Wolfram Schmidt*, Christoph Brandt-Wunderlich, Frank Kamke, Christopher Schwerdt, Jörg Kaminsky, Peter Behrens, Klaus-Peter Schmitz, Niels Grabow

Pulsatile fatigue testing of arterial stents with radially applied load

An update based on new standardization

https://doi.org/10.1515/cdbme-2024-2135

Abstract: Pulsatile fatigue testing is a basic requirement for arterial stents, however, there are several opportunities to set-up and conduct the testing. The recently published standard guide ASTM F2477:2023 provides specific guidance, in particular includes the pressure controlled test method applying an outer hydraulic pressure to the test samples. The current work describes this approach, and demonstrates that the technical requirements can be met successfully. In addition, some inherent advantages are discussed, e.g. accuracy of pressure loading, absence of stent migration and potential high test frequencies.

Keywords: Radial fatigue testing, arterial stents, pressure loading, standardization, ASTM, ISO

1 Introduction

It is one of the basic requirements for long-term implants like arterial stents to withstand cyclic dynamic loading without any loss of support function. When clinical literature reports that there were more stent fractures observed post-mortem than during patients life, the relevance of fracture rates might be subject of consideration. On the other hand, the cardiologic event rates are found systematically higher at least with severe fracture grades [1]. Calcified lesions, overlapping stents, long stents and Sirolimus eluting stents, among others, are discussed as clinical predictors [2].

For approval purposes, the assumptions on physiological load parameters, verification of test frequency for accelerated testing and the required validation of the method shall be in accordance with ISO 25539-2:2020, sect. 8.5.2.3.2 [3]. However, no specific test method is described.

The option of pressure controlled radial fatigue testing using an outer pressure on the stents was developed more than two decades before [4], but was not very popular due to the lack of standardization. The recently published new revision of ASTM F2477:2023 [5] describes a pressure controlled test principles explicitly including dynamic loading by an outer hydraulic pressure (Figure 1).

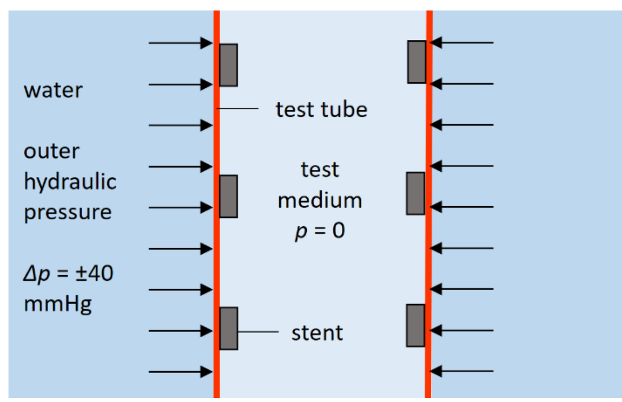

Fig. 1: Principle of pulsatile load application by outer hydraulic pressure. The flexible test tube transmits the outer pressure directly to the stent.

Arterial stents are exposed to radial loading resulting from static wall stress and arterial pulse. There is consensus that a hypertonic situation of 160 to 80 mmHg (systolic to diastolic blood pressure) is relevant resulting in a dynamic pressure of ± 40 mmHg. When using the outer pressure method, an additional static pressure is applied to ensure permanent contact between test tube and stent, as well as to avoid negative pressure in the test chamber.

Data for the expected diameter change of stented vessels are rare. Some literature is available for diameter change of native coronary vessels due to physiological arterial pressure, providing diameter compliance in the range of 2.5 – 9.3 %/100 mmHg [6,7]. It is known from various investigations that the diameter change of coronary stents due

***Corresponding author: Wolfram Schmidt:** Rostock University Medical Center, Institute for Biomedical Engineering, Rostock, Germany, e-mail: wolfram.schmidt@uni-rostock.de
Christoph Brandt-Wunderlich, Frank Kamke, Christopher Schwerdt, Jörg Kaminsky, Peter Behrens, Klaus-Peter Schmitz: Institute for ImplantTechnology and Biomaterials IIB e.V., Rostock, Germany
Niels Grabow: Rostock University Medical Center, Institute for Biomedical Engineering, Rostock, Germany

to radial loading with physiological pressure changes is expected to be much lower but measurable [8]. It depends on the radial stiffness of the stent which is determined by the stent structure and the expansion diameter. For demonstration, an experiment was conducted to measure the effect of the support function on diameter change.

High test frequencies at accelerated testing are of huge economic impact as test time can be drastically reduced if higher test frequencies can be applied. It has to be considered that a 10 years life-time simulation is requested which equals 380 to 400 mio load cycles. It has to be proven for each test configuration that the diameter change at accelerated test frequency is comparable to that at physiological pressure and frequency [5]. A suitable test setup and exemplary results will be presented.

