Radiotherapy for Desmoids tumors

MP Sunyach
Modern technics allows to decreased dose delivered to the normal structure

- Personnal immobilisation device
- Image Guided Radiotherapy :
  - Control before and during seance
- Precision of the dose distribution :
  - RC 3D
  - IMRT
  - VMAT
First stage SIMULATION

CT scanning for:

- spatial localisation of patient anatomy, including Organ At Risk and tumor contours

Immobilisation equipment
The second stage: PLANNING

3D planning takes into account the variations in dose distribution caused by heterogeneities (lung.... bones.... )

- Current computers are able to compute dose in three dimensions
Fig. 4. Axial views demonstrating isodose displays for original, conformal, and intensity-modulated radiotherapy plans for Patient 8. Red color wash contour represents gross tumor volume; light blue color wash contour, clinical target volume; and green color wash contour in anterior leg, medial, and lateral flaps.
Beam with no modulation

Open beam
Intensity modulated beam
Principe of IMRT

3DRT:
- beam

IMRT:

uniformedose

Complex dose distribution sparing critical structure
Fig. 4. Axial views demonstrating isodose displays for original, conformal, and intensity-modulated radiotherapy plans for Patient 8. Red color wash contour represents gross tumor volume; light blue color wash contour, clinical target volume; and green color wash contour in anterior leg, medial, and lateral flaps.
Dose to OAR spinal cord reduced
The last stage TREATMENT

It is important to ensure that the tumour (and normal tissues) are where you think they are.

There is a balance between reducing margins to miss normal tissues versus sufficient margins to cover the disease volume.
Checking the position

image acquisition prior to every treatment,

- with an on board imaging device,
- The target volume is identified and compared with the volume in planning.
- If significant deviation has occurred, the radiotherapy delivery may be mildly adjusted.
Accelerator able to treat and control the position by imaging 3D
Accelerator able to treat and control the position by imaging 2D
What about Desmoid tumors ????
Radiotherapy After surgery?

Local failure after excision 25\%-40\%

No phase III Study =
– No certitude
Surgery versus Radiation Therapy for Patients with Aggressive Fibromatosis or Desmoid Tumors

A Comparative Review of 22 Articles

Joost J. Nuyttens, M.D.
Philip F. Rust, M.D.
Charles R. Thomas, Jr., M.D.
Andrew T. Turrisi III, M.D.

BACKGROUND. Desmoid tumors (aggressive fibromatoses) are benign neoplasms with high rates of recurrence after surgery. Radiotherapy is sometimes reported to prevent recurrences, but not in all studies. In order to evaluate the effect of radiation, comparative analysis was performed.

METHODS. The authors conducted a MEDLINE search and collected all articles in the English language on the treatment of “desmoid tumor” or “aggressive fibromatosis” from the years 1983-1998. They categorized treatment into three groups: surgery alone (S), surgery with radiotherapy (S + RT), or radiotherapy alone (RT). The S and S + RT groups were each subdivided according to whether margins were free (–), positive (+), or unknown. Each subgroup was divided into cases with primary, recurrent, or unknown tumor.

RESULTS. The local control rates after treatment for cases in the S group with (–) margins, (+) margins, and overall were 72%, 41%, and 61%, respectively. For the S + RT group the local control rates were 94%, 75%, and 75%, respectively, significantly different when compared with the results for the S group. For the RT group, the local control was 78%, significantly superior to that of the S group (61%). Cases with primary and recurrent tumors had significantly superior local control rates with S + RT or RT versus S. Radiotherapy complications noted were fibrosis, paresthesia, edema, and fracture.

CONCLUSIONS. RT or S + RT results in significantly better local control than S. Even after dividing the groups into cases with free and positive margins and cases with primary and recurrent tumors, the best local control is achieved with RT or S + RT. Cancer 2000;85:1517-23. © 2000 American Cancer Society.

KEYWORDS: desmoid tumor, aggressive fibromatosis, surgery, radiotherapy, complications.

