medical Physics Publishing.

Rationale: The equation to determine activity at a point in time is $A(t) = A_0 \cdot \exp(-\lambda t)$. The decay constant λ is related to the half-life by $\lambda = \ln(2)/T_{1/2}$.

264. What is the role of a magnetron or klystron in a linear accelerator during photon beam production?

- A. Generates radiofrequency power for acceleration
- B. Transfers radiofrequency power to an electron beam
- C. Redirects an electron beam toward machine isocenter
- D. Creates photons from an accelerated electron beam

Key: A

Domain: 13.3

Citations: McDermott, P. N. & Orton, C. G. (2018). The physics & technology of radiation therapy (2nd ed., pp. 9-14-9- 17). Madison, WI: Medical Physics Publishing.

Rationale: The magnetron or klystron (depending on accelerator design) acts as a radiofrequency power source for a medical linear accelerator. Power from the magnetron or klystron is transferred to electrons within an accelerating waveguide. Bending and focusing magnets act on the accelerated electron beam to redirect it toward a tungsten target in line with machine isocenter. Interactions in the target convert the electron beam energy to Bremsstrahlung photons directed toward the patient.

265. Which electron beam energy is MOST appropriate when treating a target at 4 cm depth that is prescribed to the 80% isodose line?

- A. 6 MeV
- B. 9 MeV
- C. 12 MeV
- D. 15 MeV

Key: C

Domain: 13.8

Citations: McDermott, P. N. & Orton, C. G. (2018). The physics & technology of radiation therapy (2nd ed., pp. 16-5). Madison, WI: Medical Physics Publishing.

Rationale: R_{80} , the depth where dose from an electron beam falls off to 80% of the maximum, is approximated (in centimeters) by the nominal beam energy (in MeV) divided by 3. Therefore, to achieve prescription dose at 4 cm depth prescribed using the 80% isodose level, the appropriate beam energy is $4 \text{ cm} * 3 = 12 \text{ MeV}$.

266. What dosimeter should be used when performing an absolute dose output calibration of a linear accelerator?

- A. Geiger counter
- B. Ionization chamber
- C. Radiochromic film
- D. Thermoluminescent dosimeter (TLD)

Key: B

Domain: 13.8

Citations: McDermott, P. N. & Orton, C. G. (2018). The physics & technology of radiation therapy (2nd ed., pp. 8-5-8- 25). Madison, WI: Medical Physics Publishing.

Rationale: Ionization chambers are most appropriate as they can be calibrated accurately with methods traceable to primary standards laboratories to provide direct absolute dose measurements. Geiger counters are much less accurate and typically only calibrated for exposure. Film is a relative dosimeter, requiring a separate calibration to be used as an absolute dosimeter. Thermoluminescent dosimeters (TLDs) are capable of absolute dosimetry with careful pre- and post-processing, however this requires special equipment not commonly available in a clinic and still results in measurements with less accuracy and precision than an ionization chamber.

267. What does “UID” denote in the DICOM standard?

- A. Underlying dataset
- B. Uninterruptable data stream
- C. Unique identifier
- D. Universal indicator

Key: C

Domain: 13.8

Citations: NEMA PS3 / ISO 12052, Digital Imaging and Communications in Medicine (DICOM) Standard, National Electrical Manufacturers Association, Rosslyn, VA, USA (available free at <http://www.dicomstandard.org/>)

Rationale: A DICOM unique identifier (UID) is structured yet unique number that allows an aspect of a DICOM-compliant dataset to be reliably referenced to other DICOM-compliant datasets. Some areas where UIDs are necessary include establishing a common UID among all slices in an image volume, matching a UID to a frame of reference for registered image volumes, and maintaining study/series and subject/object relationships, among others. Enforcing concordance of UIDs keeps relationships structured and predictable in the presence of large amounts of data.

268. Voxel values in a computed tomography (CT) image set are MOST closely related to which property of the object being imaged?

- A. Metabolic activity
- B. Nuclear spin
- C. Photon attenuation
- D. Physical density

Key: C

Domain: 13.12

Citations: McDermott, P. N. & Orton, C. G. (2018). The physics & technology of radiation therapy (2nd ed., pp. 19-17). Madison, WI: Medical Physics Publishing.

Rationale: Computed tomography (CT) images are formed by the mathematical reconstruction of the relative attenuation of a photon beam passing through the subject being imaged. It is possible to create a mapping between CT image values and physical density using specialized phantoms, but physical density is not the fundamental material property responsible for creating the image. Positron emission tomography (PET) images are most used to evaluate metabolic activity, and magnetic resonance (MR) images are formed using properties of nuclear spin.