The influence of temperature on fatigue testing is negligible for balloon-expandable metallic stents consisting of stainless steel, CoCr or PtCr alloys. For self-expandable stents mostly made from Nitinol the austenite finish temperature may be somewhat lower than body temperature, and testing at (37±2) °C is essential as well it is for polymer-based stents.

The test medium may have an impact on fatigue resistance if corrosion or degradation effects occur (i.e. stress corrosion cracking, bioresorbable stents). ASTM F2477-2023 provides some guidance for selection of test fluid (physiologic pH buffered saline or equivalent, 0.9 % saline, modified simulated body fluid, or distilled water) [5].

Within the current work, the technical realization of the test parameters to be controlled will be demonstrated and discussed.

2 Materials and Methods

Physiological worst case pressure loading by an external hydraulic pressure is realized by a direct loading mechanism (Figure 2). The stents implanted in thin and flexible test tubes

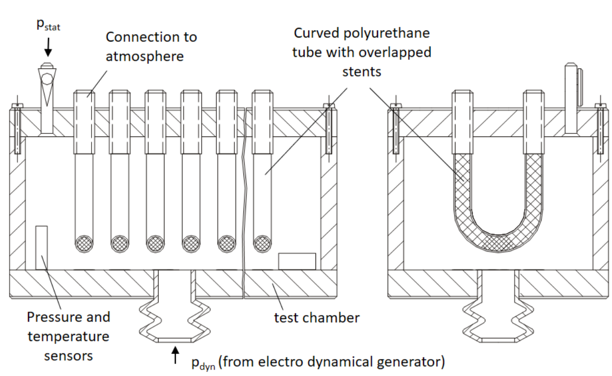

Fig. 2: Test chamber for static and dynamic loading of stents in bent condition. The chamber is filled with heated water to transmit outer hydraulic loading to the test samples [13].

(polyurethane, wall thickness 0.1 mm) are placed in the test chamber which is pressurized by a static pressure superimposed by the dynamic pressure load. The compliance of the test tubes is not of importance as they act just to transfer the outer pressure to the stent.

The pressure range to be controlled and measured is $p = p_{stat} \pm p_{dyn}$ and ranges from 10 mmHg to 90 mmHg (±40 mmHg). The setup uses a pressure sensor with a range of 0 to 250 mbar (187.5 mmHg, output 4 – 20 mA). The 16-bit resolution of the digital conversion is far better than the calibrated accuracy of ± 2 mmHg. The sensor has a response time t_{10-90} of 1 ms which is fast enough to measure pressure changes of up to 100 Hz.

The temperature in the test chamber is controlled automatically. For testing, it is checked at the beginning and ending of each test with a traceable calibrated thermometer (GMH 3750 with temperature probe GTF 401 DIN Kl. AA, extended uncertainty u_{95} = 0.05 K). The precision of temperature control was investigated while measuring temperature over a time period assessing times of heating and cooling. The measurement of the temperature directly at the test sample as implanted in the thin-walled test tube provided a temperature difference of ΔT = 0.04 K which is mainly due to measurement uncertainty.

2.1 Stent diameter change

For estimation of expected stent diameter change when exposed to dynamic pressure loading, polymeric tubes fabricated from silicone rubber were used as mock vessels. They had a nominal internal diameter of 3.5 mm, a wall thickness of 0.2 mm and a certified diameter compliance of 5 - 7 %/100mmHg when measured between 80 mmHg and 120 mmHg (Dynatek Dalta).

The outer diameter was measured at increasing steps of internal pressure (Δp = 0.05 bar = 37.5 mmHg) without stent and after implantation of a commercially available coronary stent by calibrated optical microscopy.

2.2 Test frequency for accelerated testing

It has to be shown for each test configuration that the diameter change at accelerated test frequency is comparable to that at physiological pressure and frequency [3,5]. This experimental prove is conducted using a setup as shown in Figure 3. A high resolution line camera (Basler raL8192-12gm, pixel size 3.5 µm x 3.5 µm, 8192 Pixel, used frame rate 1.2 kHz) measures the outer diameter at different positions along the stent axis. The telecentric lens enables measurement of diameter changes with a resolution of ± 2 µm. The principle setup for pressure loading (p = 50 ± 40 mmHg) is as in Figure 2.

