Ulteeva Purity™ Membrane **An alternative to traditional stent graft materials**

Ulteeva Purity™

Propelled by aging populations, increased expenditures in healthcare, and more demand for minimally invasive surgery, the global cardiovascular device market is poised to see explosive growth in the coming years.

According to GlobalData, the peripheral vascular device market in North America is worth $4.2 billion in 2024, and is expected to hit $5.9 billion by 2030.[1]

Behind the momentum of the market has been the steady growth of the aging population, and with it a sharp increase in the number of cases of cardiovascular and related diseases. The American Heart Association estimates there are currently about 127.9 million adults in the U.S. suffering from some form of coronary vascular disease, with the number of new heart attacks each year pegged at 605,000 in addition to about 200,000 incidences of recurrent attacks.[2]

On the global front, increased demand for these treatments is being fueled by a growing middle class and improved health care in countries like China and India.

Additionally, treatments like stenting, balloon angioplasty and atherectomies to treat peripheral arterial disease (characterized by the buildup of plaque on the inner walls of the arteries carrying blood from the heart to the legs, arms, stomach, or kidneys) represented about 40% of the U.S. peripheral vascular device market.[3]

Current minimally invasive surgical solutions for addressing both cardiovascular and peripheral arterial disease rely on devices such as stent grafts, typically inserted through a major artery like the carotid, iliac, or femoral, either to expand a narrowed vessel or remove a blockage.

Most commercially available devices used for endovascular stent grafts are made up of two key components: the stent, which is typically a tubular metal mesh or metal wire braid that can be either self-expandable or balloon expandable; and the graft, which is usually a tubular polymeric sleeve or membrane that can be fit to the interior, exterior or both surfaces of the stent.

To overcome external compression and mechanical forces, flexible stent materials like nitinol (nickel titanium) are used in most peripheral stent placements. Most graft material, however, is made from either polyethylene terephthalate (PET) or more commonly from expanded polytetrafluorethylene (ePTFE).

Traditionally, PET stent coverings are woven or knitted fabric made from the polyester fibers while ePTFE coverings are laminated structures based on the porous ePTFE membrane that features a node- fibril microstructure. The covering acts as a barrier and confines blood flow within the lumen (internal tubular opening) of the stent graft.

Overall, the performance of these two types of materials used in stent grafts have fared well in larger diameter uses such as aortic position. However, they have been less satisfactory due to low patency rates (ability to remain open) in small diameter uses like treating peripheral artery disease.

Today, there is an alternative to traditional ePTFE used for small diameter covered stent grafts for treatment of long lesion superficial femoral artery disease: Ulteeva Purity™ membrane by the Biomedical division of dsm-firmenich.

Ulteeva Purity™ membrane is a synthetic membrane made of ultrahigh molecular weight polyethylene (UHMWPE), a proven material in sports medicine and arthroplasty applications. Its chemical nature together with the physical properties of the membrane have the potential to improve patency rates in small diameter uses. In preclinical studies, initial prototype stent grafts made out of Ulteeva Purity™ membrane remained widely patent (open).

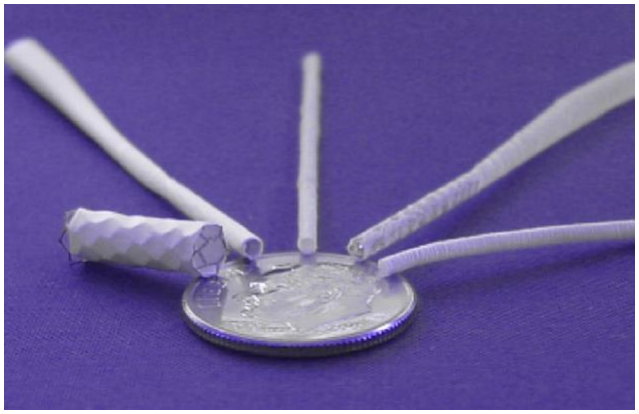
First introduced in 2013, the Ulteeva Purity™ membrane is a biocompatible and inert material. Among its many attributes, it provides improved handling at lower temperatures, making it easier to work with, while requiring lower cost tooling. Compared to ePTFE, the Ulteeva Purity™ membrane has a higher ratio of strength versus volume allowing manufacturers to produce medical devices with smaller profiles supporting better deliverability and deployment when treating patients through minimally invasive surgery.[6]

Laminated structures produced from Ulteeva Purity™ membrane are both flexible and strong. This together with the low friction supports the delivery and deployment of the device. Its high resistance to fatigue and creep is an advantage versus more traditional materials in the development of cardiovascular innovations, where continuous motion, like the beating of the heart or movement of the legs, can cause stresses in materials.

The lamination technology of the Ulteeva Purity™ membrane provides a platform for the creation of a structure that features a porosity that can accept coatings and drugs, for example, Heparin. It also can be used in combination with other materials like nylon, PET, and TPU.

In addition to having excellent biocompatibility, Ulteeva Purity™ membrane is mechanically strong and shows high resistance to creep. It can be laminated at temperatures below 150 Celsius (302 Fahrenheit), an advantage when it comes to commercial design and fabrication of covered-stents compared to those that use ePTFE.[4,5]

The material enables design of lower profile devices, which is important in the current trend of minimally invasive surgery and miniaturization. In addition, unlike ePTFE, Ulteeva Purity™ membrane retains its



Examples of various Ulteeva Purity™ membrane- covered stents

characteristics after being sterilized by high energy irradiation.

