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Third edition
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Implants for surgery — Hydroxyapatite —

Part 2: Thermally sprayed coatings of hydroxyapatite

Implants chirurgicaux — Hydroxyapatite —

Partie 2: Revêtements à base d'hydroxyapatite, obtenus par projection thermique

Reference number
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Contents

Page

Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation on the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see the following URL: www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 150, *Implants for surgery*, Subcommittee SC 1, *Materials*.

This third edition cancels and replaces the second edition (ISO 13779-2:2008), which has been technically revised.

A list of all parts in the ISO 13779 series can be found on the ISO website.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

No known surgical implant material has ever been shown to be completely free of adverse reactions in the human body. However, long-term clinical experience of the use of the material referred to in ISO 13779 has shown that an acceptable level of biological response can be expected, if the material is used in appropriate applications.

The biological response to hydroxyapatite coatings has been demonstrated by a history of clinical use and by laboratory studies (see References [1], [2], [3], [4], [5], [6]).

Implants for surgery — Hydroxyapatite —

Part 2: Thermally sprayed coatings of hydroxyapatite

1 Scope

This document specifies requirements for single layer thermally sprayed hydroxyapatite coatings applied to metallic surgical implants.

These requirements are intended to describe properties of the materials and to communicate these between organizations. These requirements are not written with the objective of replacing a company's internal operational and assessment requirements although they could be used as such.

NOTE 1 For thin coatings with a thickness of less than 50 µm, some of the test methods described in this document might be difficult to apply without modification.

NOTE 2 The requirements of the hydroxyapatite layer of dual-layer coatings (consisting of a lower layer of metallic coating and an upper layer of hydroxyapatite coating) can follow this document; however, testing methods referred to in this document cannot be applied to dual layer coatings. If this document is taken in reference for the requirements of the hydroxyapatite layer of dual layer coatings, a rationale on how the single-layer tested coupons are representative of the dual-layer coated implant might be considered necessary.

This document does not cover coatings made from glasses, glass ceramics, alpha- and beta-tricalcium phosphate, biphasic calcium phosphate or other forms of calcium phosphate.

NOTE 3 While the requirements in this document are intended to be used as specifications of a thermally sprayed coating of hydroxyapatite, it might be necessary to establish routine control procedures specifying control tests and their time intervals to make sure the characteristics of the coating stay within specified limits.

NOTE 4 This document was developed with a focus on plasma sprayed coating of hydroxyapatite. It might also be used to characterize other thermally sprayed coatings of hydroxyapatite. However, thermally sprayed coatings that do not have a history of clinical use might present different risks and might need additional characterizations beyond those identified in this document.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 4288, *Geometrical Product Specifications (GPS) — Surface texture: Profile method — Rules and procedures for the assessment of surface texture*

ISO 10993-1, *Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process*

ISO 13779-3, *Implants for surgery — Hydroxyapatite — Part 3: Chemical analysis and characterization of crystallinity ratio and phase purity*

ISO 13779-4, *Implants for surgery — Hydroxyapatite — Part 4: Determination of coating adhesion strength*

ISO 13779-6, *Implants for surgery — Hydroxyapatite — Part 6: Powders*

ASTM F1044, *Standard Test Method for Shear Testing of Calcium Phosphate Coatings and Metallic Coatings*

ASTM F1854, *Standard Test Method for Stereological Evaluation of Porous Coatings on Medical Implants*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 13779-3 and the following apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at http://www.electropedia.org/

3.1
thermally sprayed hydroxyapatite coating
coating formed by thermal spraying of hydroxyapatite powders

Note 1 to entry: For the purpose of this document, the terms "coating" and "hydroxyapatite coating" both mean "thermally sprayed hydroxyapatite coating"

4 Coating preparation

The powder used for thermal spraying of the hydroxyapatite coating shall be in accordance with ISO 13779-6.

