Using Radiation Therapy to Treat Desmoid Tumors

David Kirsch MD, PhD
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Disclosures

• Scientific Advisory Board: Lumicell Inc.
• Past Research Support from: Lumicell Inc.
• Current Research Support from: X-RAD Therapeutics, Lilly, and Merck
• Stockholder in: Lumicell Inc., X-RAD Therapeutics
• Patent: co-inventor (US patent 8,983,581) of an imaging device

- and -

• I will not discuss off label use and/or investigational use in my presentation.
Outline

• Case Studies
  – Using Radiation Therapy for Desmoid Tumors
• Evidence to Support the Efficacy of Radiotherapy
• Risks of Receiving Radiotherapy
Case #1

- 19 y/o woman presented in 2009 with recurrent desmoid tumor in right lower extremity
  - 1998 (Age 8) mass in the right calf resected
  - 2001 local recurrence treated with methotrexate, but D/C because of side effects, therefore had another resection with post-operative vinblastine
  - 2006 with multi-focal recurrence, had a debulking surgery followed by tamoxifen and sulindac
  - 2007 recurrent desmoid, had extensive resection in gastrocnemius
  - 2008 recurrent disease treated with imatinib (gleevec) and then nilotinib (tasigna), but D/C because of diarrhea and other side effects
  - Recommendation in 2009: above the knee amputation
Case #1

- MRI 8/17/09 showed interval increase of 2 enhancing masses within the soleus and gastrocnemius muscles
  - 7.2 x 6 x 3.1 cm
  - 6.5 x 3.5 x 2.7 cm
- Increasing pain in the right calf exacerbated by walking
- When walking long distances, breaks required to relieve pain
Definitive Radiation Therapy 66.6 Gy in 1.8 Gy daily fractions using a shrinking field technique: 50.4 Gy to large field, then 9 Gy to a smaller field with less margin, and then 7.2 Gy to a smaller field of gross disease.

Acute Toxicity: Moist desquamation with pain
Case #1

- MRI 5/13/10: 5 cm
- MRI 2/12/15: 3.6 cm

Able to walk long distances pain free, rock climbing
Late Toxicity: tightness in Achille’s tendon
Case #2

- 40 y/o woman with 2 year history of an enlarging mass in the left deltoid
- MRI 3/30/16 showed a 7.1 cm heterogeneous mass
- Bx 4/12/16: desmoid tumor
- Sulindac and tamoxifen with disease progression and increasing pain
- MRI 6/29/17: 8.4 cm mass
Radiation Therapy Planning and Treatment

Definitive Radiation Therapy with 60 Gy in 2 Gy fractions using a shrinking field technique: 50 Gy to large field and 10 Gy boost to smaller field
Outline

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• Risks of Receiving Radiotherapy
LONG-TERM OUTCOMES FOR DESMOID TUMORS TREATED WITH RADIATION THERAPY

B. ASHLEIGH GUADAGNOLO, M.D., M.P.H., GUNAR K. ZAGARS, M.D., AND MATTHEW T. BALLO, M.D.

Table 1. Distribution of tumor size by treatment strategy

<table>
<thead>
<tr>
<th>Tumor size (cm)</th>
<th>RT alone (n = 41)</th>
<th>CMT (n = 74*)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤5</td>
<td>10 (24)</td>
<td>25 (34)</td>
</tr>
<tr>
<td>5–10</td>
<td>17 (42)</td>
<td>35 (48)</td>
</tr>
<tr>
<td>&gt;10</td>
<td>14 (34)</td>
<td>13 (18)</td>
</tr>
</tbody>
</table>

Abbreviations: CMT = combined-modality therapy (either surgery followed by RT or RT followed by surgery); RT = radiation therapy.

* Maximal tumor size was not available for 1 patient treated with CMT.
Actuarial Local Control  

Actuarial Radiation Complications

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Guadagnolo et al., IJROBP 2008
Summary I

• Radiation Therapy is an effective treatment for desmoid tumors
• Local control can be achieved with radiation therapy alone or radiation therapy + surgery
  – No statistically significant difference in local control with (78%) or without surgery (65%)
  – For radiation therapy alone, no statistically significant difference in local control with radiation dose ≤ 56 Gy (62%) or radiation dose > 56 Gy (75%)
• Radiation Therapy can cause late toxicities
  – Risk is increased for radiation dose > 56 Gy
• Careful consideration of potential risks and benefits of radiation therapy for desmoid tumors by multi-disciplinary team
Outline

• Case Studies
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• Risks of Receiving Radiotherapy
Overall Survival

91 patients with high grade sarcoma of extremity (chemotherapy)
  47 post-op RT
  44 no RT

50 patients with low grade sarcoma of extremity
  26 post-op RT
  24 no RT

Radiation Therapy: 45 Gy with 18 Gy boost
The Incidence of Lung Carcinoma after Surgery for Breast Carcinoma with and without Postoperative Radiotherapy

Results of National Surgical Adjuvant Breast and Bowel Project (NSABP) Clinical Trials B-04 and B-06

Melvin Deutsch, M.D.¹
Stephanie R. Land, M.D.²,³
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H. Samuel Wieand, M.D.²,³
Norman Wolmark, M.D.⁵
Bernard Fisher, M.D.²
# The Incidence of Lung Carcinoma after Surgery for Breast Carcinoma with and without Postoperative Radiotherapy

