WE ARE HERNIA CARE. PROVEN RESULTS. IMPROVING LIVES.

Key parameters driving mesh performance
DEDICATED TO IMPROVING QUALITY OF LIFE

Today, our therapies improve the lives of more than two people every second.† But therapies alone are not enough. The current model of healthcare delivery is no longer sustainable. That’s why we’re working with hospitals and health systems to restructure processes, challenge the status quo, and truly transform healthcare. It’s how we’re taking healthcare Further, Together.

†Derived from Medtronic Corporate data.
DEDICATED TO IMPROVING QUALITY OF LIFE

70 MILLION LIVES IMPROVED THIS YEAR†

†Derived from Medtronic Corporate data.

160 COUNTRIES

370+ LOCATIONS

84,000+ EMPLOYEES

92 MANUFACTURING FACILITIES

4,600+ PATENTS AWARDED

†Derived from Medtronic Corporate data.
We offer a truly comprehensive hernia repair portfolio with product options spanning mesh, fixation, dissection, and biologics. You can create the complete mix of products to meet your procedural and economic needs.
TWO MILLION+
Units of meshes using ProGrip™ mesh technology manufactured since 2007

ONE MILLION+
Units of Parietex™ composite mesh manufactured between 1999 and 2017

800,000+
units manufactured annually

200 patents awarded

HEMNIA COMPLETE SOLUTIONS FOR SUCCESSFUL RESULTS

5 Key parameters driving mesh performance | September 2019
INNOVATIVE HERNIA REPAIR SOLUTIONS
YEAR AFTER YEAR

1988
Established Hernia Care base

1999
WORLD’S FIRST
Parietex™ composite mesh

2000
WORLD’S FIRST
Created laparoscopic dissection

2006
Pioneered absorbable fixation

2006
WORLD’S FIRST
ProGrip™ self-gripping polypropylene mesh

2008
Entered biologics market

2012
Established R&D center of excellence

2013
WORLD’S FIRST
Symbotex™ composite mesh

2014
ReliaTack™ articulating reloadable fixation device

6 Key parameters driving mesh performance | September 2019
ADVANCING HERNIA CARE WITH QUALITY MESH PRODUCTS

HERNIA MESH AND BIOLOGIC IMPLANTS MANUFACTURED IN TREVOUX, FRANCE

Employees in advanced manufacturing engineering, regulatory, clinical affairs, marketing, and project management.

Key parameters driving mesh performance | September 2019
Primitive Surgery:
- 2500 BC: Hernia cure described on papyrus. Use of bandages and plasters (e.g., textile, metal)
- 1st Century (AD): First description of surgical resections by Celsus (Rome)
- Henri de Mondeville (1314 AD), Cyrurgia, mainly dedicated to hernia
- Renaissance: Invasive surgery for hernia cure (castration mainly)

Historical Shift: Anesthesia (1848) and Aseptic Field (1867–1873)
- 1871: First invasive hernia cure using suture (Henry Marcy): 100 percent of recurrence at 4 years
- 1884: Assini optimizes hernia cures based on patient complex anatomy: 30 percent recurrence at 4 years
Surgery « Tension Free »:

- 1900: First silver mesh
- 1958: Polypropylene (PP) mesh (Usher)
- 1967: Rives and Stoppa use the first polyethylene terephthalate (PET) mesh
- 1987: Lichtenstein developed a tension-free hernioplasty
- 1987: Gristina describes the Race for the Surface
- 1999: First dualsided composite mesh for IPOM (Parietex™ Composite Mesh)
- 2006: ProGrip™ mesh technology
- 2015: Move towards robotic procedures
INTEGRATION CASCADE$^{3-6}$

Objective: reduce intensity and time of inflammatory period

†Results based on animal data. Results may not correlate to performance in humans.
Expected outcomes for an optimal repair

**LIMITED SCARRING**
**COMFORT AND DURABILITY**
**QUICK INTEGRATION**
**MINIMIZING VISCERAL ATTACHMENT**

Key mesh properties

**MAXIMIZED POROSITY**
**MECHANICAL PROPERTIES**
**ENHANCED HYDROPHILICITY**
**DUAL SIDED MESHES**
POROSITY AND TISSUE INGROWTH\textsuperscript{7–9}

