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Investigating the permeability properties of covered stents according to international standards and beyond

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Abstract: The permeability properties of covered stents are crucial for the therapy success treating peripheral artery disease, peripheral artery occlusive disease as well as dissections and aneurysms. For investigation of water permeability according to ISO 7198:2016 a customized test setup was developed. It enables for standardized testing regarding the integral water permeability as well as the water entry pressure and provides additional quantitative and qualitative results beyond the requirements: The first measureable flow, the maximum applicable pressure as well as photo documentation during the test were implemented. Four commercially available covered stents indicated for atherosclerotic lesions of the iliac arteries were investigated within the current study showing no measureable permeability at 120 mmHg. However, different water entry pressures and leaking patterns at higher pressures could be observed. Especially, photo documentation during the test as well as the first measureable flow enhance the informative value of standardized permeability testing.

Keywords: Endovascular prostheses, covered stent, stent graft, permeability, water entry pressure, testing

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1 Introduction

Covered stents are minimally invasive implantable endovascular prostheses for the treatment of peripheral artery disease, peripheral artery occlusive disease as well as dissections and aneurysms [1, 2]. In the therapeutic management of atherosclerosis, the cover acts as a barrier against neointimal hyperplasia, but should also allow transfer of nutrients to the arterial wall [3, 4]. During therapy of arterial dissections or aneurysms the cover functions as sealing to redirect the blood flow inside the artery [1, 5]. The permeability properties of the endovascular prosthesis are crucial for the therapy success and thus are subject of the current study.

International standards, such as ISO 25539-1:2017 and ISO 7198:2016, provide a framework for the performance of bench and analytical tests. These tests are designed to characterize endovascular prostheses in general, including their permeability properties [6, 7].

Within the current study, the requirements of international standards were implemented into a custom made test setup for investigation of the permeability properties of covered stents and exemplary commercially available devices were evaluated.

2 Requirements of international standards

ISO 25539-1:2017 provides minimum requirements for endovascular prostheses based on the state of the art regarding testing as well as clinical application. In particular, this standard designates and describes bench and analytical tests (sect. 8.5 as well as Annex D) to be performed with endovascular prostheses for treatment of aneurysms, stenoses or other vascular anomalies, such as dissections. Regarding permeability properties, the investigation of integral water leakage as well as water entry are requested. However, for more specific requirements it is referred to ISO 7198:2016 [6].

ISO 7198:2016 defines more precisely the requirements for the test equipment to measure the integral water permeability as well as the water entry pressure:

- usage of particle free water at room temperature
- usage of sample holder with appropriate dimensions for pressure tight sealing
- pressure control enabling for applying a minimum pressure of 120 mmHg
- pressure sensor with an accuracy of ± 2 mmHg
- flow sensor with an accuracy of ± 5% RD
- device for measurement of unsealed sample length

In addition, the general test sequences are provided: For measurement of integral water permeability, the sample should be filled with water and air has to be completely removed. The inner pressure should be increased up to 120 ± 2 mmHg. After stabilization of the leakage, leakage should be measured for 60 s or for another time to guarantee appropriate measurement. Integral water permeability should be given in $ml \cdot cm^{-2} \cdot min^{-1}$. For measurement of water entry pressure (*WEP*), the sample should be filled with water. A pre-defined pressure should be used as start pressure. Pressure should be stepwise increased and be held constant for at least 30 s. The pressure at which water could be observed on the outer surface of the sample is defined as *WEP*. The *WEP* should be given in kPa [7]. Neither in ISO 25539-1:2017 nor in ISO 7198:2016 any acceptance criteria or critical values to be accomplished are provided [6, 7].

3 Materials and methods

3.1 Test setup

For investigation of water permeability according to ISO 7198:2016 a customized test setup was developed. The sample to be tested is pressurized from the luminal side with water, while leaking is quantified. Therefore, the sample is fixed within a special sample holder that fits the inner diameter and is sealed with the help of an elastic film (Parafilm®, Bemis Company Inc., USA). The sample holder with sample is positioned above a reservoir in order to collect leaking fluid immediately. With the help of a centrifugal pump (type IPD-30.1-50-01, Levitronix, Switzerland), the water is directed through a flow sensor (LEVIFLOW LFS-008-Z, Levitronix, Switzerland, measurement error < 1% RD within the range of 1 to 800 ml/min) into the inflow of the sample holder and the sample. On the outflow of the sample holder a pressure sensor (type 86A, TE Connectivity, Galway, USA, measurement error < 2 mmHg within the range of 0 mmHg to 286 mmHg) is connected. Due to pressure tight sealing of the sample within the sample holder the fluid can only leak through the sample itself. For photo- and video documentation purposes, a digital camera (DFK 33UX183 with lens V1226-MPZ, The Imaging Source Europe GmbH, Germany) is integrated into the test setup. The test setup is illustrated in Figure 1.

