

図4.ブリッジの金型と寸法

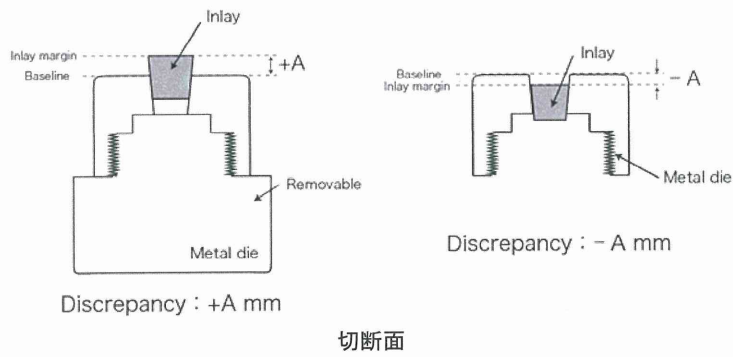


図5. I 級インレーの精度の測定方法

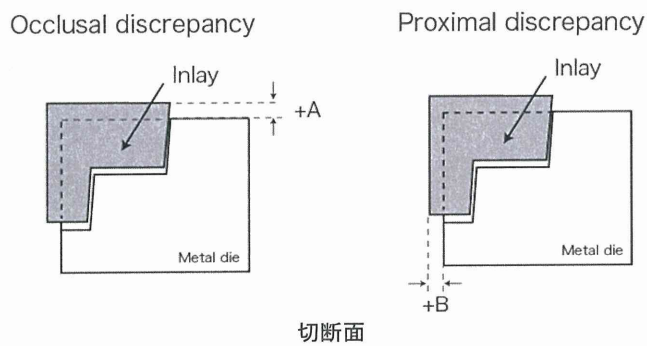


図6. II 級インレーの精度の測定方法(大きい場合)

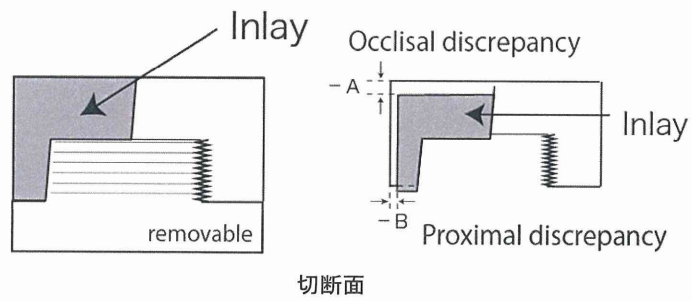


図7. II級インレーの精度の測定方法(小さい場合)

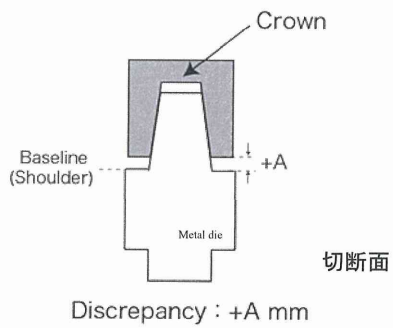


図8. クラウンの精度の測定方法(小さい場合)

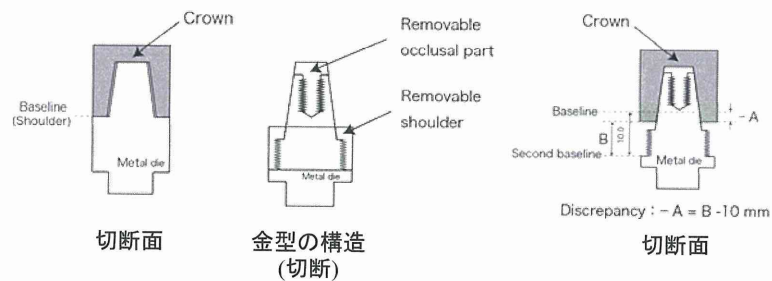
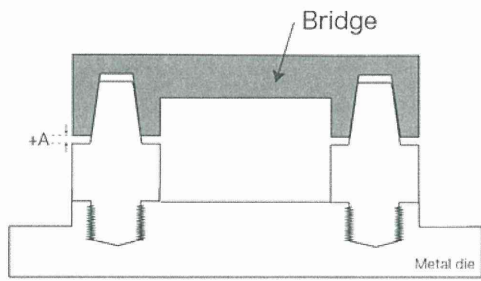
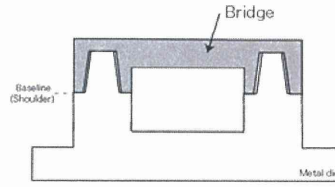


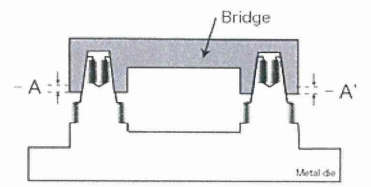
図9. クラウンの精度の測定方法(大きい場合)



切断面



切断面



切断面

図10. ブリッジの精度の測定方法(小さい場合)

図11. ブリッジの精度の測定方法(大きい場合)