\textbf{Microporosity\textsuperscript{†}:}

\textbf{Macroporosity\textsuperscript{†}:}

\textbf{Pore shape\textsuperscript{†}:}

\texttt{> 10 \(\mu\text{m}\)}

\texttt{\geq 1.5 \text{mm}}

\texttt{Hexagonal limits deformation under strain}

\texttt{Cellular penetration Limited encapsulation}

\textsuperscript{†}Based on preclinical animal data. Results may not correlate to performance in humans.
MESH POROSITY INFLUENCES INGROWTH AND SHRINKAGE$^{10,11}$

Key parameters driving mesh performance | September 2019
LOW WEIGHT DOES NOT GUARANTEE LARGE PORES\textsuperscript{12–14}

<table>
<thead>
<tr>
<th>Specifications</th>
<th>Parietex\textsuperscript{™} optimized composite mesh</th>
<th>Symbotex\textsuperscript{™} composite mesh</th>
<th>Physiomesh\textsuperscript{™} open flexible composite mesh</th>
<th>Ventralight\textsuperscript{™} ST mesh</th>
</tr>
</thead>
<tbody>
<tr>
<td>Textile type</td>
<td>Polyester multifilament</td>
<td>Polyester monofilament</td>
<td>Polypropylene monofilament</td>
<td>Polypropylene monofilament</td>
</tr>
<tr>
<td>Weight (g/m\textsuperscript{2})</td>
<td>78</td>
<td>66</td>
<td>29</td>
<td>57</td>
</tr>
<tr>
<td>Thickness (mm)</td>
<td>1.7</td>
<td>0.7</td>
<td>0.5</td>
<td>0.4</td>
</tr>
<tr>
<td>Pore size (mm) (h x l)</td>
<td>2.4 x 2.0 2.5 x 2.1</td>
<td>2.3 x 3.3</td>
<td>3.5 x 3.4</td>
<td>0.7 x 0.5 1.0 x 0.6</td>
</tr>
</tbody>
</table>
BUT LOWERING THE WEIGHT IMPACTS MESH STRENGTH

- Having large pore does not require having to accept low weight (surface density)

- Tensile strength (minimum) and surface density are correlated
CONNECTING OUTCOME TO ATTRIBUTES

Expected outcomes for an optimal repair

- Limited scarring
- Comfort and durability
- Quick integration
- Minimizing visceral attachment

Key mesh properties

- Maximized porosity
- Mechanical properties
- Enhanced hydrophilicity
- Dual sided meshes
COMBINED ENLARGED POROSITIES AND ROBUST MECHANICAL PROPERTIES INTENDED TO OFFER OPTIMAL REPAIR \(^{12,†}\)

Symbotex™ Composite Mesh

<table>
<thead>
<tr>
<th>Specifications</th>
<th>Parietex™ optimized composite mesh</th>
<th>Symbotex™ composite mesh</th>
<th>Physiomesh™ open flexible composite mesh</th>
<th>Ventralight™ ST mesh</th>
</tr>
</thead>
<tbody>
<tr>
<td>Textile type</td>
<td>Polyester multifilament</td>
<td>Polyester monofilament</td>
<td>Polypropylene monofilament</td>
<td>Polypropylene monofilament</td>
</tr>
<tr>
<td>Tensile breaking strength (N)</td>
<td>253</td>
<td>138</td>
<td>225</td>
<td>158</td>
</tr>
<tr>
<td>Suture pull-out strength (N)</td>
<td>30</td>
<td>46</td>
<td>39</td>
<td>44</td>
</tr>
<tr>
<td>Tear strength (N)</td>
<td>29</td>
<td>25</td>
<td>34</td>
<td>32</td>
</tr>
<tr>
<td>Elongation under 50N (%)</td>
<td>19</td>
<td>61</td>
<td>25</td>
<td>37</td>
</tr>
</tbody>
</table>

†Results based on internal bench tests.
CONNECTING OUTCOME TO ATTRIBUTES

Expected outcomes for an optimal repair

- LIMITED SCARRING
- COMFORT AND DURABILITY
- QUICK INTEGRATION
- MINIMIZING VISCERAL ATTACHMENT

Key mesh properties

- MAXIMIZED POROSITY
- MECHANICAL PROPERTIES
- ENHANCED HYDROPHILICITY
- DUAL SIDED MESHES
HYDROPHILICITY AND CELL ATTACHMENT

THE FIRST TO REACH THE SURFACE HAS A SIGNIFICANT ADVANTAGE
HYDROPHILIC SURFACES IMPROVE CELL ADHESION AND PROLIFERATION

The higher contact angle implies the more hydrophobic surface

Hydrophilic \( \theta < 90^\circ \)

