Risk of second cancer after breast cancer treatment

HUAN JIANG A, B
A CANCER CARE ONTARIO, 620 UNIVERSITY AVENUE, TORONTO, ONTARIO, M5G2L7, CANADA
B DALLA LANA SCHOOL OF PUBLIC HEALTH, UNIVERSITY OF TORONTO, 155 COLLEGE ST, TORONTO, ONTARIO, M5T 3M7, CANADA
Background

- During the last decade, breast cancer survival has increased considerably, largely as a result of improved screening and advances in treatment.

- As the risk of developing cancer increases with age, longer lifetimes are associated with increased probabilities of second cancer occurrence.
Background

Risk of second cancer

• Breast cancer patients have a more than two fold increased risk of developing a contralateral breast cancer

• Some studies suggest that the higher risk might relate to the use of radiotherapy or chemotherapy

• This may arise not only from therapeutic radiation but also from diagnostic doses of irradiation or mammographic screening exams.
Objectives

A population-based cohort of women diagnosed with breast cancer in Ontario in 2010-12 will be identified:

1) To compare the incidence of lung, uterine, ovarian, and acute myeloid leukemia cancer in breast cancer patients with the rates in the general population of Ontario females.

2) To assess the excess risk of secondary non-breast cancers (SNBCs) or contralateral breast cancers (CBCs) during follow-up in women who have screen-detected breast cancer compared to women with symptomatic breast cancer by different age groups in Ontario, adjusting for prognostic factors.
Methods

The cohort

• The retrospective cohort comprises women 30 to 74 years of age diagnosed with their first invasive breast cancer in Ontario in 2010-12, with follow up up to the year 2015.

• Cases will be identified through the Ontario Cancer Registry (OCR)

• Women with screen-detected breast cancer will be identified through a data linkage with the Ontario Breast Screen Program (OBSP).

• The characteristics of cancer cases will be obtained through the Activity Level Reporting (ALR) database, including information such as age at diagnosis, place of residence at diagnosis, radiotherapy (yes/no), tumor size, lymph node status, and stage
The Cohort

Omitted Cases: Zero or Negative Survival Time

**Case #1a:** Diagnosis Date is Last Contact Date  
**Case #1b:** Diagnosis Date is After Last Contact Date

<table>
<thead>
<tr>
<th>Obs</th>
<th>PERSON_KEY</th>
<th>SURNAME1</th>
<th>Diag_date</th>
<th>DEATH_DATE</th>
<th>last_contact_date</th>
<th>ft_day</th>
<th>ft_year</th>
<th>vstatus</th>
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<tbody>
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| 19  | 51764546   |          | 20JUL2010     | 01JAN1800   | 01JAN1800         | -76901 | -210.543| 0       |
| 20  | 51849599   |          | 06APR2010     | 01JAN1800   | 06APR2010         | 0      | 0.000   | 0       |
| 21  | 51929460   |          | 24FEB2012     | 01JAN1800   | 24FEB2012         | 0      | 0.000   | 0       |
| 22  | 51960004   |          | 04OCT2010     | 01JAN1800   | 04OCT2010         | 0      | 0.000   | 0       |
| 23  | 52075249   |          | 14DEC2011     | 01JAN1800   | 29MAY2006         | -2025  | -5.544  | 0       |
The Cohort

Total number of women: 20030
A total of 1574 (7.86%) women have multiple primaries:

<table>
<thead>
<tr>
<th>Number of Primary Cancers</th>
<th>Number of Women</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>1448</td>
<td>0.920</td>
</tr>
<tr>
<td>3</td>
<td>120</td>
<td>0.076</td>
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<tr>
<td>4</td>
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<td>5</td>
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</table>
The Cohort

Age of Multiple Primary Breast Cancer Patients in 2010-2016 Cohort

Age of Primary Breast Cancer Patients in 2010-2016 Cohort by Multiple Primary Class

Cancer Care Ontario
Kaplan-Meier Nonparametric Survival Curve

From First Diagnosis

From Second Diagnosis
## Standardized Incidence Ratio

<table>
<thead>
<tr>
<th>Condition</th>
<th>Observed</th>
<th>Expected</th>
<th>Incidence Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>1153</td>
<td>145.3</td>
<td>7.93</td>
</tr>
<tr>
<td>Lung and Bronchus</td>
<td>242</td>
<td>74.6</td>
<td>3.24</td>
</tr>
<tr>
<td>Uterus</td>
<td>97</td>
<td>35.95</td>
<td>2.70</td>
</tr>
<tr>
<td>Ovary</td>
<td>45</td>
<td>16.3</td>
<td>2.76</td>
</tr>
<tr>
<td>Acute Myeloid leukemia</td>
<td>17</td>
<td>1.7</td>
<td>10.00</td>
</tr>
</tbody>
</table>

N=20030
Data linkage with Ontario Breast Screening Program

<table>
<thead>
<tr>
<th>OCR</th>
<th>Breast Cancer Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>OBSP</td>
<td>Ontario Breast Cancer Screening Program</td>
</tr>
</tbody>
</table>

- **CLIENT**
  - Client Information
  - **CLIENTID**
    - ID Number for each patient in OBSP
  - **SCREEN**
    - Screening Information
    - **SCREENEDT**
      - Screening Date
    - **SCRNAGE**
      - Age at Screening
    - **FINALRES**
      - Final Result of Screening
    - **MAMDONE**
      - Mammography Done Flag

- **GIVENNAME1**
  - **SURNAME1**
  - **BIRTH_DATE**
  - **PERSON_KEY**
  - **HCN_ON**
    - Health Insurance Number
  - **HIN**
    - Health Insurance Number

Cancer Care Ontario
Linkage Between OBSP Entities and OCR

- Created wide format table for each OBSP cohort patient
- First Linkage done by HIN
  - **Matched Cases = 8,967**
  - Every observation is unique (CLIENTID and PERSON_KEY are 1-to-1)
- Second Linkage done by First Name, Surname, Birth Date
  - Linked **HIN Non-Matches** to **OCR**
  - Linkage Criteria:
    - First 9 Characters of First Name
    - First 5 Characters of Surname
    - Birth Date
  - Removed Special Characters from First Name and Surname
  - **Matched Cases = 21**
  - **HINs** (OBSP) are either missing or different from **HCN_ON** (OCR)
## Screening History and Occurrence of Multiple Primary Cancers

<table>
<thead>
<tr>
<th>Multiple Primary Type</th>
<th>Not screened in OBSP</th>
<th>Screened in OBSP</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contralateral Breast Cancers</td>
<td>95 (9.52%)</td>
<td>140 (14.03%)</td>
<td>235 (23.55%)</td>
</tr>
<tr>
<td>Secondary Non-Breast Cancers</td>
<td>281 (28.16%)</td>
<td>482 (48.30%)</td>
<td>763 (76.45%)</td>
</tr>
<tr>
<td>Total</td>
<td>376 (37.68%)</td>
<td>622 (62.33%)</td>
<td>998</td>
</tr>
</tbody>
</table>

P-value is .319
Future Works and Challenges

• Data linkage with the Activity Level Reporting (ALR) database to collect prognostic information.

• Continue to review data quality and explore inconsistencies between different data sources.

• For the majority of research questions, the ideal dataset does not exist.

• Data linkage requires expertise in several areas, including knowledge of the datasets to be linked—their limitations, skills in the use of linkage programs, and skills in statistical analysis and interpretation that comes from a multidisciplinary team.
Acknowledgement

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