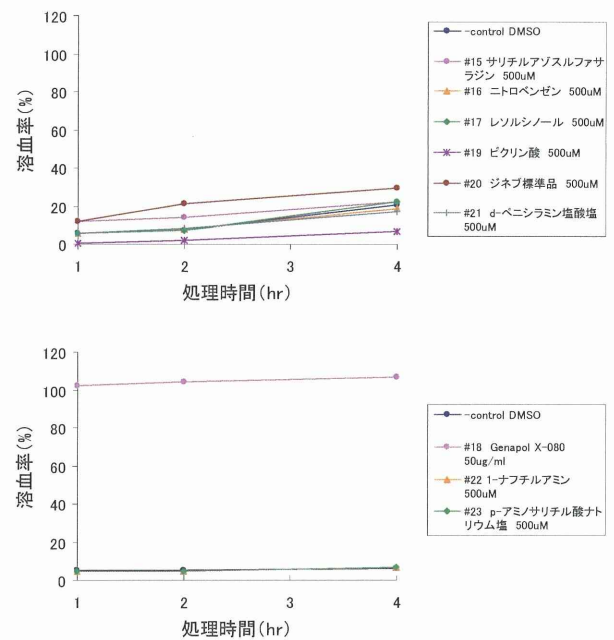
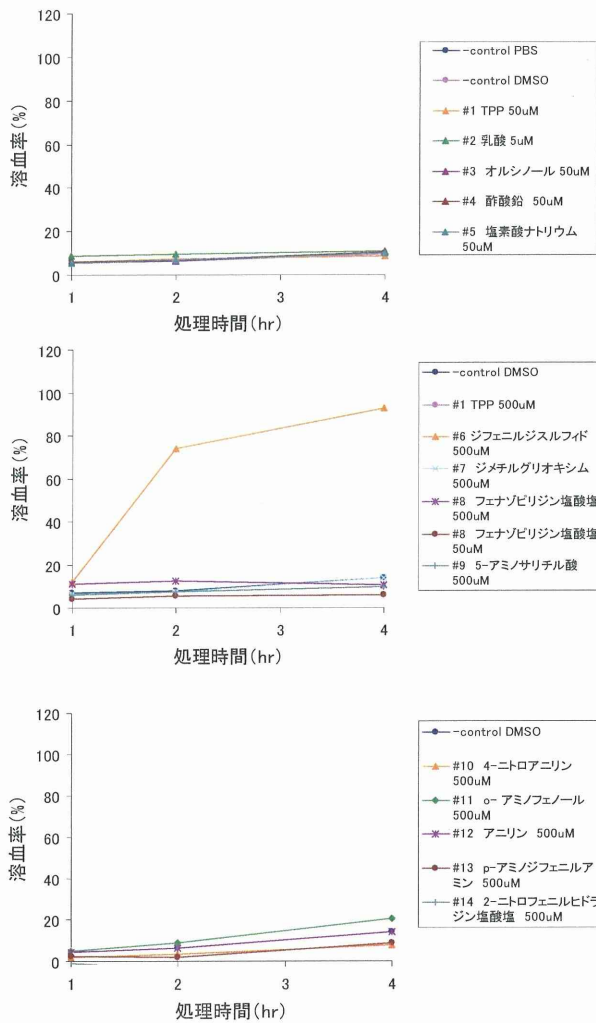


図12. 試験対象化学物質23種類の溶血性試験結果

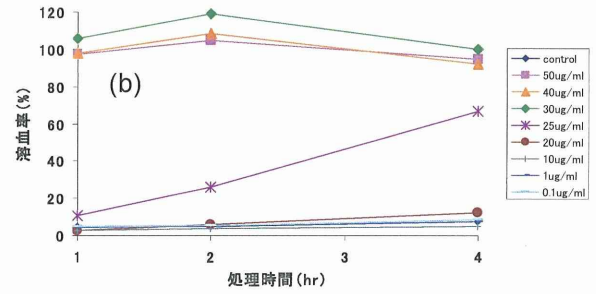
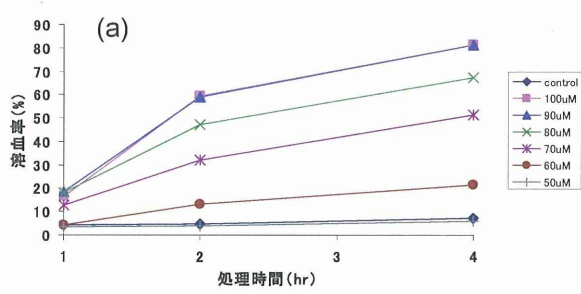


図13. ジフェニルジスルフィド (a) 及びGenapol X-080 (b) の溶血性試験結果

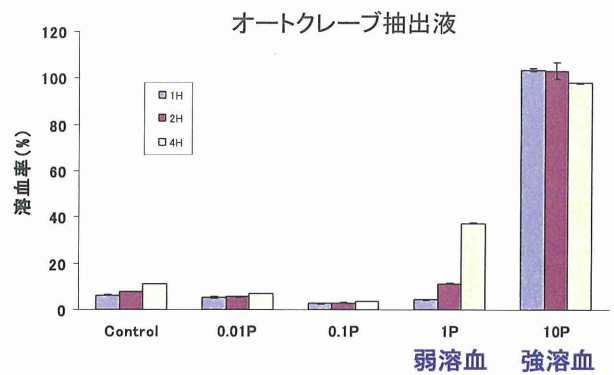
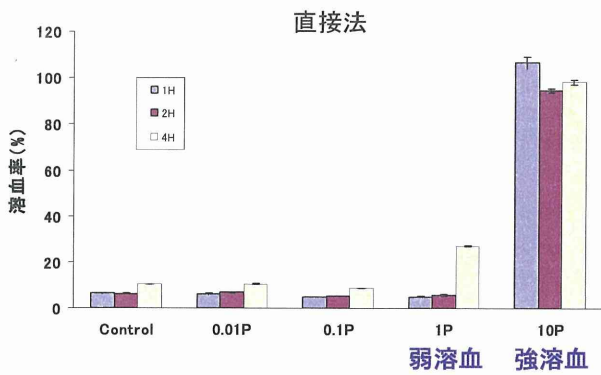


