Integra…
Overpriced, Understudied, Overrated

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February 6, 2012

Department of Surgery Grand Rounds
University of Colorado
Burn Thickness

- Epidermis
- Dermis
- Subcutaneous Tissue

Superficial

Partial Thickness

Full Thickness
Burn Center Referral Criteria

- Partial Thickness Burns > 10% TBSA
- Face, hands, feet, genitalia, perineum, major joints
- Any full thickness
- Electrical/lightening injury
- Chemical Burns
- Inhalational Injury
- Significant Comorbidities

American College of Surgeons, 2006
Initial Burn Management

• Intubation
  – GCS < 8, stridor/hoarseness, post pharyngeal burns, TBSA > 60%

• Escharotomy
  – Extremity escharotomy for compartment syndrome
  – Torso escharotomy for ↑ PAP

• Resuscitation
  – Parkland = 4 cc x weight (kg) x % TBSA
  – ½ in first 8 hours, second ½ over next 16

• Early excision and grafting
Options for Covering the Extensive Burn Wound

- Autograft
- Allograft
- Integra
- Biobrane
- Transcyte
Integra

**Pros**
- Decrease burn sepsis
- Cosmesis
- Contracture

**Cons**
- Expense
- Graft infection
- Efficacy
Artificial Dermis for Major Burns

  - Prospective, randomized, multicenter trial
  - 139 sites, 106 patients

All controls 95% versus Integra 80%
Important Points

• No mortality data
• No LOS data
• All advantages were based on subjective assessment
  – “Normalcy” of donor site, surgeon’s overall evaluation of graft, etc.

FDA Approval 1996 ➔ Treatment of severe burns
Integra Decreases LOS

• Retrospective review
  – 270 patients with > 20% TBSA burns between 1990 and 2000

J Burn Care Rehab. 2002 (23):5.
### Total Patient Population

<table>
<thead>
<tr>
<th></th>
<th>Control: No Integra&lt;sup&gt;®&lt;/sup&gt;</th>
<th>Treatment: Integra&lt;sup&gt;®&lt;/sup&gt;</th>
<th>t-test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>227</td>
<td>43</td>
<td>NA</td>
</tr>
<tr>
<td>Age (mean ± SD)</td>
<td>46 ± 20 years (range 18–94 years)</td>
<td>50 ± 21 years (range 19–83 years)</td>
<td>P = .24</td>
</tr>
<tr>
<td>Percent BSA Burned</td>
<td>42 ± 22% (range 20–97%)</td>
<td>50 ± 22% (range 25–90%)</td>
<td>P = .02*</td>
</tr>
<tr>
<td>Inhalation injury present</td>
<td>67 patients (30%)</td>
<td>31 patients (72%)</td>
<td>P &lt; .001*</td>
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<tr>
<td>Mortality</td>
<td>69 patients (30%)</td>
<td>13 patients (30%)</td>
<td>P = 1.00</td>
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</table>

### Total Survivors

<table>
<thead>
<tr>
<th></th>
<th>Control survivors</th>
<th>Integra&lt;sup&gt;®&lt;/sup&gt; survivors</th>
<th>t-test</th>
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</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>158</td>
<td>30</td>
<td>NA</td>
</tr>
<tr>
<td>Age</td>
<td>39 ± 15 years</td>
<td>43 ± 15 years</td>
<td>P = .20*</td>
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<tr>
<td>Percent BSA burned</td>
<td>36 ± 17%</td>
<td>51 ± 21%</td>
<td>P &lt; .001*</td>
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<tr>
<td>Inhalation injury present</td>
<td>42%</td>
<td>63%</td>
<td>P = .04*</td>
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<tr>
<td>Escharotomy required</td>
<td>27%</td>
<td>89%</td>
<td>P &lt; .001*</td>
</tr>
<tr>
<td>Number of mortality risk factors present</td>
<td>0.7 ± 0.7</td>
<td>1.4 ± 0.7</td>
<td>P &lt; .001*</td>
</tr>
<tr>
<td>LOS</td>
<td>47 ± 47 days</td>
<td>64 ± 23 days</td>
<td>P &lt; .001†</td>
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</table>
Subgroup Analysis

> 60 years old, > 40% TBSA, inhalational injury, escharotomy

<table>
<thead>
<tr>
<th></th>
<th>No Integra®</th>
<th>Integra®</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number patients</td>
<td>29</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Age (Mean ± SD)</td>
<td>42 ± 18 years</td>
<td>42 ± 20 years</td>
<td>Not significant</td>
</tr>
<tr>
<td>Inhalation injury present</td>
<td>100%</td>
<td>100%</td>
<td>Not significant</td>
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<tr>
<td>Percent BSA burned</td>
<td>59 ± 21% BSA</td>
<td>55 ± 19% BSA</td>
<td>Not significant</td>
</tr>
<tr>
<td>Full-thickness burn (percent BSA excised and grafted)</td>
<td>44 ± 19% BSA</td>
<td>45 ± 16% BSA</td>
<td>Not significant</td>
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<tr>
<td>Percent BSA grafted with Integra®</td>
<td>0</td>
<td>19 ± 13% BSA</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Percent of patients who required escharotomies</td>
<td>55%</td>
<td>93%</td>
<td>0.009 †</td>
</tr>
<tr>
<td>Time-to-clinically effective wound closure</td>
<td>79 ± 60 days</td>
<td>49 ± 14 days</td>
<td>0.11*</td>
</tr>
<tr>
<td>LOS</td>
<td>107 ± 60 days</td>
<td>63 ± 18 days</td>
<td>0.014*</td>
</tr>
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• Integra group all treated after 1996
  • Historical controls
  • ICU critical pathways established
  • ARDS net developed
  • Decreased OR time
  • Surgeon practice patterns changed
Postapproval Clinical Trial

- Prospective, observational study of 222 patients
  - No control arm... all patients received Integra
- 13.2% superficial infections
- 3.1% invasive infections
- 76.2% take

Increased infections and decreased take
Integra in Pediatric Populations

• Crit Care Med. 2007 (35):11.
  – Prospective, randomized trial
  – 10 children per arm
  – Integra decreased energy expenditure, increased bone density and biochemical markers
  – No difference in sepsis
  – 20% increase in cosmetic score

Statistically significant, clinically irrelevant
Debunking Allograft Myths

- Only 1 reported case of HIV transmission (none since 1987)
- No reported cases of hepatitis transmission
- Scant evidence for CMV seroconversion
- Tissue Banking increasing
Integra Cost

- $11/cm^2
- 6’ 180 lb male = ~2 m^2
- For 40% TBSA burn = $88,000
Summary

- Integra
  - No proven efficacy
  - Infection rates increased compared to allograft
  - Expensive
  - Minimal cosmetic benefit
  - Cost prohibitive
Conclusion

Integra has no proven efficacy and is cost prohibitive as a mainstray in the treatment of severe thermal injuries