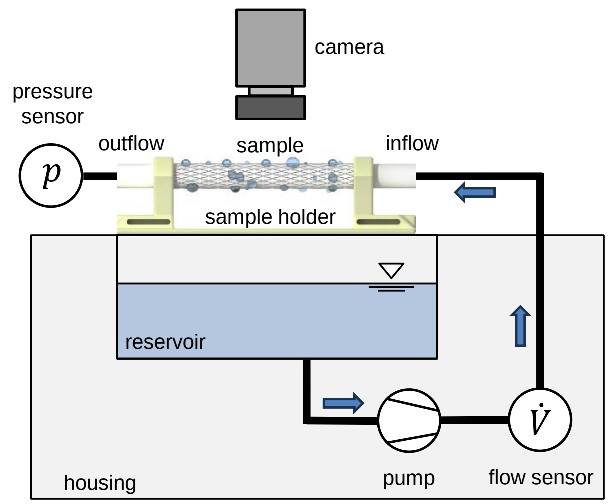

Figure 1: Schematic illustration of the customized test setup for testing water permeability of endovascular prostheses

Water for injections (e.g. AMPUWA, Fresenius Kabi, Germany) is used to prevent the test setup from particles that may impact the test results. Testing is performed at room temperature.

3.2 Permeability testing

Our measurement approach combines testing of *WEP* as well as the integral water permeability at 120 mmHg. Before mounting the sample into the permeability test setup, the outer diameter D of the sample is measured over the entire length using a custom-made test setup with a two-axis laser scanner (ODAC 32XY, Zumbach Electronic AG, Switzerland). After mounting and sealing of the sample, the non-sealed sample length L is measured by a caliper (CD-15APX, Mitutoyo, Japan). Subsequently, the air in the sample is removed and the start pressure is set to 30 mmHg. The pressure is stepwise increased by 30 mmHg and held for 30 s at each pressure step, while the volumetric flow of the leaking fluid $\dot{V}$ is measured simultaneously by the flow sensor and photo documentation is performed. However, the pressure of 120 mmHg is maintained for a minimum of 180 s, or for a greater duration if required to ensure stabilization of the flow. Integral water permeability Q can be calculated for every pressure step according to eq. 1.

$$Q = \frac{\dot{V}}{\pi \cdot D \cdot L} \quad [ml \cdot cm^{-2} \cdot min^{-1}] \qquad (1)$$

In addition to the standardized test parameters, the first measureable flow (*FMF*) as well as the maximum applicable pressure (*pMax*) can be quantified during the permeability measurements. Considering the visual appearance of the leaking provides additional information for evaluation of permeability properties of the sample.

3.3 Test samples

Permeability testing as described above was performed for four commercial available endovascular prostheses indicated for therapy of atherosclerotic lesions of the iliac arteries, namely iCast 8 x 38 mm (Getinge Deutschland GmbH, Germany), BeGraft 8 x 37 mm (Bentley InnoMed GmbH, Germany), iCover 8 x 37 mm (iVascular, Spain) and Viabahn VBX 8 x 79 mm (W. L. Gore & Associates, Inc., USA).

4 Results

Measurement data and quantitative test results of permeability testing are given in Figure 2 as well as Table 1. Exemplary images of the photo documentation during the test are given in Figure 3. Integral water permeability at 120 mmHg was not measureable for all tested endovascular prostheses. *WEP* was comparable for iCover, iCast and BeGraft (12 kPa to 16 kPa), whereas Viabahn VBX showed a considerably higher *WEP* (68 kPa). *FMF* was lowest for the BeGraft (210 mmHg) and highest for the iCover (480 mmHg). Measured flow for the Viabahn VBX did not correlate with the visual investigation, as no leaking water within the unsealed region could be observed. It is assumed, that leakage was not within the unsealed cover region, but within the sealing region and therefore should not be associated with the sample itself. For iCast, iCover and Viabahn VBX, the maximum applicable pressure was determined by the test setup itself. No failure (e.g. rupture, burst, holes) of the cover could be detected. The BeGraft showed delamination of the outer cover layer during the test, resulting in a significant diameter increase (gum bubble effect) and a rupture at 240 mmHg. However, such a loading is not likely to happen *in vivo*, due to the surrounding arterial wall.

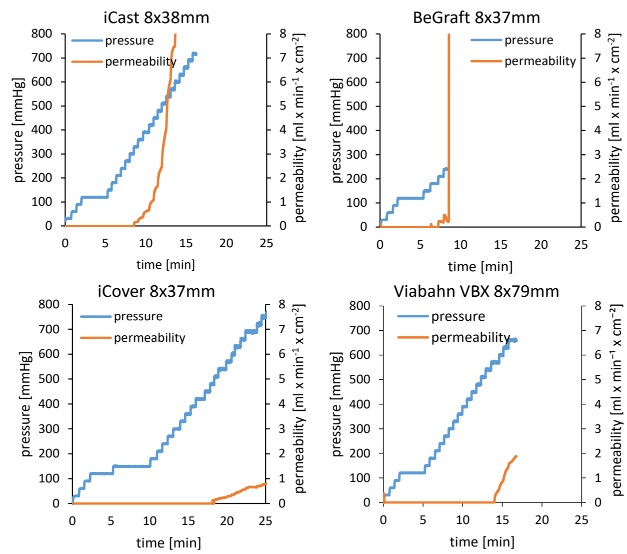

Figure 2: Pressure-time and permeability-time curves for the investigated endovascular prostheses (iCast, BeGraft, iCover, Viabahn VBX, each $n = 1$)