図14. Genapol X-080含有ヒートプレスPVCシートの溶血性試験結果

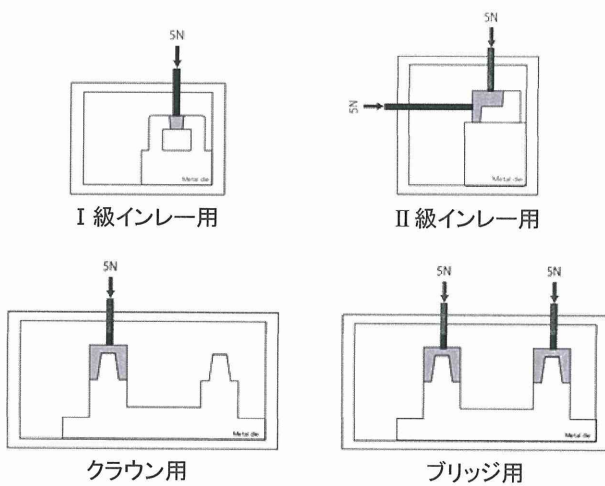


図15. 歯科用修復物の圧接方法

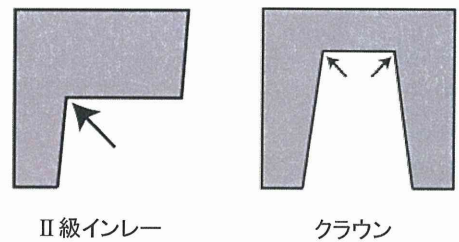


図16. 線角部の対処方法

表1. 試験対象化学物質一覧

番号	試薬群	化合物名
1	リン酸トリフェニル	リン酸トリフェニル
2	乳酸	乳酸
3	オルシノール	オルシノール
4	Lead	酢酸鉛
5	Chlorate	塩素酸ナトリウム
6	ジフェニルジスルフィド類	ジフェニルジスルフィド
7	オキシム類	ジメチルグリオキシム
8	Phenazopyridine	フェナゾピリジン塩酸塩
9	5-アミノサリチル酸	5-アミノサリチル酸
10	ニトロアニリン類	4-ニトロアニリン
11	o-,p-アミノフェノール類	o-アミノフェノール
12	アニリン類	アニリン
13	N-フェニル-p-フェニレンジアミン類	p-アミノジフェニルアミン
14	ニトロ化合物	2-ニトロフェニルヒドラジン塩酸塩
15	Salicylazosulphapyridine	サリチルアゾスルファサラジン
16	ニトロベンゼン類	ニトロベンゼン
17	Resourcin	レスルシノール
18	エチレンジグリコールアルキルエーテル類	Genapol X-080
19	2,4,6-トリニトロフェノール類	2,4,6-トリニトロフェニル
20	Zinc ethylene bisdithiocarbonate	ジネブ標準品
21	d-Penicillamine	d-ペニシラミン塩酸塩
22	二環芳香族アミン類	1-ナフチルアミン
23	p-Aminosalicylic acid	p-アミノサリチル酸ナトリウム塩

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Secretariat: JISC

Dentistry — CAD/CAM systems – Accuracy of machined indirect restorations – Test methods and marking

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Foreword

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ISO-n was prepared by Technical Committee ISO/TC 106, *Dentistry*, Subcommittee SC 9, *Dental CAD/CAD systems*.

Introduction

Dental CAD/CAM systems have been successfully used for the fabrication of indirect dental restorations such as inlays, crowns and bridges. The accuracy of these restorations is one of the most important keys for their clinical success. The proposed document provides standardized test methods to evaluate the accuracy of machined indirect using dental CAD/CAM systems as well as the evaluated accuracy for these restorations as marking information.

Dentistry — CAD/CAM systems – Accuracy of machined indirect restorations – Test methods and marking

1 Scope

This standard specifies test methods to evaluate machined indirect dental restorations such as inlays, full crowns and bridges using dental CAD/CAM systems and marking of the evaluated accuracy based on the results from the test methods.

2 Normative references

The following referenced documents are indispensable for the application 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 1942, Dentistry — Vocabulary

ISO12836, Dentistry -- Digitizing devices for CAD/CAM systems for indirect dental restorations -- Test methods for assessing accuracy

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 1942 and the following apply.

4 Requirements

The accuracy of target restoration(s) shall be evaluated using the test methods, clause 5 in this standard and shall be described both in marking and instruction for use.

5 Test methods

5.1 Target restorations

Four types of restorations, 1) Class I inlay, 2) Class II inlay, 3) full crown, and 4) four-unit bridge are the target of this standard. Choose the type(s) following the applicable restoration(s) cited by the manufacturer. If any of the four restorations is not cited applicable by the manufacturer, this restoration is eliminated from the target. In other words, the fabrication of the restoration(s) and the accuracy evaluation are carried out only for the applicable restoration(s) cited by the manufacturer.

5.2 Apparatus

Four types of metal dies given in Fig. 1-4 (Class I inlay, Class II inlay, full crown and four-unit bridge dies) are used both for the preparation of three-dimensional (3-D) data and the evaluation of the accuracy of machined restorations. As shown in Fig. 1-4, these dies have a removable structure for the evaluation of accuracy. These dies shall be prepared for the applicable restoration(s) cited by the manufacturer.

5.3 Preparation of 3-D data

To fabricate the target restorations, 3-D data for each of the restorations shall be prepared. The 3-D data are not necessarily identical to the dimensions of the dies and the data can be modified to produce accurate restorations (the data conversion is involved).

The modified data may be supplied by the manufacturer.