269. What factor principally contributes to the reduced soft tissue contrast in MV portal images as compared to diagnostic radiographs?

- A. Photon beam energy
- B. Radiation field size
- C. Source-to-detector distance
- D. Source-to-subject distance

Key: A

Domain: 13.14

Citations: McDermott, P. N. & Orton, C. G. (2018). The physics & technology of radiation therapy (2nd ed., pp. 19-8). Madison, WI: Medical Physics Publishing.

Rationale: The higher beam energy in portal images leads to reduced contrast, as the dominant attenuation mechanism is the Compton interaction (independent of atomic number) for a megavoltage beam as opposed to the photoelectric effect (varies exponentially with atomic number) for a kilovoltage beam. While differences in acquisition geometry may affect the magnification or signal, detector response for a given acquisition is relatively uniform across the panel and therefore image contrast is independent of the geometry.

270. In general, which set of treatment techniques is correctly ordered from least MU to most MU when treating a given target to the same dose prescription?

- A. 3D CRT, fixed-gantry IMRT, VMAT
- B. 3D CRT, VMAT, fixed-gantry IMRT
- C. VMAT, fixed-gantry IMRT, 3D CRT
- D. VMAT, 3D CRT, fixed-gantry IMRT

Key: B

Domain: 13.14

Citations: Teoh, M., Clark, C. H., Wood, K., Whitaker, S., & Nisbet, A. (2011). Volumetric modulated arc therapy: a review of current literature and clinical use in practice. *Brit J Rad.* 84(1007), 967–996. doi:10.1259/bjr/22373346

Rationale: While there are variations among treatment sites and planning approaches, estimates in literature suggest that fixed gantry IMRT treatment plans generally require 2-3 times more MU as compared to a 3D conformal technique to deliver equivalent dose to a given target. Arc-based IMRT is more time- and MU-efficient than fixed gantry IMRT, but as an intensity-modulated technique still requires more MU than for an equivalent 3D conformal plan.

271. There are two types of accelerating waveguides for medical linear accelerators: standing wave and traveling wave. Standing wave linac waveguides are _____ in length than traveling wave but both employ _____ to increase the energy of electrons.

- A. Shorter; magnetic fields
- B. Shorter; microwaves
- C. Longer; magnetic fields
- D. Longer; microwaves

Key: B

Domain: 13.3

Citations: The Physics and Technology of Radiation Therapy, 2nd ed. by McDermott & Orton, Medical Physics Publishing, 2018.

Rationale: Linac standing wave waveguides are approximately half the length of traveling wave waveguides because they employ side cavity coupling. In both types of waveguide, the electrons are accelerated by the electric field of the microwaves that are fed into the waveguide. A magnetic field cannot do work on charged particles and thus cannot increase their energy.

272. The AAPM Task Group 51 report for linac beam calibration requires that the absolute dose output calibration be performed at least _____ with a dosimeter placed in a _____ phantom.

- A. Monthly, water
- B. Monthly, tissue equivalent solid
- C. Annually, water
- D. Annually, tissue equivalent solid

Key: C

Domain: 13.6

Citations: The Physics and Technology of Radiation Therapy, 2nd ed. by McDermott & Orton, Medical Physics Publishing, 2018.

Rationale: The TG51 report requires that calibration be performed at least annually in a water phantom. Solid phantoms are not permitted.

273. The absorbed dose, D_1 , in a linac beam is measured using an ion chamber placed at depth, d_1 , within a large water phantom. Water is added to the phantom without moving the ion chamber, and as a result, the ion chamber is now at a depth, d_2 . With no change in the linac configuration, what is the dose at d_2 ?

- A. $D_1 \times \text{TMR}(d_2)/\text{TMR}(d_1)$
- B. $D_1 \times \text{TMR}(d_1)/\text{TMR}(d_2)$
- C. $D_1 \times \text{PDD}(d_2)/\text{PDD}(d_1)$
- D. $D_1 \times \text{PDD}(d_1)/\text{PDD}(d_2)$

Key: A

Domain: 13.6

Citations: The Physics and Technology of Radiation Therapy, 2nd ed. by McDermott & Orton, Medical Physics Publishing, 2018.

Rationale: This is based on the definition of TMR as the ratio of two doses measured at different depths but at the same distance from the source.

