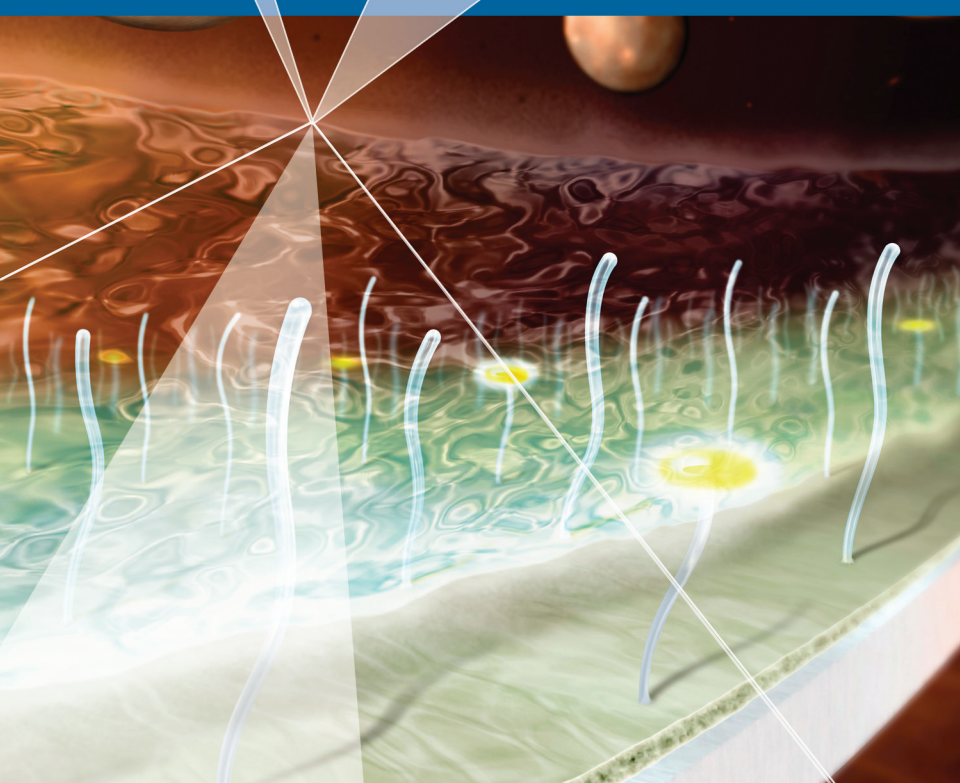
Medtronic

Balance™ Biosurface

Balance



Why use biocompatible surfaces for extracorporeal circulation circuits?

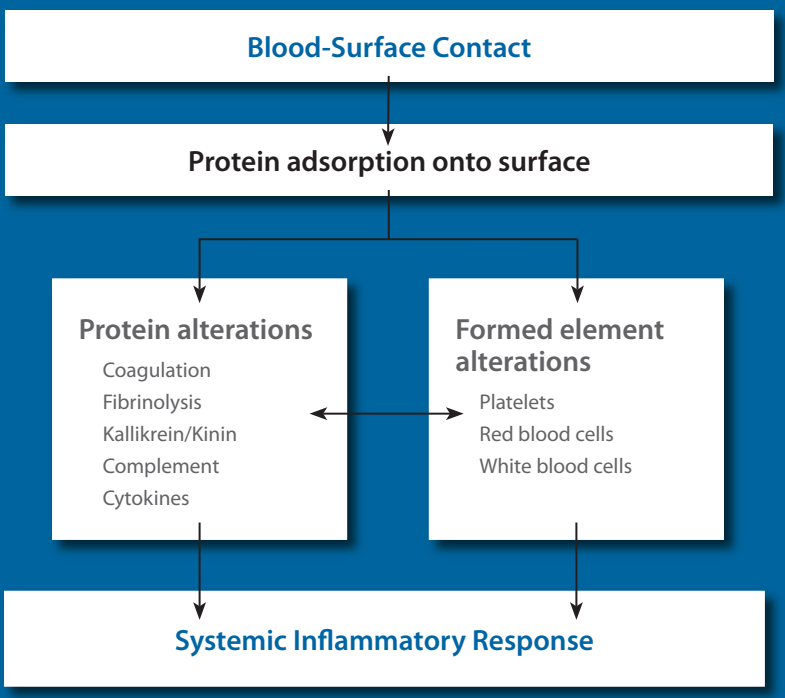
Blood is naturally compatible with vascular endothelium, not artificial surfaces

Blood is compatible with the healthy vascular endothelium, a single layer of cells that lines all blood vessels and the heart.

