Harmonization of Breast Cancer Surveillance Recommendations for Childhood Cancer Survivors
International Meeting Summary
Amsterdam, The Netherlands
September 28, 2011

Participants: Saro H. Armenian, Smita Bhatia, Louis S. Constine, Mary Dwyer, Riccardo Haupt, Tara Henderson, Lars Hjorth, Melissa M. Hudson, Yasushi Ishida, Hiroyuki Ishiguro, Shunicho Kato, Leontien Kremer, Wendy Landier, Gill Levitt, Miho Maeda, Renee Mulder, Kevin C. Oeffinger, Liedeke Postma, Cecile Ronckers, Roderick Skinner, Elvira van Dalen, Marry van den Heuvel, Helena van der Pal, Flora van Leeuwen, Hamish Wallace

1. Leontien Kremer welcomed the attendees and outlined the agenda and objectives of meeting.

2. Kevin Oeffinger presented an overview of the evidence summaries evaluating the areas of discordance and concordance in the published breast cancer surveillance recommendations [detailed in summary booklet distributed before meeting and attached slides]. The following research questions were formulated according to the areas of discordance:

   - What is the risk of breast cancer in childhood and young adult cancer survivors treated with 1-19 Gy chest radiation? By radiation categories: 1-4, 5-9, 10-14, 15-19 Gy?
   - What is the risk of breast cancer in childhood and young adult cancer survivors treated with TBI?
   - What is the risk of breast cancer in childhood and young adult cancer survivors treated with high abdominal field radiation (with or without chest radiation)?
   - Does alkylating agent chemotherapy lower the risk of breast cancer in childhood and young adult cancer survivors treated with chest radiation? If so, how much does the risk decrease?
   - What is the diagnostic value of a breast MRI and a mammogram compared to a breast MRI (additional value mammogram) to detect breast cancer in an early stage in women aged 25-35 years?
   - What is the diagnostic value of a mammogram, compared to a breast MRI, to detect breast cancer in an early stage in women in a young age group compared to another age group?
   - What is the additional value of screening with a mammogram in childhood and young adult cancer survivors?
   - What is the diagnostic value of a clinical breast exam to detect breast cancer in an early stage in women aged <25 years?

   Attendees agreed with evidence summaries presented. In addition, several general comments from discussion of evidence tables follow:
   - The different methods for the calculation of the RT dose should be described.
   - That fact that control groups are represented largely by low dose groups should be clarified in the conclusion.
   - Consider asking Lois Travis to calculate risks for her cohort in the 0-10 and 10-20 Gy exposure groups.
   - Note existing evidence for higher breast cancer risk among populations exposed to low dose radiation for conditions other than cancer (e.g., radiation for thymic hyperplasia)

- Compared to alkylating agent exposure, premature menopause represents a better indirect determinant of hormonal exposure influencing breast cancer since young women will variably maintain ovarian function after alkylating agent.
- Flora mentioned that Andrea Ng had new unpublished data in Hodgkin survivors supporting the superiority of dual imaging with MRI and mammography in facilitating diagnosis of early stage lesions. This is important because detection of early stage breast cancer early may offer survival benefit by minimizing need for (cardiac) toxic treatment.
- The group was informed about a recent manuscript that focused on updated evidence and recommendations for screening women who are at average risk for breast cancer (Warner E. Breast-cancer screening. N Engl J Med 2011;365:1025-32).

3. Melissa Hudson moderated the discussion to harmonize recommendations for breast cancer surveillance. The group considered the evidence and formulated recommendations considering the quality of the evidence, the benefits versus harms of the screening intervention, and the need to maintain flexibility across health care systems [summary presented in attached slides].

4. Representatives from DCOG, USCOG, and UKCCLG presented existing recommendations for cardiomyopathy screening. A core group will be defining research questions related to the areas of concordance and discordance (slides attached), undertaking the work of the evidence review, and organizing a summary.

5. Renee Mulder presented background about the Delphi methodology and preliminary results from Round 1 derived from responses of the late effects experts participating in the harmonization effort. The purpose of the Delphi survey is to identify, clarify and achieve consensus regarding the priority of late effects the harmonization will consider. Round 2 surveys were distributed; attendees were encouraged to rank late effects that were of high prevalence, severe in nature, had accurate screening measures to detect in early stage, and for which identification of an early versus a later stage would confer a better prognosis.

6. A discussion was held regarding next steps:

   The core group involved in preparing the breast cancer surveillance evidence summary will outline a draft of a white paper regarding the harmonization process and outcome.

   A core group will be assembled to undertake the cardiomyopathy surveillance evidence review and organize the evidence summary. Individuals should e-mail Leontien regarding questions to include in the evidence review and their interest in performing the evidence review. The timeline will be to complete the review and organize the summary before the next meeting of the harmonization group.

7. The next meeting of this group will be held in Williamsburg Lodge, likely before the International Conference on Late Complications of Childhood Cancer (scheduled for June 8-9, 2012).