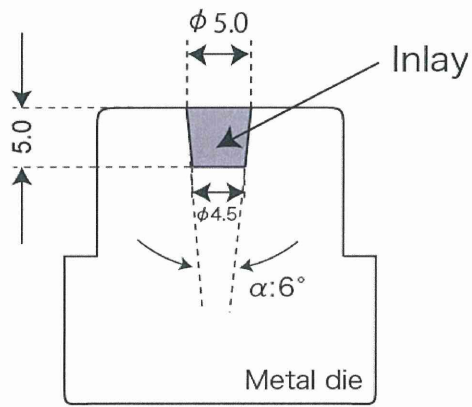


Fig. 1-a Class I inlay die, Cross section

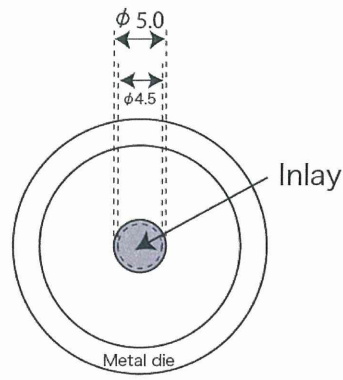


Fig. 1-b Class I inlay die, Upper view

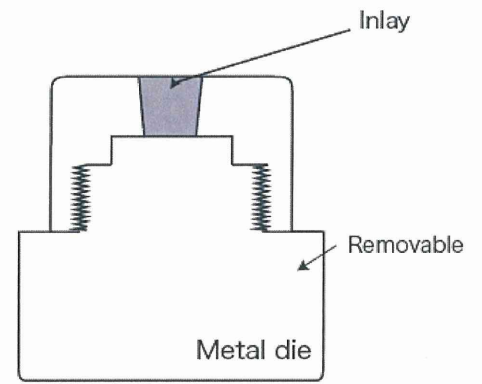


Fig. 1-c Class I inlay die, Removable structure

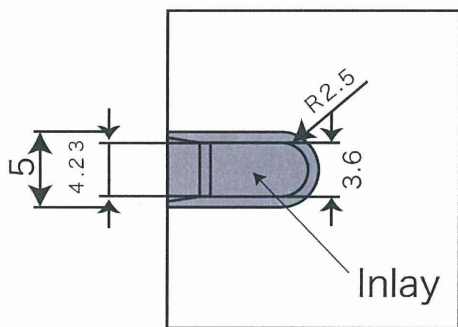


Fig. 2-a Class II inlay die, Upper view

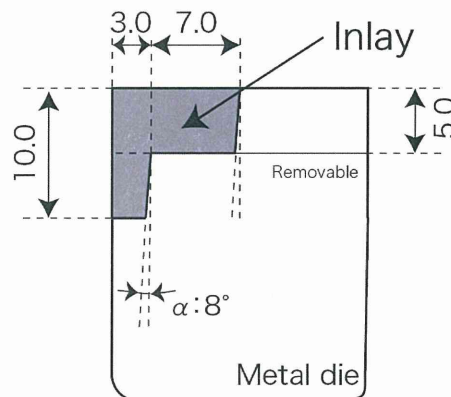


Fig. 2-b Class II inlay die, Cross section

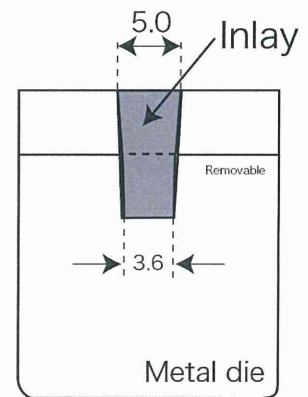


Fig. 2-c Class II inlay die, Proximal view

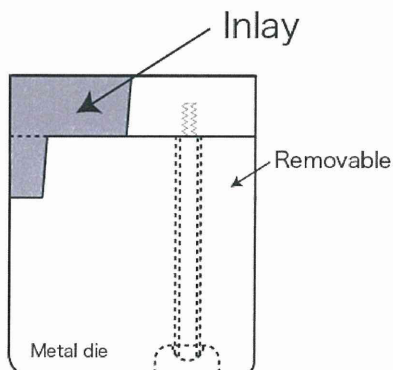


Fig. 2-d Class II inlay die, Removable structure

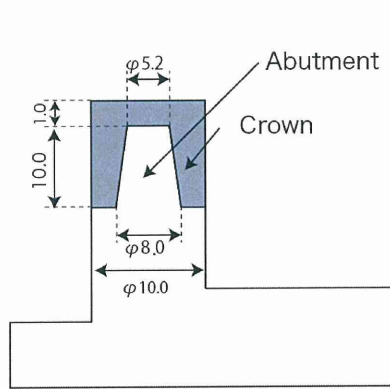


Fig. 3-a Full crown die, Cross section

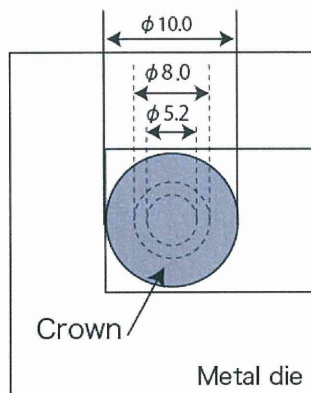


Fig. 3-b Full crown die, Upper view

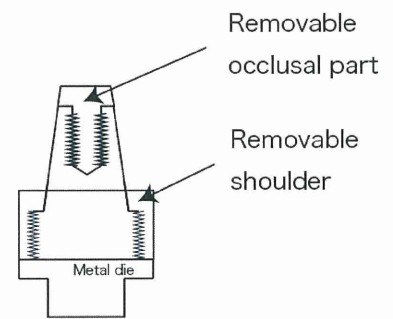


Fig. 3-c Full crown die, Removable structure

Note: For a full crown die either left part or right part of the bridge die (Fig. 4) can be used. Fig. 3 shows the left part of the bridge die

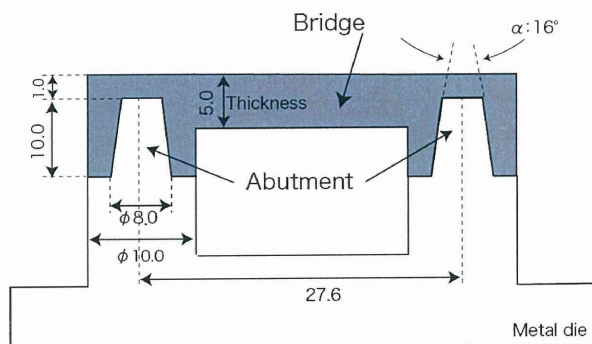


Fig. 4-a Bridge die (cross section)

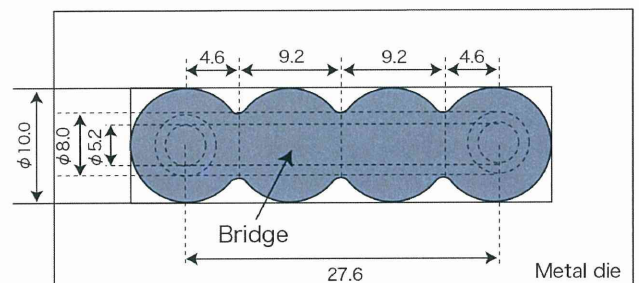


Fig. 4-b Bridge die (upper view)

Note: The removal structure of the bridge die is the same as that of the full crown die (Fig. 3-c). The shapes and dimensions of the full crown and bridge dies are identical to those specified by ISO 12836.

5.4 Machining of restorations

The prepared 3-D data are input into the machining device and a target restoration is machined following the manufacturer's instruction. The material specimen (blank) shall be used following the manufacturer's instruction. Fabricate six restorations for each of the target restorations.

