TC 150

International Standard 5840

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Implants for surgery — Cardiovascular implants — Cardiac valve prostheses

Implants chirurgicaux — Implants cardiovasculaires — Prothèses valvulaires

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Every member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work.

Draft International Standards adopted by the technical committees are circulated to the member bodies for approval before their acceptance as International Standards by the ISO Council. They are approved in accordance with ISO procedures requiring at least 75 % approval by the member bodies voting.

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0 Introduction

Twenty years of intensive and continuous research and development has failed to result in the ideal valve replacement. Indeed, at the time of writing, many would argue that not even a particular type of valve can be singled out as nearest the optimum. This is due to many conflicting factors in valve design. For example, a prosthesis with excellent hydraulic characteristics may have a poor record of thromboembolic complication; a second valve, satisfactory from the haemodynamic point of view, may have limited durability; and a third may be too noisy for the patient to tolerate. Thus there is no clear-cut choice for the surgeon.

This International Standard has been prepared by a group well aware of the problems associated with prosthetic heart valves and their development. In several areas, this International Standard has deliberately been left open, for there was no wish to inhibit valve improvement. It intentionally makes no attempt to specify minimum performance requirements for the finished product, since standard performance criteria do not exist and, in fact, may vary according to the needs of a specific patient.

The areas with which this International Standard is concerned are thus intended to be those which will aid the surgeon in his choice of valve and ensure that the prosthesis will be presented in a convenient form at the operating table. Emphasis has therefore been placed on labelling and packaging aspects of the device and on the reporting of *in vitro* hydraulic and durability data.

With regard to testing and reporting, the document has been restricted to cover the important pulsatile hydraulic characteristics of the valve; because various test methods in current use are also in a state of evolution and improvement, the exact method of test has not been specified. Similarly, in the case of accelerated fatigue testing, only a description of the method of test and the results obtained are required.

It is recognized that this International Standard is incomplete, but it is intended that it be updated as knowledge and techniques in prosthetic heart valve technology improve.

1 Scope and field of application

This International Standard specifies basic requirements for test reporting, packaging, labelling and terminology for prosthetic heart valves (aortic/pulmonary and mitral/tricuspid).

2 Definitions

2.1 arterial diastolic pressure: Minimum value on the central aortic pressure wave form during the diastolic phase.

2.2 arterial systolic pressure: Maximum value on the central aortic pressure wave form during the systolic phase.

2.3 ball valve: A prosthetic heart valve which employs an occluder of spherical shape constrained in such a manner that fluid forces move the sphere away from the orifice area such that forward fluid flow is permitted, and conversely, fluid forces in the opposite direction move the sphere to occlude the orifice, thereby preventing fluid flow in the reverse direction.

2.4 cardiac valve prosthesis: Prosthetic device used to replace or supplement natural valves of the heart as follows:

a) arterial outflow valves (aortic/pulmonary);

b) ventricular inflow valves (mitral/tricuspid).

2.5 cycle rate: Number of complete cycles per unit time, usually expressed in terms of number of cycles per second (f) (or cycles per minute).

2.6 cycle time: Time, in seconds, during which a complete cycle is performed

$$T = \frac{1}{f}$$

where

T is the cycle time in seconds;

f is the cycle rate in cycles per second.

2.7 disc valve: The same as a ball valve except that the occluder element is disc-shaped.

2.8 external annulus diameter: (Also know as *mounting diameter*.) The diameter of the prosthetic valve where it is intended to mate with the smallest diameter of host tissue.

2.9 frustum: (Also known as *secondary valve orifice*.) The minimum built-in area available for flow other than at the primary valve orifice.

2.10 hinged disc prosthetic heart valve: (Also known as *pivoted disc prosthetic heart valve*.) Prosthetic heart valve in which flow and occlusion are controlled by one or more hinged rigid occluders.

2.11 leaflet prosthetic heart valve: A prosthetic heart valve consisting of one or more flexible leaflets attached to a ring in such a manner that fluid forces will cause them to flex between the open and closed positions, allowing flow in one direction and restricting it in the other.

2.12 mean flow rate: Mean (average) rate of flow across the valve being tested either during the systolic ejection phase (outflow valve) or during the diastolic filling phase (inflow valve).

2.13 mean pressure difference (deprecated term: *mean pressure gradient*): Mean (average) value of the pressure difference wave form across a valve under test during the whole of the systolic ejection phase (outflow valve) or diastolic filling phase (inflow valve).

2.14 mounting diameter: [See 2.8, *external annular diameter*.]

2.15 occluder: The components of a prosthetic valve that move to inhibit retrograde flow, either totally or partially.

2.16 pivoted disc prosthetic heart valve: [See 2.10, *hinged disc prosthetic heart valve*.]

2.17 primary valve orifice: Space available through open valve at narrowest point of valve inlet.

2.18 regurgitant fraction: That proportion of the stroke volume which flows in a retrogade manner across the test valve.

2.19 secondary valve orifice: [See 2.9, *frustum*.]