*Results of National Surgical Adjuvant Breast and Bowel Project (NSABP) Clinical Trials B-04 and B-06*

## TABLE 1
Incidence of Subsequent Lung Carcinomas According to Breast Carcinoma Treatment

<table>
<thead>
<tr>
<th></th>
<th>NSABP B-04</th>
<th></th>
<th></th>
<th>NSABP B-06</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RM</td>
<td>TM</td>
<td>TM + RT</td>
<td>P value</td>
<td>RM</td>
<td>TM</td>
<td>TM + RT</td>
</tr>
<tr>
<td></td>
<td>n = 654</td>
<td>n = 365</td>
<td>n = 646</td>
<td></td>
<td>n = 589</td>
<td>n = 633</td>
<td>n = 628</td>
</tr>
<tr>
<td>Confirmed ipsilateral lung carcinoma</td>
<td>1</td>
<td>2</td>
<td>9</td>
<td>0.013</td>
<td>2</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Confirmed and probable ipsilateral lung carcinoma</td>
<td>3</td>
<td>3</td>
<td>10</td>
<td>0.066</td>
<td>3</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>All confirmed and probable ipsilateral plus contralateral lung carcinomas</td>
<td>6</td>
<td>3</td>
<td>14</td>
<td>0.029</td>
<td>13</td>
<td>8</td>
<td>9</td>
</tr>
</tbody>
</table>

NSABP: National Surgical Breast and Bowel Project; RM: radical mastectomy; TM: total mastectomy; RT: radiotherapy; L: lumpectomy.

* P value refers to comparison of the radiotherapy arm with the treatment arms without radiotherapy.
No Increased Risk of Second Cancer After Radiotherapy in Patients Treated for Rectal or Endometrial Cancer in the Randomized TME, PORTEC-1, and PORTEC-2 Trials


Patients included in the TME, PORTEC-1, and PORTEC-2 trials (N = 2,672)

Excluded
(n = 117)
Did not meet eligibility criteria (n = 117)

Randomly assigned
(n = 2,555)

Allocated to EBRT
Received EBRT (n = 1,264)
Received no RT (n = 16)
Received VBT (n = 5)

Allocated to no RT
Received no RT (n = 1,078)
Received EBRT (n = 88)
Lost to follow-up (n = 1)

Allocated to VBT
Received VBT (n = 213)
Received EBRT (n = 1)
Received no RT (n = 3)

Analyzed in the EBRT group
(n = 1,332)

Analyzed in the no-RT group
(n = 1,008)

Analyzed in the VBT group
(n = 214)
Table 3. SIRs for All Types of Second Cancer*

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Observed</th>
<th>Expected</th>
<th>SIR</th>
<th>95% CI</th>
<th>AER†</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>449</td>
<td>151</td>
<td>2.98</td>
<td>2.82 to 3.14</td>
<td>154</td>
</tr>
<tr>
<td>Male sex</td>
<td>167</td>
<td>52</td>
<td>3.23</td>
<td>2.98 to 3.50</td>
<td>178</td>
</tr>
<tr>
<td>Female sex</td>
<td>282</td>
<td>101</td>
<td>2.78</td>
<td>2.58 to 3.00</td>
<td>140</td>
</tr>
<tr>
<td>Age ≤ 60 years</td>
<td>121</td>
<td>22</td>
<td>5.47</td>
<td>4.73 to 6.31</td>
<td>151</td>
</tr>
<tr>
<td>Age &gt; 60 years</td>
<td>328</td>
<td>119</td>
<td>2.76</td>
<td>2.60 to 2.93</td>
<td>163</td>
</tr>
</tbody>
</table>

*Excluding basal cell carcinomas.
†Per 10,000 persons per year.

Abbreviations: AER, absolute excess risk; SIR, standardized incidence ratio.

Wiltink et al., JCO 2015
TWENTY-YEAR FOLLOW-UP OF A RANDOMIZED TRIAL COMPARING TOTAL
MASTECTOMY, LUMPECTOMY, AND LUMPECTOMY PLUS IRRADIATION
FOR THE TREATMENT OF INVASIVE BREAST CANCER

BERNARD FISHER, M.D., STEWART ANDERSON, PH.D., JOHN BRYANT, PH.D., RICHARD G. MARGOLESE, M.D.,
MELVIN DEUTSCH, M.D., EDWIN R. FISHER, M.D., JONG-HYEON JEONG, PH.D., AND NORMAN WOLMARK, M.D.

A  Total Deaths

B  Deaths in Women with Recurrent or Contralateral Breast Cancer

C  Deaths in Women without Recurrent or Contralateral Breast Cancer

Cumulative Incidence (%)
Summary II

• Radiation Therapy is an effective treatment for desmoid tumors
• Local control can be achieved with radiation therapy alone (56-66 Gy) or radiation therapy (50 Gy) + surgery
• Radiation Therapy can cause acute and late toxicities
• Careful consideration of potential risks and benefits of radiation therapy for desmoid tumors by multi-disciplinary team

• Initial presentation- consider observation vs. surgery alone
• At recurrence consider Radiation Therapy + Surgery vs. Radiation Therapy alone depending on the location and the consequences of surgery
Acknowledgments

The Kirsch Lab