The endothelium plays an active biological role in maintaining homeostasis, or a balance, among the various body defense systems in a manner that simultaneously provides a state of readiness and avoids the trigger of adverse responses. [1,2]

The blood-contacting surfaces of endothelial cells are highly negatively charged, a characteristic that may repel the negatively charged platelets and be important in limiting the hemostatic reaction.[3]

Responses to Blood-Material Contact



Blood recognizes the extracorporeal circuit surfaces as "foreign," triggering coagulation and inflammatory events that may lead to adverse patient outcomes

Within seconds of blood exposure to artificial, non-endothelial surfaces, there is a rapid adsorption of proteins from the blood onto the surface of the foreign material.[4]

Adsorption onto a surface may result in protein denaturation, such as the denaturation of adsorbed fibrinogen, and ultimately lead to activation of the plasma proteolytic systems.[1] Subsequent events, including cell adhesion, are mediated by the adsorbed protein layer.[1]

The blood's formed elements and other specific protein groups in the blood that are associated with the body's defense systems may then interact with the material and its new protein layer.[1,2]

Ultimately, the biological reactions associated with the defense systems may affect the heart, lungs, brain and other organs, causing conditions that have been described as the "systemic inflammatory response syndrome."[5]

Biocompatible surfaces for Medtronic extracorporeal circulation technologies mimic critical characteristics of the vascular endothelium

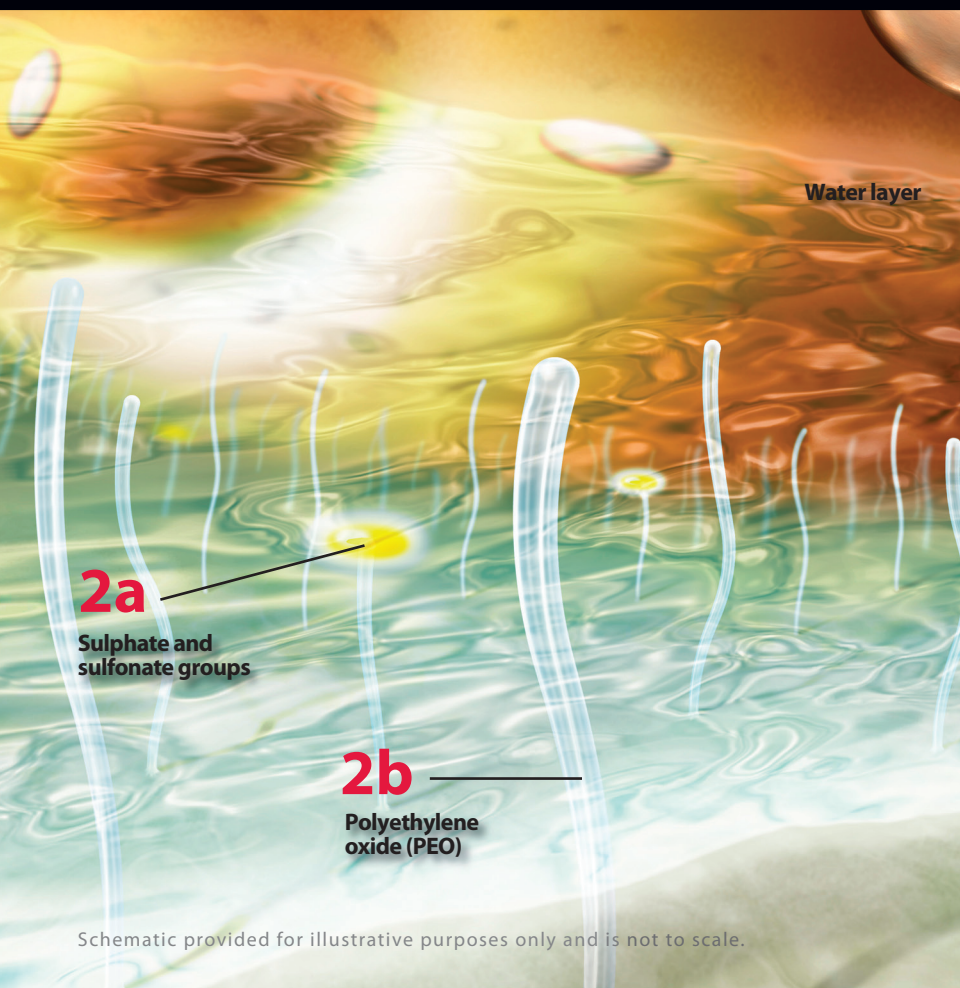
These biocompatible surfaces mitigate the foreign body response that occurs when blood comes in contact with non-endothelial surfaces.

