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研究課題名(和文) 組織工学の手法を用いた新しい分岐部人工気管の開発

研究課題名(英文) Development of a Y-shaped tissue-engineered artificial trachea for carinal reconstruction.

研究代表者

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研究成果の概要(和文)：本研究の目的は、胸腔内でも安全に使用し得る分岐部人工気管を開発することであった。そこで、これまで私たちが開発してきた自己組織再生型人工気管のコラーゲン部分に、新たな分子構造をもち早期に自己組織化が期待できるコラーゲンを用いることにより、安全性を向上させた。気道内面は粘膜上皮が再生するが、本研究では患者自身の組織由来幹細胞を応用することによって安全性と効果の向上をめざすため、これを大型実験動物を使って評価し、並びに分岐部気管の安全な再建術式に関しても検討した。

研究成果の概要(英文)：The aim of this study was to develop a tracheal prosthesis for carinal reconstruction. We have studied more than 20years tracheal reconstruction with the base of the concept of in situ Tissue Engineering., where the inner surface is designed to be replaced with regenerated host epithelium. Newly developed tracheal prosthesis were evaluated in the animal experiment in terms of feasibility and its safety.

In this project, several types of Y-shaped artificial trachea were manufactured in our laboratory. The material of the tracheal wall were Marlex mesh or bioabsorbable Vicryl mesh. Tracheal bifurcations were reconstructed on 26 beagle adult dogs, Azygos vein was cut, then the tracheal carina was replaced with prosthesis and wrapped the greater omentum. Bronchoscope and CT examinations were performed to evaluate patency of airway and luminal tissue regeneration. These results were now prepared to report on JTCVS.

研究分野：呼吸器外科学、人工臓器学、再生医学

キーワード：人工気管 組織工学 コラーゲン 気道再建 胸部外科 分岐部気管 再生 生体内再生

## 1. 研究開始当初の背景

1940年代から人工気管による気道再建研究がはじまったが、現在なお臨床に安全に使い得る人工気管は世界的にも皆無である。我々は生体親和性の高いコラーゲンのコンポジットを用いて代用気管を作製し、動物実験において有用性・安全性を確認してきた。その結果 2002年より京都大学医学部・福島県立医科大学倫理委員会の審査を経て、現在までにすでに20例以上の患者に自己組織再生型人工気管を使用し、良好な結果を得ていた (Omori, K., Nakamura, T., et al. *Annals of Otolaryngology & Rhinology* 113: 623-627, 2004)。しかしながらこれらは耳鼻科領域の頸部気管の再建であるため、胸部外科領域の再建、すなわち気管分岐部や左主気管支幹において使える安全性の高い人工気管の開発を行いたいと考えた。

## 2. 研究の目的

我々の代用気管は現在すでに10年前から耳鼻科領域の気道再建で患者に使われている実績があり、本研究で、直ちに三つの技術開発と動物実験に取りかかれば、本研究期間内に胸部外科領域の縦隔内の気管の置換に応用可能であると予想される。これまでは左肺全摘しかできなかった左の主気管支の狭窄の患者も、安全に使用できる人工気管が開発されれば左肺機能を本研究に対する期待は大きかった。

そこで本研究は、最近の組織幹細胞を使う新しい *in situ Tissue Engineering* であり、ES細胞や脳死移植など倫理的に高いハードルのある技術を使っていない。このため直ちに臨床応用が可能である。本研究はその

第一歩となる必要不可欠な動物実験であり、胸部外科領域の応用研究に関しては世界初の試みとして実験を行なった。

## 3. 研究の方法

本研究においては平成25年度にコラーゲン部分の改良で代用気管の生体親和性の向上と改良を行った。胸部外科領域、とりわけ胸腔内での置換に耐え得る代用気管の完成を目指すとともに、上皮化の促進のために組織幹細胞の応用と新たな術式を検討した。

そこで、本研究課題の具体的な目標として次の3点を行なった。

- (1) 安全性の向上ためのコラーゲンの気密性の向上
- (2) 分岐部再建術式の検討(大綱や遊離組織移植を含めた)
- (3) 組織幹細胞の導入による早期上皮化の促進

平成25、26年度には、分岐部用の人工気管の開発と臨床での需要の多い左主気管支の置換モデルの実用化を行い、さらに組織由来幹細胞導入をして成績の向上をめざした。そのため動物実験による安全性の確認をビーグル犬への埋込実験で行なった。

## 4. 研究成果

本研究では、胸腔内でも安全に使用し得る分岐部人工気管を開発することを目的とした。これまで開発してきた自己組織再生型人工気管に、新たなコラーゲンをを用いて安全性を向上させるべく人工気管の改良を行なった。気道内面に粘膜上皮再生を促すため自己組織由来幹細胞を含浸させた系も加えた。作成したY字型人工気管を大型実験動物の気管再建で評価し、併行して安全な再建術式も検討した。

膜様部構造を持った代用気管はメッシュ筒の全周 2/3 にだけステントを入れた新しいタイプの人工気管 (L=50mm) であり、気管壁の素材はマーレックスメッシュとバイクリルメッシュの二種類のものを作成した。気管内腔の虚脱を防止するため、ポリプロピレンステントをメッシュに 1mm 間隔で入れている。

Y 字型コラーゲンとメッシュ複合体人工気管を用いてビーグル成犬 (体重 10-12kg) の気管分岐部を再建した。右後側方開胸で奇静脈を切断し分岐部の背方からアプローチして、左気管支、気管、右気管支の順に吻合し、腹腔より経横隔膜的に右胸腔に挙上した大綱でラッピングし組織再生を促進させた。コントロールを含めて都合 26 頭のビーグル成犬に再建を行った。動物実験における長期観察として、再建した気管分岐部を気管支鏡と CT で評価した。内腔保持力と気管の変形、組織再生の病理的検討を行っており、結果を JTCVS に投稿すべく準備している。

## 5 . 主な発表論文等

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〔図書〕(計 0 件)

〔産業財産権〕  
出願状況 (計 0 件)

取得状況 (計 0 件)

〔その他〕

ホームページ

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## 6 . 研究組織

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