Aggressive fibromatosis is a benign neoplasm that arises from fascial and musculoskeletal tissues. These tumors lack a capsule, infiltrate along fascial planes, and invade adjacent neurovascular structures. Local recurrences may occur even after a wide resection. Some recurrences may be malignant. Disfigurement may be avoided in some instances by radiotherapy, either alone or after conservative surgery, without compromising in local control. Radiotherapy has a relapse rate of 31% for unresectable tumors. There seems to be evidence that radiotherapy is helpful in the management of aggressive fibromatosis, although the role and precise indication for its modality has not been defined clearly. In an attempt to put the multimodal management of the desmoid tumor in some perspective, a comparative review of 22 articles regarding the roles of surgical and radiotherapy for aggressive fibromatosis was performed.
(Nuyttens JJ, Cancer. 2000 Apr 1;88(7):1517-23.)

Publications 83-98.
22 articles
718 pts
FU: 6 y.
RESULTS: Local control
surgery 61%
Surgery + RT 75%
RT alone 78%

Toxicity: RT complications fibrosis, paresthesias, edema, fractures

Conclusion: RT or surgery + RT results in significantly better local control than surgery alone

RTE is effective after surgery R1 and R0

**Table 3**

<table>
<thead>
<tr>
<th>Local Control for Free Margins, Positive Margins, or Unknown Margins Treated with Surgery Alone, Surgery with Radiotherapy, or Radiotherapy Alone</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Surgery alone</strong></td>
</tr>
<tr>
<td>No.</td>
</tr>
<tr>
<td>Free margins</td>
</tr>
<tr>
<td>Positive margins</td>
</tr>
<tr>
<td>Unknown margins</td>
</tr>
<tr>
<td>Total</td>
</tr>
</tbody>
</table>

RT: radiotherapy; No.: number of patients with local control, NA: not available.

*aAll patients treated with radiotherapy alone had macroscopic disease.*

*bP value in comparison with surgery alone.*
The impact of radiotherapy in the treatment of desmoid tumours. An international survey of 110 patients. A study of the Rare Cancer Network

Brigitta G Baumert*1,2, Martin O Spahr1, Arthur Von Hochstetter3, Sylvie Beauvois4,25, Christine Landmann5, Katrin Fridrich6,24, Salvador Villà7, Michael J Kirschner8,22, Guy Stormes9, Peter Thum10, Hans K Streuli11, Norbert Lombriser12, Robert Maurer13, Gerhard Ries14, Ernst-Arnold Bleher15, Alfred Willi16, Juerg Allemann17, Ulrich Buehler18, Hugo Blessing19,26, Urs M Luetolf1, J Bernard Davis1, Burkhardt Seifert20 and Manfred Infanger2

An international study of the Rare Cancer Networkthe 110 patients, the addition of radiation therapy after surgery was an independent positive prognostic factor for local recurrence and overall survival
The impact of radiotherapy in the treatment of desmoid tumours. An international survey of 110 patients. A study of the Rare Cancer Network

Brigitta G Baumert*1,2, Martin O Spahr1, Arthur Von Hochstetter3, Sylvie Beauvois4,25, Christine Landmanns, Katrin Fridrich6,24, Salvador Villà7, Michael J Kirschner8,22, Guy Storme9, Peter Thum10, Hans K Streuli11, Norbert Lombriser12, Robert Maurer13, Gerhard Ries14, Ernst-Arnold Bleher15, Alfred Willi16, Juerg Allemann17, Ulrich Buehler18, Hugo Blessing19,26, Urs M Luetolf1, J Bernard Davis1, Burkhardt Seifert20 and Manfred Infanger2

Results: Recurrences:

- Post surgical E RT: 17/68 patients (25%)
- Surgery alone: 12/38 patients (32%)

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Surgery and radiotherapy

Surgery alone

p = 0.0028
Group EBRT: Recurrences were seen:

- at the field borders in 7 cases
- within the field in 10 cases.
- in areas where the dose was less than 50 Gy in 65% of cases.