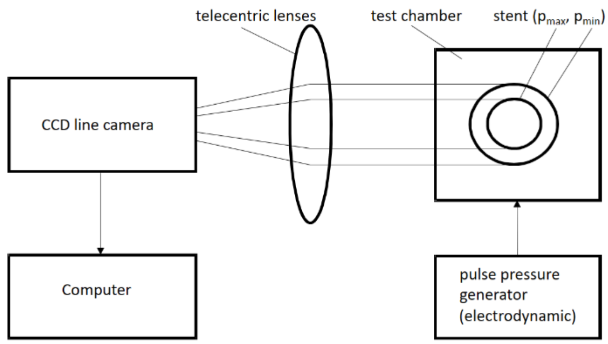

Fig. 3: Test setup for measurement of stent diameter as a function of test frequency

3 Results

3.1 Stent diameter change

Under the same simulated physiological conditions (mean arterial pressure p_{mean}=100 mmHg, p_{diast}/p_{syst} = 80/120 mmHg) the compliance of the unstented artery was C = 5.467 %/100 mmHg while the compliance of the stented artery was found to be an order of magnitude smaller (C = 0.489 %/100 mmHg) (Figure 4).

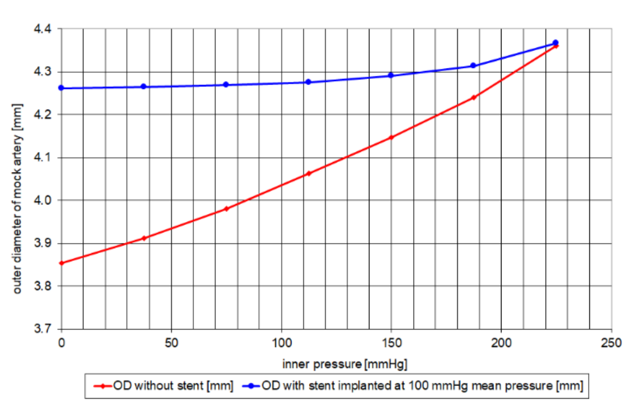

Fig. 4: Diameter of unstented and stented mock vessel as a function of internal pressure. The diameter compliance is the slope of the curve at 100 mmHg inner pressure

3.2 Test frequency

The stent outer diameter change at dynamic pressure loading with p_{dyn} = ± 40 mmHg is shown in Figure 5 for test frequencies of 1, 50 and 100 Hz.

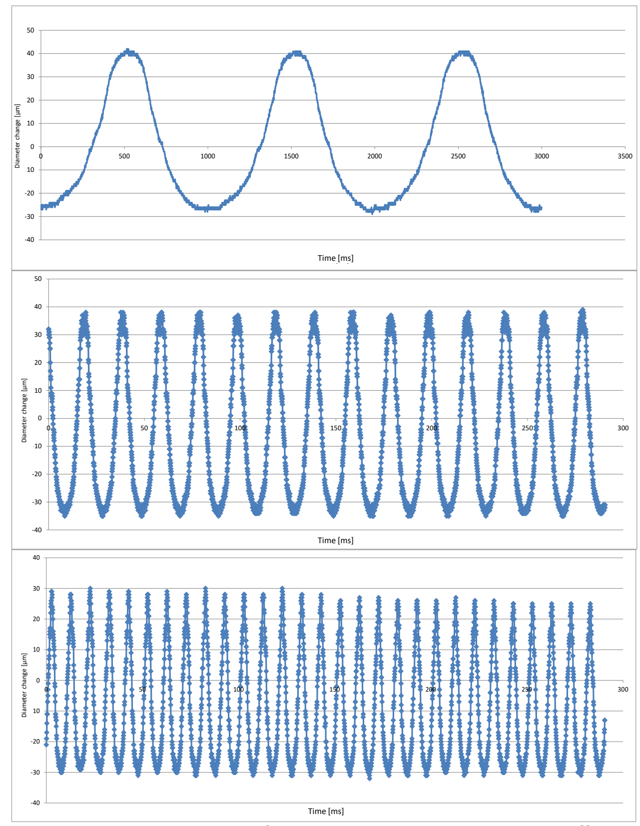

Fig. 5: Diameter change of a dynamically loaded stent at different test frequencies: 1 Hz, 50 Hz, 100 Hz. Measured by CCD line camera (sample rate 1.2 kHz)

It is obvious that the stent outer diameter follows the pressure load and thus the stent actually experiences the pressure load. In the presented case, the amplitude of diameter change is comparable between 1 Hz and 50 Hz, but reduced at 100 Hz. As the conclusion, the test frequency would have to be lower than 100 Hz.

4 Discussion

The results demonstrate that the required parameters can be appropriately adjusted and controlled.

The presented radial fatigue testing is designed as a test to success. Long-term results are obtained at visual inspections during the test and final inspections of the test samples for loss of support function, initial tearing or cracks in the structure, or fretting corrosion. The latter is done using microscopic imaging. Light microscopy and SEM inspection of stents after fatigue testing was demonstrated before. It is effective even for assessment of coating integrity without sample preparation [9]. All observations have to be reported. The assessment of pass or fail depends on the risk analysis considering the results and the specific stent application.

