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Standard Test Methods for *in vitro* Pulsatile Durability Testing of Vascular Stents[1]

This standard is issued under the fixed designation F2477; the number immediately following the designation indicates the year of original adoption or, in the case of revision, the year of last revision. A number in parentheses indicates the year of last reapproval. A superscript epsilon (ε) indicates an editorial change since the last revision or reapproval.

1. Scope

1.1 These test methods cover the determination of the durability of a vascular stent by exposing it to physiologically relevant diametric distension levels by means of hydrodynamic pulsatile loading. This testing occurs on a stent test specimen that has been deployed into a mock (elastically simulated) vessel. The typical duration of this test is 10 years of equivalent use (at 72 beats per minute), or at least 380 million cycles.

1.2 These test methods are applicable to balloon-expandable and self-expanding stents fabricated from metals and metal alloys. It does not specifically address any attributes unique to coated stents, polymeric stents, or biodegradable stents, although the application of this test method to those products is not precluded.

1.3 These test methods do not include recommendations for endovascular grafts ("stent-grafts") or other conduit products commonly used to treat aneurismal disease or peripheral vessel trauma or to provide vascular access, although some information included herein may be applicable to those devices.

1.4 These test methods are valid for determining stent failure due to typical cyclic blood vessel diametric distension. These test methods do not address other modes of failure such as dynamic bending, torsion, extension, crushing, or abrasion.

1.5 These test methods do not address test conditions for curved mock vessels.

1.6 These test methods do not address test conditions for overlapping stents.

1.7 The values stated in SI units are to be regarded as standard. No other units of measurement are included in this standard.

1.8 *This standard does not purport to address all of the safety concerns, if any, associated with its use. It is the responsibility of the user of this standard to establish appropriate safety, health, and environmental practices and determine the applicability of regulatory limitations prior to use.*

1.9 *General Caveat—This document contains guidance for testing as is currently carried out in most laboratories. Other testing techniques may prove to be more effective and are encouraged. Whichever technique is used, it is incumbent upon the tester to justify the use of the particular technique, instrument, and protocol. This includes the choice of and proper calibration of all measuring devices. Deviations from any of the suggestions in this document may be appropriate but may require the same level of comprehensive justification that the techniques described herein will require.*

1.10 *This international standard was developed in accordance with internationally recognized principles on standardization established in the Decision on Principles for the Development of International Standards, Guides and Recommendations issued by the World Trade Organization Technical Barriers to Trade (TBT) Committee.*

2. Referenced Documents

2.1 *Other Documents:*

ISO 7198: 1998(e), 8.10, Determination of Dynamic Compliance[2]

FDA Guidance Document 1545, Non-Clinical Tests and Recommended Labeling for Intravascular Stents and Associated Delivery Systems, (issued January 13, 2005)[3]

3. Terminology

3.1 *Definitions of Terms Specific to This Standard:*

3.1.1 *cardiac cycle, n*—defined as one cycle between diastolic and systolic pressures.

3.1.2 *compliance, n*—the change in inner diameter of a vessel due to cyclic pressure changes. Compliance, if calculated, shall be expressed as a percentage of the diameter change per 100 mm Hg and defined per ISO 7198, 8.10.5:

$$\%\text{Compliance/100 mm Hg} = \frac{(Dp2 - Dp1) \times 10^4}{(Dp1(p2 - p1))} \quad (1)$$

where:

$Dp1$ = inner diameter at the pressure of $p1$,

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[2] Available from American National Standards Institute (ANSI), 25 W. 43rd St., 4th Floor, New York, NY 10036, http://www.ansi.org.

[3] Available from Food and Drug Administration (FDA), 5600 Fishers Ln., Rockville, MD 20857, http://www.fda.gov. This document available at http://www.fda.gov/cdrh/ode/guidance/1545.pdf.

$Dp2$ = inner diameter at the pressure of $p2$,
$p1$ = lower pressure value (diastolic), in mm Hg, and
$p2$ = higher pressure value (systolic), in mm Hg.

3.1.3 *diametric strain, n*—a change in mock artery diameter divided by the initial diameter. This term does not relate to the mechanical strain seen in the stent material. The diametric strain can be identified as:

$$\text{diametric strain} = \frac{(Dp2 - Dp1)}{Dp1} \tag{2}$$

that is,

$$\text{diametric strain} = \frac{(\text{maxID} - \text{minID})}{\text{minID}}$$

3.1.4 *distension, n*—the change in diameters; such as the inner diameter (ID) of a vessel due to a pressure change. The term "diametric distension" is meant to represent the change in inner diameter of a blood vessel during each pulse of blood circulation. As an example, the change in diameter between the diastolic and systolic pressure for each pulse of blood circulation.