Around the world, leading cardiovascular surgery teams adopt biocompatible surfaces offered by Medtronic as a critical component of comprehensive, multi-modal strategies to achieve the best possible outcomes for their patients undergoing extracorporeal circulation.

Balance™* Biosurface is a hydrophilic polymer coating without heparin for cardiopulmonary bypass circuit devices that reduces platelet adhesion and activation and preserves platelet function. Representing Medtronic's commitment to perfusion solutions, Balance Biosurface expands options used by cardiovascular surgery teams for comprehensive strategies to achieve the best possible outcomes for their patients undergoing cardiopulmonary bypass.

Warning: A strict anticoagulation protocol should be followed and anticoagulation should be routinely monitored during all procedures. The benefits of extracorporeal support must be weighed against the risk of systemic anticoagulation and must be assessed by the prescribing physician.

Caution: Federal law (USA) restricts devices coated with Balance™ Biosurface to sale by or on the order of a physician. For a listing of indications, contraindications, precautions and warnings, please refer to the Instructions for Use which accompanies each product.



Schematic provided for illustrative purposes only and is not to scale.

1 Prime coat

A priming layer is strongly bonded to the artificial surface.

2 Functional layer

The hydrophilic ("water loving") functional layer is strongly bonded to the prime coat and provides the key endothelial-like benefits for the blood contacting surfaces of cardiopulmonary bypass circuits:

2a *Negative charge*

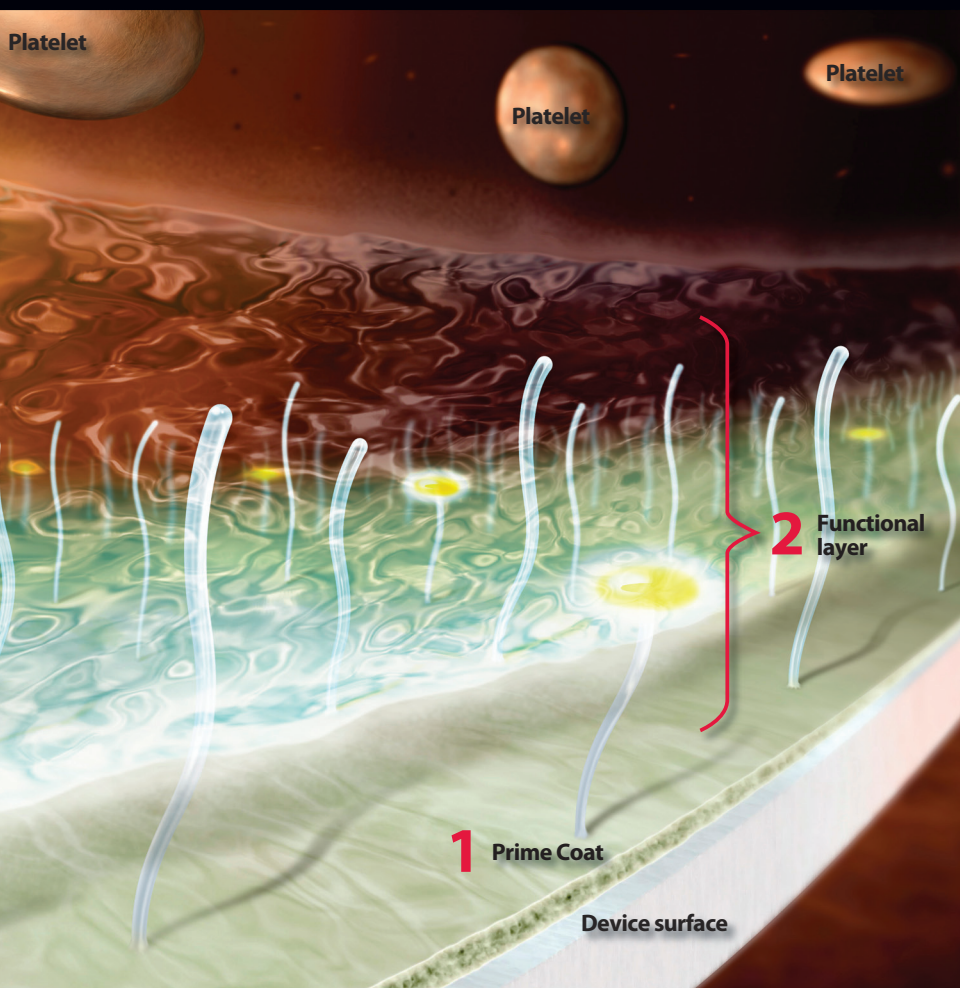
Sulphate and sulfonate groups are incorporated into the Balance Biosurface functional layer to mimic the negative charge of the vascular endothelium.

