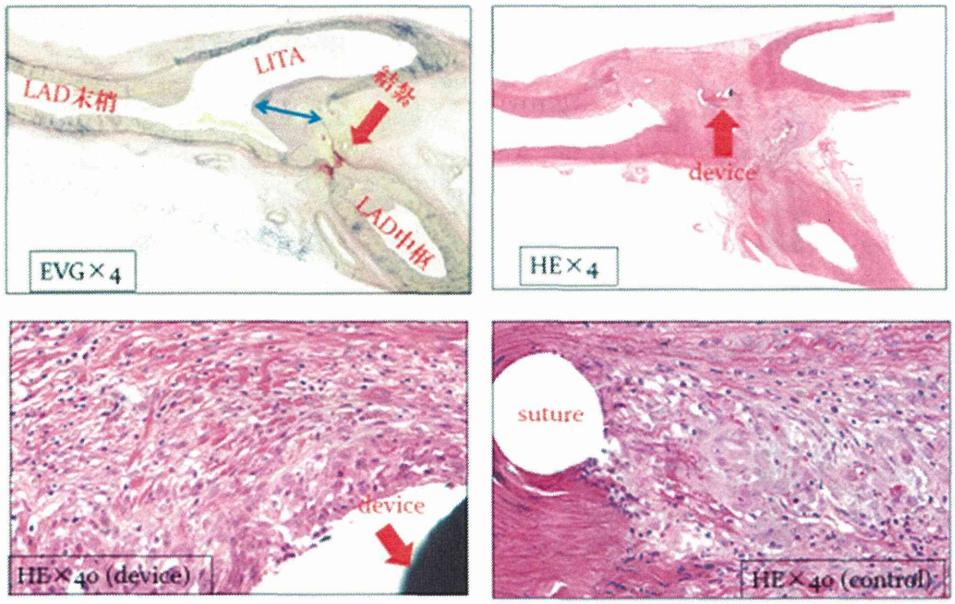
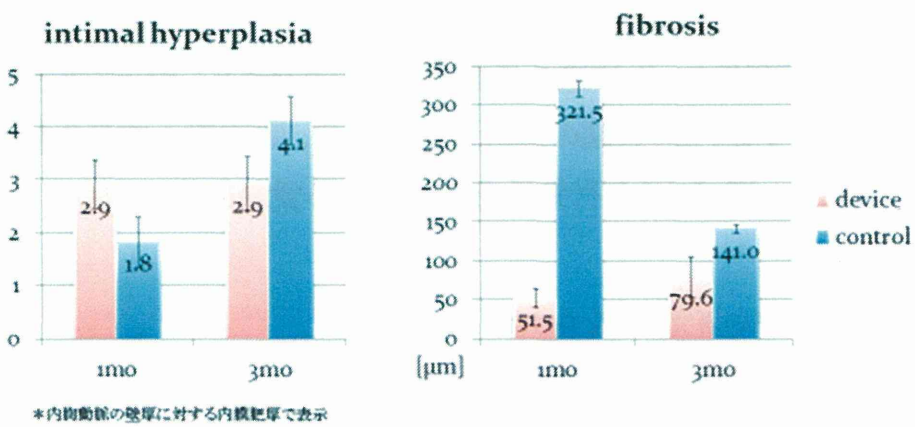
Results -histopathology-



Results -histopathology-



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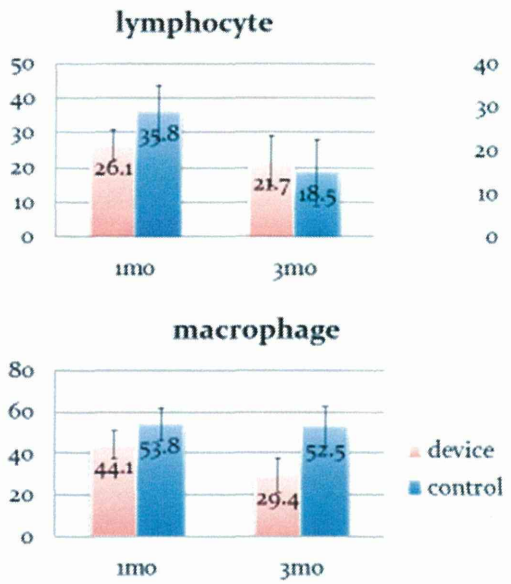
Results -histopathology-



＊吻合部のデバイス/糸周囲で2ヵ所の×40の高倍率視野で各炎症細胞の数をカウントし平均化した値

Conclusion

- 今回、ブタ冠動脈を用いた慢性実験において、我々が開発した吻合デバイスは、冠動脈末梢側吻合用デバイスとして十分な開存性と、生体適合性を有し、有効であることが確認された。今後、より長期の埋め込み実験や、胸腔鏡下での手術を行い、デバイスの有効性を評価する必要がある。

- 付記：下記の研究助成を受けた
平成23年度文部科学省科学研究費助成事業
平成24年度文部科学省橋渡し研究加速ネットワークプログラム
平成25年度厚生労働科学研究費補助

新しい冠動脈末梢側吻合用デバイスの研究
－慢性期動物実験モデルでの報告－

○井戸田佳史[a]，Nirmal Panthee[a]，安藤岳洋[b]，佐久間一郎[b]，小野稔[a]
[a]東京大学　心臓外科
[b]東京大学工学部精密工学科
Yoshifumi Itoda[a], Nirmal Panthee[a], Takehiro Ando[b], Ichiro Sakuma[b], and Minoru Ono[a]
[a] *Department of Cardiac Surgery, The University of Tokyo, Tokyo, Japan*
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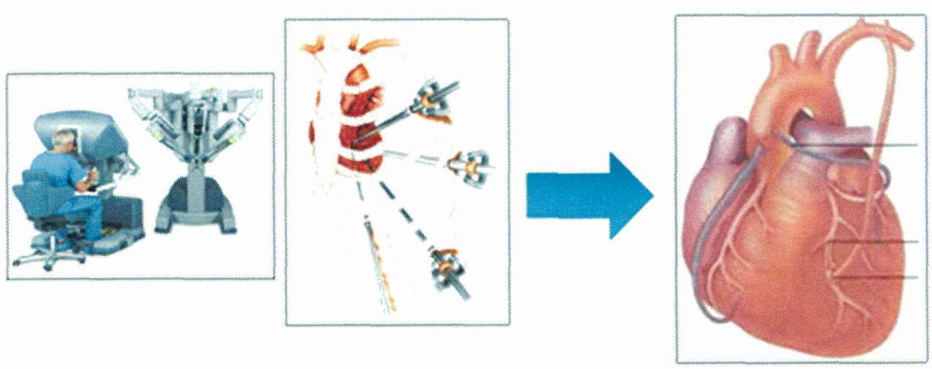
東京大学
THE UNIVERSITY OF TOKYO

2014 2/19 JSCVS @ Kumamoto

Background

- 心臓外科領域に低侵襲手術が導入されて久しいが、内視鏡下手術やロボット手術といった低侵襲手術は普及していない。



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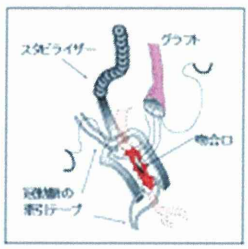
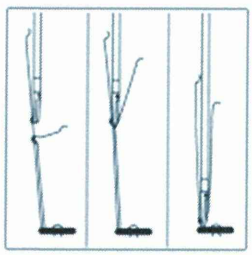
Background

