# Self-Assessment Module
# 2017 ASTRO Annual Meeting

## *Late Toxicity of Radiation for Breast Cancer: Overblown or Underappreciated?*

Drs. Wazer, Taghian, Wong, Hamilton, and Wright

**Question 1:**

The population-based case-controlled study of cardiac morbidity/mortality after breast irradiation by Darby et al NEJM 2013 estimated cardiac radiation dose by extrapolation from 2D treatment planning. In the validation study of van den Bogaard et al JCO 2017, heart doses were measured via contemporary 3D treatment planning. After 9 years of follow up, both studies found a linear relationship between the risk of cardiac events and mean heart dose suggesting a relative risk of what percent per gray of mean heart dose?

a) 7%
b) 16%
c) 35%
d) 53%

**Answer**:
B

**Feedback**:
The value found in both papers was approximately 16% within the first 9 years of follow-up. The maximum duration of follow-up in the Darby et al paper (20+ years) was considerably longer than in the van den Bogaard et al study (9 years). For the overall duration of follow-up (20+ years), Darby et al found a cumulative increase in relative risk of 7.4% per Gray.

**Location**:
Slide numbers 6, 7, 10, 11 (in draft version of presentation)

**References**:
Darby et al. NEJM 2013;368(11):987-998.
Van den Bogaard et al. J Clin Oncol 2017;35(11):1171-1178.

*- - - End of Question 1 - - -*

**Question 2:**

Which of the following systemic therapy was shown to result in the highest increase in the 5-year cumulative incidence of heart failure and/or cardiomyopathy?

a) Aromatase inhibitor
b) Anthracycline alone
c) Trastuzumab alone
d) Anthracycline in combination with trastuzumab

**Answer**:
D

**Feedback**:
The combination of anthracycline plus trastuzumab has generally been recognized as resulting in greater risk of heart failure/cardiomyopathy than either agent alone. Aromatase inhibitor has been correlated to risk of dysrhythmia, valve dysfunction, and pericarditis – but not heart failure or cardiomyopathy.

**Location**:
Slide numbers: 50,51,54 in draft presentation

**Reference**:
Bowles et al. *J Natl Cancer Inst* 2012;104:1293-1305
Haque et al. *JAMA Oncol* 2016;2(12):1590-97

*- - - End of Question 2 - - -*
-

**Question 3:**

The most acceptable definition of lymphedema is:

a) Absolute increase of arm circumference by 2 cm
b) Absolute increase of arm volume by 200 ml
c) Absolute volume difference by >10%
d) Relative increase in volume by 10%
e) All of the above

**Answer**:
D
**Feedback**:
There is no universal definition for lymphedema. Each definition mentioned above was used in a large number of studies. The absolute volume change correlates with pre-operative arm volume, patient weight and body mass index. The Relative volume change is independent of pre-operative arm volume, patient weight and body mass index. In the last few years, there is a tendency to define lymphedema at a relative increase of volume of 10% taking in consideration the baseline volume.

**Reference**:
Armer JM, Stewart BR. A comparison of four diagnostic criteria for lymphedema in a post-breast cancer population. Lymphat Res Biol. 2005;3:208–217.

Ancukiewicz M, Miller CL, Skolny MN, et al. Comparison of relative versus absolute arm size change as criteria for quantifying breast cancer-related lymphedema: the flaws in current studies and need for universal methodology. *Breast Cancer Res Treat.* Aug 2012;135(1):145-52.

*- - - End of Question 3 - - -*

**Question 4:**

Risk of lymphedema after axillary lymph node dissection and regional lymph node radiation is

a) <5%
b) 5-10%
c) 10-20%
d) >20%

**Answer**:
D

**Feedback:**
In a prospective study on >1,500 patients screened for lymphedema, Warren et al showed that the risk of lymphedema (defined as >10% relative increase in arm volume), was 18% for patients treated with axillary lymph node dissection (ALND) and 24% for patients with ALND and regional lymph node radiation (RLNR). In patient with positive sentinel node and RLNR, the risk of lymphedema varied between 7 and 10%.

**Reference**:
Warren LE, Miller CL, Horick N, Skolny MN, Jammallo LS, Sadek BT, Shenouda MN, O'Toole JA, Macdonald SM, Specht MC, **Taghian AG.** The Impact of Radiation Therapy on the Risk of Lymphedema After Treatment for Breast Cancer: A Prospective Cohort Study. Int J Radiat Oncol Biol Phys. 2014 Mar 1;88(3):565-71. doi: 10.1016/j.ijrobp.2013.11.232. Epub 2014 Jan 7.

*- - - End of Question 4- - -*

**Question 5:**
What is the estimated absolute increased risk of lung cancer mortality after breast RT for long-term continuing smokers?

a) 0.4%

b) 2.4%
c) 4.4%
d) 6.4%

Answer:
c) 4.4%

**Feedback:**
Taylor *et al.* estimated a 4.4% absolute increased risk of death from lung cancer in breast cancer patients who continued to smoke after adjuvant RT. The estimated absolute increased risk in a patient who stopped smoking at the time of adjuvant RT was 1.3% and the risk in non-smokers was 0.3%.

**Reference:**
Taylor, C. Correa, C. Duane, FK *et al.* Estimating the risks of breast cancer radiotherapy: evidence from modern radiation doses to the lungs and heart and from previous randomized trials. *J Clin Oncol.* 2017:35:1641-649.

*- - - End of Question 5 - - -*