274. An 8-bit gray scale image has _____ shades of gray.

- A. 8
- B. 16
- C. 64
- D. 256

Key: D

Domain: 13.10

Citations: The Physics and Technology of Radiation Therapy, 2nd ed. by McDermott & Orton, Medical Physics Publishing, 2018.

Rationale: An 8 bit gray scale contains $2^8 = 256$ shades of gray.

275. What is the approximate average annual effective dose received by individuals in the US population, including background, medical and consumer exposure?

- A. 5 mSv
- B. 50 mSv
- C. 150 mSv
- D. 500 mSv

Key: A

Domain: 13.10

Citations: The Physics and Technology of Radiation Therapy, 2nd ed. by McDermott & Orton, Medical Physics Publishing, 2018.

Rationale: The average effective dose received annually by a member of the US population is 6.2 mSv. This includes exposure from background, medical exams and consumer products.

276. In magnetic resonance imaging (MRI), what is “relaxation”?

- A. The magnetic susceptibility of the tissue reaching saturation
- B. The magnetization of the protons returning to equilibrium
- C. The detection of an echo from the tissue voxels
- D. A magnetic pulse that flips the spin of the protons

Key: B

Domain: 13.10

Citations: The Physics and Technology of Radiation Therapy, 2nd ed. by McDermott & Orton, Medical Physics Publishing, 2018.

Rationale: In MRI, “relaxation” refers to the return of proton magnetization to its equilibrium value with time- scales T1 and T2.

277. Why does ICRU 83 define “near minimum” and “near maximum” dose parameters of a target volume?

- A. The absolute minimum and maximum dose are difficult to determine
- B. The absolute maximum dose is always 100% of the prescribed dose
- C. Single voxels may have extreme values
- D. The absolute minimum dose is always zero

Key: C

Domain: 10.10

Citations: The Physics and Technology of Radiation Therapy, 2nd ed. by McDermott & Orton, Medical Physics Publishing, 2018.

Rationale: The absolute minimum and maximum dose can be deceiving because they may only occur in a single small voxel and represent an extreme outlier.

278. What is a difference between pencil beam scanning (PBS) and passive scattering delivery techniques for proton therapy?

- A. Dose delivery interplay due to organ motion is less of a problem for PBS
- B. Neutron contamination is higher for PBS
- C. PBS requires no patient specific beam modifiers
- D. Passive scattering does not use a spread-out Bragg peak approach

Key: C

Domain: 13.17

Citations: The Physics and Technology of Radiation Therapy, 2nd ed. by McDermott & Orton, Medical Physics Publishing, 2018.

Rationale: Interplay is more problematic when an organ is moving while it is being scanned by the pencil beam. Passive scattering relies on a spread out Bragg peak for target coverage along the beam axis. For passive scattering, distal conformity is achieved with a physical compensator but proximal conformity is more difficult to achieve due to the fixed extent of the spread out Bragg peak.

279. As compared to a flattened 6 MV photon beam, how does the x-ray energy spectrum of a 6 MV flattening filter free (FFF) beam differ?

- A. Lower maximum photon energy
- B. Higher maximum photon energy
- C. Larger percentage of lower energy photons
- D. Larger percentage of higher energy photons

Key: C

Domain: 13.2

Citations: Ali ES, Rogers DW. Functional forms for photon spectra of clinical linacs. *Phys Med Biol.* 2012 Jan 7;57(1):31-50.

Rationale: The maximum photon energy will not change between a flattened 6 MV beam and a 6 MV FFF beam. However, since there is no flattening filter to filter the 6 MV FFF beam, the 6 MV FFF beam will have a higher percentage of lower energy photons as compared to the flattened 6 MV beam due to beam hardening attributed to the flattening filter.

280. What is the purpose of a scattering foil in a linear accelerator?

- A. Increase electron energy
- B. Eliminate photon contamination
- C. Flatten photon beam profile
- D. Broaden the electron field

Key: D

Domain: 13.2

Citations: Khan, F. M. *The Physics of Radiation Therapy*, 5th Edition (2014). Baltimore, MD: Lippincott Williams & Wilkins.

Rationale: The scattering foil is located inside of the treatment head, and it broadens the electron beam to enable delivery of large field sizes.

281. What is the MOST probable interaction of a 6 MV photon with water?

- A. Compton
- B. Pair production
- C. Photo electric
- D. Nuclear interaction

Key: A

Domain: 13.2

Citations: Khan, F. M. The Physics of Radiation Therapy, 5th Edition. (2014). Baltimore, MD: Lippincott Williams & Wilkins.