- 狭いスペースでの連続縫合
- それに続く結紮(通常5回以上)
- 多枝病変での吻合の困難さ





- 新しい吻合デバイス

  最も慣れた*手縫いによる連続縫合*

  *結紮部分*をワンタッチで可能に

  優れた*生体適合性*

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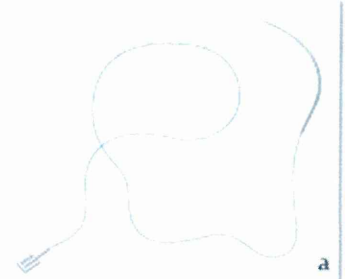
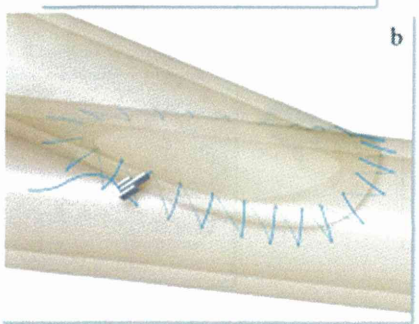
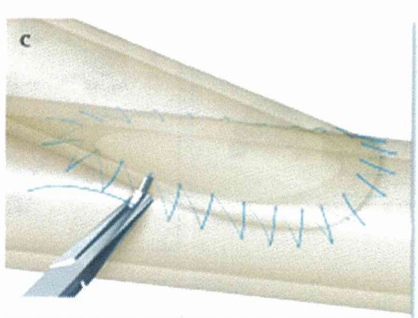
Device Design



- SUS316L stain-less steel
- YAG laserにより作成
- 1.0 mm × 0.5 mm イカリ状の形
- 糸は通常の7-0 polypropylene糸
- 通常の連続吻合の後に糸を通して持針器で摘まむことで糸が固定される



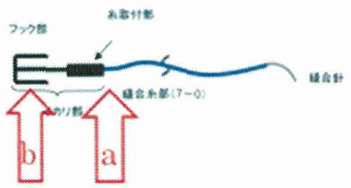


Device Design

試験材料：
縫合デバイス本体引っ張り試験

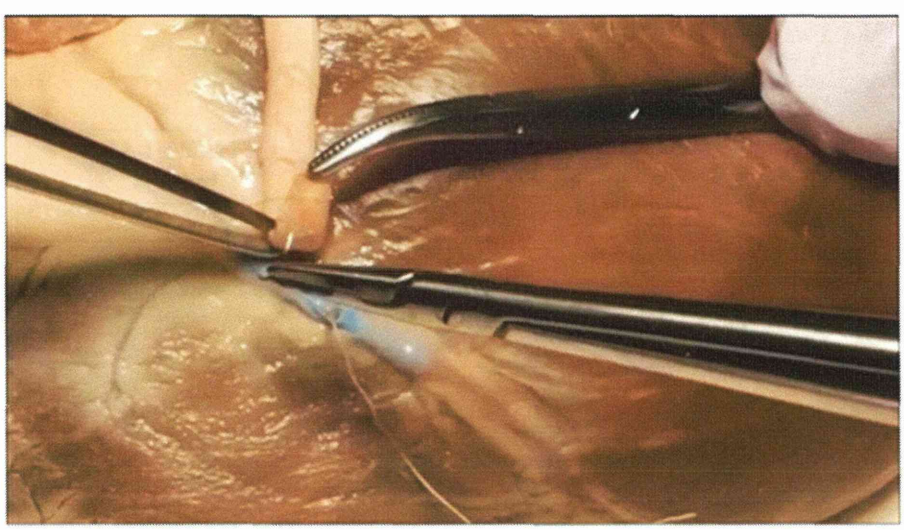
a. デバイスと7-0縫合糸接続部（n = 10）
強度　1.008 N

b. 縫合糸カシメ部（n = 10）
強度　1.531 N



(Reference：7-0縫合糸破断強度規格：1.08 N)

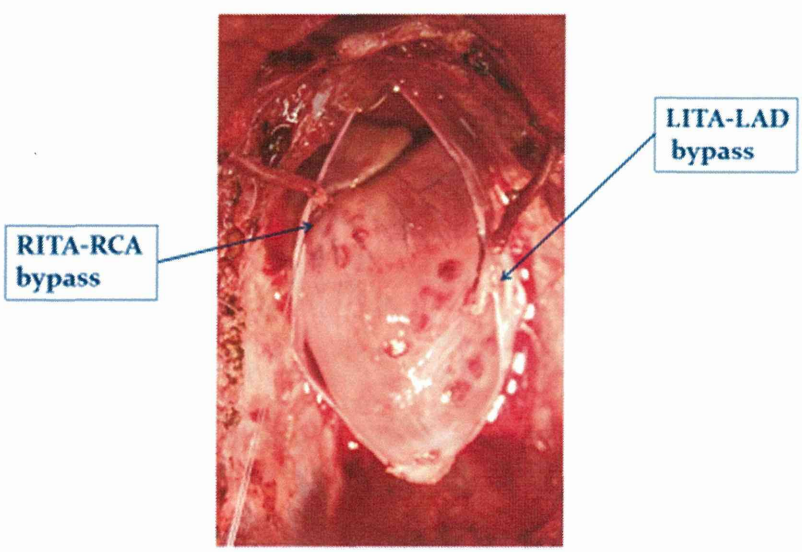
Anastomosis procedure



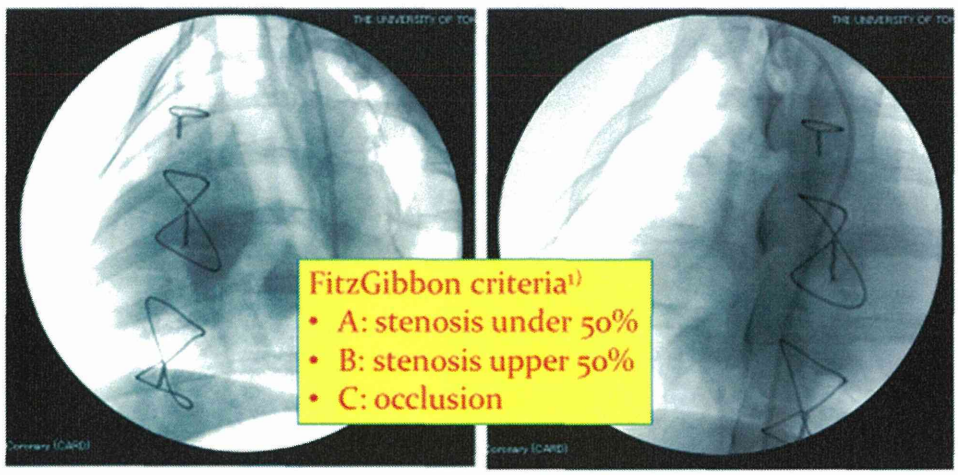
Experimental protocol

- ブタ冠動脈バイパスモデルによる長期埋め込み実験。
- クラウンミニブタ 25-30kg ♂
- 両側内胸動脈(LITA、RITA)を剥離し
  LITA-LAD及びRITA-RCA吻合を施行。
- *吻合時間*および*吻合後の血流量*を測定
- 11頭のブタを用い、9頭はdeviceを用いて吻合。
- 2頭はcontrolとして従来の7-0ポリプロピレン糸で吻合。
- 6頭は術後1ヶ月で、5頭は術後3ヶ月で遠隔期評価した。
- 遠隔期は*血管造影*、*吻合部の病理評価*を行った。