2.20 stroke volume: Volume of blood ejected from the ventricle during one systolic ejection flow phase or entering the ventricle during one diastolic filling flow phase. In test rigs the stroke volume usually refers to the volume moved across the test valve, it being assumed that no leakage occurs at the other valve.

2.21 systolic ejection flow phase (deprecated term: *systolic ejection phase*): That phase of a cycle during which forward flow occurs accross the test outflow valve.

NOTE — The term "systolic ejection phase" has been commonly used to denote both systolic ejection flow phase and systolic ejection pressure phase but these are not equivalent. The use of the term "systolic ejection phase" without further qualification is consequently to be deprecated. Similarly the term "diastolic filling phase" is deprecated.

2.22 systolic ejection pressure phase (deprecated term: *systolic ejection phase*): That phase of a cycle during which the ventricular pressure exceeds that on the opposite side of the test outflow valve. See also note to 2.21.

2.23 systolic phase: That phase of a cycle during which a force is applied to drive the ventricle, including the stage during which the force builds up.

2.24 tilting disc prosthetic heart valve: A prosthetic heart valve in which flow and occlusion are controlled by the tilting of a disc.

2.25 transvalvular pressure difference: Indirect measure of the energy lost in transporting the test fluid across the valve. Depending on the method of use (see below) and the particular measure used, this should always be specified.

2.26 ventricular (cardiac) output: Net forward flow during one minute. It is defined as:

stroke volume × (1 − regurgitant fraction) × cycle rate

or

(stroke volume − regurgitant volume) × cycle rate

3 Materials, design and manufacture

3.1 The size of the prosthetic heart valve shall be designated by the mounting diameter of the heart valve where it is intended to mate with the host tissue, expressed in millimetres.

3.2 Materials used in the construction of prosthetic heart valves shall be corrosion resistant and of adequate mechanical strength, and, in the finally processed condition, not be incompatible with the human tissue with which they are intended to be used.

3.3 All construction processes and techniques shall be performed in accordance with good manufacturing practice. (An example is provided as annex B.) In addition, all construction processes shall be adequately qualified by *in vitro* and/or *in vivo* testing as applicable with respect to mechanical or corrosion resistant properties of the material.

4 Methods of test or inspection

4.1 *In vitro* haemodynamic testing

4.1.1 Principle

In vitro haemodynamic testing is conducted to assess the performance of prosthetic heart valves.

4.1.2 Apparatus

4.1.2.1 The test apparatus shall be a prosthetic heart valve pulse duplicator system which is a simplified analogue of the human circulatory system. An ideal analogue of the human circulatory system cannot be realized because of the pulsatile nature of flow in a constantly varying geometry of both the mounting of the natural valve and the inflow/outflow tracts.

4.1.2.2 The pulse duplicator system should simulate pertinent variables of the human circulatory system such as mean cardiac output, normal heart rate, pertinent chamber and vascular dimensions, systolic and diastolic blood pressures and durations. The system should also permit basic haemodynamic measurements such as pressure and flow as dependent variables of time.

4.1.3 Procedure

4.1.3.1 At least four conveniently spaced measurement points shall be chosen covering the intended range of flow rates and cyclic rates.

4.1.3.2 The test shall be conducted at 37 ± 2 °C.

4.1.3.3 The density of the test liquid shall be 1,100 ± 0,1 kg/l at the temperature specified in 4.1.3.2.

4.1.3.4 The test liquid viscosity shall be in the range of 0,7 to 4 cP at the temperature specified in 4.1.3.2.

4.1.3.5 The systolic duration shall be between 30 and 50 % of the simulated cardiac cycle.

4.1.3.6 The volume displacement wave form shall have a configuration between and including a rectangular wave and sine wave.

4.1.4 Test report

The test report shall include the following information:

4.1.4.1 Specifications of the valve tested, including:

a) valve type (ball, caged-disc, pivoting/tilting disc, leaflet, other) and designation;

b) mounting diameter, primary orifice area, and secondary orifice area, and methods of determination;

c) density, weight and travel of occluder, if applicable;

d) materials of valve body and occluder or leaflet.

4.1.4.2 Specific description of the pulse duplicator and major components of the test loop and associated apparatus, including a schematic diagram of the system.

4.1.4.3 Specific description of the test conditions.

4.1.4.4 Specific description of instrumentation used for all measurements during the testing.

4.1.4.5 The following haemodynamic quantities at the four measurement points chosen in 4.1.3.1:

a) cyclic rate;

b) systolic duration as a percentage of the simulated cardiac cycle;

c) forward stroke volume;

d) simultaneous pulsatile pressure versus time graphs on both sides of the valve;

e) simultaneous pulsatile flow rate through the valve and pulsatile pressure drop across the valve versus time graphs;

f) regurgitant fraction;

g) regurgitant volume per stroke.