Rationale: From about 150 KeV to 10 MV photon energies, Compton effect is the most dominant interaction in water.

282. When using a vented ion chamber, why is it necessary to correct the ion chamber reading for ambient air temperature and pressure?

- A. To account for the mass of air within the ion chamber active volume
- B. To account for the change in linac dose output with atmosphere
- C. To account for polarity effects of the ion chamber
- D. To account for ion recombination within the ion chamber

Key: A

Domain: 13.6

Citations: Khan, F. M. The Physics of Radiation Therapy, 5th Edition. (2014). Baltimore, MD: Lippincott Williams & Wilkins.

Rationale: An unsealed ion chamber is affected by both air temperature and pressure because the density of air depends on temperature and pressure. The output of the linac, chamber polarity and ion recombination are not affected by temperature and pressure.

283. Geometric penumbra is independent of which of the following parameters?

- A. Beam energy
- B. Beam focal spot size
- C. Source to Surface Distance (SSD)
- D. Source to Collimator Distance (SCD)

Key: A

Domain: 13.6

Citations: Khan, F. M. The Physics of Radiation Therapy, 5th Edition. (2014). Baltimore, MD: Lippincott Williams & Wilkins.

Rationale: Geometric penumbra is caused by the finite size of the focal spot and is dependent on the distance from the source and the distance the collimator is from the source. The beam energy influences the radiative and transmission penumbra due to the lateral scattering range of the secondary electrons and the transmission through the jaw/MLC with higher energies.

284. For a remote afterloading HDR unit, what is the source positioning accuracy tolerance for daily QA?

- A. 0.5 mm
- B. 1.0 mm
- C. 2.0 mm
- D. 3.0 mm

Key: B

Domain: 13.11

Citations: Kubo HD, Glasgow GP, Pethel TD, et al. High dose-rate brachytherapy treatment delivery: report of the AAPM Radiation Therapy Committee Task Group 59. Med Phys. 1998; 25:375-403.

Rationale: According to TG-59 and NRC regulations, the required accuracy in source positioning for a remote afterloading HDR Ir-192 source is 1.0 mm.

285. What is the planning target volume (PTV)?

- A. Volume accounting for uncertainties in treatment setup
- B. Volume accounting for changes in target shape over treatment course
- C. Volume defining the beam block margins to ensure target dose coverage
- D. Volume defining the GTV motion during physiological movements

Key: A

Domain: 13.11

Citations: Khan, F. M. *The Physics of Radiation Therapy*, 5th Edition (2014). Baltimore, MD: Lippincott Williams & Wilkins.

Rationale: The PTV is created to account for patient movement and set up uncertainties.

286. Which process is responsible for the generation of photons in the target of a linear accelerator?

- A. Photoelectric effect
- B. Bremsstrahlung interaction
- C. Compton scattering
- D. Elastic scattering

Key: B

Domain: 13.2

Citations: Chang, D. S., Lasley, F. D., & Das, I. J. (2014). *Basic Radiotherapy Physics and Biology*. New York: Springer.

Rationale: Bremsstrahlung is the interaction by which electrons interact very closely with nuclei in the target and are strongly accelerated while irradiating their energy in the form of x-ray photons. The photoelectric effect and Compton scattering are both photon interactions, not electron interactions. Elastic scattering is when the total kinetic energy is conserved, which is not the case in the production of photons.

287. When a 6 MeV electron beam strikes a target to produce a photon beam, what is the maximum possible energy of the photon beam?

- A. 2 MV
- B. 4 MV
- C. 6 MV
- D. 8 MV

Key: C

Domain: 13.5

Citations: Attix, F. H. (2004). Introduction to Radiological Physics and Radiation Dosimetry. Madison, WI: Wiley.

Rationale: The spectrum of a photon beam produced by the Bremsstrahlung interaction is polyenergetic with any energy equal to or less than the initial energy of the electron possible. In this case, the photons in the beam can have any energy less than or equal to 6 MV.

288. For AP/PA photon fields, when is treating with a higher energy beam preferable to a lower beam energy?

- A. Patient with a pacemaker
- B. IMRT
- C. Superficial target
- D. Large treatment area separation

Key: D

Domain: 13.7

Citations: Khan, F. M. The Physics of Radiation Therapy, 5th Edition (2014). Baltimore, MD: Lippincott Williams & Wilkins. p. 186-187.