Experimental protocol

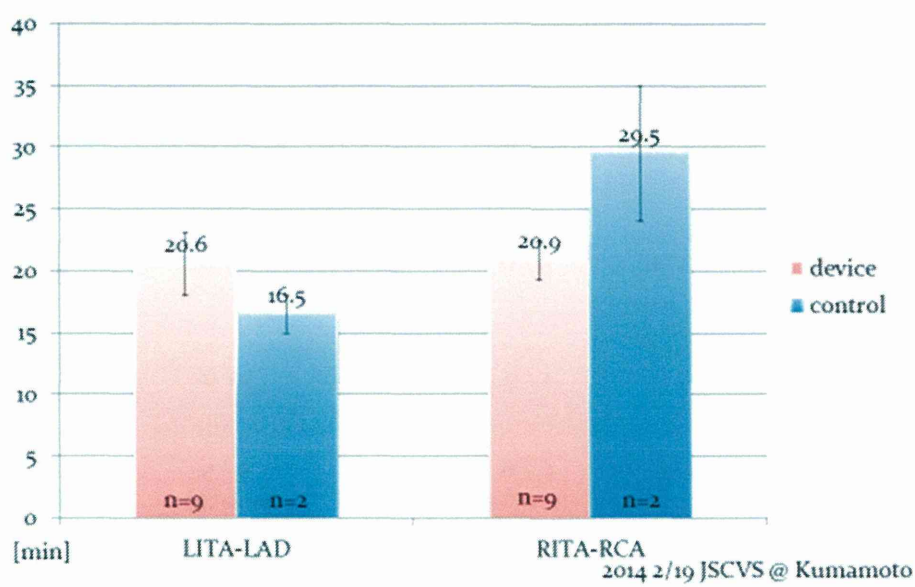


Angiography-



[1)] Fitzgibbon GM, Kafka HP, Leach AJ. Coronary bypass graft fate and patient outcome: angiographic follow-up of 5,065 grafts related to survival and reoperation in 1,388 patients during 25 years. J Am Coll Cardiol. 1996;28(3):616-26

Results - suture time -



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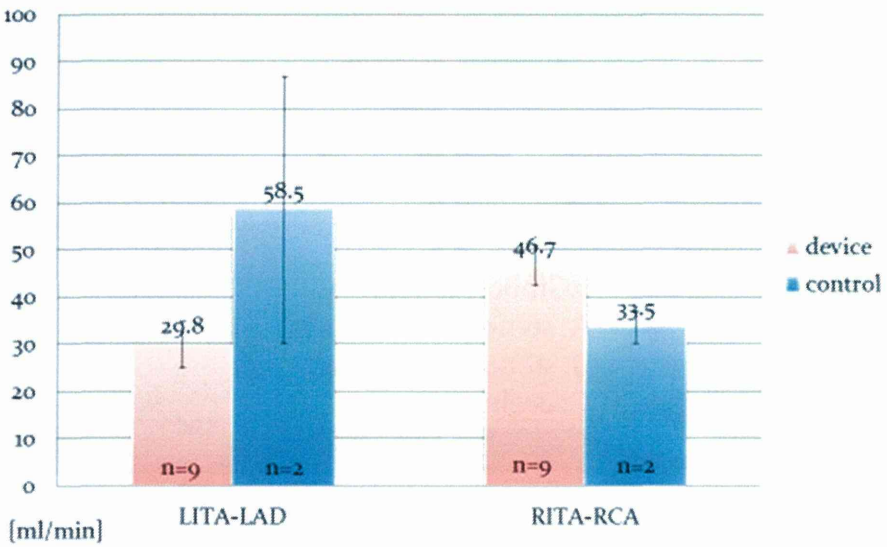
Results - graft flow -



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Results - FitzGibbon criteria -

	1 mo model		3 mo model		
	LITA-LAD	RITA-RCA	LITA-LAD	RITA-RCA	% of A
Device群 (A / B)	5 / 0	5 / 0	4 / 0	4 / 0	18 / 18 (100 %)
Control群 (A / B)	1 / 0	1 / 0	1 / 0	1 / 0	4 / 4 (100 %)
% of A	6 / 6 (100 %)	6 / 6 (100 %)	5 / 5 (100 %)	5 / 5 (100 %)	22 / 22 (100 %)

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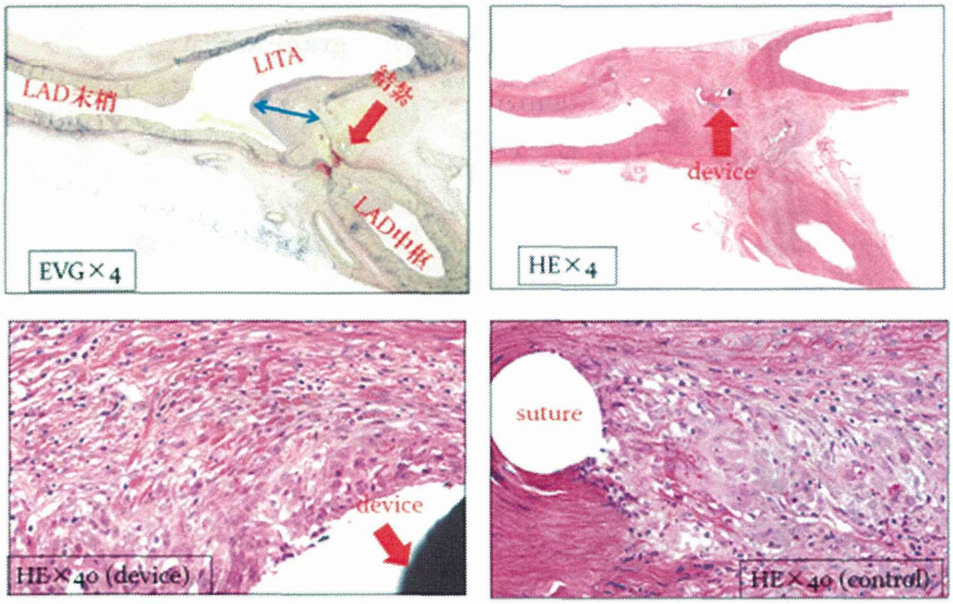
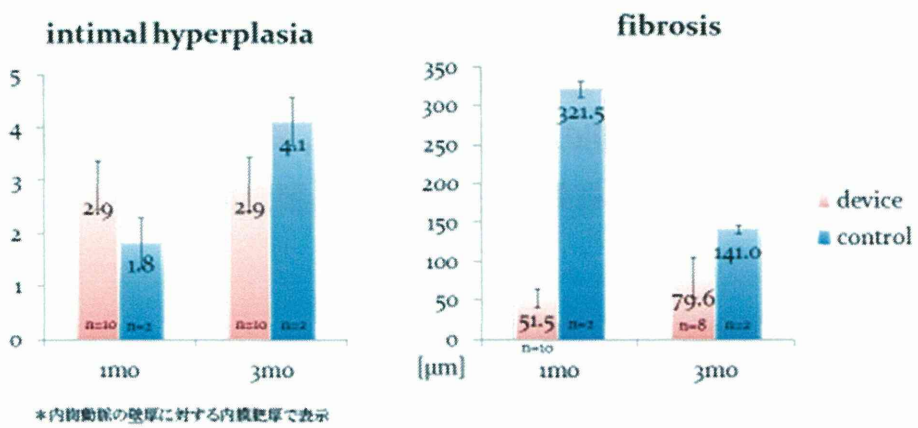
Results -histopathology-



