Desmoid Tumors

- Rare, slow growing, mesenchymal proliferations
- Fibroblastic/myofibroblastic differentiation
- Increased activity of β-catenin (CTNNB1 mutation)
- Benign Histologic appearance
- No metastatic potential
- Poorly circumscribed
- Invade and infiltrate surrounding tissues
- Local growth and invasion may result in:
  - Pain
  - Death when vital organ involved
  - Deformity
  - Functional impairment

Sleijfer. Eur J Cancer 2009
Heterogeneous Presentation

• Sporadic
  – Extremity
  – Trunk
  – Intra-abdominal
    β Pregnant or Post-Partum women
    β Children

• Associated with Familial Adenomatous Polyposis
Unpredictable behavior

• Regression without treatment
• Multiple recurrence despite radical excisions and multi-modality treatment (25-60% at 5 years)
• Tumor related mortality is very rare
• Disfigurement and loss of function that may result from tumor progression or from treatment may be significant
Treatment Options

Whether, When and How to treat??

• Surgery remains the mainstay of treatment for symptomatic desmoids arising in almost all sites
• Observation alone

• imatinib
• Chemotherapy
• Radiation

• Hormones
• Non-Steroidal Anti-Inflammatory
• COX-2 inhibitors
Surgical treatment

Tailored based on
  – Anatomic location
  – Presentation

• What type of resection?
• How extensive a resection?
• The optimal therapeutic approach
  – should differ based on the site and etiology of the desmoid
  – should employ multimodality treatment
  – Should aim to achieve the least morbidity without compromising the chance of definitive cure
Sporadic Extra-Abdominal (EA) Desmoids
Sporadic EA Desmoids

37-38% trunk
30-34% extremities
8-10% Head and Neck
5-24% Abdominal cavity
2-4 cases/million individuals
2\textsuperscript{nd} - 3\textsuperscript{rd} decade of life
60% in women
Association with tissue trauma?
Association with partum? C-section?

Sporadic EA Desmoids

- Goal should be resection with negative margins
- Widely negative margins do not decrease recurrence rates compared to negative macroscopic margins but may compromise functional results
- Prognostic significance of microscopic positive margins is controversial
- Amputation reserved to non-functional limbs or other tumor-related complications

## Margin status and recurrences

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Wide or R0</th>
<th>R1</th>
<th>R2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ballo</td>
<td>1998</td>
<td>27%</td>
<td>54%</td>
<td></td>
</tr>
<tr>
<td>Bataini</td>
<td>1988</td>
<td>0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Easter</td>
<td>1989</td>
<td>76%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Goy</td>
<td>1997</td>
<td>12%</td>
<td>68%</td>
<td></td>
</tr>
<tr>
<td>Karakousis</td>
<td>1993</td>
<td>31%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lev</td>
<td>2007</td>
<td>16%</td>
<td>19%</td>
<td></td>
</tr>
<tr>
<td>McKinnon</td>
<td>1989</td>
<td>5%</td>
<td>43%</td>
<td></td>
</tr>
<tr>
<td>Merchant</td>
<td>1999</td>
<td>73%</td>
<td>75%</td>
<td></td>
</tr>
<tr>
<td>Mirabell</td>
<td>1990</td>
<td>0%</td>
<td>22%</td>
<td>100%</td>
</tr>
<tr>
<td>Posner</td>
<td>1989</td>
<td>15%</td>
<td>54%</td>
<td>50%</td>
</tr>
<tr>
<td>Pritchard</td>
<td>1996</td>
<td>15%</td>
<td></td>
<td>50%</td>
</tr>
<tr>
<td>Rao</td>
<td>1987</td>
<td>11%</td>
<td>84%</td>
<td></td>
</tr>
<tr>
<td>Spear</td>
<td>1998</td>
<td>23%</td>
<td>44%</td>
<td>50%</td>
</tr>
</tbody>
</table>
## Margin status and recurrences