Rationale: The tissue lateral effect demonstrates that a higher beam energy results in a more homogeneous dose than a lower beam energy, an advantage particularly apparent as the patient thickness increases. A higher beam energy is not preferred for either a pacemaker or for IMRT due to neutron dose. A higher beam energy is also not preferred when treating a superficial target since it will have more skin sparing than a lower energy beam.

289. Which of the following approaches increases the skin dose of an electron beam?

- A. Decreasing the electron beam energy
- B. Placing a bolus on the patient surface
- C. Ensuring the electron beam is perpendicular to the patient surface
- D. Mixing a photon beam with the electron beam

Key: B

Domain: 13.7

Citations: Gerbi, B. J., Antolak, J. A., Deibel, F. C., Followill, D. S., Herman, M. G., Higgins, P. D., et al. Recommendations for clinical electron beam dosimetry: Supplement to the recommendations of Task Group 25. Med Phys. 2009. 36(7): p. 3257.

Rationale: A bolus will move the skin to a deeper portion of the percent depth dose curve, thereby increasing the skin dose. Decreasing the beam energy will decrease surface dose. Orthogonal beam angles will decrease surface dose as compared to oblique incidence. Adding a photon beam will lower the skin dose since photon beams have more skin sparing.

290. A full, absolute dose calibration of a megavoltage photon beam using the TG-51 calibration protocol is recommended on what temporal basis?

- A. Daily
- B. Weekly
- C. Monthly
- D. Annually

Key: D

Domain: 13.7

Citations: Klein, E. E., Hanley, J., Bayouth, J., Yin, F.F., Simon, W., Dresser, S., et al. Task Group 142 report: Quality assurance of medical accelerators. Med. Phys. 2009. 36(9): p. 4201.

Rationale: Calibration is recommended (and required by many regulations) on an annual basis by Task Group 142. Verification of the output via spot checks should be performed on a more frequent basis.

291. For a HDR vaginal cylinder treatment with a dose prescription point 5mm from the cylinder surface, how does the choice of cylinder diameter influence the surface dose?

- A. Diameter size does not affect the surface dose
- B. Smaller diameter cylinder will lead to a lower surface dose
- C. Larger diameter cylinder will lead to a lower surface dose
- D. Depends on the HDR radioisotope being used

Key: C

Domain: 13.11

Citations: Qian, J. M., Stahl, J. M., Young, M. R., Ratner, E., & Damast, S. (2017). Impact of vaginal cylinder diameter on outcomes following brachytherapy for early stage endometrial cancer. *Journal of gynecologic oncology*, 28(6), e84.

Rationale: With a larger diameter cylinder, the surface and prescription points are farther from the source. The inverse square effect becomes less severe with increased distance from the source resulting in less variation between the surface and prescription point. Since in either case the prescription point is getting the same dose, the only difference will be that in the case of a larger diameter, the surface point is not as increased as it would be for a smaller diameter. This physics principle also applies to other radioisotopes and is not exclusive for Ir-192.

292. What type of image is a port film compared to, in order to quantify patient setup offsets?

- A. Digitally reconstructed radiograph (DRR)
- B. Treatment planning CT
- C. Scout image taken at CT simulation
- D. Cone-beam CT (CBCT) taken prior to treatment

Key: A

Domain: 13.14

Citations: Goyal, S., & Kataria, T. (2014). Image guidance in radiation therapy: techniques and applications. *Radiology research and practice*, 2014, 705604. <https://doi.org/10.1155/2014/705604>

Rationale: A port film is a 2D image and must be compared with a radiographic representation of the patient's anatomy at the time of simulation which is typically digitally reconstructed in the treatment planning system.

293. Why does an IMRT treatment require higher confidence in both delivery accuracy and patient setup reproducibility?

- A. Uses higher doses per fraction thereby increasing the severity of a geometrical miss
- B. Treatment is less susceptible to patient anatomy changes
- C. Treatment uses a lower photon beam energy resulting in different effects on surface dose
- D. Creates dose distributions with high conformity and sharp dose gradients

Key: D

Domain: 13.14

Citations: Treece, S. J., et. al. (2013). The value of image- guided intensity-modulated radiotherapy in challenging clinical settings. The British journal of radiology, 86(1021), 20120278.

<https://doi.org/10.1259/bjr.20120278>

Rationale: The high dose gradients in IMRT are less forgiving to setup errors than those of open fields with margins in the beam aperture typical of 3D radiation therapy.

294. If a linac is programmed (i.e. moded up) to generate a photon beam, but the hardware incorrectly configures itself to generate an electron beam, how will the dose rate detected at the monitor chambers change?