Results -histopathology-



＊内膜動脈の壁厚に対する内膜肥厚で表示

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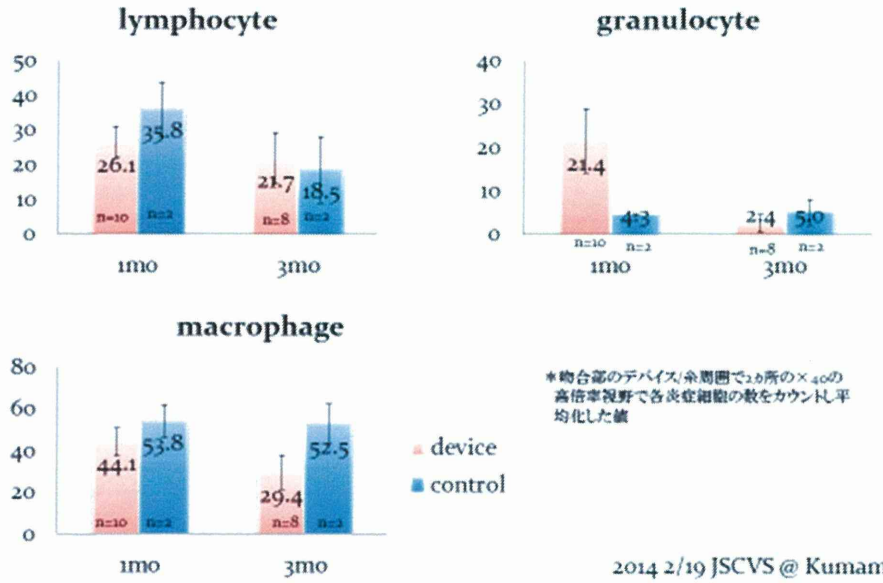
Results -histopathology-



＊吻合部のデバイス(糸周囲で2ヵ所の×40の高倍率視野で各炎症細胞の数をカウントし平均化した値

Conclusion

- 今回、ブタ冠動脈を用いた慢性実験において、我々が開発した吻合デバイスは、冠動脈末梢側吻合用デバイスとして十分な開存性と、生体適合性を有し、有効であることが確認された。今後、より長期の埋め込み実験や、胸腔鏡下での手術を行い、デバイスの有効性を評価する必要がある。

- 付記：下記の研究助成を受けた

平成23年度文部科学省科学研究費助成事業
平成24年度文部科学省橋渡し研究加速ネットワークプログラム
平成25年度厚生労働科学研究費補助

Ⅳ．研究成果の刊行に関する一覧表

研究成果の刊行に関する一覧表

雑誌

論文タイトル名	発表者氏名	発表誌名	巻号	ページ	出版年
Use of a new device for distal coronary anastomosis – pig model -	Itoda Y, Panthee N, Ando T, Sakuma I, Ono M	IEEE-EMBC	2013	3166	2013
新しい冠動脈吻合用デバイスの研究～ブタ冠動脈バイパス手術での前臨床試験	井戸田佳史、Nirmal Panthee, 安藤岳洋、佐久間一郎、小野　稔	日本コンピュータ外科学会雑誌	15-2	160-161	2013
Development of a suturing device for anastomosis for small caliber arteries	Itoda Y, Panthee N, Ando T, Sakuma I, Ono M	Journal of Artificial Organs	17-1	88-94	2014
インテリジェント手術支援ロボット－その要素技術と周辺機器の開発－	小野　稔、小林英津子、安藤岳洋、許　俊鋭、佐久間一郎	医工学治療	26-1	40-46	2014

Ⅴ．研究成果の刊行物・別冊

Use of a new device for distal coronary anastomosis -pig model-

Yoshifumi Itoda, Panthee Nirmal, Takehiro Ando, Ichiro Sakuma, and Minoru Ono

Abstract— OBJECTIVE: Different devices have been developed for distal coronary anastomosis for minimally invasive coronary artery bypass surgery. But none of these devices have been universally adopted. In this study, we describe the safety and efficacy of a new anastomotic device that we developed using swine coronary bypass model. METHODS: The device enables us to skip manual ligation with easy pinching motion after conventional suturing. Five miniature pigs were used for this study. Bilateral internal thoracic arteries were harvested and anastomosed to right coronary artery and left descending artery, respectively using new device (n=4), and conventional mono propylene suture (n=1). After 1 month of operation, pigs were sacrificed and evaluated. RESULTS: Suture time measured during surgery revealed no significant difference between device group and conventional sample. Angiography after 1 month showed good patency (FitzGibbon A). Pathological findings revealed no specific inflammatory change around devices and surrounding tissues. CONCLUSION: The device we developed was feasible for distal coronary anastomosis in present swine model.

I. Headings

In recent years, robotically assisted surgery has been introduced to cardiovascular surgery as a minimally invasive procedure. But it was pointed out that there were several obstacles to apply robotics to coronary artery bypass. Main points of these problems include difficulty to perform a running suture and tying without tactile feedback in limited space. In previous reports, different devices including various adhesives and one shot type systems for coronary distal anastomosis. But none of them have been universally adopted for some reasons; patency, handling, indication, and costs. We developed the new device which has feasibility for minimally invasive surgery followed by robotic surgery for coronary distal anastomosis. In this report, its effectiveness and safety was evaluated using swine coronary bypass model.

II. Methods and Materials

The device was designed simply with biocompatible stain-less steel combined to the free end of the ordinary mono-propylene suture (figure 1). The device enables us to skip manual ligation with easy pinching motion after conventional suturing. Five healthy male pigs (Crown miniature pig, 25-30kg) were used in this study. Under general anesthesia, chest was opened and left internal thoracic artery (LITA) and right internal thoracic artery (RITA) were harvested in skeletonized fashion. Heart was stabilized with heart positioner and left descending coronary artery (LAD) and right coronary artery (RCA) were

Figure 1. The device we developed for distal coronary anastomosis

dissected. Using coronary shunt and retractor tape, coronary anastomoses were done (LITA to LAD, RITA to RCA, respectively). New device were used in four of five pigs. Conventional mono propylene suture was used in the remain. After the operation, 100mg of oral aspirin was administered for one month and finally pigs were sacrificed and anastomoses were evaluated by following way. (1) Suture time was measured during operation. (2) Angiography was done using C-arm X-ray system after 1 month of operation. (3) Anastomotic sites were resected and histologically examined about inflammatory change.

Results

(1) Suture time using new device was 16.75 min. and 18.25 min. in LITA-LAD and RITA-RCA respectively. This time was as equal as conventional sample (18 min. and 24 min.).