Conclusion of the author is:
- Dose at least of 50 Gy has to be delivered
- Field margin has to be at least 5 cm.
But no value prognostic value for surgical margin

Looking for relevant prognostic factor

To select patients who need post operative radiation therapy

AGE ? Tumor site ?
Beta cathehine ?
News factors ?
Curative or exclusive EBRT

Are demsmoid tumor radiosensitiv ?
<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Local control</th>
<th>Doses RT</th>
<th>Site or recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Gluck et al. 787-92) Michiganan 1984 200 95 pts 8-87 ans</td>
<td>13</td>
<td>3 y : 92.3%</td>
<td></td>
<td>In field : 5 pts 3</td>
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<tr>
<td>(Rutenberg et al. 1978 2008 30 pts 8-30 ans)</td>
<td>15</td>
<td>15 ay 67%</td>
<td>55-65 Gy</td>
<td>ne</td>
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<tr>
<td>(Zlotecki et al. 177-81) 1975-2000 65 pts 10-78 ans</td>
<td>32</td>
<td>5 y 78%</td>
<td>50-54 Gy</td>
<td>In field : 2 pts Fields margins 9</td>
</tr>
<tr>
<td>(Micke and Seegenschmiedt 882-91) 112 institutions 1976</td>
<td>204</td>
<td>81 %</td>
<td>36-65 Gy</td>
<td>ne</td>
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<tr>
<td>(Baumert et al. 12)</td>
<td>0</td>
<td>ne</td>
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<tr>
<td>(El-Haddad et al. 775-80) 1990 2006 AS 54 pts 2-63 ans</td>
<td>0</td>
<td>ne</td>
<td>45 - 60 Gy</td>
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<tr>
<td>Study</td>
<td>TTT</td>
<td>age</td>
<td>Site t</td>
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<td>(Rutenberg et al.) 1978-2008 30 pts 8-30 ans</td>
<td>NS</td>
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<tr>
<td>(Gluck et al. 787-92) Michigan 1984-2004 95 pts 8-87 ans</td>
<td>NS</td>
<td>NE</td>
<td>0.035</td>
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<td>NS</td>
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<tr>
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<td>NS</td>
<td>0.01 Abdo pénjoratif</td>
<td>NE</td>
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<tr>
<td>(El-Haddad et al. 775-80)</td>
<td>NS</td>
<td>NE</td>
<td>0.010</td>
<td>NS</td>
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<tr>
<td>Study (Authors, Year, Location)</td>
<td>Recurrence</td>
<td>FU</td>
<td>TTT</td>
<td>Local Control</td>
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<tr>
<td>(Gluck et al., 1984-2004, Michigan)</td>
<td>23/95</td>
<td>38 ms</td>
<td>Surgery: 54 pts, Surgery + Rte: 28 pts, Rte: 13 pts</td>
<td>3 y 84.6%, 69% 92.3%</td>
</tr>
<tr>
<td>(Zlotecki et al., 1975-2000, 65 pts, 10-78 ans)</td>
<td>42/65</td>
<td>6 y</td>
<td>Xie + Rte: 32 pts, Rte: 33 pts</td>
<td>5 y 78%, 87%</td>
</tr>
<tr>
<td>(Mice and Seegenschmiedt, 1976, 882-91, 112 institutions, 345 pts)</td>
<td>50% &gt;2 xie</td>
<td>43 ms</td>
<td>Xie + Rte: 141 pts, Rte: 204 pts</td>
<td>81% 79.6%</td>
</tr>
<tr>
<td>(Baumert et al., 2012)</td>
<td>6 y</td>
<td>Xie + Rte: 68 pts, Surgery + Rte: 42 pts, Rte: 0 pts</td>
<td>10 y 93%, 62%</td>
<td>No second cancer, 4 severe bowel injuries</td>
</tr>
<tr>
<td>(El-Haddad et al., 1990-2006, AS, 54 pts, 2-63 ans)</td>
<td>28 rec./54</td>
<td>7.3 y</td>
<td>Surgery + Rte: 54 pts</td>
<td>10 y 67%</td>
</tr>
</tbody>
</table>
toxicities

• 3 second cancers / 1322 pts
• Résultats satisfaisants même en récidive
• Nombreuses complications de la RTE en particuliers douleurs et troubles fonctionnels
RT for desmoid