5.5 Evaluation of accuracy

5.5.1 General

The accuracy of the machined restorations is expressed by the discrepancy between the margin of a restoration and baseline (cavity margin for inlays and abutment shoulder for crown and bridge). The measurement is carried out using a dial gauge or 3-D measuring microscope at the accuracy of 1/200 mm or higher. The measured value shall be expressed in mm to two decimal places.

5.5.2 Class I inlay

Place the machined inlay in the cavity of a metal die and apply a load of 50 N for 30 sec on the center of the inlay. Remove the load and examine where the margin of the inlay is located.

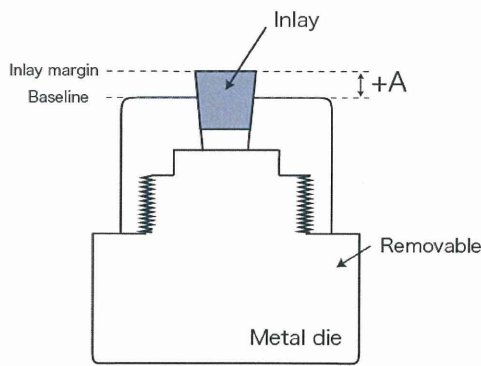
When the inlay margin is located higher than the baseline (cavity margin), measure the discrepancy between the inlay margin and the baseline (Fig. 5-a). The measured value is expressed with plus sign.

When the inlay margin is located at the same level of the baseline or beneath the baseline, remove the cavity base of the die and place the inlay in the die cavity. Apply a load of 50 N and remove it after 30 sec. Measure the discrepancy between the inlay margin and the baseline same as above (Fig. 5-b). The measured value is expressed with minus sign. If the inlay margin is still located at the same level of the baseline, the discrepancy is 0, 00 mm.

For both cases (measurements with and without removable part), the measurement shall be carried out at four points (Fig. 5-b) for each of the six fabricated inlays and the four measured data of one inlay are averaged to represent the

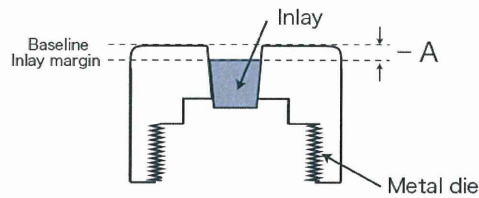
discrepancy of that inlay. Calculate the average of the six representative discrepancy values and the standard deviation to express the accuracy of the machined inlay.

Describe the average discrepancy and standard deviation (SD) in the marking and the instruction for use as follows;
Accuracy of class I inlay: $+A \pm SD$ mm, or $-A \pm SD$ mm



Discrepancy : $+A$ mm

Fig. 5-a Discrepancy measurement with removable part



Discrepancy : $-A$ mm

Fig. 5-b Discrepancy measurement without removable part

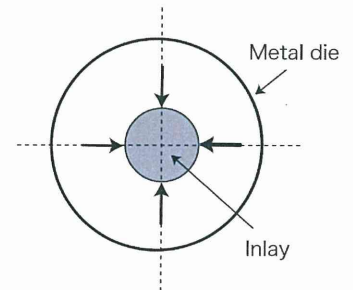


Fig. 5-c Measurement points indicated by thick arrows

5.5.3 Class II inlay

Place the machined inlay in the cavity of a metal die and apply a load of 50 N for 30 sec at the middle of the occlusal surface of the inlay. Remove the load and examine where the margin of the inlay is located.

When the occlusal margin of the inlay is located higher than the occlusal baseline (occlusal margin of the die cavity), measure the discrepancy between the inlay margin and the baseline (Fig. 6-a). Similarly, when the proximal margin of the inlay extrudes from the proximal baseline (proximal margin of the die cavity), measure the discrepancy between the inlay margin and baseline (Fig. 6-b) The measured values for both occlusal and proximal discrepancies are expressed with plus sign.

When the occlusal and proximal margins of the inlay are located at the same level of the baseline or beneath the baseline, remove the cavity base and place the inlay in the die cavity. Apply a load of 50 N and remove it after 30 sec. Measure the discrepancies between the occlusal inlay margin and the occlusal baseline and between the occlusal inlay margin and the proximal the baseline (Fig. 6-c). The measured values are expressed with minus sign. If the inlay margin is still located at the same level of the baseline, the discrepancy is 0, 00 mm.

For both cases (measurements with and without removable part), the measurement shall be carried out at three points for the occlusal discrepancy (Fig. 6-d) and at four points for the the proximal discrepancy (Fig. 6-e). The measured discrepancy data of one inlay are averaged to represent the discrepancy of that inlay. Calculate the average of the six representative discrepancy values and the standard deviation to express the accuracy of the machined inlay.

Describe the average discrepancies and standard deviation (SD) in the marking and the instruction for use as follows;

- Accuracy of class II inlay: 1. Occlusal accuracy $+A \pm SD$ mm, or $-A \pm SD$ mm
2. Proximal accuracy $+B \pm SD$ mm, or $-B \pm SD$ mm

