Patterns of Care in Patients with Cervical Cancer:

Power and Pitfalls of Claims-Based Analysis

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Acknowledgments

• Dr. Sharon Giordano
• Ms. Jing Jiang
• Dr. Patricia Eifel
Background: Cervix Ca Treatment

• In cervical cancer, bulky and invasive disease typically unresectable.

• Definitive chemoradiation is foundational curative treatment for this group.
Background: Standard of Care

• Minimum standard of care, **multi-modality**, carefully sequenced tx:
  
  1. External beam radiation
  2. Intracavitary brachytherapy (internal radiation)
  3. Concurrent chemotherapy
  4. Preferably within duration of 56 days
Background: Standard of Care

1. External beam radiation
Background: Standard of Care

2. Intracavitary brachytherapy (internal radiation)
Background: Standard of Care

2. Intracavitary brachytherapy (internal radiation)
Background: Standard of Care

2. Intracavitary brachytherapy (internal radiation)
Background: Standard of Care

- 45 Gy (#25)
- 85 Gy (#2-8)
- 60-66 Gy (#3-5)
3. Concurrent chemotherapy

- Typically platinum, delivered weekly
- Goal of 6 cycles
4. Within duration of 56 days (8 weeks)
4. Within duration of 56 days (8 weeks)

Facility: Operating room or brachytherapy suite

Supplies: Tandem and ovoid

Personnel: Coordination with gynecologic oncologist (surgeon) or another radiation oncologist; Anesthesia

Rad Onc Team: Physicists and dosimetrist
Background: Standard of Care

4. Within duration of 56 days (8 weeks)
Background: Standard of Care

4. Within duration of 56 days (8 weeks)

Toxicity
Coordinating with gyn oncologist or medical oncologist
Multimodality Treatment

• Is complex!
• Is needed!

Locoregional control and overall survival benefits associated with:
  – Brachytherapy use and dose
  – Concurrent chemotherapy use, agent, and dose
  – Total Duration ≤ 56 days

Viswanathan, Gynecol Oncol 2012
Han, IJROBP 2013
Green, Lancet 2001
Eifel, JCO 2004
Is multi-modality care being delivered?

• Prior studies are unclear:
  – Brachytherapy completion: 58% to 82%
  – Chemotherapy completion: 67% to 74%
  – Duration >70 days: 36% to 43%

• Older studies, smaller sample sizes, survey self-report, non-USA
Trends in the Utilization of Brachytherapy in Cervical Cancer in the United States

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*Radiation Medicine Program, Princess Margaret Hospital, University Health Network, Toronto, Ontario, Canada; †Department of Biostatistics, Princess Margaret Hospital, Toronto, Ontario, Canada; and ‡Department of Radiation Oncology, Dana-Farber Cancer Institute/Brigham and Women’s Hospital, Boston, Massachusetts

Prior study: Brachytherapy

• SEER database

• Cervix cancer patients
  – Stage I to IV
  – No metastatic disease
  – Diagnosed 1988 to 2009
  – SEER 18 registries

• Brachytherapy use dropped from 83% to 58%
Fig. 1. Brachytherapy use rate between 1988 and 2009 in 18 (a) and the original 9 (b) SEER registries.
Is multi-modality care being delivered?

58%  70%  83%
Gaps in the literature...

• Recent trends in receipt of multi-modality therapies are still unclear

• Influence of newer techniques unexplored
Aims

• In a national cohort, we characterized recent trends in completion of:
  – Standard external radiation
  – Brachytherapy
  – Newer radiation techniques
  – Chemotherapy

• Sought to answer these questions using claims-based approach
Why Health Services Research?

• The tools of HSR—claims data—may provide novel insights on complex, multimodality care...
  
  – Describe how such care is delivered
  – Evaluate quality of care delivered
  – Identify predictors of successful delivery
  – Understand barriers to delivery
Data Sources to Study Cervix Cancer

- SEER-Medicare? Older
- SEER? No Claims
- Marketscan
Methods: Data Source

• The MarketScan® Commercial Claims & Encounters database

• Employment-based healthcare claims

• Employees, spouse, dependent beneficiaries

• Age <65 years
Methods: Cohort Selection

Women RT procedure code between 1999 and 2011 (N=333,406)

