Second Tumors Working Group

Williamsburg, VA
June 2012
Second Tumors Working Group

Group Membership

• Joseph Neglia – Minnesota (chair)
• Sue Hammond – Nationwide Children’s
• Greg Armstrong – St. Jude
• Smita Bhatia – City of Hope
• Tara Henderson – U Chicago
• Marilyn Stovall – MD Anderson
• Peter Inskip – NCI

• Aaron McDonald – St. Jude
# Distribution of Biologic Material Available for Subsequent Neoplasm Cases

<table>
<thead>
<tr>
<th>SMN</th>
<th>Total case reported</th>
<th>Total with path reports</th>
<th># with host tissue</th>
<th>Host tissue (any kind) and MRAF data</th>
<th>Total with MRAF data</th>
<th>Total with SMN tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Buccal cells</td>
<td>Oragene</td>
<td>Blood</td>
<td>Total with MRAF data</td>
</tr>
<tr>
<td>Breast</td>
<td>222</td>
<td>206</td>
<td>116</td>
<td>87</td>
<td>107</td>
<td>140</td>
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<tr>
<td>Meningioma*</td>
<td>210</td>
<td>186</td>
<td>126</td>
<td>102</td>
<td>103</td>
<td>142</td>
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<tr>
<td>Other CNS</td>
<td>78</td>
<td>70</td>
<td>23</td>
<td>17</td>
<td>18</td>
<td>27</td>
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<tr>
<td>Thyroid</td>
<td>157</td>
<td>144</td>
<td>81</td>
<td>63</td>
<td>76</td>
<td>106</td>
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<tr>
<td>Sarcoma</td>
<td>87</td>
<td>79</td>
<td>33</td>
<td>21</td>
<td>23</td>
<td>39</td>
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<tr>
<td>Leukemia</td>
<td>51</td>
<td>35</td>
<td>14</td>
<td>8</td>
<td>9</td>
<td>15</td>
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<tr>
<td>Bone</td>
<td>54</td>
<td>46</td>
<td>14</td>
<td>4</td>
<td>11</td>
<td>16</td>
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<tr>
<td>Melanoma</td>
<td>55</td>
<td>39</td>
<td>24</td>
<td>18</td>
<td>23</td>
<td>31</td>
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<tr>
<td>Lymphoma</td>
<td>45</td>
<td>41</td>
<td>18</td>
<td>16</td>
<td>18</td>
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<tr>
<td>Renal Cell</td>
<td>26</td>
<td>26</td>
<td>15</td>
<td>14</td>
<td>12</td>
<td>17</td>
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<tr>
<td>Other Carcinoma</td>
<td>114</td>
<td>109</td>
<td>48</td>
<td>31</td>
<td>38</td>
<td>56</td>
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<tr>
<td>NMSC*</td>
<td>1,295</td>
<td>1,147</td>
<td>832</td>
<td>658</td>
<td>311</td>
<td>906</td>
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<tr>
<td>All Other</td>
<td>64</td>
<td>41</td>
<td>18</td>
<td>16</td>
<td>13</td>
<td>21</td>
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<tr>
<td><strong>TOTALS</strong></td>
<td>2,458</td>
<td>2,169</td>
<td>1,362</td>
<td>1,055</td>
<td>762</td>
<td>1,541</td>
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As of 1/2012
New Neoplasms from 2007 Follow Up

645 Malignancies reported during Follow-Up 2007

Pursued path report for 510 malignancies from FU07 + 58 from prior surveys (N = 568)

Pathology report obtained n = 402 (71%)
- Malignancies confirmed n = 334
- Not a malignancy (benign/unable to classify) n = 68

Pathology report not obtained n = 166 (29%)
- Passive non-responder (HIPAA/additional information) n = 102
- Active refusal to sign HIPAA n = 13
- Participant expired (no HIPAA) n = 6
- Hospital/clinic did not have record n = 45

Report Date 5/2012
• Nathan et al: Screening and surveillance for second malignant neoplasms in adult survivors of childhood cancer: A Report from the Childhood Cancer Survivor Study Ann Int Med 2010


Recent Publications

Second Tumors Working Group Activities

December 2010 Meeting in Memphis

- Internal audit of selected cases
- Semantics of Second Neoplasm coding
- Processes for adjudication of SMNs without path reports
- ICDO 3 transition
- Global database audit
- Creation of SMN SOP
<table>
<thead>
<tr>
<th>Date Received</th>
<th>Title</th>
<th>Author/ Institution</th>
<th>Secondary Working Group(s)</th>
<th>Date Investigator Notified</th>
<th>Concept to Publication Committee</th>
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<tbody>
<tr>
<td>10.28.10</td>
<td>Primary Tumor Recurrence and SMN After Pregnancy</td>
<td>Rokitka/Roswell Park</td>
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<td>11.9.10</td>
<td>SMN After Diabetes Mellitus</td>
<td>Chang/UCSF</td>
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<td>Breast Cancer Risk Factors</td>
<td>Inskip/NCI</td>
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<td>Radiation Dose and Risk of Meningioma</td>
<td>Rajaraman/NCI</td>
<td>Epi/Biostats</td>
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<td>02.3.11</td>
<td>Renal Cell Carcinoma</td>
<td>Wilson/SJCRH</td>
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<td>03.09.11</td>
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<td>04.13.11</td>
<td>Gynecological Malignancies</td>
<td>Nathan/Sick Kids</td>
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<td>05.03.11</td>
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<td>Development and validation of an absolute risk prediction model for thyroid cancer in childhood cancer survivors</td>
<td>Ronckers/Netherlands</td>
<td>Epi/Biostats</td>
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<td>Testicular Cancer Following Pediatric Cancer</td>
<td>Oeffinger/MSKCC</td>
<td>Chronic Disease</td>
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<tr>
<td>Date Received</td>
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<td>Development of Radiobiologic Models of Second Cancer Risk for Childhood Cancer Patients Treated with Radiation Therapy</td>
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<td>Epi/Biostats</td>
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<td>Risk of Breast Cancer in Survivors Not Exposed to Chest Radiation</td>
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<td>Genetics</td>
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<td>Subsequent neoplasms in adult survivors of childhood cancer in relation to weight and physical activity</td>
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<td>Late Second Neoplasms in Long-Term Survivors of Childhood Cancer</td>
<td>Turcotte/University of Minnesota</td>
<td>Epi/Biostats</td>
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• Second Neoplasm AOIs
  – Nine of Fourteen with Concepts Pending
  – Active follow up with holders of approved AOIs for timelines / barriers
• Selected Reports
  – Nottage; Late Occurring Leukemia
  – Armstrong; Multiple SMNs
  – Moskowitz; Breast Cancer Risk
Long-Term Risk of Leukemia
- Nottage et al (Blood 2011)