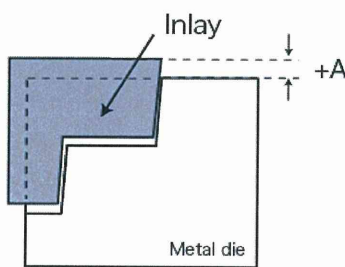


Fig. 6-a Occlusal discrepancy measurement With removable part

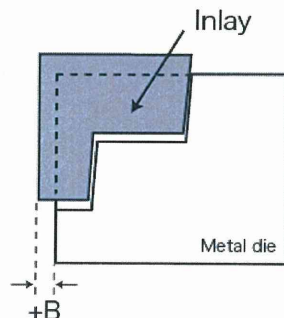


Fig. 6-b Proximal discrepancy measurement With removable part

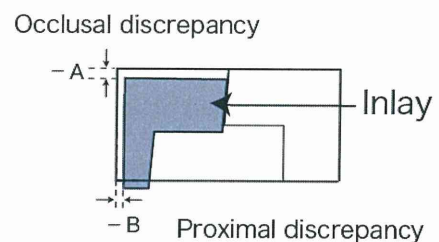


Fig. 6-c Occlusal & proximal discrepancy measurements Without removable part

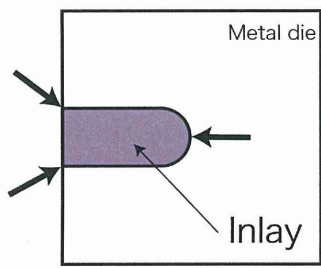


Fig. 6-d Measurement points for occlusal discrepancy

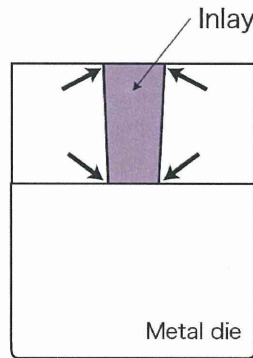


Fig. 6-e Measurement points for proximal discrepancy

5. 5. 4 Full crown

Place the machined crown on the abutment of a metal die and apply a load of 50 N for 30 sec on the center of the occlusal surface of a crown. Remove the load and examine where the margin of the crown is located.

When the crown margin is located higher than the baseline (abutment shoulder), measure the discrepancy between the crown margin and the baseline which is an abutment shoulder (Fig. 7-a). The measured value is expressed with plus sign.

When the crown margin attaches the baseline, remove the head part and shoulder ring. Place the crown on the abutment without two removal parts. Apply a load of 50 N and remove it after 30 sec. Measure the discrepancy between the crown margin and the second baseline which is 10 mm lower from the original baseline (Fig. 7-b). Subtract 10 mm from the measured value and obtain the discrepancy between the crown margin and the original baseline. The obtained discrepancy value is expressed with minus sign.

For both cases (measurements with and without removable parts), the measurement shall be carried out at four points (Fig. 7-c) for each of the six fabricated crowns and the four measured data of one crown are averaged to represent the discrepancy of that crown. Calculate the average of the six representative discrepancy values and the standard deviation to express the accuracy of the machined crown.

Describe the average discrepancy and standard deviation (SD) in the marking and the instruction for use as follows;

Accuracy of full crown: $+A \pm SD$ mm, or $-A \pm SD$ mm

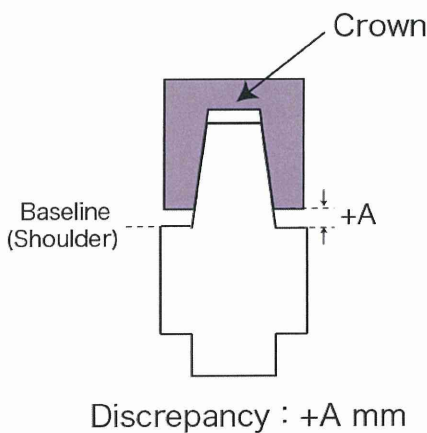


Fig. 7-a Discrepancy measurement of crown With removable parts

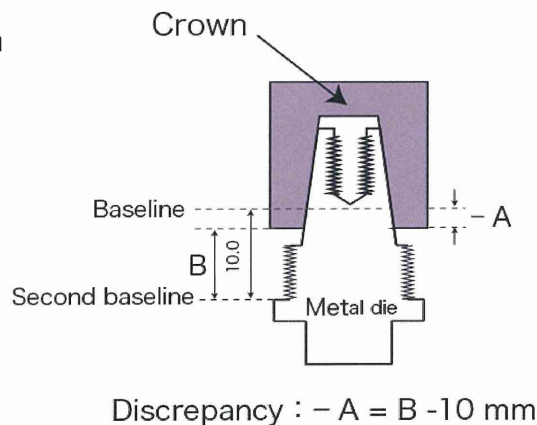


Fig. 7-b Discrepancy measurement of crown Without removable parts

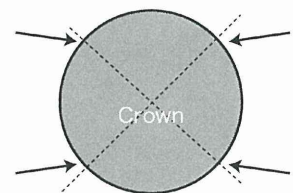


Fig. 7-c Measurement points (intersection points of crown margin and two orthogonal lines at optional diametral)

5. 5. 5 Four-unit bridge

Remove the two abutment parts from the bridge die and measure the discrepancies of two single crowns individually using the same procedure described in 5. 5. 4.

Fix the removed abutments to the bridge die and place the machined bridge on the bridge die. Apply a load of 50 N on each of the two crowns at the center of the occlusal surface for 30 sec. Remove the load and examine if the crown margin attaches the baseline (abutment shoulder).

When the crown margin is located higher than the baseline, measure the discrepancy between the crown margin and the baseline (Fig. 8-a). The measured value is expressed with plus sign.

When the crown margin attaches the baseline, remove the head parts and shoulder rings of two abutments. Place the crown on the abutment without two removal parts. Apply a load of 50 N on each of two crowns and remove it after 30 sec. Measure the discrepancy between the crown margin and the second baseline which is 10 mm lower from the original baseline (Fig. 8-b, described as D). Subtract 10 mm from the measured value (D) and obtain the discrepancy between the crown margin and the original baseline. The obtained discrepancy value is expressed with minus sign.

For both cases (measurements with and without removable parts), the measurement shall be carried out at four points for each of two crowns (Fig. 7-c) of one bridge, and obtain the average of the eight measured values in total to represent the discrepancy of that bridge. After this measurement is carried out for six bridges, calculate the average of the six representative discrepancy values and the standard deviation to express the accuracy of the machined crown.