Table 1: Permeability *Q* at 120 mmHg, water entry pressure (*WEP*), first measurable flow (*FMF*) and maximum applicable inner pressure (*pMax*) for the investigated endovascular prostheses ($n = 1$), *presumably, leakage was not through the cover but through the sealing

	iCast	BeGraft	iCover	Viabahn VBX
Q (@120 mmHg) [$ml \cdot cm^{-2} \cdot min^{-1}$]	0	0	0	0
WEP [kPa (mmHg)]	16 (120)	16 (120)	12 (90)	68 (510)
FMF [mmHg]	330	210	480	570*
pMax [mmHg]	>720	240	>750	>660

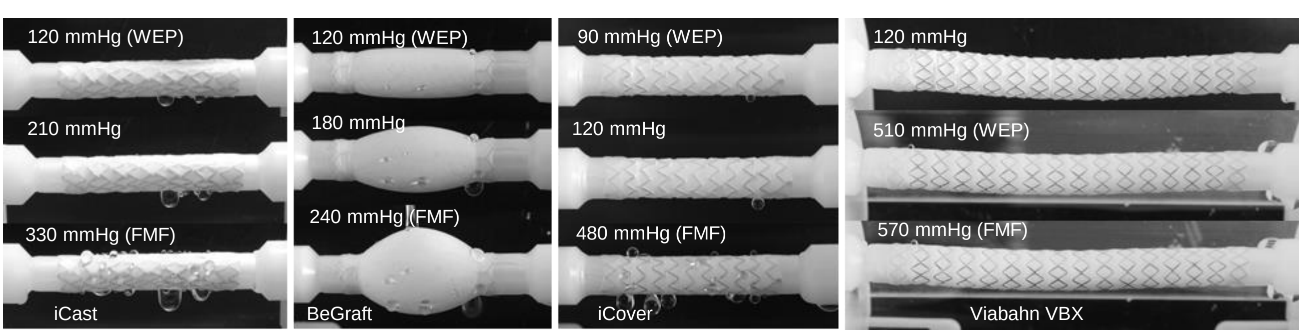

Figure 3: Visual observation during water permeability testing of different endovascular prostheses at several intraluminal pressure steps. Water entry pressure (*WEP*), first measurable flow (*FMF*) as well as general leaking appearance for Gettinge iCast 8 x 38 mm, Bentley BeGraft 8 x 37 mm, iVascular iCover 8 x 37 mm and GORE Viabahn VBX 8 x 79 mm

5 Discussion

From the literature it is known that water permeability of endovascular prostheses differs depending on the cover composition and on the cover materials used. While braided prostheses or prostheses with electrospun cover show water permeability between 1 $ml \cdot cm^{-2} \cdot min^{-1}$ and 15 $ml \cdot cm^{-2} \cdot min^{-1}$, covered stents with expanded polytetrafluorethylene (ePTFE) covers show no water leaking at a transluminal pressure of 120 mmHg [8, 9, 10]. The tested covered stents within the current study all consist of an ePTFE cover and showed no measureable water permeability as expected. However, it has been demonstrated elsewhere that porosity-mediated water permeation is conducive to the transfer of nutrients to cells within the tissue [4], confirming the relevance of permeability characterization in general.

The WEP of the tested samples investigated by visual observation could be verified by photo documentation within our customized test setup. However, the informative value of the WEP is limited, as it does not include any information regarding the amount of leakage. From our perspective, the FMF may be considered a more suitable option in this regard, given its capacity to address both the pressure of occurrence and a certain amount of leakage.

The application of hyperphysiological hydraulic pressures to endovascular prostheses facilitates the characterization of the cover strength or the bond strength between cover and stent frame, respectively. In our study, three of four test samples showed no signs of failure until maximum pumping capacity was achieved. However, the maximum applicable pressure may serve as additional criterion for assessment of endovascular prostheses.

In conclusion, the presented test setup is suitable to perform permeability measurements according to the requirements of international standards. We introduced additional quantitative results for better assessment of the permeability properties, which are in particular of interest during development of new endovascular prostheses or cover materials. Especially, photo documentation during permeability testing seems reasonable, as typical leaking patterns can be observed even below measureable flow. In addition, leakage through the sealing can be identified by photo documentation, helping to prevent from misinterpretation of measured flow. FMF may serve as an additional quantitative parameter to evaluate permeability properties of covered stents.

Author Statement

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