With regard to d) and e) above the measurement points shall show variation of mean pulsatile pressure difference (in conventional millimetres of mercury) with variation of mean pulsatile flow rate (in millilitres per second) and may be presented in either graphic or tabular form. The mean pulsatile pressure difference measurements shall be corrected to the density of blood as follows:

$$\bar{P}_{dc} = \frac{1{,}055 \times \bar{P}_d}{\varrho}$$

where

$\bar{P}_{dc}$ is the density corrected mean pressure drop, in kilopascals (or in conventional millimetres of mercury);

$\bar{P}_d$ is the measured mean pressure drop, in kilopascals (or in conventional millimetres of mercury), using liquid of density ϱ, in grams per millilitre;

1,055 is the density, in grams per millilitre, of blood at 37 °C.

The test liquid, its temperature, density and viscosity shall be stated.

4.2 Accelerated wear testing

4.2.1 Principle

Accelerated wear testing is conducted to facilitate assessment of prosthetic heart valve durability.

4.2.2 Apparatus

Any test apparatus capable of meeting the requirements of 4.2.3 may be used.

4.2.3 Procedure

4.2.3.1 The accelerated wear test shall be conducted by means of the *in vitro* cycling of a prosthetic heart valve at rates substantially greater than 72 cycles per minute.

4.2.3.2 The manufacturer shall test the opening and closing mechanism for 380 million cycles or to failure, whichever occurs first, and report the results in accordance with 4.2.4.

4.2.3.3 The maximum speed at which these tests can be performed will vary with different valve configurations and materials. The fluid used in the test apparatus will affect results. Although wear per cycle may change with increased speed, present knowledge does not allow an exact correction factor to be applied.

4.2.3.4 In view of these variables, and to make results obtained by one investigator readily comparable with others, the test results shall be reported in accordance with 4.2.4.

4.2.4 Test report

The test report shall include the following information:

4.2.4.1. Specifications of the valve tested, including:

a) valve type (ball, caged-disc, pivoting/tilting disc, leaflet, other) and designation;

b) mounting diameter, primary orifice area, and, if applicable, secondary orifice area, and methods of determination;

c) density, weight and travel of occluder, if applicable;

d) materials of valve body and occluder or leaflet.

4.2.4.2 Test speed in cycles per minute.

4.2.4.3 The gas or liquid in which the test was performed, and its temperature, viscosity and density.

4.2.4.4 Specific description of the accelerated wear test and associated apparatus, including a schematic diagram of the system.

4.2.4.5 Specific description of the test conditions.

4.2.4.6 Specific description of instrumentation used for all measurements during the testing.

4.2.4.7 Total number of cycles. The total reported should not exceed the number at which valve function is impaired.

4.2.4.8 Degradation description.

5 Sterility

5.1 The manufacturer may dispatch heart valves in a sterile or non-sterile condition as specified by the purchaser.

5.2 The method of sterilization employed or recommended by the manufacturer shall not produce changes that will render the product incompatible with human tissue or cause detectable deterioration in mechanical or other properties.

5.3 Where the prosthetic heart valve may be sterilized or re-sterilized by the user, the manufacturer shall supply full details of the recommended procedures for sterilization of the valve, including the maximum number of cycles which may be undertaken by the user.

6 Packaging, labelling and marking

6.1 Packaging

6.1.1 The prosthetic heart valve shall be individually packaged in a suitable unit container.

6.1.2 Where the prosthetic heart valve may be sterilized or re-sterilized by the user, the unit container shall permit sterilization of the contents *in situ*, and shall provide adequate physical protection against mechanical damage to the prosthesis during sterilization.

6.1.3 The packaging material within the unit container shall not cause significant particulate contamination of the prosthesis.

6.1.4 The unit container shall be sealed in such a way that once the container is opened it is obvious that the seal has been broken.

6.1.5 The unit container shall be so designed as to permit the prosthesis to be presented for use in an aseptic manner.

6.1.6 The unit container shall be packaged within an individual outer container or containers which shall be sufficiently robust to protect the unit container from damage during normal conditions of handling, transit or storage.

6.1.7 Where the prosthesis is dispatched in a sterile condition, the package system (which comprises the unit container packed within one or more outer containers) shall be designed to maintain sterility of the prosthesis under normal conditions of handling, transit and storage.

6.2 Labelling

6.2.1 Unit container

Each unit container shall display the following:

a) description of contents including name, type, model and serial number of prosthetic heart valve and the size of the valve in accordance with 4.1.4.1;

b) the words "contents sterile" or "contents not sterile";

c) date of sterilization (year and month) and/or expiration date (year and month) where applicable;

d) the name and place of business of the manufacturer or distributor and country of origin.

6.2.2 Package insert

Each unit container shall be accompained by a product information text which includes the following items, where applicable:

a) concept/description;

b) indications for use;

c) contraindications;

d) warnings;

e) precautions;

f) complications;

g) technique/directions for use;

h) accessories;

j) how supplied;

k) storage;

m) sterilization (or re-sterilization);

n) patient identification system (see 6.2.3 and annex C);

p) references;

q) the common and/or chemical names of all materials which come into contact with blood or tissue.

6.2.3 *Patient identification system*

The manufacturer shall supply a system of identification for the hospital, surgeon, manufacturer and patient. An example of a patient identification system is provided as annex C.