Superficial Radiation Therapy (SRT) in the Treatment of Keloids

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Disclosure of Industry Relationships

Radiation Treatment of Keloids - Brian Berman, MD, PhD

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Off FDA labeled usages are discussed

The clinical problem:

Keloid Recurrences after Excision
Keloid Recurrence Rates

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>Excision</th>
<th># Patients</th>
<th>% of Recurrence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neesin</td>
<td>1992</td>
<td>Scalpel</td>
<td>12</td>
<td>87%</td>
</tr>
<tr>
<td>Arnold</td>
<td>1990</td>
<td>Scalpel</td>
<td>16</td>
<td>80%</td>
</tr>
<tr>
<td>Conway</td>
<td>1990</td>
<td>Scalpel</td>
<td>20</td>
<td>65%</td>
</tr>
<tr>
<td>Cossman</td>
<td>1991</td>
<td>Scalpel</td>
<td>25</td>
<td>54%</td>
</tr>
<tr>
<td>Cossman</td>
<td>1972</td>
<td>Scalpel</td>
<td>3</td>
<td>57%</td>
</tr>
<tr>
<td>Cossman</td>
<td>1974</td>
<td>Scalpel</td>
<td>20</td>
<td>73%</td>
</tr>
<tr>
<td>Nardini&lt;br&gt;</td>
<td>1974</td>
<td>Scalpel</td>
<td>104</td>
<td>86%</td>
</tr>
<tr>
<td>Osserman</td>
<td>1974</td>
<td>Scalpel</td>
<td>41</td>
<td>92%</td>
</tr>
<tr>
<td>Ahlberg</td>
<td>1990</td>
<td>Laser</td>
<td>8</td>
<td>89%</td>
</tr>
<tr>
<td>Mancini</td>
<td>1990</td>
<td>Laser</td>
<td>25</td>
<td>74%</td>
</tr>
<tr>
<td>Berman</td>
<td>1994</td>
<td>Scalpel</td>
<td>4</td>
<td>50%</td>
</tr>
<tr>
<td>Kim</td>
<td>2004</td>
<td>Scalpel</td>
<td>9</td>
<td>44%</td>
</tr>
</tbody>
</table>

Weighted Average Recurrence = 71.2%

Recurrence Rate of Excised Keloids

JAAD 1997; 37:755-757
Recurrence Rates of Excised Keloids:
Effect of Number of Post-Op TAC Injections

<table>
<thead>
<tr>
<th>Recurrence (%)</th>
<th>Single</th>
<th>2 or More</th>
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</thead>
<tbody>
<tr>
<td>n=38</td>
<td>47.4</td>
<td>52.6</td>
</tr>
</tbody>
</table>

NS (p=0.652)  
JAAD 1997; 37:755-757

Recurrence Rates of Excised Keloids:
Effect of Post-Op TAC Concentration

<table>
<thead>
<tr>
<th>Recurrence (%)</th>
<th>10 mg/cc</th>
<th>&gt;20 mg/cc</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=38</td>
<td>55.3</td>
<td>44.7</td>
</tr>
</tbody>
</table>

NS (p=0.366)  
JAAD 1997; 37:755-757

Post-Excision Radiation and Keloid Recurrences
X-Ray Radiation in the Electromagnetic Spectrum

DNA / RNA Damage due to Ionizing Radiation

Ionizing Radiation on Wound Healing

- Full-thickness, 2-cm-diameter, dorsal rat skin, with and without prior local irradiation with 521 rad, was excised
- **Control wounds** contained:
  - prominent BrdU-positive proliferating cells, at days 3-9 &
  - minimal TUNEL-positive apoptotic cells during healing
- **Irradiated wounds** had:
  - fewer BrdU-positive proliferating cells and
  - **significant** TUNEL-positive apoptotic cells at days 3-9, &
  - persistent lower proportion of G2/M phase cells
- Radiation-induced **inactive cell proliferation, greater apoptosis**, and **cell cycle arrest** at days 3-9 post-wounding may be cellular mechanisms responsible for **delayed wound healing**

Post-Excision Radiation & Keloids

- In a retrospective study of 80 keloidectomy patients treated with postoperative single-fraction 10Gy radiotherapy
  - 9% of keloids relapsed after 1 year
  - 16% of keloids relapsed after 5 years


Post-Excision Radiation of Auricular Keloids

- Retrospective study of suturing lines of 60 keloidectomy patients (76 ear keloids)
- Treated 1-3 days post-operatively with 5 Gy/wk, 25-45 Gy total dose, contact or superficial radiotherapy
- 5 year relapse-free rate of 79.84%
- No pigmentation or telangiectasias