Hydrophobic \( \theta > 90^\circ \)

\[ \begin{align*}
\text{Col} & : 52^\circ \\
\text{PET} & : 75^\circ * \\
\text{PP} & : 90^\circ ** \\
\text{PTFE} & : 105^\circ
\end{align*} \]

Cell number on the shallow gradient after days 1 (--), 2 (--) and 3 (--) plotted against the corresponding Water Contact Angle (WCA)

†Internal measurements.
HYDROPHILICITY AND CELL ATTACHMENT†

In vitro fibroblasts’ proliferation on bicomponent textiles

PET/PLA WCA 75°

PP WCA 90°

Hydrophilic

Hydrophobic

† Based on internal data.
BACTERIA ARE INDIFFERENT TO SURFACE HYDROPHILICITY$^{21,22,†}$

Staph A. proliferation on bicomponent textiles

†Results based on internal bench tests.
CONNECTING OUTCOME TO ATTRIBUTES

Expected outcomes for an optimal repair

- Limited scarring
- Comfort and durability
- Quick integration
- Minimizing visceral attachment

Key mesh properties

- Maximized porosity
- Mechanical properties
- Enhanced hydrophilicity
- Dual sided meshes
MINIMIZING TISSUE ATTACHMENT

Surgical trauma of serosal surfaces ± foreign body

Vascular phase of the inflammation → fibrin exsudate

Fibrin bridges between injured surfaces

Healing remodelling → fibrous adhesions

Key parameters driving mesh performance | September 2019
MINIMIZING TISSUE ATTACHMENT

Key parameters driving mesh performance

- Surgical trauma of serosal surfaces ± foreign body
- Vascular phase of the inflammation → fibrin exudate
- Mesh integration + neoperitoneum

Barrier effect
Barriers:
- Resorbable films
- (e.g., Collagen, Polyesters)

Abdominal wall reinforcement:
- Macroporous permanent mesh (e.g., Polyester, Polypropylene)

Minimizing visceral attachment and facilitating tissue ingrowth\textsuperscript{24,25,†}

†Based on preclinical study. Results may not correlate to performance in humans.
Polyester versus Collagen versus expanded Polytetrafluoroethylene (ePTFE) barrier (D7)

Absorbable Collagen barrier WCA 52°

Absorbable Polyester barrier WCA 72°

Permanent ePTFE barrier WCA 105°

†Based on internal data.
Parietex™ composite mesh: 1 week after implantation†,‡

Hydrogel film
Mesh superficial thread
Mesh deep thread
Abdominal wall

Neoformed mesothelial layer
Active tissue ingrowth

†Results based on animal data. Results may not correlate to performance in humans.
‡Based on internal data.
After resorption of the hydrogel film†

Mesh superficial thread

Mesh deep thread

Abdominal wall

Continuous neoperitoneum

Differentiated tissue in-growth

Intimate attachment of the mesh to the wall

Transversal section 6 weeks after implantation

†Results based on animal data. Results may not correlate to performance in humans.
MINIMIZING VISCERAL ATTACHMENT: KEY FOR SAFETY

Parietex™ composite mesh: scanning electronic microscopy (SEM) after 6 weeks†‡

Mesh covered by a continuous neoperitoneum

Non-reinforced abdominal wall

Differentiated mesothelial cell

Mesothelial layer

Mesh fibers

Connective tissue ingrowth

†Results based on animal data. Results may not correlate to performance in humans.
‡Based on internal data.
PERFORMANCE OF DIFFERENT BARRIERS$^{24,25,*}$

†Results based on animal data. Results may not correlate to performance in humans.
Adhesion coverage of mesh surface at 7 days in an animal model

†Results based on animal data. Results may not correlate to performance in humans.
COMPLETE TISSULAR INTEGRATION FREE FROM EXTENSIVE INFLAMMATION\textsuperscript{16,†}

Symbotex™ Composite Mesh

Neoperitoneum \quad \text{Tissue ingrowth in the pores without fibrosis}

Fascia transversalis \quad \text{Retroperitoneal space} \quad \text{Minimized inflammation limited to the yarns}

\textsuperscript{†}Results based on animal data. Results may not correlate to performance in humans.
COMPLETE TISSULAR INTEGRATION FREE FROM EXTENSIVE INFLAMMATION

Parietene™ DS Composite Mesh

Parietene™ DS composite mesh **8 weeks**

- Neoperitoneum
- Tissue ingrowth in the pores without fibrosis
- Polypropylene monofilament yarn
- Fascia transversalis
- Minimized inflammation limited to the yarns