Dx claims code Cerv Ca on a date of RT

Continuous enrollment -12 mo to +12 wks

Exclude metastatic cases

Exclude adjuvant cases

Exclude “history” code

RT simulation code

>10 RT fractions

Increase specificity

Ensure complete claims

Definitive

Exclude prevalent cases

Increase specificity

6,000

3,275

2,906

1,938

1,774

1,690

1,508
Methods: Variables

• Radiation Treatment:
  – Any claims for external radiation treatment within 12 weeks of the first fraction → CPT, ICD-9
    • IMRT (intensity modulated radiation therapy)
    • SABR (stereotactic ablative radiation)
  – Any claims for brachytherapy treatment (12 wks)
    • HDR (high dose rate) versus LDR (low dose rate)
Methods: Variables

• Radiation Treatment:
  – “IMRT boost” criteria
    • Received $\geq 25$ fractions
    • Did not receive brachytherapy
    • Received $\geq 1$ fraction of IMRT after 25$^{\text{th}}$ fraction

  – “SABR boost” also explored

  – **Proxy measure**: central vs nodal targeting undetermined
Methods: Variables

• Radiation Treatment Duration:
  – Dates of claims (last minus first)
  – Prolongation > 9 weeks, >10 weeks

• Number of fractions:
  – Technical delivery charges
  – **Limitation:** ~30% no technical; weekly professional charges
  – **Solution:** [CPT 77427 X 5] + [CPT 77431 X 1]
Algorithm

• If # claims (unique dates) were missing, proxy used.

• If both...

• If proxy < 20, then use # claims as long as \( \leq 30 \)

• If 20 < proxy \( \leq 40 \), use # claims as long as between 20 and 40.

• If proxy > 40, then use # claims
Proxy Variable Solution

• Unanswered question: WHY
  – Not associated with:
    • Employee status
    • Insurance type
    • State
    • Total charges
Methods: Variables

• Chemotherapy:
  – Any claims for chemo delivery from -1 week to +20 weeks → CPT, ICD-9
    • Platinum agents (J codes)
    • NDC codes did not add a substantial number of new patients (<5)

  – Number of cycles determined by unique claim dates.
Methods: Variables

• Other covariates:
• Enrollment file:
  – Age
  – Geographic region
  – Employee vs spouse/dependent
  – Insurance type
• Claims files:
  – Year of treatment
  – Regional lymph node involvement
  – “Hydronephrosis”/ ureteral stent/ nephrostomy tube/ indwelling catheter
Methods: Variables

- Linkage to the Area Health Resource File:
- County-level:
  - Population density
  - Income (normalized by quartile-year)
  - Radiation oncologist density
    - HAS level
Methods: Statistical Analysis

• Raw frequencies: Treatment use (single and multiple), duration/prolognation

• Cochran Armitage test: Temporal trends in use
  – Brachytherapy
  – IMRT
  – HDR
  – Chemotherapy
Methods: Statistical Analysis

• Logistic regression: Predictors of use
  – Covariates P<0.25
  – Model fit: Hosmer-Lemeshow
  – Missing variables: dummy variables

• SAS v 9.2, assume 2-tail alpha=0.05
Results: Patient characteristics

• Median follow-up: 1.3 years (IQR 0.7-2.6)

• Median age: 51 years (IQR 44-57)

• Regional nodal involvement: 15%

• Hydronephrosis: 14%
Results: Patient characteristics

- PPO: 61%, HMO 13%
- Employee: 66%
- South: 49%
Results: External RT and Brachy

• Median # external fractions: 27 (IQR 25-30)
  – 93% ≥20 fractions, 85% ≥25 fractions
  – 83% received brachytherapy
Brachytherapy Use Over Time

HDR: 25%

Brachy = 83%
HDR = 62%

P-trend = 0.82
P-trend < 0.001
## Brachytherapy Use: Predictors

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Adjusted OR</th>
<th>95% CI</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (interquartile range)</td>
<td>0.96</td>
<td>0.95</td>
<td>0.98</td>
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<tr>
<td>Pelvic/ paraaortic node involvement</td>
<td>0.538</td>
<td>0.362</td>
<td>0.801</td>
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<tr>
<td>Hydronephrosis or stent placement</td>
<td>0.445</td>
<td>0.306</td>
<td>0.649</td>
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<tr>
<td>Received any concurrent chemotherapy</td>
<td>1.597</td>
<td>1.107</td>
<td>2.303</td>
</tr>
<tr>
<td>Any IMRT</td>
<td>2.844</td>
<td>1.615</td>
<td>5.005</td>
</tr>
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</table>

