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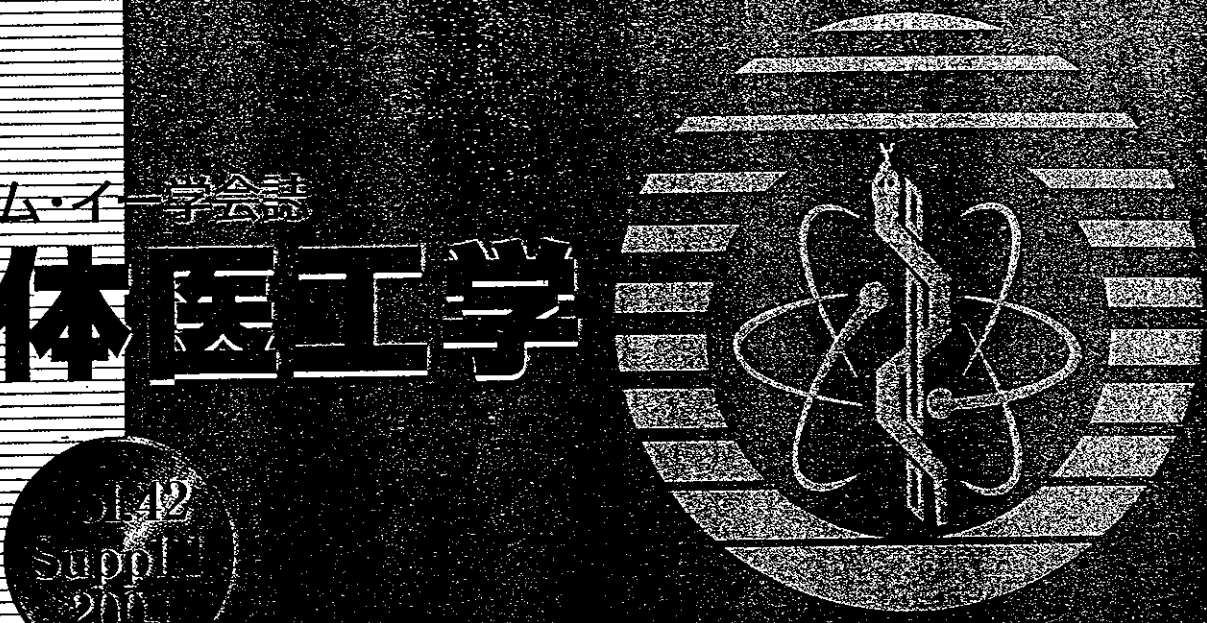

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体内完全埋め込み型人工心臓システム開発の現況

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Current Status of a totally implantable artificial heart system

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1．緒言

当センターで開発を行っている完全埋め込み型電気油圧駆動式全人工心臓（EHTAH）システムは、ダイアフラム型血液ポンプ、油圧アクチュエータ、体内回路、経皮的エネルギー伝送（TET）システム、経皮的情報伝送システムから構成される。従来型システムは血液ポンプとアクチュエータをオイルコンデュイットにより分離し体内へ配置する方式をとっていたが、アクチュエータの小型・軽量化により、オイルコンデュイットを廃止し、血液ポンプとアクチュエータの一体化に成功した。

2．システムの概要

一体化により血液ポンプ駆動ユニットは、左右血液ポンプ部、アクチュエータ部の体積がそれぞれ 314 mL と 156 mL、重量は 1100 g まで小型・軽量化された。従来型、一体型の各血液ポンプ駆動ユニットを、模擬循環回路を用いた in vitro 試験で評価したところ、拍出量特性は従来型では 11 L/min (130 bpm) で飽和していたが一体型では 12 L/min (150 bpm) まで線形的に増加した。システム効率特性は一体型の効率が従来型よりも全拍動数において上回り、最大効率も 12.5 %から 14.4 %に上昇した。またシステムの耐久試験では 3 年以上の動作を確認しており、現在も継続中である。