†Results based on animal data. Results may not correlate to performance in humans.
MARKED INFLAMMATION LEADING TO FIBROTIC CAPSULE\textsuperscript{26}

Ventralight\textsuperscript{TM*} ST Mesh

†Results based on animal data. Results may not correlate to performance in humans.
Physiomesh™ Flexible Composite Mesh

†Physiomesh™ flexible composite mesh was removed from the market by its manufacturer.
‡Results based on animal data. Results may not correlate to performance in humans.
THE IDEAL MESH

Expected outcomes for an optimal repair

- LIMITED SCARRING
- COMFORT AND DURABILITY
- QUICK INTEGRATION
- MINIMIZING VISCERAL ATTACHMENT

Key mesh properties

- MAXIMIZED POROSITY
- MECHANICAL PROPERTIES
- ENHANCED HYDROPHILICITY
- DUAL SIDED MESSES

- Meshes long term tolerance depends on their physical and mechanical properties
- Macroporosity should reach 1.5 mm for optimal tissue ingrowth and shrinkage minimization\(^27\)
- The weight, as sole parameter, does not matter
- When in contact with viscera, the meshes should be protected by a continuous smooth barrier to minimize visceral attachment adhesions
- Smooth and continuous resorbable barriers outperform hydrophobic permanent barriers in preclinical models
**OUR MESH TECHNOLOGIES**

Complete solutions for all types of hernias

<table>
<thead>
<tr>
<th>Symbotex™ composite mesh</th>
<th>Parietex™ optimized composite mesh</th>
<th>Parietene™ DS composite mesh</th>
<th>Parietex™ composite ventral patch</th>
<th>Versatex™ monofilament mesh</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Symbotex image" /></td>
<td><img src="image2" alt="Parietex optimized image" /></td>
<td><img src="image3" alt="Parietene DS image" /></td>
<td><img src="image4" alt="Parietex ventral patch image" /></td>
<td><img src="image5" alt="Versatex monofilament image" /></td>
</tr>
<tr>
<td>ProGrip™ self-gripping polyester mesh</td>
<td>Parietene™ macroporous mesh</td>
<td>Parietex™ hydrophilic anatomical mesh</td>
<td>ProGrip™ laparoscopic self-fixating mesh</td>
<td>Duatene™ bilayer mesh</td>
</tr>
<tr>
<td><img src="image6" alt="ProGrip image" /></td>
<td><img src="image7" alt="Parietene macroporous image" /></td>
<td><img src="image8" alt="Parietex hydrophilic image" /></td>
<td><img src="image9" alt="ProGrip laparoscopic image" /></td>
<td><img src="image10" alt="Duatene bilayer image" /></td>
</tr>
</tbody>
</table>

38 Key parameters driving mesh performance | September 2019
We have a team of 1,500 people at one of our largest manufacturing facilities. We’re dedicated to making quality surgical products that can be trusted by surgeons and patients around the globe.
COMPLETE RANGE OF FIXATION DEVICES

AbsorbaTack™ fixation device
Strong, temporary mesh fixation, leaving no foreign material in the body over time\textsuperscript{28,29}

ReliaTack™ articulating reloadable fixation device
A fixation device with a one-of-a-kind articulating technology, interchangeable reloads, and screw-like tack designs for hernia repair

ProTack™ fixation device
A sterile, single-use device for fixation of prosthetic materials, such as hernia mesh, to soft tissue
AbsorbaTack™ fixation device

ReliaTack™ articulating reloadable fixation device
Mesh shift following laparoscopic ventral hernia repair. Liang MK, Clapp ML, Garcia A, Subramanian A, Awad SS.

ProTack™ fixation device
Prospective randomized trial of mesh fixation with absorbable versus nonabsorbable tacker in laparoscopic ventral incisional hernia repair. Colak E, Ozlem N, Kucuk GO, Aktimur R, Kesmer S, Yildirim K.
REFERENCES


REFERENCES

24. Based on NAMSA Study #198929. Minimizing tissue attachment barrier performance, local tissue effects and tissue integration of Parietene™ DS composite mesh in a rat cecal abrasion model. Based on occurrence rates of cecal soft tissue attachment to the mesh through macroscopic observations in the rat (n = 18 test articles versus n = 12 bare mesh; p < 0.05). Oct. 2016.
REFERENCES

25. Based on internal test report #162750, Evaluating local tissue effects, tissue integration and minimizing tissue attachment performance of Symbotex™ composite mesh versus Parietex™ optimized composite mesh. May 2013.


WE ARE HERNIA CARE.
PROVEN RESULTS.
IMPROVING LIVES.