- A. Increase slightly
- B. Increase significantly
- C. Decrease slightly
- D. Decrease significantly

Key: B

Domain: 13.3

Citations: Khan, F. M. The Physics of Radiation Therapy, 5th Edition. (2014). Baltimore, MD: Lippincott Williams & Wilkins.

Rationale: Due to inefficiencies in x-ray production, the linac operates at a significantly higher dose rate for photon beams compared to electron beams. Furthermore, in this situation, the flattening filter would not have been in place for the photon beam, which also would increase the dose rate incident on the monitor chambers.

295. When a 10 MV photon beam interacts with a metal prosthesis, why is there an increase in the dose at the proximal edge of the metal interface?

- A. Backscatter
- B. Attenuation
- C. Pair production
- D. Photoelectric absorption

Key: A

Domain: 13.7

Citations: AAPM TG-65 Tissue Inhomogeneity Corrections for Megavoltage Photon Beams 2004.

Rationale: The increased dose is due to an increase in backscatter at the metal-tissue interface. Attenuation within the metal causes decreased dose downstream. Pair production and photoelectric absorption do not cause increased dose at the interface.

296. Compared to a hospital EMR, what is a unique feature of a radiation oncology record and verify system?

- A. Supplies information that controls radiation treatment delivery
- B. Stores medical notes and billing codes
- C. Has modules for patient data entry
- D. Has settings required to maintain patient security

Key: A

Domain: 13.10

Citations: AAPM TG-201 Information technology resource management in radiation oncology 2009.

Rationale: The RO EMR and EMRs for other clinics both contain medical notes and billing codes. There are different vendors for RO EMR's and EMR's. Both types of EMR's require multiple tasks and settings to maintain security. What makes the RO EMR unique is that it contains technical parameters that are used by treatment machines to deliver radiation.

297. What happens if the applicator treatment length of an HDR treatment channel is entered incorrectly in the treatment plan?

- A. The source will dwell at times that are different than intended
- B. The source will move to a location different than intended
- C. The source step size will be different than the plan
- D. The source activity will be different than the plan

Key: B

Domain: 13.11

Citations: Kubo et al. High dose-rate brachytherapy treatment delivery: Report of the AAPM Radiation Therapy Committee Task Group NO. 59. Med. Phys. 25(4). 1998.

Rationale: The applicator treatment length in the HDR plan communicates to the afterloader the maximum distance the source can move to. Source dwell positions are then relative to this maximum distance. If the treatment length in the plan does not match the actual length of the applicator and transfer guide tube system, then the source will move to a position that doesn't match the intended anatomical treatment position.

298. What anatomical structure appears larger in a deep inspiration breath hold (DIBH) CT compared with a free breathing CT?

- A. Heart
- B. Lung
- C. Esophagus
- D. Trachea

Key: B

Domain: 13.12

Citations: Dieterich, et. al, Practical Radiation Oncology Physics, 1st Ed., 2016.

Rationale: In a deep inspiration breath hold CT, the lung tidal volume is maximized, thus resulting in an increased lung volume in the image. The volume of the heart, esophagus, and trachea aren't affected by the breath hold.

299. For the opposed, lateral brain fields of a 3D CRT craniospinal treatment, what limits the maximum extent of the inferior beam edge?

- A. Jaw position limits
- B. MLC interdigitization limits
- C. Mandible position
- D. Shoulder position

Key: D

Domain: 13.13

Citations: Bentel, Radiation Therapy Planning, 2nd Edition 1995.

Rationale: When the inferior edges of the CSI brain fields are too low, they enter through the shoulders, resulting in an unacceptable dose distribution and unnecessary doses in the shoulders. Jaw position limits, while factor affecting spine fields, do not affect the brain fields. MLC interdigitization limits are not factors for CSI treatments. The maximum extent of the superior edge of the spine field will be limited by the field exiting through the face.

300. A patient treated for a lung tumor using protons experiences fluid filling around the tumor. Assuming the tumor location does not change, how will the location of the Bragg peaks for each treatment field change relative to their original positions?

- A. Peaks will be more distal
- B. Peaks will be more proximal
- C. Peaks will not change location
- D. Peaks will change selectively based on beam energy

Key: B

Domain: 13.17

Citations: Pawlicki, et al. Hendee's Radiation Therapy Physics, 4th Ed. 2016.

References: There would be a higher density tissue surrounding the periphery of the lung tumor as compared to the original treatment plan. The increased density would cause the Bragg Peaks to be located more proximal to the original peak location.