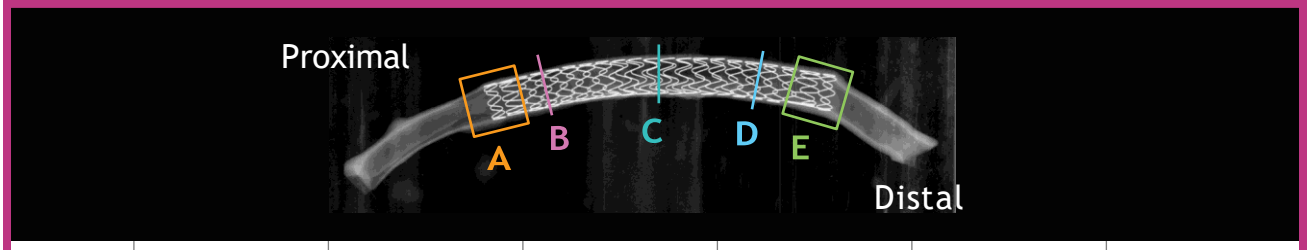
The proprietary manufacturing process of Ulteeva Purity™ membrane involves a gel-extrusion and bi-axially stretching process that combines UHMWPE powder with a solvent to form a suspension. That, in turn, is introduced into a screw-extruder at an elevated temperature to form the so-called base tape. After the solvent evaporates, the base tape is stretched at elevated temperatures and through several other steps formed into a highly porous and thin membrane.

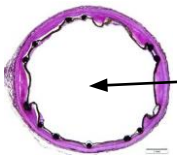
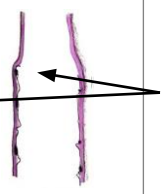
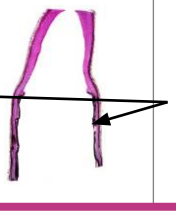
The process gives Ulteeva Purity™ membrane a very distinct mechanical behavior compared to typical ePTFE, making the membrane much stronger and showing no significant directional mechanical variations, compared to typical ePTFE membrane at comparable porosity and pore size.[6]

To further illustrate the effectiveness of the Ulteeva Purity™ membrane, researchers conducted preclinical and clinical studies in which they developed a prototype stent and compared it to an alternative small diameter covered stent with ePTFE. In the preclinical studies, four sheep each received a Ulteeva Purity™ membrane-CS device and a control device (commercially available stent graft containing ePTFE).

The development team used a Ulteeva Purity™ membrane covered-stent designed to improve adherence to the vessel wall when implanted.

AN EXAMPLE OF HISTOLOGICAL GRAPHS FROM RIGHT CAROTID ARTERY



	A Proximal longitudinal	B Proximal	C Middle	D Distal	E Distal longitudinal	
Ulteeva SG						Widely open lumen
Control SG						Stent graft implanted

The results indicated a favorable similar/non- inferior comparison, in both the preclinical and clinical studies.

By combining Ulteeva Purity™ membrane with other materials, such as Ulteeva Purity™ woven fiber, it can create a reinforced substrate that doesn't require suturing or stitching to keep it in place on a frame or stent. This allows for additional choices in design in more challenging anatomical environments.

Based on outcomes from angiography, radiography and histology, both test devices and control devices in all four sheep were widely patent (open) at 90 days.

"The results of the study were very encouraging and our expectations for further development and uses of the Ulteeva Purity™ membrane in this arena are high," said Dr. Renu Virmani, MD, FACC and President of CV Path Institute.

While the Ulteeva Purity™ membrane was initially developed for use in the design of peripheral stent grafts (next to stent grafts for use outside the arterial/ venous system such as biliary stents), it is expected that the material will be useful in other areas where tubular structures or conduits are required.

Examples being researched are skirts for heart valves. Due to the membrane's potential to be loaded with therapeutic compounds, it can be used in the design of drug eluting devices.

While the future of the Ulteeva Purity™ membrane is very bright and we are committed to exploring all of the possible applications for its use, the real motivator is seeing the positive effects it has on medical device developments and, most importantly, improved patient outcomes.

Currently, there is a master file in place for the Ulteeva Purity™ membrane with the U.S. Food and Drug Administration, and medical device companies interested in working with the material and the technology can contact the Biomedical division of dsm-firmenich for more information.

1 GlobalData Intelligence Center, May 2024. Data can be found at https://medical.globaldata.com/sector/MarketGridEdit?sectorId=1900044

2 American Heart Association, 2024, Heart Disease and Stroke Statistics Update Fact Sheet. Available from https://www.heart.org/-/media/PHD-Files-2/Science-News/2/2024-Heart-and-Stroke-Stat-Update/2024-Statistics-At-A-Glance-final_2024.pdf

3 iData Peripheral Vascular Devices and Accessories Market Report, 2016-2022. Available from https://idataresearch.com/product/us-peripheral-vascular-devices-market-2016-medsuite/

4 Gogoleva OV, et al., FarEastCon - Materials and Construction II, 992 MSF: 2020, pp.398-402.

5 UHMWPE Biomaterials Handbook Ultra High Molecular Weight Polyethylene in Total Joint Replacement and Medical Devices Book, Third Edition, 2015.

6 Data on file at Biomedical: T-20418

For more information on Ulteeva Purity™ membrane please visit our website

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