(2) Angiography after 1 month of operation revealed FitzGibbon A (without stenosis up to 50%) in all anastomoses. No evidences of parse-string suture and device specific stenosis were shown (figure 2).

(3) Pathological study showed general inflammatory response including cell filtration, fibrosis and neointimal hyperplasia. But there were no specific change by using new devices; invasiveness to vessels and surrounding tissues (figure 3).

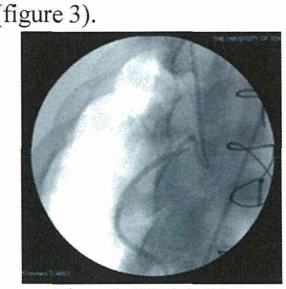


Figure 2. RITA-RCA

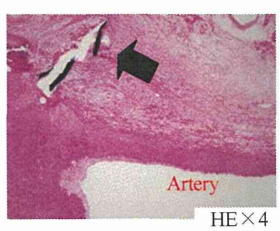


Figure 3. Device (arrow)

Conclusion

It was confirmed that the device we developed has feasibility to use in coronary artery bypass surgery in this mid-term chronic study. Now we are challenging more long period model. Evaluating efficacy of this devise in closed or limited operative space, further research is necessary.

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Takehiro Ando and Ichiro Sakuma were with Department of Precision Engineering, The University of Tokyo, Hongo, 7-3-1, Bunkyo-ku, Tokyo, Japan.

新しい冠動脈吻合用デバイスの研究

～ ブタ冠動脈バイパス手術での前臨床試験～

○井戸田佳史[a]，Nirmal Panthee[a]，安藤岳洋[b]，佐久間一郎[b]，小野稔[a]

[a]東京大学　心臓外科

[b]東京大学工学部精密工学科

Development of A New Device for Distal Coronary Artery Anastomosis

Yoshifumi Itoda[a], Nirmal Panthee[a], Takehiro Ando[b], Ichiro Sakuma[b], and Minoru Ono[a]

[a] *Department of Cardiac Surgery, The University of Tokyo, Tokyo, Japan*

[b] *Department of Precision Engineering, The University of Tokyo, Tokyo, Japan*

Introduction: For minimally invasive and robotic surgery, we developed a new suture device that enables us to skip manual ligation by pinching motion after conventional suturing. **Methods**: Thirteen pigs were used in this study. Left internal thoracic artery was anastomosed to left anterior descending artery (LITA-LAD). And right internal thoracic artery was anastomosed to right coronary artery (RITA-RCA). Suture time was measured. Eleven of thirteen pigs were operated upon using the suture device (group D), and the remaining by conventional 7-0 monopropylene suture (group C). Six animals of group D and one of group C underwent angiography just after anastomosis. The remaining underwent angiography at one month after operation. Histopathological examination of anastomosis was performed after animals were euthanized. **Results**: LITA-LAD anastomosis was done in 18.4±1.2 min in group D, 16±2.0 min in group C (p=0.42). RITA-RCA anastomosis was done in 20.1±1.2 min in group D and 24.5±0.5 min in group C (p=0.0055). Angiography demonstrated FitzGibbon B in one anastomosis of each group, the remaining were FitzGibbon A. Histopathologic examination showed common inflammatory responses in both groups. Device-specific inflammatory changes were not observed. **Conclusions**: This new suture device showed an excellent safety and quality in this porcine model.

Keywords: minimally invasive surgery, robotic surgery, coronary anastomosis, suture device

【目的】心臓外科領域で低侵襲手術が導入されて久しい[1)]が、冠動脈バイパス手術においては吻合自体が高度な技術を伴うことや多枝病変の吻合は困難なことなどから、内視鏡下手術やロボット手術といった低侵襲手術はさほど普及していないのが現状である。我々は、当大工学部および企業との連携により狭小スペースや深部術野での吻合を容易にする、半自動吻合デバイスを開発した。本研究ではブタ冠動脈を用いて動物実験を行い、デバイスの有効性、安全性を評価した。

【デバイス】我々が開発したデバイスは、市販されているポリプロピレン糸の自由端にステンレス製の錨状の器具を圧着させた単純な構造をしており、従来の連続縫合の後ワンタッチで器具と糸が固定され結紮を省略できるというものである（Figure1）。器具は生体適合性を有する SUS316L ステンレス鋼を YAG レーザー加工により切り出して作製したもので、高さ 0.9mm, 横幅 0.5mm, 奥行き 0.5mm の錨の形状をしている。錨の溝状の部分に糸を挟んだ状態で持針器を用いて溝を外側からつまむことで器具と糸とを固定することができ、通常 7 回程度結紮する手間を省くことができる。結紮の困難な、狭小スペースや深部での血管吻合をより容易にする可能性がある。

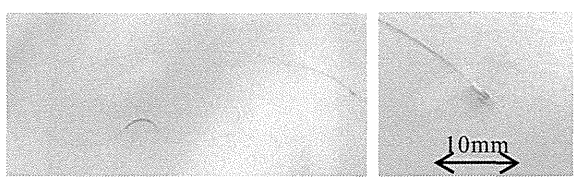

Figure1 the suture device

【実験】動物実験は US National Institute of Heath の "Guide for the Care and Use of Laboratory Animals,"に基づいて計画され、東京大学動物実験倫理委員会に承認された。(承認番号：11-P-84). 実験は 13 頭のブタ（急性期実験は全農三元豚、慢性期実験はジャパンファームクラウンミニブタ）を用いてオフポンプ冠動脈バイパス手術を行った。ブタを全身麻酔下、気管挿管下に開胸し両側内胸動脈を剥離。左内胸動脈を左前下行枝に（LITA-LAD）、右内胸動脈を右冠動脈に（RITA-RCA）吻合し吻合時間、吻合後の血液流量を測定した。13 頭中 11 頭については開発したデバイスで吻合を行い（D 群）、残りの 2 頭は従来通りの polypropylene suture（7-0 Prolene® Ethion, Somerville, NJ, USA）（C 群）で吻合を行った。また D 群のうち 6 頭と C 群のうち 1 頭は急性期実験として吻合後に血管造影検査を、残りの D 群 5 頭と C 群 1 頭は慢性期実験として 1 ヶ月後に血管造影を行い、KCl の静注による安楽死後、吻合部を切除して病理

評価を行った。術後 1 ヵ月間はバイアスピリン 100mg/日を内服させた。

【成績】吻合時間はそれぞれ、LITA-LAD 吻合は D 群 18.4±1.2 分、C 群 16±2 分（p=0.42）、RITA-RCA 吻合は D 群 20.1±1.2 分、C 群 24.5±0.5 分（p=0.0055）であった。LITA-LAD 吻合では両群に有意差を認めなかったが RITA-RCA 吻合では D 群の吻合時間が有意に短かった。吻合後の血液流量はそれぞれ、LITA-LAD 吻合が D 群 29.7±4.0ml/min、C 群 48.0±39.0ml/min（p=0.72）、RITA-RCA 吻合が D 群 48.7±4.9ml/min、C 群 28±9.0ml/min（p=0.20）で両群に有意差は認めなかった。急性期での血管造影検査は D 群、C 群にそれぞれ 1 吻合ずつ FizGibbon [1]B（50%以上の狭窄）が見られたがその他の吻合はすべて FizGibbon A（50%以下の狭窄）であった。慢性期の血管造影では D 群、C 群ともにすべての吻合で FizGibbon A が得られた（Figure2）。慢性期の病理ではデバイス周囲に炎症細胞の浸潤や線維増生、吻合血管の内服肥厚がみられたものの C 群と比較しデバイスに固有のものではなく、デバイスによる血管損傷や組織障害もみられなかった（Figure3）。