Unless documented and justified by the manufacturer, all test specimens shall be prepared using the same production methods of regular implant components, including initial hydroxyapatite powder, substrate material, production installations, substrate surface preparation process, coating process parameters, cleaning and sterilization.

5 Requirements

5.1 General

The minimum requirements for the hydroxyapatite coating are established in 5.2 to 5.8.

Other characterization tests, such as those described in A.2, A.3 and A.4, might also be requested (e.g. in order to satisfy applicable national or regional regulation).

NOTE 1 In addition to the tests described in 5.2 to 5.8, some regulatory bodies can request the tests given in Annex A to characterize the hydroxyapatite coating.

5.2 Calcium to phosphorus ratio (*Ca:P*)

Coating shall be scraped from the substrate before testing.

The calcium to phosphorus ratio, *Ca:P*, of the hydroxyapatite ceramic coating shall be determined in accordance with ISO 13779-3.

The calcium to phosphorus ratio, *Ca:P*, shall have a value in the range of 1,61 to 1,76 for the atomic ratio.

NOTE Calcium to phosphorous ratio is usually not influenced by the thickness of the coating.

5.3 Trace elements

Coating shall be scraped from the substrate before testing. The amount of sample required for chemical analysis is dependent on the chemical analysis technique used. The amount of sample used shall be sufficient to achieve adequate quantification limits. The technique used to remove the coating shall

minimize the chance of contamination of the coating: care shall be taken to use appropriate tools and avoid contamination with particles coming from the substrate.

The trace element concentrations shall be determined as specified in ISO 13779-3. Heavy metals shall be as specified in ISO 13779-3.

The maximum allowable limits of specific trace elements and heavy metals for hydroxyapatite coatings are given in Table 1.

Any trace element likely to be present with more than 1 000 mg/kg shall be identified. These elements shall be quantified and if present with more than 1 000 mg/kg, their influence on biocompatibility shall be assessed according to ISO 10993-1 as well as their influence on bone healing.

Table 1 — Limits of specific trace elements

Trace element	Maximum limit mg/kg
Arsenic	3,0
Cadmium	5,0
Mercury	5,0
Lead	30,0
Heavy metals (total)	50,0

5.4 Foreign crystalline phases

Coating shall be scraped from the substrate before testing.

The foreign crystalline phases content, expressed as the foreign crystalline phase to crystalline hydroxyapatite ratio, shall be determined as specified in ISO 13779-3. The sum of α-tricalcium phosphate, β-tricalcium phosphate and tetracalcium phosphate shall not exceed 30,0 % and the CaO content shall not exceed 5,0 %.

NOTE 1 For coatings with a thickness over 50 µm the foreign crystalline phases content is usually not influenced by the thickness of the coating.

NOTE 2 A rationale on the limits set for foreign crystalline phases content is included in Annex B.

NOTE 3 Within the limits allowable per the present document, any increase of the α-tricalcium phosphate, β-tricalcium phosphate and tetracalcium phosphate total content might increase the solubility of the coating. A significant variation in this total content might impact the functionality of the coating.

5.5 Crystallinity ratio

Coating shall be scraped from the substrate before testing.

The crystallinity ratio shall be determined following the method described in the ISO 13779-3.

The crystallinity ratio shall be not less than 45 %.

NOTE 1 The crystallinity ratio of the coating can be influenced by the thickness of the coating. First deposited layers of the coating can have a lower crystallinity ratio than upper layers. Therefore, it might be sensible within a validation process to determine crystallinity ratio on coupons with a coating thickness within or below the lowest quartile of the specification for the thickness of the coating.

NOTE 2 A method to evaluate the thickness of the coating can be found in ASTM F1854. This method requires to prepare metallographic sections and is thus destructive. However, it can be correlated to, but might not provide identical results as, non-destructive methods like Eddy current or micrometer.