Research reports that negatively-charged sulphonated polymers:

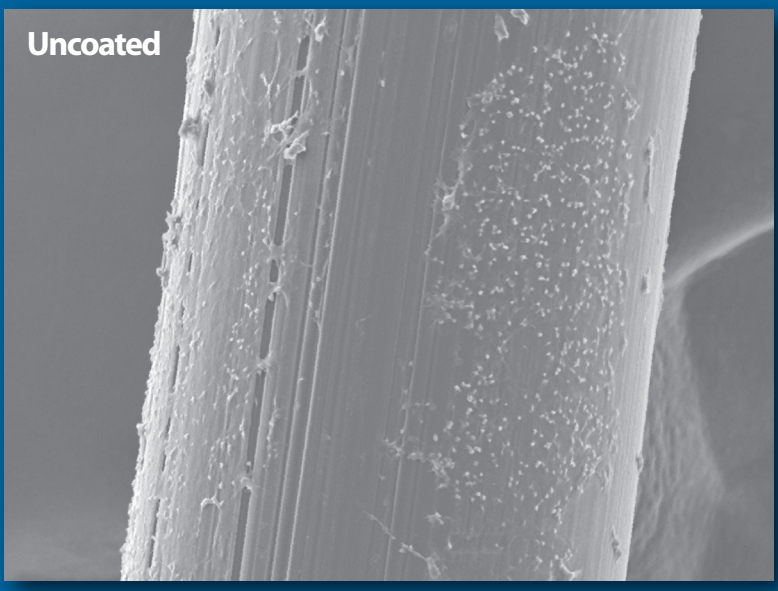
- Repel platelets, which are negatively charged [6,7,8]
- Inhibit thrombin by binding to antithrombin in a heparin-like manner [9,10,11]
- May impair additional processes required for thrombus formation [9,12]

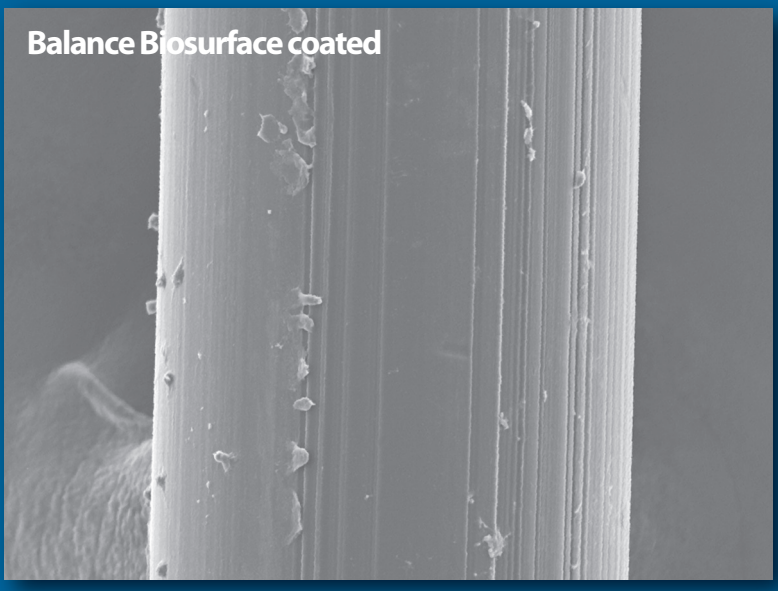
2b *Hydrophilicity*

Polyethylene oxide (PEO) polymer is a second functional layer component. PEO is a hydrophilic molecule. In the primed circuit, PEO creates an "insulating" water layer structure between the blood and artificial surface to resist cell adhesion and protein deposition.