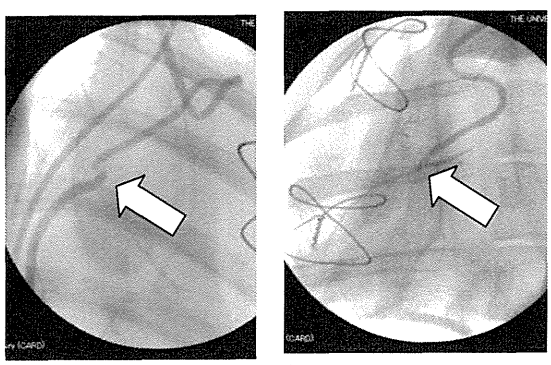

Figure2.a b
Angiography 1 month after operation revealed FitzGibbon A in both LITA-LAD（a）and RITA-RCA（b）anastomosis. (⇒: suture device)

【考察】我々は、すでにウサギ頸動脈バイパスモデルを用いてこの吻合デバイスの有効性、安全性を実証している。頸動脈を同側顎静脈を用いてバイパスし、1 ヵ月、3 ヶ月、6 ヵ月の遠隔期において吻合時間、開存性、生体組織に与える炎症反応を評価した結果、全項目において従来の吻合方法と有意差を認めなかった。つまり従来の polypropylen 糸と同等に小口径血管の吻合に使用可能と結論できることができた。今回の実験では、ブタ冠動脈を用いて実際の冠動脈吻合に使用可能かどうかを評価することが目的であった。

吻合時間については、RITA-RCA 吻合は D 群

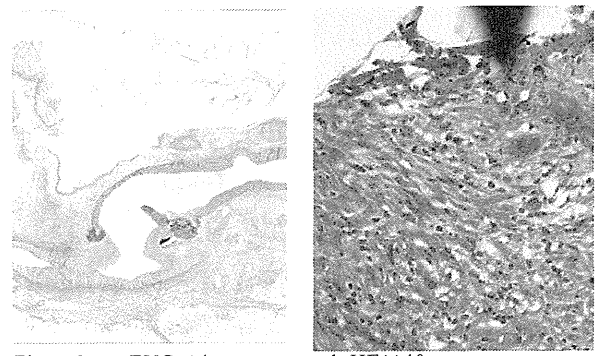

Figure3.a EVG×4 b HE×40
Hitopathological study showed common inflammatory responses including intimal hyperplasia, fibrosis (a), and cell infiltration (b).

で優位に吻合時間が短い結果が得られた。ブタ冠動脈では右冠動脈が細く、吻合可能な範囲は心右側面の深部になってしまうため、解放術野であってもやや深部での結紮を要する。このため深部での操作を想定したデバイスが吻合に有効であったと考えられた。

血管造影検査では急性期で 1 例の吻合部狭窄（FitzGibbon B）を認めたものの、慢性期を含むその他はすべて良好な開存性を示しており、十分に臨床応用できる結果であった。

血管吻合部の病理学的変化としては、内膜損傷（吻合操作による）に起因する内膜肥厚、ステンレスや糸などの異物に対する炎症細胞浸潤、線維増生などが知られており [2]、今回の実験でもこれらの変化が確認された。デバイスの周囲にはマクロファージ、リンパ球、好酸球などの炎症細胞の浸潤および異物肉芽種が見られたが polypropylen 糸を使用した場合と程度の変化はなく、デバイスによる血管損傷や、吻合部の狭窄なども見られなかった。

【結論】今回、ブタ冠動脈を用いた急性および慢性実験において、我々が開発した吻合デバイスは、従来の方法と同等に有効であることが証明された。今後、より長期の埋め込み実験や、胸腔鏡下での手術を行い、デバイスの有効性を評価する必要がある。

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Development of a suturing device for anastomosis for small caliber arteries

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Abstract The use of minimally invasive and robotic operations has been increasing for coronary artery bypass surgery; however, no suturing devices have been universally adopted for use in these procedures. We developed a new suturing device that enables omission of manual ligation after a running suture. Twenty-two rabbits were used in this study. In 22 rabbits, the right carotid artery was bypassed using an autologous jugular vein graft. Half of the animals were operated on using the new device and the other half using conventional suturing methods. Postoperative evaluations were performed at 1, 3, and 6 months. Suturing time was 15.6 ± 2.4 min in the device group and 16.6 ± 4.4 min in the control group ($p = 0.34$). Graft patency and blood flow measurements were not significantly different between the two groups. Histopathological examination of the anastomotic site showed common inflammatory responses in both groups. No particular histopathological change was seen related to the device. In conclusion, the safety of the new suturing device was confirmed, and its efficacy was equal to that of the conventional suturing technique.

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Keywords Anastomosis · Coronary artery bypass graft · Device · Robotics · Animal model

Introduction

In recent years, robotically assisted techniques have been introduced for cardiovascular surgery. However, several obstacles still exist in the application of robotic techniques to coronary artery bypass graft (CABG) procedures. One such problem is diffi in performing a running suture and tying a knot in a limited space. Despite the development of several devices that eliminate suturing and/or tying a knot, none have been widely adopted for performing coronary distal anastomoses. The Ventrica Magnetic Vascular Positioner (Ventrica Inc., Fremont, CA) enabled anastomosing with magnetic power and was expected to have excellent patency and good handling [1]. However, this device was not suitable for arteriosclerotic lesions, and it was diffi to add a hemostatic stitch, so it was withdrawn from the market. Although a U-clip (Coalescent Surgical, Inc., Sunnyvale, CA) enabled satisfactory anastomoses and eliminated knot tying in minimally invasive cardiac procedures [2, 3], it was also withdrawn from the market. Currently, the only system available for distal coronary anastomoses is the C-Port (Cardica Inc., Redwood City, CA), which enables the cutting and suturing of vessels simultaneously with an embedded cutter and staples. However, high cost is a limiting factor for this device. We developed a new device that can eliminate knot tying after completion of running suturing. The effi and safety of this new suturing device were evaluated in a rabbit carotid artery bypass graft model.

Materials and methods

Device design and anastomosis procedure

This device is simply composed of a commercially available monofilament propylene suture with an anchoring mechanism connected to the free end of a suture. The anchoring mechanism is made of biocompatible stainless steel (SS316L) and manufactured by laser molding. The size of the mechanism is 1.0 mm height, 0.5 mm width, and 0.5 mm depth. After a common running suture, in an end-to-side fashion, surgeons pass the suture through a slot in the mechanism and pull the suture to control hemostasis, then pinch the slot of the mechanism with regular force by a needle holder to complete the anastomosis. Figure 1 shows the structure of the device and anastomotic procedures for using the device, which enables the performance of interrupted, running, or other preferred suture patterns and the omission of manual knot tying by hands or needle holder.