3.1.5 *hydrodynamic loading, n*—causing a change in the inner diameter (ID) of a mock vessel by injecting a volume of fluid into the confined test volume.

3.1.6 *mock vessel, n*—a simulated vessel typically manufactured from an elastomeric material. The mock vessel is made to approximate the ID and diametric distention of a native vessel at physiological pressures (see A1.2.2 and A2.4.2) or at non-physiological pressures (see A2.4.4).

3.1.7 *native vessel, n*—defined as a natural healthy blood vessel.

3.1.8 *strain control, n*—a term to describe control of diametric distention, relative to an initial diameter of the mock vessel, not to be confused with controlling the strain in the stent material.

3.1.9 *vascular stent, n*—a synthetic tubular structure that is implanted in the native or grafted vasculature and is intended to provide mechanical radial support to enhance vessel patency over the intended design life of the device. A stent is metallic and not covered by synthetic textile or tissue graft material.

4. Summary of Test Methods

4.1 These test methods cover fatigue/durability testing of vascular stents that are subjected to hydrodynamic loading that simulates the loading and/or change in diameter that the stent will experience *in vivo*. The stent shall be deployed into mock vessels that can be used to produce a cyclic diameter change of the stent. This document details two test methods that are currently used.

4.1.1 *Physiological Pressure Test Method*—This test method (provided in Annex A1) requires the use of mock vessels that possess similar diametric compliance properties to native vessels at physiological pressure and rate of pulsation as well as at higher testing frequencies.

4.1.2 *Diameter Control Test Method*—(Sometimes called a strain control test method.) This test method (provided in Annex A2) requires the use of a diameter measurement system and mock vessels to ensure that the desired minimum and maximum stent diameters, or the equivalent change in stent diameter and mean stent diameter, are being achieved at the test frequency. For conditions where a direct measurement of the stent is not possible, measurements are typically made over the OD of the mock vessel and a relationship is determined and justified for the ratio of the stent OD versus measured mock vessel OD.

5. Specimen Size, Configuration, and Preparation

5.1 Unless otherwise justified, all samples selected for testing shall be taken from fully processed, implant quality product. Sterilization should be required unless it can be shown not to influence the fatigue/durability test results.

5.2 The number of specimens tested for each stent geometry should be sufficient to support any claims to be made based on the test results. Fatigue/durability shall be evaluated for the worst case labeled diameter, and a rationale shall be provided stating why the particular labeled diameter is considered worst case.

5.3 *Mock Vessels:*

5.3.1 The choice of inside diameter of the mock vessel is critically important to the effectiveness of any durability test to be carried out. The mean non-stented mock vessel ID over a cardiac cycle shall be consistent with the worst case stent OD, for the stent being tested, over the full test duration.

5.3.2 See Annex A1 and Annex A2 for specific requirements.

5.4 The sample size, in combination with other tests, animal and clinical tests, analysis (such as FEA (Finite Element Analysis), and/or comparisons to predicate devices shall be sufficient to enable demonstration of an adequate justified reliability. In these test methods, one stent shall be considered one sample. The reliability justification may reference additional testing and/or analysis used to establish stent durability.

6. General Apparatus Requirements

6.1 For test methods requiring precision measurement and control of pressure, dimensions, or cycle counts, verification of the dynamic performance of these systems shall be performed and documented with justification of the means used.

6.2 *Pressure Measurement System*—Pressure transducers should be chosen that allow for the accurate evaluation of the pressures within the tubes at the frequency of the test. See Annex A1 and Annex A2 for method specific requirements. The pressure measuring system must be calibrated and justified.

6.3 *Dimensional Measurement Devices,* such as linear variable displacement transducers, lasers, and high-speed cameras must be calibrated and justified.

6.4 *Cycle Counting System*—The apparatus shall include a cycle counting system for measuring the number of load cycles applied to the stent/mock artery combination.

6.5 *Temperature Control System*—The apparatus shall include a calibrated temperature control and measurement system to provide the testing temperature for stents being tested.