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients</th>
<th>Desmoid</th>
<th>Year</th>
<th>R0</th>
<th>R1</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posner</td>
<td>131</td>
<td>All, FAP</td>
<td>1989</td>
<td>15%</td>
<td>54%</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Spear</td>
<td>107</td>
<td></td>
<td>1998</td>
<td>23%</td>
<td>44%</td>
<td>0.017</td>
</tr>
<tr>
<td>Ballo</td>
<td>189</td>
<td>All, FAP</td>
<td>1998</td>
<td>27%</td>
<td>54%</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Merchant</td>
<td>105</td>
<td>E/T</td>
<td>1999</td>
<td>73%</td>
<td>75%</td>
<td>0.51</td>
</tr>
<tr>
<td>Gronchi</td>
<td>203</td>
<td>E/T</td>
<td>2003</td>
<td>23%</td>
<td>26%</td>
<td>0.5</td>
</tr>
<tr>
<td>Lev</td>
<td>146</td>
<td>All</td>
<td>2007</td>
<td>16%</td>
<td>19%</td>
<td>NS</td>
</tr>
</tbody>
</table>
### Margin status and recurrences

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients</th>
<th>Desmoid</th>
<th>Year</th>
<th>R0</th>
<th>R1</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posner</td>
<td>131</td>
<td>All, FAP</td>
<td>1989</td>
<td>15%</td>
<td>54%</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Spear</td>
<td>107</td>
<td></td>
<td>1998</td>
<td>23%</td>
<td>44%</td>
<td>0.017</td>
</tr>
<tr>
<td>Ballo</td>
<td>189</td>
<td>All, FAP</td>
<td>1998</td>
<td>27%</td>
<td>54%</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Merchant</td>
<td>105</td>
<td>E/T</td>
<td>1999</td>
<td>73%</td>
<td>75%</td>
<td>0.51</td>
</tr>
<tr>
<td>Gronchi</td>
<td>203</td>
<td>E/T</td>
<td>2003</td>
<td>23%</td>
<td>26%</td>
<td>0.5</td>
</tr>
<tr>
<td>Lev</td>
<td>146</td>
<td>All</td>
<td>2007</td>
<td>16%</td>
<td>19%</td>
<td>NS</td>
</tr>
</tbody>
</table>
Margin status and recurrences

- Positive margins per se influence subsequent adjuvant treatment
- Microscopically positive margins do not necessarily predict a recurrence
- A local recurrence does not necessarily portend to uncontrolled tumor growth
- For tumors that require extensive/disfiguring operation the focus should be on preservation of organ function and quality of life, rather than on striving for R0
Sporadic Intra-Abdominal (IA) Desmoids
IA Sporadic Desmoids

- Few sporadic desmoids (5-24%) are located in the abdominal cavity
- Most abdominal desmoids (74-87%) are sporadic
- Associated with definite mortality (complications of progression/treatment)
IA Sporadic Desmoids

- Mesenteric desmoids usually too large for complete excision
- Resection of desmoids in proximity to mesenteric vessels may compromise viability of small bowel \(\Rightarrow\) short bowel syndrome
- Mortality 3%
- Severe morbidity 13%
- Recurrence rate 11%
IA Sporadic Desmoids

Burke 1990

• 113 patients
  – positive margins 47% (R1? R2?)
• 10 patients not resected
  – 2 died of other causes
  – 8 alive without evidence of disease

Smith 2000

• 16 resected
  – positive margins 68%
  – local recurrence 37%
• 8 not resectable
• 10-year survival 73% (p = 0.73)
IA Sporadic Desmoids

• No definitive information on influence of positive margins on recurrence/outcomes
• Chances of obtaining negative margins are low
• Heroic resections that endanger viability of the small intestine should be avoided
FAP-associated Desmoids
FAP-associated Desmoids

- 9-29% of FAP patient develop desmoids
- 850-fold frequency increase
- 75% intra-abdominal
- 82-86% develop after abdominal operation
FAP-associated Desmoids