Experimental protocol

Institutional guidelines for the care and use of laboratory animals were observed. This animal experiment was designed according to the humane care guidelines of the United States National Institute of Heath "Guide for the Care and Use of Laboratory Animals" and was approved by the Animal Ethics Committee at The University of Tokyo (11-P-71). A total of 22 healthy male New Zealand White rabbits (weight 3.0–3.5 kg; age 15–20 months) were purchased for this study. All animals were anesthetized with an intramuscular injection of ketamine (100 mg/kg) and xylazine (50 mg/kg). An auricle vein was used for infusion. A median neck incision was made exposing a 3-cm segment of the right carotid artery. Heparin (100 units) was administered, and the ipsilateral jugular vein was harvested as a graft vessel. The jugular vein was anastomosed to the carotid artery; a 1.25-mm- or 1.5-mm-diameter coronary shunt tube was placed in the carotid artery during anastomosis. Finally, native carotid artery

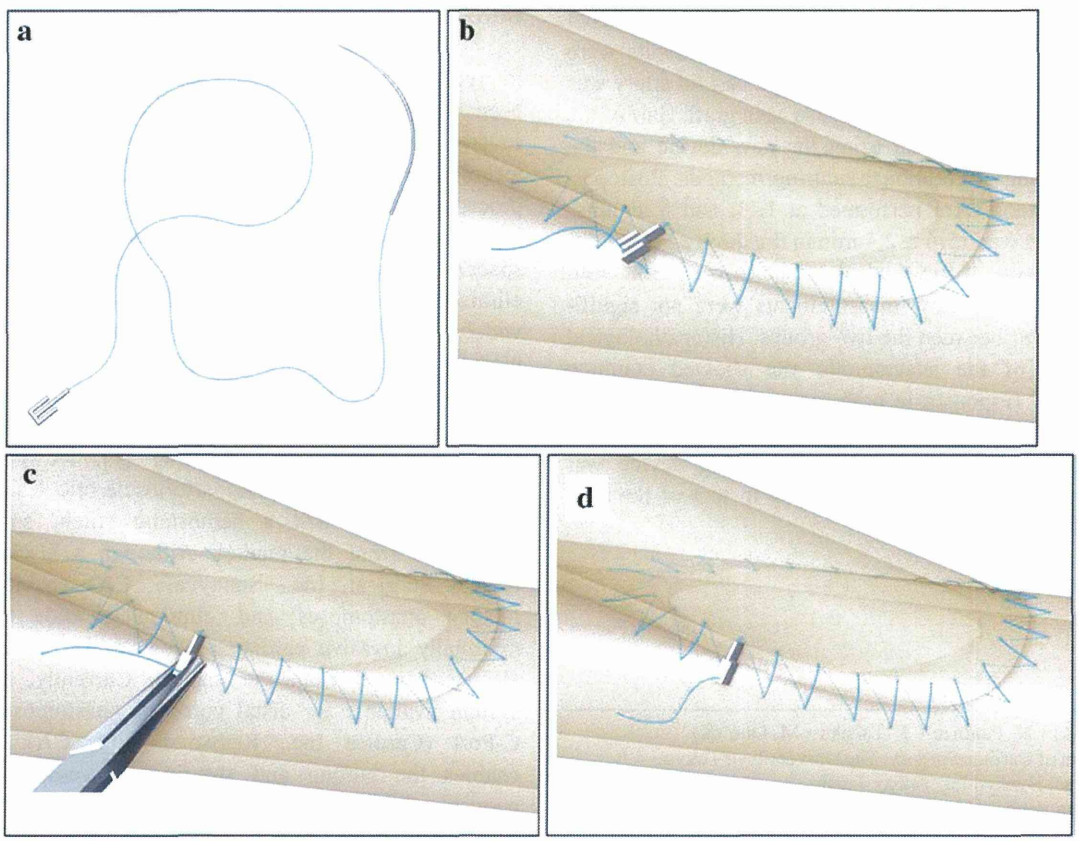

Fig. 1 Device design. a The suturing device consists of a polypropylene suture with an anchoring stainless steel mechanism attached to the free end of the suture. b After a running suture, the suture goes through the anchoring mechanism. c The surgeon can fix the suture by pinching the mechanism using a needle holder. d Completed anastomosis with the suturing device

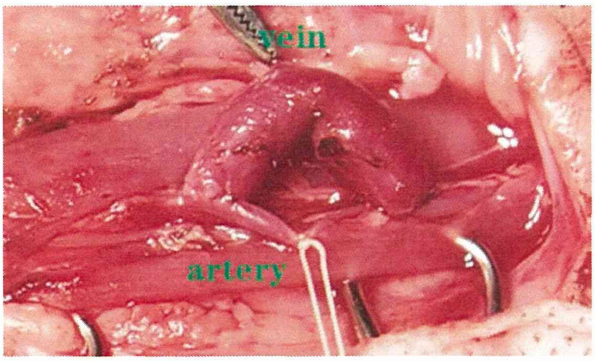

Fig. 2 Bypass design: an arch-shaped bypass with two anastomoses of the rabbit carotid artery and jugular vein. Carotid artery is ligated between anastomoses

was ligated between the anastomoses once completed (Fig. 2). The new suturing device was used on 11 rabbits (group D), and conventional suturing (group C) using 8-0 monofilament polypropylene suture (8-0 Prolene® Ethicon Inc., Somerville, NJ) was performed on the other 11 rabbits. Because of the fragility of the vein graft, we initially fixed the vein graft in two edges of the arteriotomy of the carotid artery. Two devices/sutures were used to complete one anastomosis. This meant one rabbit needed four devices/sutures for the operation. The skin incisions were closed, and the rabbits were returned to their cages after full recovery from anesthesia. All animals had free access to water and feed. Dissolved aspirin (10 mg) was administered by direct oral feeding every day after the operation. At 1, 3, and 6 months after the operation, 4, 5, and 2 rabbits from each group were anesthetized and evaluated, respectively. Suturing time, which was the time required to complete anastomosis and insure hemostasis, was measured and compared between the two groups. BeriQ® (Nippon BXI Inc., Tokyo, Japan) was used for graft flow measurements just after completion of anastomosis and at each evaluation period (1, 3, and 6 months). Angiography was also performed at each evaluation period using a C-arm X-ray system (Siemens Medical Solutions, Germany) with iomeprol (Iomeron®, Eisai, Tokyo, Japan) contrast media. A guiding catheter was inserted into the right carotid artery via the femoral artery. Images were obtained from an angle at which anastomosis could be observed from a horizontal direction (Fig. 3). Graft patency was evaluated during each period using the Fitz-Gibbon criteria [4]. At study completion, the rabbits were killed by cardiac injection of potassium chloride. Anastomotic sites were resected and fixed in 5 % formalin for histopathological examination. Sections (5 lm) were cut from paraffin-embedded blocks in a way that all elements (a device or a suture, vein graft, and carotid artery) were included in one slide. Hematoxylin & eosin and Elastica

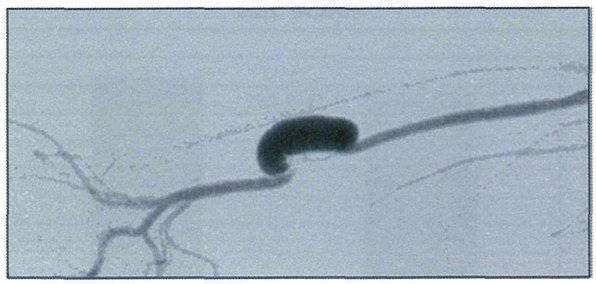

Fig. 3 Graft angiogram

van Gieson staining was performed. Inflammatory cells including lymphocytes, macrophages, and granulocytes were counted in six random high-power fields. Intimal hyperplasia (IH) and fibrosis at the anastomosis site were measured as inflammatory response indicators.

