Harmonization of Breast Cancer Surveillance Recommendations for Childhood Cancer Survivors
International Meeting Summary
Boston, Massachusetts
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1. Melissa Hudson outlined the objectives of meeting and provided a brief overview of issues surrounding development of clinical consensus. Full details in Attachment #1: Harmonizing Health Surveillance Recommendations_Overview_SIOP_10-21-2010.

2. Background information regarding the rationale used to determine breast cancer screening recommendations in each guideline under discussion was presented by participants from each of the groups [See attachments 2-5 for details]:
   a. COG Guidelines – Hybrid process of (1) considering strength of evidence from literature regarding association of exposure with late effect and (2) consensus of expert panel regarding screening recommendation
   b. DCOG LATER Guidelines – Screening based on NABON (National Breast Cancer Organisation Netherlands) guideline. Very high risk group defined as patients having RR $\geq$ 4, which is comparable to risk seen in patients with BRCA1 and BRCA2 mutations. High risk group defined as patients with RR 2-<4. Determinations were made based on data from Travis 2003.
   c. UKCCLG Guidelines – Based on Department of Health Directive from 2003; there was no evidence in UK cohort available at that time on which to base further recommendations
   d. Japan – No current guideline in place, but comments regarding recommendations were provided from the group. It was noted that Hodgkin lymphoma is rare in Japan and thus there is no population-based evidence on which to base a Japanese guideline
   e. New Zealand/Australia – Guidelines currently in development, would benefit from international consensus to support this process
   f. Italy – No national guideline; current guidelines are institution-specific.

3. Breast cancer surveillance in childhood cancer survivors: Areas of consensus reached and areas determined to require further research are indicated in the table below.

| PARAMETER | AREAS OF CONSENSUS | AREAS REQUIRING FURTHER RESEARCH |
|---|---|---|
| Definition of risk groups | No radiation – not at risk<br>≥ 20 Gy radiation – at highest risk<br>1-19 Gy radiation – risk unknown | Define risk and screening for patients who received chest radiation doses between 1-19 Gy (determine magnitude of risk and relevant screening based on risk). |
| Age at initiation of surveillance | 25 years*<br>*If evaluating AYA patients, screening should begin at age 25 OR 8 years following completion of radiation, whichever occurs last. | None |
| Frequency of surveillance | Yearly between 25 and 50 years of age | Not enough information to determine optimal frequency of screening for women older than age 50 with a history of chest irradiation. Although there is agreement that there is increased risk of breast cancer in irradiated women over age 50 compared to women in the general population, there is not agreement regarding how often these women should be screened. Current guidelines are generally based on recommendations of the local health care system |
| Surveillance modality: Clinician exam | Not enough evidence to recommend clinical breast exams in this population; there was agreement that guidelines should not be precise when describing clinician exam as a screening modality (e.g., in COG, Clinical Breast Exam will be removed as a screening recommendation and displayed in the 'Further Considerations' box; instructions will be provided to indicate that the patient should be counseled to visit their healthcare provider regularly in order to closely monitor breast health).<br>There was consensus that the recommendations for Breast Self Exam should be similarly changed | Not enough evidence to support a recommendation for clinical breast exam or breast self-exam in breast cancer surveillance among women at increased risk for breast cancer. |
| Surveillance modality: MRI | Highest risk patients between 25 and 50 years of age should be screened yearly with MRI | Not enough evidence on which to base recommendation for MRI as a screening modality in patients ≥ 50 years of age.<br>Note: Statistical modeling could be used to determine if yearly or twice-yearly surveillance with MRI is optimal. |
| Surveillance modality: Mammogram | Annual Mammography plus MRI as screen for high-risk patients age 30-50 | Determination needs to be made regarding screening with mammography prior to age 25 and after age 50. UK guideline varies depending on presence/ absence of fatty breasts – is there evidence to support this? |

4. Additional research currently planned/underway by group members:
    a. Pancare – comprehensive evidence review (should be completed in about 4 years; evidence regarding targeted areas may be available prior to 4 years)
    b. Oeffinger – statistical modeling to predict risk in CCSS cohort (collaboration with Dutch)
    c. Bhatia/City of Hope – R21 application submitted re: cost effectiveness of COG breast cancer surveillance guidelines
    d. Hudson/St. Jude – cost effectiveness/yield of screening with MRI and mammography
    e. Haupt – case-control study using dosimetry
    f. Bhatia/COG – results from Key Adverse Events cohort, currently in progress should be available in 2 to 3 years

5. CONCLUSIONS: A discussion was held regarding next steps. The group will review the areas where consensus was reached and areas for future research identified during this meeting and will then make a determination as to whether the consensus is adequate to move forward with authoring a white paper versus the need to pursue further refinement prior to reaching an acceptable consensus agreement. The group will also define a research agenda based on areas lacking evidence identified at this meeting.

6. Leontien Kremer offered to develop a booklet to guide preparation of evidence tables, the focus of which will be on the preparation of tables that can be easily and frequently updated as new literature emerges.

7. The need was identified for an "evidence bank" or database to store materials used in guideline preparation. Lars Hjorth indicated that Pancare may be able to assist with this.

8. The next meeting of this group will be held in Amsterdam on September 28, 2011 just prior to the European Late Effects meeting (scheduled for September 29-30, 2011). The next focus of this group will be on cardiac screening. A smaller working group will be formed to evaluate the evidence over the next several months in preparation for the larger meeting in September 2011.