• Higher chance of complications
  – Bowel obstruction 27%
  – Ureteral obstruction 24%
  – Bowel perforation 9%
  – Entero-cutaneous fistula 4%
  – Bleeding 4%

• Recurrence 41%

• Mortality 10-15%

Sleijfer. Eur J Cancer 2009
FAP-associated Desmoids

Burke 1990

- 10 patients with FAP-IA desmoids operated on
- 90% had recurrence
- 60% Overall mortality
- 50% Surgical-related mortality

Berk 1992

- 13/40 patients with FAP-IA operated on
- 85% had recurrence
- 53% desmoid-related mortality
FAP-associated IA Desmoids

Clark 1999
• 22/68 patients operated on for intra-abdominal
• 71% (10/14) had recurrence
• 37% (8/22) Surgical mortality
• 42% (6/14) Short bowel syndrome requiring long-term TPN

Smith 2000
• 5 patients operated on for intra-abdominal
• 2 patients operated on † death
• 3 unresected ‡ alive at 36 mo f/u
FAP-associated IA Desmoids

Resection is:

- *Technically challenging*
- *Associated with high morbidity*
- *Frequently followed by early recurrence*

Unclear if negative margins would decrease recurrence rates

Spontaneous regression documented in 4-17%

Surgery should be restricted to complications and failure of non-operative treatment

Melis 2008
Jones, Ann Surg 1986
Reitamo. Arch Surg 1983
Multi-Modality Treatment
Adjuvant Radiation (XRT)

- Post-Operative XRT might offset the adverse impact of positive margins on recurrence
- At least 3 recent retrospective review showed no benefit of adjuvant XRT, even when margin status was accounted for
- Complications (fibrosis, paresis, edema, fractures, second malignancies) in 23% patients
- Ineffective for IA or FAP desmoids
- Should not be used in children

Ballo. J Clin Oncol 1999
Merchant. Cancer 1999
Definitive XRT

Several series report recurrence rates comparable or lower than surgery.
Rapid resolution of the mass should not be expected.
Not an option if impending complication.

Neoadjuvant XRT

Does not improve rates of resection with negative margins.
Medical treatment

Good option for FAP-associated, locally advanced or unresectable desmoids

- Chemotherapy
- Imatinib
- Anti-estrogens
- NSAIDS
Wait & See
What about... No treatment?

![Graph showing survival rates with different treatments over years.]

Bonvalot.. Eur J Surg Oncol 2008
What about... No treatment?

3 spontaneous regressions (4% of primary desmoids)

Putting It All Together
Sporadic Extra-Abdominal Desmoids

- Small, asymptomatic
  - Consider observation
  - Negative margins
    - Follow-up
    - Immediate re-excision
      - Follow-up
  - Microscopic positive margins
    - Re-resectable without functional or cosmetic impairment
    - Re-resectable only with functional or cosmetic impairment
      - Consider radiation therapy
        - Follow-up
  - Gross residual disease
    - Adjuvant radiotherapy
    - Reconsider for surgery if definite progression
      - Follow-up
    - Not a radiotherapy candidate
      - Consider systemic therapy trial. Close follow-up
    - Reassess and reconsider for surgery in the future
- Large or with progression or symptoms
  - Not resectable without functional or cosmetic impairment
  - Radiotherapy and/or systemic chemotherapy
Intra-Abdominal Desmoids

Intra-abdominal desmoids (± FAP)

- Follow-up
  - No symptoms
  - No complications
  - No progression

- Symptoms and/or progression
  - Consider systemic therapy trial

- Complications
  - Supportive treatment

Success
- Consider systemic therapy trial

Failure
- Surgical palliation
  - Avoid extensive procedure
Take-Home messages

We cannot predict which tumor would respond best to various treatments
Therapeutic selection is challenging
Watchful waiting is an option
Surgery must be tailored to what is achievable in terms of negative margins while preserving function
Thank you!!
Questions?
marcovalerio.melis@nyumc.org