- Larges volumes
- Dose 50-55 Gy
Expérience CLB

<table>
<thead>
<tr>
<th>Pts</th>
<th>Rec</th>
<th>Dose Gy</th>
<th>fu</th>
<th>DN réponse</th>
<th>douleurs</th>
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<tbody>
<tr>
<td>Pt1</td>
<td>oui</td>
<td>56</td>
<td>5A</td>
<td>RN : 60-40 mm</td>
<td>NON</td>
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<tr>
<td>Pt2</td>
<td>oui</td>
<td>56</td>
<td>7A</td>
<td>RP</td>
<td>OUI</td>
</tr>
<tr>
<td>Pt3</td>
<td>oui</td>
<td>56</td>
<td>8A</td>
<td>RC</td>
<td>NON</td>
</tr>
<tr>
<td>Pt4</td>
<td>oui</td>
<td>56</td>
<td>4A</td>
<td>PR champ</td>
<td>OUI</td>
</tr>
<tr>
<td>Pt5</td>
<td>oui</td>
<td>54</td>
<td>6A</td>
<td>RC</td>
<td>OUI</td>
</tr>
<tr>
<td>Pt6</td>
<td>oui</td>
<td>56</td>
<td>8A</td>
<td>PR bordure</td>
<td>OUI</td>
</tr>
<tr>
<td>Pt7</td>
<td>oui</td>
<td>56</td>
<td>4A</td>
<td>RC 96-60 mm</td>
<td>NON mieux</td>
</tr>
<tr>
<td>Pt8</td>
<td>oui</td>
<td>56</td>
<td>4A</td>
<td>PR bordure</td>
<td>NON</td>
</tr>
<tr>
<td>Pt9</td>
<td>oui</td>
<td>56</td>
<td>3A</td>
<td>RP</td>
<td>NON</td>
</tr>
<tr>
<td>Pt10</td>
<td>oui</td>
<td>56</td>
<td>3A</td>
<td>RP 78-40 mm</td>
<td>NON</td>
</tr>
</tbody>
</table>
conclusion

• Not always efficient for dolor....
• Tumor regression after several years
• Marginal recurrence
To evaluate the efficacy of radiotherapy for inoperable desmoid tumors, the Soft Tissue and Bone Sarcoma Group of the European Organization for Research and Treatment of Cancer (EORTC) performed a pilot study (EORTC 62991) assessing moderate-dose radiotherapy for aggressive fibromatosis in patients not amenable to resection without significant function loss. Patients received radiotherapy for a total of 56 Gy in 28 fractions. This nonrandomized, phase II study finalized recruitment with 44 patients in April 2008, and patients are still under followup; the final analysis is awaited after 3 years of follow-up in the second quarter of 2011.
Toxicities

Bones fractures
  - Reduced by modern RT

Fibrosis necrosis
  - Reduced by modern RT

Second cancer
  - ????
  - Low risk
  - Very long term risk
  - Probably not reduced by modern radiotherapy
Observation before radiation

They may grow progressively larger over time, but growth is indolent, and periods of growth arrest are not uncommon.

Medical treatment need 24 months to induced responce.
When it may be proposed?

In case of evolutive inoperable symptomatics disease?

- Abdominal
  - New IMRT and VMAT
  - gaves news possibilities in selectiv case

- Appendix head and neck or parietal
  - For evolutive symptomatics disease after failure of medical treatment
After surgery
Lack of selections criteria
Recurrence with second R2 resection and

Role for postop RT is not clear;

It is currently not recommended for R1 resection,

It may be offered for R2 resection, particularly if there are concerns about local disease progression and morbidity/mortality
Why irradiated?

To preserved the quality of life

Decreased dolor

Preserved function

Increased local control after surgery
Conclusion

• Desmoid tumors are a challenging clinical condition with locally aggressive behavior and a strong tendency for recurrence.

• Management options include:
  – observation, surgical resection, radiotherapy, conventional chemotherapy, hormonal agents, and newer molecular targeted agents. A multidisciplinary approach tailored to the individual patient is usually needed, depending on the location, local effects, and clinical course.