Wound Healing Revealed by a Novel Automated Indentation Technique

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Disclosure

Eric Quenneville and Martin Garon are the cofounders of the company Biomomentum Inc.
The desire in wound healing is to regenerate tissues in a manner that the functional and structural properties of the wounded tissue are restored. Additionally, the appearance of the scar shall be intact.
Introduction

Additionally, there is a desire to reduce the appearance of the scar.

Images taken from www.dillerlaw.com
Introduction

Conventional mechanical test

Sample  Excised strips  Uniaxial tensile tests

Invasive  Disruptive

Only tensile test as an indicator of the wound healing state is insufficient
Introduction

Proposed mechanical test

Sample

Indentation tests

Non-destructive

Preserves the integrity of the surrounding tissue of the wound while testing
In this study, we wanted to test the ability of a novel automated indentation technique to non-destructively characterize mechanical properties of the entire wound and its integration with the surrounding skin.
Methods

Samples

- 2 wounded pig skin samples
- Size: 4 x 8 cm
- Centered 3 cm incision length
Methods

Mechanically controlled surface mapping

- Camera-registration system
- Top view image
- Position grid superimposed
- Conversion of position coordinates pixels into metrics
Methods

Automated Indentation Equipment

Multiaxial mechanical tester
Mach-1 v500css
Biomomentum Inc.

Spherical indenter
diameter=6.35mm
Excision of strips for tensile test

Excised dumbbell-shape strips were taken adjacent to each other in a vertical plane.
Methods

Indentation at each position

- Non-invasive **thickness measurement** was performed by finding the contact of the skin surface at each position prior to indentation
- Indentation tests at each position
- **Indentation** amplitude of 1.7 mm at 0.2 mm/s
Methods

Uniaxial tensile test

- Each strip was **installed in fixtures** and then **mounted** on the chamber plate of the mechanical tester.
- The mechanical tester applied a gradually **increasing tensile load** until tissue rupture.
Results

Mapping of maximum load and thickness

High-resolution mapping of maximum load and thickness were generated (about 30s per position).

These mappings revealed significant spatial variation of the mechanical properties and thickness over the wound region compared to the uniform properties of the intact skin observed at least 1cm away from the incision site.
**Results**

**Quantitative assessment**

- **Softer scar tissue** (region I) than the surrounding skin (region II and region III).
- For the thickness, the scar is found thicker (region I) with a progressive thinner tissue in region II and in region III.

<table>
<thead>
<tr>
<th>Region</th>
<th>Maximum Load</th>
<th>Thickness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Region I</td>
<td>3.2 ± 2.4 N (n=36)</td>
<td>5.0 ± 0.6 mm (n=36)</td>
</tr>
<tr>
<td>Region II</td>
<td>6.3 ± 6.0 N (n=53)</td>
<td>4.2 ± 0.6 mm (n=53)</td>
</tr>
<tr>
<td>Region III</td>
<td>13.3 ± 5.3 N (n=72)</td>
<td>3.5 ± 0.2 mm (n=72)</td>
</tr>
</tbody>
</table>
Results

Quantitative assessment

The mechanical properties of region I and region II are higher than region III.
The thickness of all three regions are similar.

<table>
<thead>
<tr>
<th>Region</th>
<th>Maximum Load (N)</th>
<th>Thickness (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Region I</td>
<td>11.7 ± 6.7</td>
<td>3.5 ± 0.3</td>
</tr>
<tr>
<td>Region II</td>
<td>12.4 ± 8.1</td>
<td>3.6 ± 0.3</td>
</tr>
<tr>
<td>Region III</td>
<td>6.7 ± 2.9</td>
<td>3.6 ± 0.1</td>
</tr>
</tbody>
</table>
Results

Quantitative hypertrophy/atrophy through thickness

Scar A revealed a 12.25 mm²/mm of wound hypertrophy while scar B does not reveal significant hypertrophy.
Results

Load at rupture

<table>
<thead>
<tr>
<th>Scar</th>
<th>Load at rupture (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A-a</td>
<td>2053</td>
</tr>
<tr>
<td>A-b</td>
<td>2266</td>
</tr>
<tr>
<td>B-a</td>
<td>2922</td>
</tr>
<tr>
<td>B-b</td>
<td>3729</td>
</tr>
</tbody>
</table>
## Results

### Indentation vs Tensile properties

<table>
<thead>
<tr>
<th>Scar</th>
<th>Tensile Load at rupture (g)</th>
<th>Indentation Maximum Load (N)</th>
<th>Thickness (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scar A-a</td>
<td>2053</td>
<td>1.71</td>
<td>5.08</td>
</tr>
<tr>
<td>Scar A-b</td>
<td>2266</td>
<td>3.21</td>
<td>4.80</td>
</tr>
<tr>
<td>Scar B-a</td>
<td>2922</td>
<td>7.13</td>
<td>3.87</td>
</tr>
<tr>
<td>Scar B-b</td>
<td>3729</td>
<td>12.79</td>
<td>3.49</td>
</tr>
</tbody>
</table>

A trend could be observed between the thickness and the maximum load obtained in indentation and the load at rupture obtained in tension.

- As the sample is thinner ➞ a higher load in indentation and at rupture
- As the sample is thicker ➞ a lower load in indentation and at rupture
Conclusion

These preliminary results indicate that performing different mechanical tests on wounded skin samples provide complementary information to quantify the healing outcomes.

- Tension rupture test provides insight on the basic mechanical function of the scar along its surface (maintaining the wound closed).

- Novel automated indentation mapping technique was able to reveal the spatial variation in the compressive stiffness and thickness of the scar and its surrounding. These mappings could be used to quantify other characteristics of the scar like an hypertrophic healing or the presence of stiffer scar tissue.
• Since the novel technique is non-destructive for the sample, it allows additional analyses (tensile, relaxation or shear mechanical tests, histology or biochemical assessment) to be performed at matched positions.

• This high spatial resolution and non-destructive technique provides new opportunities when studying wound healing where the number of animals involved could be significantly reduced.
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Questions