7. General Test Parameters

7.1 *Temperature*—The temperature shall be 37 ± 2°C. If other temperatures are to be used, a rationale shall be provided stating why the particular temperature is considered worst case or equivalent. The unit is to be stable over the intended period of the test and maintained within the established parameters.

7.2 Actual temperatures and precisions shall be documented by the user with accompanying justifications.

7.3 *Solutions*—The test solution shall be phosphate buffered saline (PBS) or equivalent unless testing in a different environment (such as in distilled water or in air) can be justified. Rationale for use of a different environment shall be provided.

7.4 *Physiological Pressure*—The pressure change in the intended blood vessel. A suggested range for coronary stent pulsatile fatigue evaluation is 80 to 160 mm Hg.

NOTE 1—Selection of the systolic and diastolic pressures should be based on the patient population for which the stent is indicated.

7.5 *Physiological Pulse Rate*—For the purposes of these test methods, determined to be 1.2 Hz or 72 beats per minute.

7.6 Biological growth can inhibit post-test evaluation of the stent surface characteristics. Use of a biological growth inhibitor (such as algaecides or chemical agents) may be used unless such use would negatively impact the test by unintended degradation of the stent or the test set-up.

7.7 The ID of the non-stented mock vessel is to be empirically verified on the test instrument after the mock vessel(s) have been mounted in their initial test position.

7.8 *Vessel Degradation*—Mock vessels made of materials that may degrade with exposure to environmental factors (such as UV light) shall be protected from such exposure.

7.9 *Stent Deployment*—The stent shall be deployed in the mock vessel in such a manner as to minimize end effects where the vessel is connected to the test article and at a sufficient distance from other stents that may be deployed in the same vessel (see X2.5).

7.10 *Test Frequency*—See Annex A1 and Annex A2 for test specific details.

7.11 *Test Validation*—The investigator shall demonstrate that the stent to be tested maintains contact with the ID of the vessel to be used in the durability test throughout the cycle, when evaluated with the same pressures and frequencies to be used in the durability test. This is not required for every sample. This and any justifications shall be documented in the test report. Rationale: The functionality of a test method used to test a stent inside a vessel depends on the stent remaining in contact with the ID of the vessel throughout the distension cycle of that vessel.

7.12 *Acceptance Criteria*—A detailed test protocol shall be written that describes all procedures unique to the stent being evaluated. This protocol shall include any specific failure modes to be identified, and inspections to be performed to identify those failures in any acceptance/rejection criteria. (See Appendix for examples.)

8. Test Report

8.1 The test report shall include a complete summary of the materials, methods, and results including any rationale for deviations from this procedure. The effects of any such deviations on the significance of the test results shall be reported. All real, artifact, and anomalous observations shall be reported, including a justification for considering negative findings as artifacts or discounting their clinical significance.

8.2 Test reports should include:

8.2.1 Test parameters and acceptance criteria:

8.2.1.1 Test parameters (such as):

(1) Mock vessel dimensions.

(2) Fluid temperature.

(3) Fluid pressure range and variability, or desired change in stented vessel diameter.

8.2.1.2 Acceptance criteria (such as):

(1) Minimum level of pulsatile distention to define acceptance.

(2) Maximum number of failures to define acceptance.

(3) Minimum number of cycles required to define acceptance.

8.2.2 Test specimen information:

8.2.2.1 Number of test specimens.

8.2.2.2 Size (diameter, length, or other relevant dimensions) of all test specimens.

8.2.2.3 Rationale for the number of test specimens and sizes used.

8.2.2.4 Whether the specimens are representative of the finished product.

8.2.2.5 Sterilization parameters and number of sterilization cycles applied to the test specimens.

8.2.2.6 Traceability information.

8.2.3 Materials used:

8.2.3.1 Test equipment.

8.2.3.2 Mock vessels.

8.2.3.3 Test fluid/solutions.

8.2.3.4 Measurement devices.

8.2.4 Test protocol, including all justifications and rationales required by these test methods.

8.2.5 Protocol deviations.

8.2.6 Raw data.

8.2.7 Test results.

8.2.8 Data analysis

8.2.9 Fracture reporting:

8.2.9.1 Report any fractures that occur during the test.

8.2.9.2 Fracture information should include number of cycles to failure, number and locations of all fractures along the length of the stent, type of fracture such as transverse or spiral, with or without dislocation, and any root cause analysis performed to determine the reason for the fracture.

8.2.10 Conclusions.

9. Precision and Bias

9.1 Intralaboratory and interlaboratory reproducibility has not been systematically determined.