• Presumed that risk of secondary leukemia plateaus at 10 – 15 years form diagnosis
• Typically AML
  – Alkylator associated (changes on 5 or 7), five to 7 year latency
  – Epipodophyllotoxin associated (MLL), two to three year latency
• Recognized 13 pathologically confirmed cases of secondary leukemia after 15 years in the cohort
Long-term incidence and overall survival of subsequent leukemia.

- 13 path confirmed cases
- 7 cases of AML
  - 2 APL
  - 2 preceding MDS
  - No MLL changes
- 4 cases of ALL
  - 2 B lineage
  - 1 T lineage
  - 1 unidentified
- 1 T-cell large granular
- 1 Leukemia NOS

- Mean Latency 21.6 years
- Risk > 15 years from diagnosis
  - Leukemia: SIR 3.5 (1.9-6.0)
  - AML: SIR 5.3 (2.1-10.9)

- Too few cases to describe specific associations
Multiple Subsequent Neoplasms in the Childhood Cancer Survivor Study (CCSS) Cohort

Greg Armstrong, Wei Liu, Sue Hammond, Smita Bhatia, Joseph P. Neglia, Marilyn Stovall, Wendy Leisenring, Yutaka Yasui, Kumar Srivastava, Leslie Robison

Department of Epidemiology and Cancer Control
Describe the cumulative incidence and risk factors for development of multiple subsequent neoplasms (SNs) among survivors of childhood cancer diagnosed 1970-1986.
Cumulative Incidence: SN1 → SN2

At risk: 1377 574 219 76 21

33.4%  46.9%
Cumulative Incidence: SN1 → SN2
By Primary Diagnosis

- HD: 50%
- CNS: 45%
- Kidney: 21%
- NB: 7%
Cumulative incidence of a subsequent malignant neoplasm among radiotherapy-exposed patients after nonmelanoma skin cancer (NMSC) as first subsequent neoplasm (SN; blue line) and subsequent malignant neoplasm (SMN) as SN1 (gold line).

Armstrong G T et al. JCO 2011;29:3056-3064

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Multiple SNs are common in long-term survivors and most common after Hodgkin lymphoma (50% at 15 years)

Increased risk associated with RT exposure, older age at SN1 and female sex
New insights into the risk of breast cancer in childhood cancer survivors treated with chest radiation:
A report from the Childhood Cancer Survivor Study and the Women’s Environmental Cancer and Radiation Epidemiology Study

Chaya S. Moskowitz, Ph.D.
Associate Member
Department of Epidemiology and Biostatistics
Purpose

• Based on substantially extended period of follow-up, estimate breast cancer risk in childhood cancer survivors treated with chest radiation

• Contrast risk with breast cancer risk in other known high risk population
  – Carriers of a BRCA1 or BRCA2 mutation

• Study subpopulations of childhood cancer survivors
• **Childhood cancer survivors (CCSS)**
  – Cumulative incidence estimated non-parametrically
  – Competing risk of death
  – Standardized incidence ratios (SIRs) estimated using age-, sex-, and calendar-year-specific incidence rates from the general US population

• **BRCA1 and BRCA2 mutation carriers**
  – Cumulative incidence estimated using kin-cohort method
  – WECARE study (Women’s Environmental Cancer and Radiation Epi)

• **US population**
  – From Surveillance, Epidemiology, and End Results (SEER) Program
  – Population incidence estimated using age-specific rates
  – Weighted to account for the calendar year in which members of the CCSS cohort were at risk of breast cancer
Conclusions

- Come to tomorrow’s session
• Short Term
  – Assure the quality of the CCSS SMN data set: Audit of all SMNs this summer
  – Reconcile the availability of biologic specimens across sites
  – ICDO 3 Migration
  – Outline the high priority analyses for the CCSS II cohort
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Short Term Priorities

• Long Term
  – Assure the consistency of the CCSS SMN data set through rigorous use of SOPs
  – Build further links between biology and epidemiology
  – Link to GWAS Analysis
  – CCSS I and II comparisons
  – “Screen-able” Cancers
• Long Term
  – Pooled analysis of secondary brain tumors
    • CCSS/European Childhood Cancer Survivors
    • Radiation for benign conditions
    • Pediatric CT scan recipients
    • Atomic bomb survivors
  – Influence of Lifestyle on site-specific SMN risk