Reduced platelet and cell adh



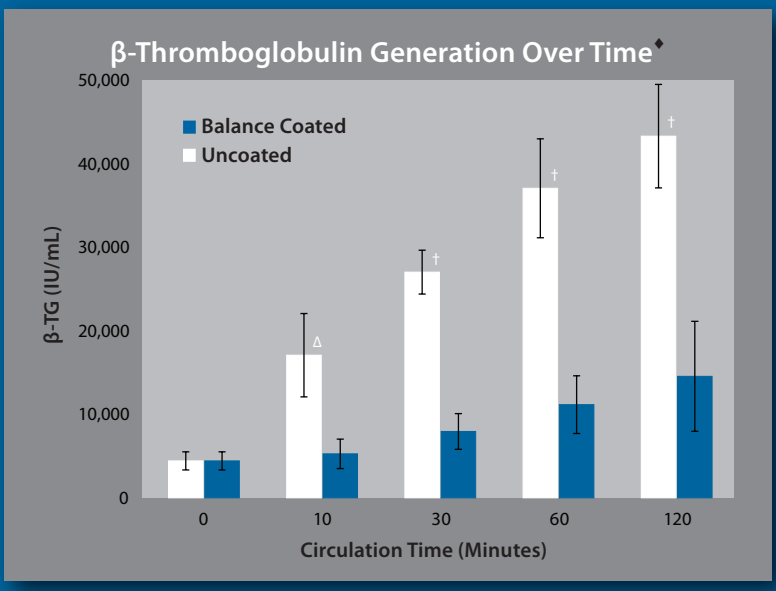


Scanning electron micrographs (SEM) of oxygenator fiber surfaces after two hours of *in-vitro* circulation in a closed circuit using heparinized, human blood (200X magnification)

Uncoated oxygenator fiber SEM (top) shows extensive platelet and cell deposition and activation on the fiber surface. In contrast, minimal deposition and activation is seen on the Balance Biosurface SEM (bottom)

Ask your Medtronic Representative today about Medtronic perfusion technologies available with Balance™ Biosurface

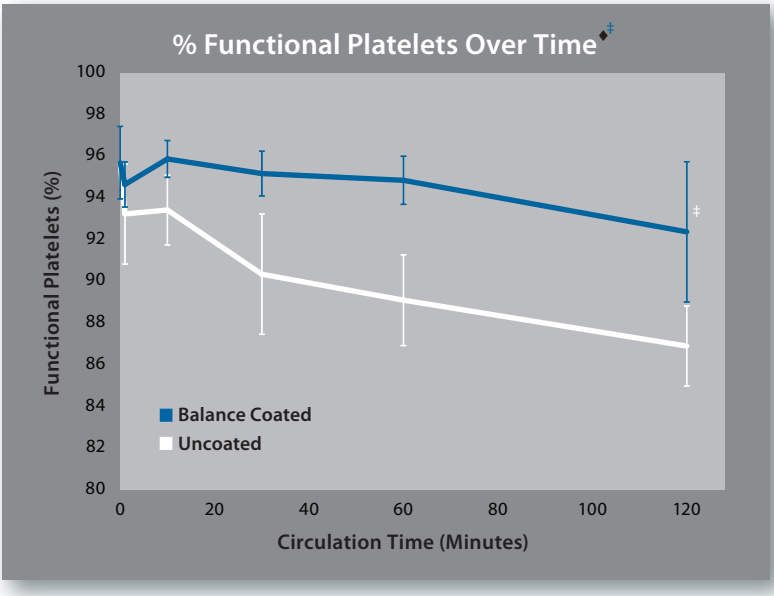
esion and activation



Generation of beta-thromboglobulin (β-TG), a marker of platelet activation, over time.

Balance™ Biosurface is associated with a reduction in platelet activation as marked by reduced β-TG generation ($^{\Delta}$ p < 0.001, † p < 0.0001).

Preserved function of circulating platelets



Comparison between Balance-coated and uncoated *in vitro* bench test circuits of percentage of platelets that are activated with adenosine diphoshpate (ADP @ 20 µM) in circulating heparinized human blood over time.

Balance Biosurface is associated a greater percentage of functional platelets (‡ p < 0.02 at 10, 30, 60 and 120 minutes).

◆ Comparison between Balance Biosurface-coated and uncoated *in vitro* bench test circuits circulating heparinized human blood over time at device maximum rated flow rate.

References

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