Describe the average discrepancy and standard deviation (SD) in the marking and the instruction for use as follows;

Accuracy of crown 1: $+A \pm SD$ mm, or $-A \pm SD$ mm

Accuracy of crown 2: $+B \pm SD$ mm, or $-B \pm SD$ mm

Accuracy of whole bridge: $+C \pm SD$ mm, or $-C \pm SD$ mm

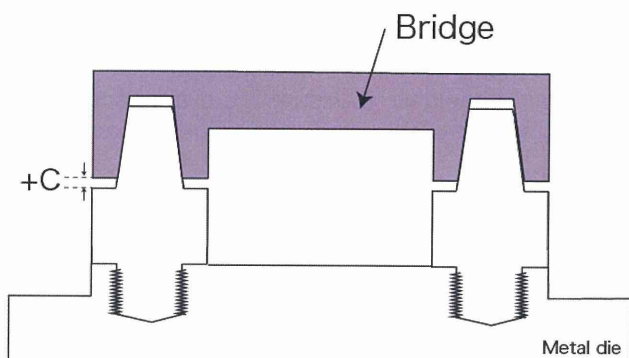


Fig. 8-a Discrepancy measurement of whole bridge With removable parts

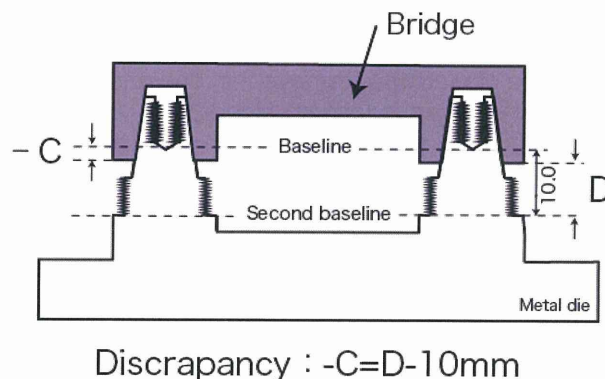


Fig. 8-b Discrepancy measurement of whole bridge Without removable parts

分担研究報告書

平成 24 年度厚生科学研究費補助金（地球規模保健課題推進）研究事業
国際標準化機構（ISO）及び国際電気標準会議（IEC）における医療機器の各種国際規格の
策定に関する研究（H23-地球規模-指定-003）

分担研究課題名

ISO/TC 194/WG 9 ラウンドロビンテスト支援研究

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研究要旨

ISO/TC 194/WG 9 (医療機器の生物学的評価 - 血液適合性 WG) は、担当文書 ISO 10993-4:2002 及び Amd 1:2006 の改正に向け、溶血性試験に関する多施設国際共同検証試験（ラウンドロビンテスト）の実施を計画した。今年度、本研究班から参加の 2 機関が、WG 9 Convenor Dr. Michael Wolf のとりまとめる溶血性試験プロトコルの最終化作業に参画し、サンプル選定と文書校正を完了させた（文書発行 2012 年 11 月 19 日）。プロトコルは、医療機器の溶血性試験で国際的に広く用いられている ASTM 法、NIH 法、MHLW 法（薬食機発 0301 第 20 号¹⁾）の 3 法で構成されている。またラウンドロビンテストの実施は、第一段階の Pilot Run と第二段階の Actual に分けて行うこととなった。上記 2 機関により今年度末までに Pilot Run の第一回目の試験が実施される運びとなっている。

また本研究班で試験精度管理の目的で開発中の陽性対照材料（Genapol X-080 含有 PVC シート）を、前述のラウンドロビンテストのプロトコルにて性能評価を実施し、ラウンドロビンテスト用サンプルの 1 つとして提供することを目的として、その基本性能を詳細に評価した。Genapol X-080 含有量依存的に溶血性が認められ、精度管理目的の陽性対照材料の候補として、その基本性能が確認された。

A. 研究目的

血液に接触する医療機器には安全性上の不具合を生じないように、ISO 10993-4 で規定される血液適合性評価が求められているが、具体的で標準化された試験法が明記されていない点が大きな課題となっている。ISO/TC 194：医療機器の生物学的評価 技術委員会では、WG 9 が主体と

なって発行文書 ISO 10993-4（2002 年に発行された本体及び 2006 年に発行された Amendment で構成）の改正作業が始まっている。血液適合性評価の中に赤血球に及ぼす影響を評価する試験法として確立された「溶血性試験」がある。国際的には、米国で規格化された ASTM 法、NIH 法、及び日本の MHLW 法（薬食機発 0301 第 20 号

¹⁾が国際的に広く用いられている(表1)。WG 9ではISO 10993-4への記載のため、この3法を比較検討するためのラウンドロビンテストの実施が決まった(図1)。ラウンドロビンテスト参加者は日中米欧の12試験機関で構成されている(表2)。

ラウンドロビンテストのプロトコルの最終化と試験検体の決定は、参加する試験機関の意見の一致に時間を要し難航していたが、電話会議を重ね、2012年11月19日完了した。またラウンドロビンテストの実施は、第一段階のPilot Runと第二段階のActualに分けて行うこととなった(図1)。Pilot Runの試験概要を図2に示す。陰性対照材料(非溶血)としてポリエチレンを用いるほか、さまざまな溶血程度を有するゴム材料を5種類試験して、第二段階(Actual)のラウンドロビンテストで用いる検体を選択する目的も含まれている。

B. 研究方法

1. 試験材料

ラウンドロビンテストの試験検体は図2に示す6種類(Polyethylene, Nitrile glove, Latex glove #12, EPDM Rubber #3, EPM Rubber #4, Buna rubber (Aero Rubber Co. 製))が提供されることになっている。さらに、本研究では試験精度管理の目的で開発中の陽性対照材料(Genapol X-080含有PVCシート)を用い、溶血性能を評価した。各試験法のインキュベーション時間は、プロトコルに従い、ASTM法(直接接触及び抽出液法):3時間、NIH法(直接接触法):1時間、MHLW法(抽出液法):4時間で実施した。

2. 実験方法

試験方法は2012年11月19日付ラウンドロビンテストのテストプロトコルに従った。

ただし、Genapol X-080含有PVCシートについてはウサギ血液での実施とし、間接接触法における抽出条件は表面積あたり6 cm²/mLの抽出溶媒量、121 ± 2℃、1 ± 0.1時間とした。

3. 倫理面への配慮

動物血液の採取については、所属機関(財団法人ヒューマンサイエンス振興財団の動物実験実施施設認証認定番号12-005(秦野研)及び12-030(テルモ))の規定する動物実験指針に従い、動物に対する苦痛が最小となるよう務めた。又、動物実験倫理委員会の承認を得た(承認番号:1120331A(秦野研)及び120163(テルモ))。

C. 研究結果

陽性対照材料の溶血性試験結果を図3及び表3-6に示す。Genapol X-080 10 phrシートはすべての試験法で溶血率がほぼ100%の高い溶血性を示した。またGenapol X-080 0.1 phr及び0.01 phrシートはすべての試験法で陰性であった。一方、Genapol X-080 1 phrシートはASTM直接接触法で20%程度の溶血率を示したが、その他の試験では陰性であった。