5.6 Morphology

The morphology of the Hydroxyapatite coating (thickness, roughness and microscopical observation) shall be assessed on the final device, if possible. If the morphology tests are not performed on the final device because the requirements of the applied standard cannot be met due to geometry of the device, coupons may be used and their representativeness to the final device shall be justified.

The average thickness and the tolerances, in µm, shall be determined in accordance with ASTM F1854. No acceptance criterion is defined in this International Standard for average thickness. The acceptance criteria for tolerances of average thickness of the Hydroxyapatite coating in the different areas of the implant shall be defined and documented for each implant.

Roughness (R_a or R_t), in µm, shall be determined in accordance with ISO 4288. No acceptance criterion is defined in this International Standard for roughness. The acceptance criteria for tolerances of roughness (R_a or R_t) of the Hydroxyapatite coating shall be defined and documented.

Scanning Electron Microscopy (SEM) or optical microscopy observation of the Hydroxyapatite coating surface and cross-section shall be performed. No acceptance criterion is defined in this International Standard for this test. The aim is to characterize qualitatively the porosity of the coating and the profile of the surface of the coating.

NOTE The data obtained by observation of the Hydroxyapatite coating surface and cross-section can be used to help evaluate an intended process change or to compare two different Hydroxyapatite coatings.

5.7 Coating strength

Whether tensile or shear adhesion strength are appropriate properties to be tested depends on the application. Static tensile adhesion strength testing according to ISO 13779-4 or static shear adhesion strength testing according to ASTM F1044 shall be performed. If the application demands both static tensile and static shear adhesion strength, both tests shall be performed.

If tensile adhesion strength testing is performed, the mean tensile coating adhesion strength shall be not less than 15 MPa and no individual result shall be less than 10 MPa.

NOTE 1 ISO 13779-4 provides requirements on the number and geometry of coupons to use for tensile strength testing.

If shear adhesion strength testing is performed, the mean shear coating adhesion strength shall be not less than 15 MPa and no individual result shall be less than 10 MPa.

For shear adhesion strength testing, a minimum of 10 coupons shall be used.

The coating might affect the fatigue properties of the implant. ASTM F1160 can be useful to compare fatigue properties of the substrate before and after coating. The fatigue properties of the implant might have to be investigated on the final product.

NOTE 2 The adhesion strength results might be influenced by the thickness of the coating. High thickness coatings might result in lower adhesion strength results. Therefore, it might be sensible within a validation process to determine adhesion to the substrate on coupons with a coating thickness within or above the highest quartile of the specification for the thickness of the coating.

NOTE 3 A method to evaluate the thickness of the coating can be found in ASTM F1854. This method requires to prepare metallographic sections and is thus destructive. However, it can be correlated to non-destructive methods like Eddy current or micrometer.

5.8 Accuracy of test methods

Accuracy of test methods shall be determined.

NOTE ISO 13779-3 provides requirements for the determination of accuracy of chemical analysis, foreign phases content, crystallinity ratio and *Ca:P* ratio test methods.

6 Test report

The test report shall include at least the following information:

a) reference to this document, i.e. ISO 13779-2:2018;

b) identification of the test sample, including: source, references, coating thickness, form, date of receipt;

c) number of test samples used for each test;

d) the reference to the test method used and accuracy (see 5.8);

e) calcium to phosphorous ratio results (see 5.2);

f) trace elements method and results (see 5.3);

g) foreign crystalline phases analysis results (see 5.4);

h) crystallinity ratio results (see 5.5);

i) specified minimum and maximum average thickness and results of the measurements of the average thickness and tolerances of the Hydroxyapatite coating in the different areas of the implant (see 5.6);

j) specified minimum and maximum roughness (R_a or R_t) and results of the measurements of roughness (R_a or R_t) (see 5.6);

k) Scanning Electron Microscopy (SEM) or optical microscopy observations of the Hydroxyapatite coating (see 5.6);

l) rationale for choosing the static tensile strength test or the static shear strength test (see 5.7);

m) coating adhesion strength or shear strength results, including: individual results on each coupon, mean value and standard deviation (see 5.7);

n) if applicable, the results of the tests described in Annex A;

o) dates of the tests;

p) identification and accreditation of the laboratory carrying out the test.