In the past, the test principle itself was subject of discussions. Does the application of an outer pressure actually represent relevant loading for fatigue testing of arterial stents? We proved that the loading of the stents with a dynamic outer pressure of ± 40 mmHg results in comparable diameter change as pressure values from 160 to 80 mmHg as they are generally accepted. The stent experiences the relevant dynamic load.

The reduced amplitude of diameter change compared to unstented natural arteries was confirmed by other authors, who reported that the compliance of the stented rabbit aorta was significantly lower than the unstented aorta [10]. A significant change of diameter compliance due to stenting was also measured in the case of unstented and stented human carotid arteries [11]. Finite element modeling of a Palmaz stented artery indicated that the compliance of the stented artery was only 10% of that of the unstented artery [12].

The presented test principle has several advantages: The load is directly applied, measured and controlled. There is no influence of the test tube as far it is thin enough to transfer the load to the stent. High test frequencies are possible limited only by the inertia of water displacement and the moved stent mass (which are low) and the mass/power of the dynamic pressure generator itself. No stent migration occurs due to permanent contact between tube and stent resulting from the static pressure load higher than the minimum dynamic pressure. The stents are visible through the thin and clear test tubes enabling steady visual inspections. The closed and small volume inside the stent enables for measurement of particle release during fatigue test (chronic coating durability) [13]. A limitation is that the stent has to support all of the pressure load without collapse. This may be critical for weak stents with a low collapse pressure (large diameter stents).

The used technical approach is not as intuitive as the method applying internal pressure. However, this is not a technical limitation but requires description and justification to customers and authorities. The recently published standard ASTM F2477:2023 will be helpful for acceptance.

5 Conclusion

The presented test method for pulsatile fatigue testing of stents is suitable to meet the requirement resulting from assumed physiological worst-case condition for arterial stents exposed to arterial pulse. The technical parameters can be adjusted and controlled with relevant precision. The test method is in accordance to related standardization and has several advantages which may help to increase acceptance.

Author Statement

Research funding: The author state no funding involved. Conflict of interest: Authors state no conflict of interest. Informed consent: Not applicable. Ethical approval: Not applicable.

References

[1] Nakazawa G, Finn AV, Vorpahl M et al. Incidence and predictors of drug-eluting stent fracture in human coronary artery a pathologic analysis. J. Am. Coll. Cardiol. 2009; 54: 1924–1931

[2] Conway C. Coronary Stent Fracture: Clinical Evidence Vs. the Testing Paradigm. Cardiovasc Eng Technol 2018; 9: 752–760

[3] ISO 25539-2:2020 - Cardiovascular implants - Endovascular devices - Part 2: Vascular stents

[4] Schmitz KP, Behrens P, Schmidt W, Behrend D, Kaminsky J, Lootz D, Enzenross P: Anordnung und Verfahren zur Prüfung von Gefäßimplantaten, DE 19903476B4

[5] ASTM F2477:2023 - Test Methods for in vitro Pulsatile Durability Testing of Vascular Stents. ASTM International

[6] Nakatani S, Yamagishi M, Tamai J, Goto Y, Umeno T, Kawaguchi A et al. (1995): Assessment of coronary artery distensibility by intravascular ultrasound. Application of simultaneous measurements of luminal area and pressure. In: Circulation 1995;91(12), 2904–2910.

[7] Numao T, Ogawa K, Fujinuma H, Furuya N. Pulsatile diameter change of coronary artery lumen estimated by intravascular ultrasound. In: J Cardiol 1997; 30(1), 1–8.

[8] Schmidt W, Kaminsky J, Behrens P et al. Stentdeformation bei beschleunigter radialer Gefäßbelastung in Abhängigkeit von der Belastungsfrequenz. Biomed.Techn/Biomed.Eng. 2003; 48: 68–69

[9] Wiemer M, Butz T, Schmidt W et al. Scanning electron microscopic analysis of different drug eluting stents after failed implantation: from nearly undamaged to major damaged polymers. Catheter Cardiovasc Interv 2010; 75: 905–911

[10] Vernhet H, Demaria R, Juan JM et al.: Arterial stenting and overdilatation: does it change wall mechanics in small-caliber arteries? J Endovasc Ther. 2002; 9(6):855-62

[11] Vernhet H, Jean B, Lust S et al.: Wall mechanics of the stented extracranial carotid artery. Stroke 2003; 34:e222-e224

[12] Berry JL, Manoach E, Mekkaoui C et al.: Hemodynamics and wall mechanics of a compliance matching stent: In vitro and in vivo analysis. J Vasc Interv Radiol 2002; 13:97-105

[13] Schmidt W, Brandt-Wunderlich C, Kurzhals A, Schmitz K-P, Grabow N: Method to determine particle release during long-term loading for assessment of coating durability of cardiovascular stents. In: Current Directions in Biomedical Engineering 7(2021)2, S. 704–707