Integra: A Valuable Cost Effective Tool in Burn Care

Grand Rounds
2/6/11
Matthew Fox
R3
How will I get this covered?
What Is Integra?

- 2 Layered Dermal Regeneration Template
  - Epidermal Substitute – Silicone
  - Dermal Substitute - Porus matrix of fibers of cross-linked Collagen/Glycosaminoglycan (GAG) (type 1 bovine tendon collagen/chondroitin 6-sulfate)
    - Serves as matrix for infiltration of fibroblasts, macrophages, lymphocytes and capillaries

- Not A Substitute for Autograft

- $2000 for 8 x 10 inch sheet!!!!!!
Clinical Sequence

Day 1

Day 7-14
Clinical Sequence
Integra
Integra
Integra
Integra
Integra
Integra
“Artificial Dermis for Major Burns – A Multi-Center Randomized Clinical Trial”

- 11 Burn centers, 106 patients with 136 burn sites
- Extensive flame or scald burns with life-threatening injuries
- Average TBSA burn - 46%
- Artificial Dermis vs Control Sites (Autograft/Allograft)
“Artificial Dermis for Major Burns – A Multi-Center Randomized Clinical Trial”

**Fig. 3.** Graphic representation of “take” of artificial dermis compared with all control sites.

**Fig. 4.** Graphic representation of “take” of artificial dermis compared with cadaver allograft.
“Artificial Dermis for Major Burns – A Multi-Center Randomized Clinical Trial”

- Donor Sites
  - .013” vs. .006”
  - Average Healing Time 14.3 days vs. 10.6 days
    - More Often Re-excised Epidermis

- Subjective Assessment
  - 72 % “more normal”
  - 42% less hypertrophic scarring (57% the same)
“Artificial Dermis for Major Burns – A Multi-Center Randomized Clinical Trial”

Conclusions

- Better appearing wound than widely meshed autograft
- “Takes” as well as other Allograft substitutes
- Does not reject or need to be removed
- Very thin donor sites
- No increased hospital stay for extensive burns
- NOT TO BE USED IN PLACE OF AUTOGRRAFT
“Multicenter Clinical Trial of Integra Dermal Regeneration Template for Burn Treatment”

- 216 Patients with 841 burn sites From 13 burn centers over 2 year period
- Full Thickness or Deep Partial Thickness Burns
- End Points:
  - Infection at Integra treated sites
  - Integra and thin epidermal autograft take
“Multicenter Clinical Trial of Integra Dermal Regeneration Template for Burn Treatment”

Figure 3. Percentages of burn wound sites at which various percentages of take were observed for (A) Integra and (B) thin epidermal autograft placed over Integra.

Figure 2. Incidence of superficial, invasive and total infection at sites receiving (A) Integra® and (B) thin epidermal autograft subsequent to Integra®. Error bars represent 95% confidence intervals.
“Multicenter Clinical Trial of Integra Dermal Regeneration Template for Burn Treatment”

- Infection 13.9% Integra / 3.4% Integra plus Autograft
- Take 76.2% Integra / 87.7% Integra plus Autograft

Conclusion

- Infection and Take rates acceptable in extensively burned patients
- Integra take improved with application protocols
“Use of Integra Artificial Skin is Associated with Decreased Length of Stay for Severely Injured Adult Burn Survivors”

- 270 Acutely Burned Patients, > 20% TBSA Burn
- Integra only used with full thickness burns
- Primary End Points
  - Mortality
  - Length of Stay
  - Time to wound closure
“Use of Integra Artificial Skin is Associated with Decreased Length of Stay for Severely Injured Adult Burn Survivors”

Table 2. Characteristics of surviving patients comparing patients treated with Integra® and those who were not

<table>
<thead>
<tr>
<th></th>
<th>Control survivors</th>
<th>Integra® survivors</th>
<th>t-test</th>
</tr>
</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>
</tr>
<tr>
<td>Percent BSA burned</td>
<td>36 ± 17%</td>
<td>51 ± 21%</td>
<td>P &lt; .001*</td>
</tr>
<tr>
<td>Inhalation injury present</td>
<td>42%</td>
<td>63%</td>
<td>P = .04*</td>
</tr>
<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>
</tr>
</tbody>
</table>

* Student’s t-test.

Note that while Integra® patients stayed longer, they were older, they had significantly more extensive burns, more inhalation injury, more often required escharotomy and had a higher number of mortality risk factors present than the control survivors. Because of this, a longer length of stay would be expected in the Integra® patients based on a previous statistical model, possibly masking a treatment effect of Integra® on length of stay.

LOS, length of stay; NA, not applicable
† Wilcoxon signed-rank test.

Mortality Risk Factors: age > 60, total burn area > 40%, inhalation injury
“Use of Integra Artificial Skin is Associated with Decreased Length of Stay for Severely Injured Adult Burn Survivors”

**Table 3. Results of survivor LOS subgroup analysis**

<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>
</tr>
<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>
</tr>
<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>
</tbody>
</table>

*LOS, length of stay.*

* Wilcoxon signed-rank test.

Characteristics of surviving patients with burn size ≥20% BSA and with ≥2 risk factors present stratified by treatment with Integra® during their acute burn course.

† Student’s t-test.
“Use of Integra Artificial Skin is Associated with Decreased Length of Stay for Severely Injured Adult Burn Survivors”

- Integra is associated with decreased hospital stay (potentially decreased cost) in the most severely injured burn patients
- No difference in mortality
Longitudinal assessment of Integra in primary burn management:
A randomized pediatric clinical trial*

- Burn size 50% TBSA and 40% TBSA full-thickness burn
- Patients admitted within 72 hrs of injury
- Patients not septic at admission
- Randomized to Integra vs Conventional Autograft, Allograft
- 10 patients in each arm (7 died)
Longitudinal assessment of Integra in primary burn management:
A randomized pediatric clinical trial

- Cardiac Function (heart rate, stroke volume, CI using echo)
- Liver Size (Ultrasound)
- Metabolism (resting energy expenditure, basal metabolic rate)
- Body Composition (Total weight, lean body mass, bone mineral content, and bone mineral density)
- Sepsis score/Infection rate
- Cosmetic Appearance (4 blinded clinicians)
- Functional Outcome and Cost (OR time, number of reconstructive procedures up to 2 years out)
Longitudinal assessment of Integra in primary burn management:
A randomized pediatric clinical trial

- Cardiac Function - No Difference
- Liver Size Metabolism – No Difference
- Metabolism – Transferrin and Albumin Significantly Improved with Integra
- Body Composition – Trend Towards Improvement with Integra
- Sepsis score/ Infection rate – No Difference
- Cosmetic Appearance - Improved 12,18,24 month appearance
Longitudinal assessment of Integra in primary burn management: A randomized pediatric clinical trial
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- Metabolism – Transferrin and Pre-Albumin Significantly Improved with Integra
- Body Composition – Trend Towards Improvement with Integra
- Sepsis score/ Infection rate – No Difference
- Cosmetic Appearance - Improved 12,18,24 month appearance
- Functional Outcome and Cost – No Difference
Conclusions

- Integra is an important tool for difficult large burns
- Improved appearance, less hypertrophic scar
- Much thinner donor sites
- "Take" rates similar to allograft
- No change in mortality
- Possible decrease length of stay in large burns