し、精度管理目的の陽性対照材料の候補としての基本性能が確認され、ラウンドロビンテスト用サンプルになりうると思われた。また本材料における溶血性の検出は、ASTM直接接触法が最も感度良く確認できた。

D. 考察

赤血球の溶血現象には、(1) 浸透圧変化、(2) レオロジー作用、(3) 生化学的要因の 3 つの作用が関与しており、医療機器の臨床使用においては、単独あるいはこれらが複合的に作用して不具合としての溶血が生じると考えられる。ラウンドロビンテストで取り上げられた溶血性試験は、医用材料の有する潜在的な毒性として主に (3) の作用による赤血球膜が破壊される現象の有無とその程度を確認する試験法である。(3) の作用の中には、界面活性作用による膜破壊や高/低 pH 等による膜たんぱく質の変性作用などが例として挙げられる。

本研究班の開発した陽性対照材料は、非イオン界面活性剤である Genapol X-080 が抽出液やインキュベーション中の試験液に溶出することで、赤血球膜のリン脂質 2 分子膜を破壊する作用を有することが溶血性の機序と考えられる。研究結果から、本陽性対照材料における溶血性の閾値は、ASTM 直接法で 0.1 phr と 1 phr の間の用量、その他の試験では 1 phr と 10 phr の間の用量に、それぞれあると考えられる。材料中の Genapol X-080 量の精密なチューニングはこれからの作業となるが、本実験結果から、本材料のコンセプトは証明され、溶血試験法陽性対照材料としての有用性が確認できたと判断できる。

E. 結論

ISO/TC 194/WG 9 (血液適合性) で企画された RRT への、国内 2 機関の参加への支援を継続した。平成 25 年 3 月中旬に試験材料を配布するとの情報が、オーガナイザーよりよせられたが、当該研究班の報告には間に合わないため、本研究班で

試験精度管理の目的で開発中の陽性対照材料を用いて、ウサギ血でその基本性能を評価した。その結果 Genapol X-080 含有量依存的に溶血性が認められ、陽性対照材料候補としての基本性能が確認できた。

得られたデータは、平成 25 年 4 月開催予定の ISO/TC 194/WG 9 パヴィア会議で報告する。

F. 研究発表

なし。

G. 参考

1) 平成 24 年 3 月 1 日付け厚生労働省医薬食品局審査管理課 医療機器審査管理室長通知 薬食機発 0301 第 20 号「医療機器の製造販売承認申請等に必要な生物学的安全性評価の基本的考え方について」

表1. 溶血性試験3法の実験条件比較

		ASTM	NIH	MHLW
試験に用いる血液の種類		クエン酸血 (ヒト or ウサギ)	シュウ酸血 (ウサギ)	脱繊維血 (ウサギ)
血液濃度の調整		10 mg Hb/mL	採取した血液と生理食塩液を混合し、吸光度 A_{545} が0.9~1.00になるよう調節	希釈なし
血液接触比率	抽出液法	抽出液7 mL (媒体: PBS) と1 mLの濃度調整血液を混合	抽出液10 mL (媒体: 生理食塩液) と0.2 mLの濃度調整血液を混合 *Pilot Runでは実施計画なし	抽出液10 mL (媒体: 生理食塩液) と0.2 mLの血液を混合
	直接接触法	7 mLのPBSと1 mLの濃度調整血液を混合し、60 cm ² 分の被験物質を添加	10 mLの生理食塩液と0.2 mLの濃度調整血液を混合し、5 gの被験物質を添加	/
インキュベーション時間・振盪条件		3時間 振盪 (60 rpm)	1時間±5分 振盪なし	1、2、及び4時間 *ラウンドロビンテストでは4時間に固定 振盪なし

表2. ラウンドロビンテスト参加者リスト

Role	Name (affiliation)	Facility
Principal Investigator	Michael F. Wolf Medtronic Inc. - USA	Medtronic Inc. Minneapolis, MN 55432, USA
Study Biostatistician	Dr. Sebastian Hoffmann seh consulting + services - Germany	seh consulting + services Germany
Study-Coordinator	Michelle Lee, B.S., RM(NRCM), ASQ CQA Nelson Laboratories - USA	Nelson Laboratories SLC, UT 84123, USA
1. Co-Investigator	Keisuke Sakaguchi (and/or Takahiro Tanigawa) TERUMO Corporation, Japan	TERUMO Corporation Japan
2. Co-Investigator	Tomoko Shindo Hatano Research Institute - Japan	Hatano Research Institute Japan
3. Co-Investigator	Hou Li Shandon Quality Inspection Center - China	Shandong Quality Inspection Center for Medical Devices, China
4. Co-Investigator	Anita Y. Sawyer, MS MTASCP Becton Dickenson Corp. - USA	BD Biological Sciences, Corporate PreClinical Development and Toxicology, NJ 07417, USA
5. Co-Investigator	Melissa Cadaret (and/or Joe Carraway) (NAMSA)	NAMSA Northwood, OH 43619, USA
6. Co-Investigator	Michelle Lee, B.S., RM(NRCM), ASQ CQA (Nelson Laboratories, USA)	Nelson Laboratories SLC, UT 84123, USA
7. Co-Investigator	Lisa Olson and/or Bev Lundell WuXiAppTec - USA	WuXiAppTec MN 55120, USA
8. Co-Investigator	Andrew Walsh Medtronic Inc. - USA	Medtronic Inc. Minneapolis, MN 55432, USA
9. Co-Investigator	Kathy Laffan (and/or Christine Eoff) Medtronic Inc. - USA	Medtronic CardioVascular CA 95403, USA
10. Co-Investigator	Ron Brown (FDA - USA)	FDA MD 20993, USA
11. Co-Investigator	Jean Pierre Boutrand, Catherine Tremolieres, Gaëlle Clermont NAMSA - France	NAMSA France
12. Co-Investigator	Ed Reverdy, Boston Scientific (tentative)	Boston Scientific Corporation MA 01760, USA