Superficial Radiation Therapy for the Prevention of Keloids After Surgery

- A BED value of 30 Gy can be obtained with
  - a single acute dose of 13 Gy
  - two fractions of 8 Gy
  - three fractions of 6 Gy
  - a single dose of 27 Gy at low dose rate
- The radiation treatment should be administered within 1-2 days after surgery

Kal HB, Veen RE. Keloid Dose and Fractionation Schemes
**Keloidectomy + BED 30 SRT**
- 297 keloids were surgically completely excised
- Starting on post-operative day 1 the suture closure line, with a 5 mm margin, received a BED 30 of superficial radiation 70 or 100 kV
- Almost all, three 6 Gy fractions on POD 1, 2 & 3
- Follow-up: 3m to >3 yrs (majority >6m)
  - **9/297 recurrences (3.0%)**
- Transient hyperpigmentation was most frequent AE

**SRT (BED 30) Post-Keloidectomy**

<table>
<thead>
<tr>
<th></th>
<th>BL</th>
<th>Post-Excision</th>
<th>6 m</th>
<th>12 m</th>
</tr>
</thead>
</table>

Schmieder, EADV Geneva, 2017

**Keloidectomy + BED 30 SRT: Chart Review**
- Retrospective, chart review study of 96 excised keloids + SRT (61 patients) with ≥1 year followup (or recurrence noted prior to 1 year), at 4 US sites
- Usually 3, 6-Gy fractions, on POD 1, 2 & 3 (BED 30 SRT 70 or 100 kV) to the suture closure line, with a 5 mm margin
- 10/96, **10.4%** treated keloids noted to recur within 12 months - 5/10 were clinically significant; 1 additional recurrence by 18 months f/u
- 8/11 recurred within the first 6 months; 2/11 within 6 to 12 months and 1/11 within 12 to 18 months; Kaplan-Meier Survival Probability Estimate **cure rate** of 85.6% from 24 months post-SRT treatment end onwards
- By 18 months, 86/96 SRT-treated keloidectomy sites **specifically** noted whether a recurrence was present (11; **12.7%)** or absent (75; **87.2%)**
- Greater rate of recurrence if keloid had previously recurred or was on chest
- If 1 recurred, not all keloids recurred in patients with multiple treated keloids
Consensus Guidelines on the Use of Superficial Radiation Therapy for Treating Nonmelanoma Skin Cancers and Keloids

11.1 Post-surgical treatment of keloid excision suture lines with several fractions of SRT significantly reduces keloid recurrence rates.

11.2 Fractionation of the SRT dose reduces the risk of hyperpigmentation and other adverse events. The optimal treatment protocol is a biologically effective dose of 3000 cGy in three fractions of 600 cGy on post-operative days 1, 2 and 3.

11.3 There is little evidence that exposing keloid or surrounding healthy skin to SRT at a 3000 cGy dosing causes skin cancer.


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SRT Post-Keloidectomy

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SRT ports for large keloid excision site treatment

12.7 cm diameter 18 cm x 8 cm at 25 cm SSD at 30 cm SSD
Surgical Keloid Excision With/Without External Beam Radiation vs Brachytherapy

- 10 year retrospective analysis
- 264 excised keloids in 128 patients: 28 excised alone, 197 received post-excision EBRT (9-30 Gy over 1-10 daily doses) and 39 received post-excision HDR (8-12 Gy) interstitial Iridium-192 brachytherapy, all but 1 within 36 hrs post excision
- 54% recurred post-excision alone (9m f/u)
- 13% recurred post-excision + EBRT (12m f/u, p < .01)
- 23% recurred post-excision + brachytherapy (12m f/u, p < .01)
- Longer time to keloid recurrence after EBRT than after brachytherapy (mean difference of 2.5 years, p < .01)
- No development of malignancy

Superficial Brachytherapy and Post-Excision Keloid Recurrence

- 36 keloidectomy scars were treated with high-dose-rate superficial brachytherapy after keloidectomy
  - 20 Gy delivered in 3 or 4 daily fractions to 2 mm below skin surface
- 9.7% (3/32) keloid recurrence rate at a median follow-up period of 18 months (range, 9 to 29 months)

Post-Keloidectomy e-Beam Radiotherapy

- Treated 91 keloids with a combination of surgical excision and postoperative electron beam radiation
  - 20 Gy: 5 Fractions (Ear: 16 Gy: 4 Fractions)
- 44% keloid recurrence rate (include symptoms)
Radiation Treatment of Keloids Literature Review for Associated Malignancy

- A computerized literature search of MEDLINE and PubMed Central between 1901 and March of 2009 located 5 cases of carcinogenesis that were associated with radiation therapy for keloids
- Basal cell carcinoma, thyroid carcinoma, breast carcinoma and fibrosarcoma
- However, it was unclear whether an appropriate dose of radiation or sufficient protection were used
- The authors conclude radiation therapy is acceptable as a keloid treatment modality

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Thank you!