Received Brachytherapy Boost
Hosmer-Lemeshow P=0.96
# HDR Use: Predictors

<table>
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<tr>
<th>Characteristic</th>
<th>Adjusted OR</th>
<th>95% CI</th>
<th>P</th>
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<tbody>
<tr>
<td>Median age (interquartile range)</td>
<td>1.01</td>
<td>1.00</td>
<td>1.03</td>
</tr>
<tr>
<td>[Year at diagnosis]</td>
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<tr>
<td>&lt;0.001</td>
<td>0.13</td>
<td>0.013</td>
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<tr>
<td>2000</td>
<td>0.11</td>
<td>0.03</td>
<td>0.41</td>
</tr>
<tr>
<td>2001</td>
<td>0.17</td>
<td>0.07</td>
<td>0.44</td>
</tr>
<tr>
<td>2002</td>
<td>0.22</td>
<td>0.11</td>
<td>0.46</td>
</tr>
<tr>
<td>2003</td>
<td>0.20</td>
<td>0.11</td>
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<tr>
<td>2004</td>
<td>0.29</td>
<td>0.16</td>
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</tr>
<tr>
<td>2005</td>
<td>0.39</td>
<td>0.22</td>
<td>0.67</td>
</tr>
<tr>
<td>2006</td>
<td>0.56</td>
<td>0.32</td>
<td>0.98</td>
</tr>
<tr>
<td>2007</td>
<td>0.7</td>
<td>0.41</td>
<td>1.20</td>
</tr>
<tr>
<td>2008</td>
<td>0.88</td>
<td>0.53</td>
<td>1.46</td>
</tr>
<tr>
<td>2009</td>
<td>0.88</td>
<td>0.53</td>
<td>1.45</td>
</tr>
<tr>
<td>2010</td>
<td>1.44</td>
<td>0.87</td>
<td>2.39</td>
</tr>
<tr>
<td>2011</td>
<td>-</td>
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## HDR Use: Predictors

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<tr>
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<tr>
<td>Geographic Region</td>
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<tr>
<td>Northeast</td>
<td>1.21</td>
<td>0.81</td>
<td>1.81</td>
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<tr>
<td>Midwest</td>
<td>1.32</td>
<td>0.98</td>
<td>1.80</td>
</tr>
<tr>
<td>South</td>
<td>-</td>
<td></td>
<td></td>
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<tr>
<td>West</td>
<td>1.80</td>
<td>1.16</td>
<td>2.80</td>
</tr>
<tr>
<td>Hydronephrosis or stent placement</td>
<td>0.64</td>
<td>0.44</td>
<td>0.93</td>
</tr>
</tbody>
</table>

Received HDR Technique
Hosmer-Lemeshow P=0.99
IMRT Use Over Time

- IMRT: 83%
- "Boost": 3.5%
- P-trend: <0.001
## IMRT Use: Predictors

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<tr>
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<tbody>
<tr>
<td>Year at diagnosis</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>2003</td>
<td>0.02</td>
<td>0.003</td>
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<tr>
<td>2004</td>
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<td>2005</td>
<td>0.12</td>
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<tr>
<td>2006</td>
<td>0.29</td>
<td>0.15</td>
<td>0.56</td>
</tr>
<tr>
<td>2007</td>
<td>0.27</td>
<td>0.15</td>
<td>0.50</td>
</tr>
<tr>
<td>2008</td>
<td>0.40</td>
<td>0.24</td>
<td>0.66</td>
</tr>
<tr>
<td>2009</td>
<td>0.64</td>
<td>0.40</td>
<td>1.03</td>
</tr>
<tr>
<td>2010</td>
<td>0.97</td>
<td>0.63</td>
<td>1.49</td>
</tr>
<tr>
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# IMRT Use: Predictors

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<tbody>
<tr>
<td>Metropolitan</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;1,000,000 vs &lt;=1,000,000</td>
<td>1.47</td>
<td>1.03</td>
<td>2.10</td>
</tr>
<tr>
<td>Pelvic/ paraaortic node involvement</td>
<td>1.64</td>
<td>1.12</td>
<td>2.39</td>
</tr>
<tr>
<td>Hydronephrosis or stent placement</td>
<td>0.89</td>
<td>0.58</td>
<td>1.37</td>
</tr>
<tr>
<td>Received any concurrent chemotherapy</td>
<td>2.62</td>
<td>1.58</td>
<td>4.33</td>
</tr>
</tbody>
</table>
Chemo Use Over Time