Annex A
(informative)

Other possible characterization tests

A.1 General

The characterization tests, such as those described in A.2 and A.3, might be requested (e.g. in order to satisfy applicable national or regional regulation).

A.2 Dissolution

Coating shall be scraped from the substrate before testing.

Dissolution of the sample obtained should be assessed in accordance with ASTM F1926[7].

Initial and final dissolution rates and pH shall be recorded.

The data obtained can be used for characterization purposes of the coating and to help evaluate process change or to compare two different Hydroxyapatite coatings.

A.3 Infrared spectroscopy

Coating shall be scraped from the substrate before testing.

Fourier Transformation Infrared Spectroscopy (FT-IR) shall be conducted on the sample obtained.

NOTE A detailed method for FT-IR analysis is described in Reference [8].

All functional groups of HA should be detected. At least the presence of the functional groups of oxyapatite, nitrate, carbonate, and hydrogen-phosphate impurities should be assessed. The presence of any of these impurities shall be documented and justified.

The data obtained can be used for characterization purposes of the coating and to help evaluate process change or to compare two different Hydroxyapatite coatings.

A.4 Shear fatigue strength

Shear fatigue adhesion strength should be assessed in accordance with ASTM F1160[9].

At least 5 coupons shall be tested at a minimum of 10 MPa and all coupons shall withstand at least 10^7 cycles without failure.

Annex B
(informative)

Comparison of foreign crystalline phases content limits

A common limit was set for α-tricalcium phosphate, β-tricalcium phosphate and tetracalcium phosphate total content because these foreign phases have a similar biological effect: they can promote bone growth but are more resorbable than hydroxyapatite. In the 2008 version of this document, the limit was set to 5 w% for each of the α-tricalcium phosphate, β-tricalcium phosphate and tetracalcium phosphate content, expressed as weight percent relative to the total mass of coating (a thermally sprayed coating of hydroxyapatite is composed of crystalline hydroxyapatite, crystalline foreign phases and amorphous phase). Moreover, per the 2008 version of this document, the crystalline hydroxyapatite content had to be 50 w% or greater, expressed as weight percent relative to the total mass of coating. Therefore, when expressed as percentage relative to the crystalline hydroxyapatite, the maximum limit of the 2008 version of this document for each foreign phase was 10 % and the limit for the sum of α-tricalcium phosphate, β-tricalcium phosphate and tetracalcium phosphate was 30 %. This limit was adopted in the current version of this document.

With respect to CaO, as this foreign phase might impair the biocompatibility of the coating and as thermally sprayed coatings of hydroxyapatite usually don't exceed 5 % of CaO expressed as a percentage relative to the crystalline hydroxyapatite, a limit of 5 % was set.