Statistical analysis

Data were collected in a computerized database (Excel for Windows, Microsoft Inc., Redmond, WA). Suturing time, flow measurement, and cell count data are expressed as mean ± standard deviation (SD). Differences between the groups were analyzed by Student's *t* test using SPSS for Windows statistical software package (SPSS Inc., Chicago, IL).

Results

Suture time

Figure 4 shows suturing time in both groups. In group D, all suturing devices functioned as intended. Average suturing times were 15.6 ± 2.4 min in group D and 16.6 ± 4.4 min in group C. No significant difference was observed between the two groups ($p = 0.34$).

Angiography

Anastomosis patency in both groups C and D was 75 % (3/4), 80 % (4/5), and 100 % (2/2) at 1, 3, and 6 months, respectively, and all were Fitzgibbon A grade.

Blood flow

No significant difference in blood flow was observed between the two groups at all time periods evaluated (Fig. 5).

Histopathological evaluation

Figure 6 shows the histological images of anastomoses. There were no findings of damage to vessel walls or

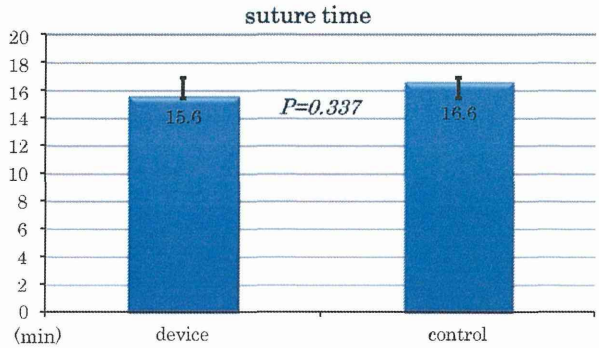

Fig. 4 Suture time: this table shows device and control anastomotic time. No significant difference was observed between the two groups

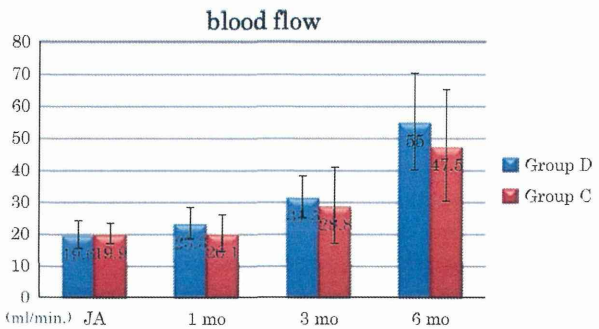

Fig. 5 Blood flow at each evaluation period: *JA* just after anastomosis. Blood flows of both groups increased gradually with time. And there was no significant difference between the groups

surrounding tissues from the device. Figure 7 shows histopathological changes [fibrosis, intimal hyperplasia (IH), lymphocyte, granulocyte, and macrophage] at each evaluation phase. Figure 8 shows histopathological images. Fibrosis was markedly observed at 1 month particularly around the monofilament polypropylene suture and gradually diminished at 3 and 6 months in both groups. IH at the anastomosis site was detected to some degree, but no significant difference was observed in average thickness between the two groups. At 1 month, inflammatory cell infiltration was equally observed around the anastomoses in both groups. Cell infiltration was attenuated at 3 and 6 months.

Discussion

The carotid artery-jugular vein bypass model of a rabbit has commonly been used to evaluate the quality of adhesives and suturing devices [5, 6]. When two vessels were anastomosed using the conventional suturing technique, some degree of histopathological change was observed

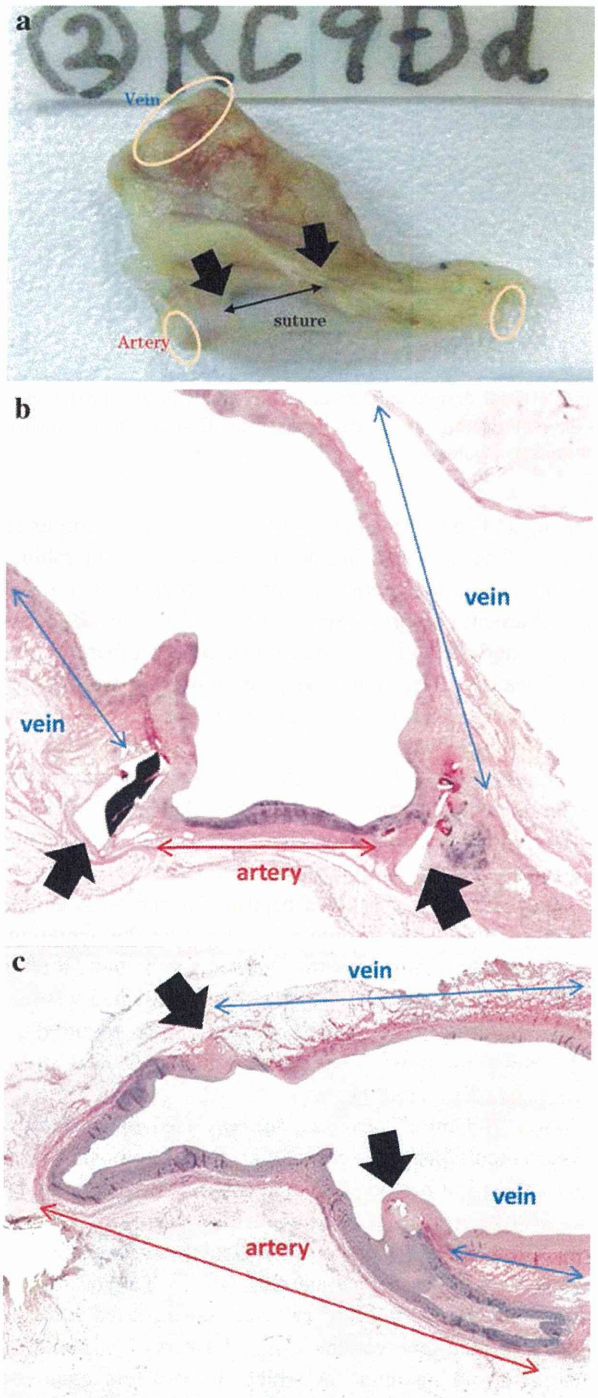

Fig. 6 Histopathological evaluation: histopathological sections were made from resected anastomotic sites (a). *Two arrows* are pointing at the used devices/sutures. Embedded block of the specimen was cut by a surface including these two devices/sutures. Section of anastomotic site with used device (b) and conventional suture (c) showed no damage to vessel walls or surrounding tissues. a Resected specimen from anastomosis site. b Anastomosis by the device. c Anastomosis by conventional suture