Chemo = 74%
P-trend = <0.001

% Chemo Use:
- 1999: 67%
- 2000: 74%
- 2011: 86%

Years:
- 1999
- 2000
- 2001
- 2002
- 2003
- 2004
- 2005
- 2006
- 2007
- 2008
- 2009
- 2010
- 2011
## Chemo Use: Predictors

<table>
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<tr>
<td>Median age (interquartile range)</td>
<td>0.97</td>
<td>0.96</td>
<td>0.99</td>
</tr>
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<td></td>
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<td>0.88</td>
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<tr>
<td>2000</td>
<td>0.83</td>
<td>0.24</td>
<td>2.82</td>
</tr>
<tr>
<td>2001</td>
<td>0.47</td>
<td>0.19</td>
<td>1.14</td>
</tr>
<tr>
<td>2002</td>
<td>0.63</td>
<td>0.30</td>
<td>1.35</td>
</tr>
<tr>
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<td>0.55</td>
<td>0.29</td>
<td>1.05</td>
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<tr>
<td>2005</td>
<td>0.44</td>
<td>0.25</td>
<td>0.79</td>
</tr>
<tr>
<td>2006</td>
<td>0.87</td>
<td>0.45</td>
<td>1.67</td>
</tr>
<tr>
<td>2007</td>
<td>0.94</td>
<td>0.51</td>
<td>1.74</td>
</tr>
<tr>
<td>2008</td>
<td>1.10</td>
<td>0.61</td>
<td>1.99</td>
</tr>
<tr>
<td>2009</td>
<td>0.95</td>
<td>0.53</td>
<td>1.70</td>
</tr>
<tr>
<td>2010</td>
<td>0.88</td>
<td>0.51</td>
<td>1.53</td>
</tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Any IMRT</td>
<td>2.31</td>
<td>1.51</td>
<td>3.54</td>
</tr>
<tr>
<td>Any HDR</td>
<td>1.73</td>
<td>1.33</td>
<td>2.62</td>
</tr>
</tbody>
</table>

- Proxy indicators of providers’ available resources
- Year no longer significant (P=0.15)
Duration

• All: Median 56 days (IQR 47-65)

• Completed boost: 57 days (IQR 50-66)

• >9 weeks: 32%

• >10 weeks: 15%
Duration Over Time

![Bar Chart

The chart shows the duration over time from 1999 to 2011. The duration peaks in 1999 and decreases in subsequent years.
Encouraging Results?

• Encouraging results?
• In 2011...
  – 82% of patients received brachytherapy
  – 85% received chemotherapy
  – 81% of these (69% of sample) received ≥4 cycles
  – 86% within 70 days (49% of sample in 56 days)

• At least 1 of 3? 99%
• Encouraging results?
• In 2011...
  – 82% of patients
  – 85% received chemotherapy
  – 81% of these (69% of sample) received ≥4 cycles
  – 86% within 70 days (49% of sample in 56 days)

• At least 1 of 3? 99%
Should I be encouraged or discouraged?

Oh wait... let me run just one more “PROC FREQ”...
Encouraging Results?

- At least 1 of 3? 99%
- Brachy + 4 cycles chemo? 55%
- Brachy + 4 cycles chemo + 56 days? 25%
- Brachy + 4 cycles chemo + 63 days? 36%
How to Reconcile these Results?

- At least 1 of 3? **99%**
- Brachy + 4 cycles chemo? **55%**
- Brachy + 4 cycles chemo + 56 days? **25%**
- Brachy + 4 cycles chemo + 63 days? **36%**
• Brachy + 4 chemo + 56 days? **25%**

• Brachy + 4 chemo + 63 days? **36%**

**MDACC**

70-80%

>90%
Normally, I'm not an optimist, but in this case the glass is half full.
Discussion

• High ability to achieve individual benchmarks

• Extraordinarily low ability to achieve multiple benchmarks

• Physicians are able to do ONE thing, but are struggling to do MANY things.
Discussion

• High ability to achieve individual benchmarks  
  → **Not a knowledge gap**

• Extraordinarily low ability to achieve multiple benchmarks

• → **A complexity gap?**
  A **coordination gap?**
Discussion

• Temporal trends in improvement of basic benchmarks have been stagnant since 2003-2006.

• In contrast, uptake of newer HDR and IMRT rose rapidly and persistently.

• Newer technologies may be associated with even greater treatment planning complexity.
Final Comments

• An approach using claims data to evaluate cancer treatment in younger patients is...
  – Feasible
  – Challenging
  – Powerful

• When carefully analyzed, weave novel, complex story about treatment patterns and quality.