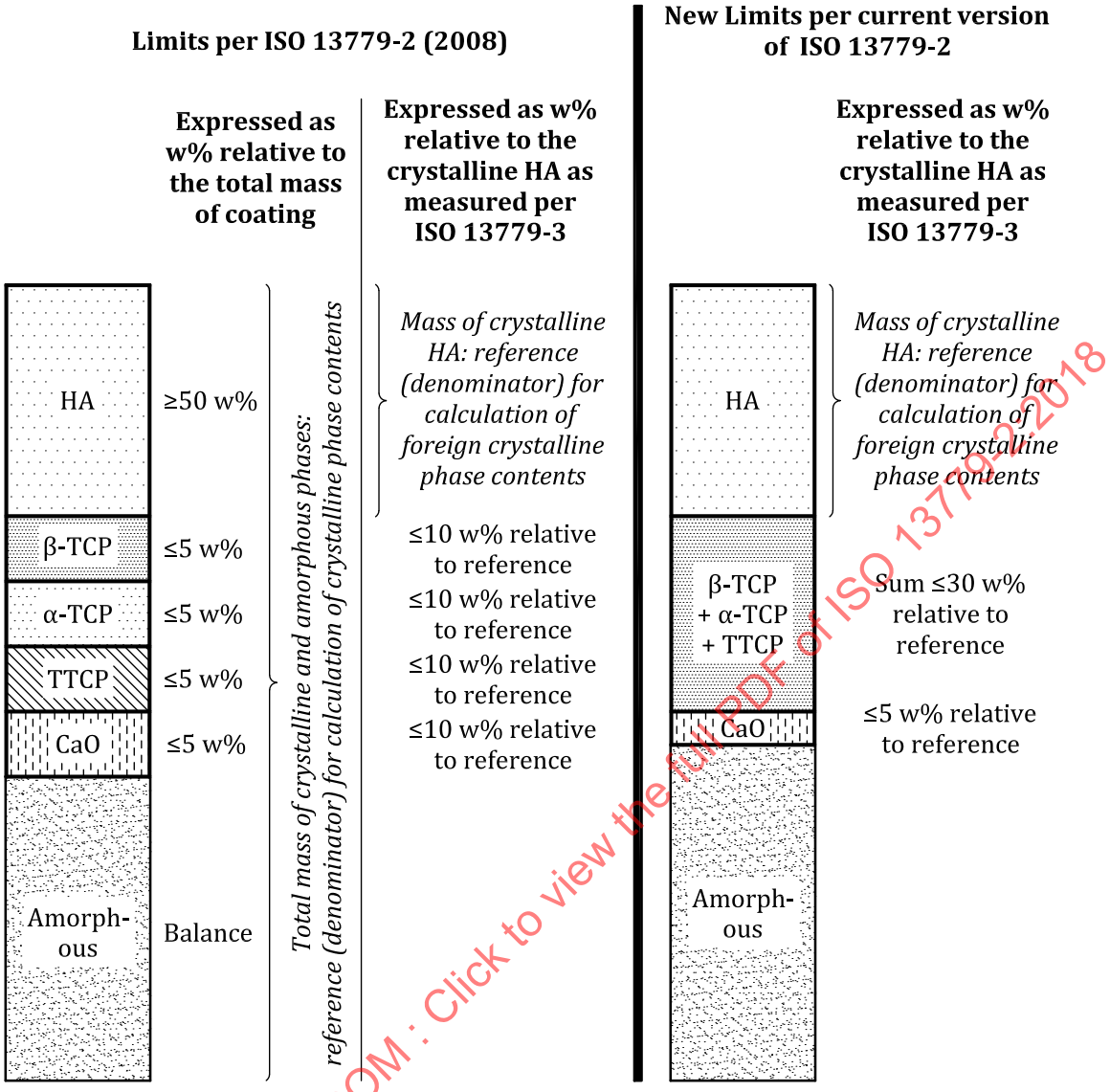

Figure B.1 — Comparison of foreign crystalline phases content limits

To complement the explanation in the text and the figure above, the following example is included:

EXAMPLE If a coating is composed of:

— 66,0 w% HA, expressed as weight percent relative to the total mass of coating;

— 2,0 w% β-TCP, expressed as weight percent relative to the total mass of coating;

— 3,0 w% α-TCP, expressed as weight percent relative to the total mass of coating;

— 4,8 w% TTCP, expressed as weight percent relative to the total mass of coating;

— 1,8 w% CaO, expressed as weight percent relative to the total mass of coating;

— 22,0 w% amorphous phase, expressed as weight percent relative to the total mass of coating.

The w% of foreign crystalline phases, relative to the crystalline HA as measured per ISO 13779-3 are:

— 3,0 w% β-TCP, relative to the crystalline HA;

— 4,5 w% α-TCP, relative to the crystalline HA;

— 7,3 w% TTCP, relative to the crystalline HA;