3．動物実験評価

システムの in vivo 評価として、従来型血液ポンプ駆動ユニットを体重 73 kg の仔牛に埋め込んだ慢性動物実験では、87 日間の国内最長生存記録を達成し、一体型血液ポンプ駆動ユニットを体重 78 kg の仔牛に埋め込んだ慢性動物実験では、21 日間の生存を記録した。さらに一体型血液ポンプ駆動ユニット、体内回路、体内電池、TET システムの全ユニットからなるトータルシステムを体重 63 kg の仔牛に埋め込んだ慢性動物実験では現時点で 30 日間の生存を記録し、全実験期間を通じて、TET を用いた電力伝送によるシステムの駆動と体内電池の充電、毎日約 1 時間の体内電池によるシステムの駆動が問題なく行われることを確認した。TET システムのエネルギー伝送効率も約 80 %近くを記録した。

4．結論

以上の結果から、本システムは完全体内埋め込み型システムとして十分な性能を有していると考えられる。

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機械弁でのキャビテーション現象に関する研究

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A Study on the Cavitation Phenomenon of the Mechanical Heart Valves

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1. はじめに

以前、我々は本研究室で開発した電気油圧型人工心臓を用い、異なる形状のmonoleaflet弁を対象にてキャビテーション気泡の発生のメカニズムを検討してきた[1]。しかし、最近臨床では、bileaflet弁が主に使用されている。本研究では、monoleaflet弁としては25 mmのBjörk-Shiley monostrut弁、Medtronic Hall弁と23 mmのOmnicarbon弁を、bileaflet弁としては21 mmのSJ弁、ATS弁とSorin弁を対象とし、キャビテーション気泡の発生のメカニズムを比較することにした。

2. 方法

機械弁を僧帽弁に装着し、電気油圧型人工心臓を用いて心拍数60-100 bpmで駆動し、弁の閉鎖運動、圧力低下およびキャビテーション気泡の撮影を行った。閉鎖中に弁の運動が観察できるようにアクリル製のチャンバーを製作した。チャンバー上部に高速度カメラ（fx-6000, nac）を設置し、弁表面に生じるキャビテーション気泡を10,000 fpsで記録した。閉鎖中の弁の軌跡はCCDレーザ変位センサ（LC-2450, Keyence）を用いて検討した。さらに、閉鎖中に弁表面近傍での圧力低下を小型圧力センサ（105C02, PCB Piezotronics）を用いて計測した。

3. 結果と考察

閉鎖速度と圧力低下共にmonoleaflet弁のほうがbileafletより大きくなっていた。また、monoleaflet弁の場合には閉鎖速度は速い際にはsqueeze flowとwater hammerによるキャビテーション気泡が観察された（図1, 2）。Bileaflet弁の場合には閉鎖速度がmonoleaflet弁より遅くなったため、squeeze flowによるキャビテーション気泡のみが観察された（図3, 4）。

図 1. Medtronic Hall弁でのCavitation bubbles (100 bpm)

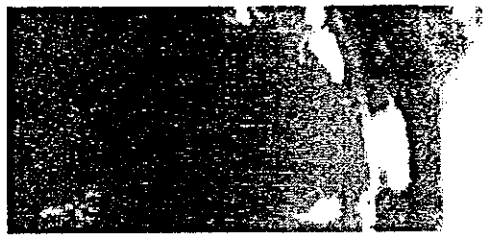

図 2. Omnicarbon弁でのCavitation bubbles (100 bpm)

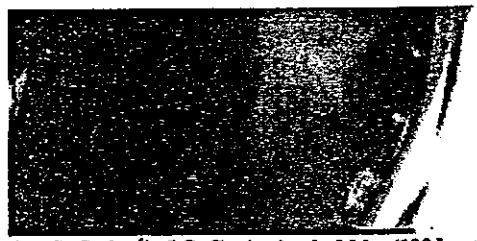

図 3. St. Jude弁でのCavitation bubbles (100 bpm)

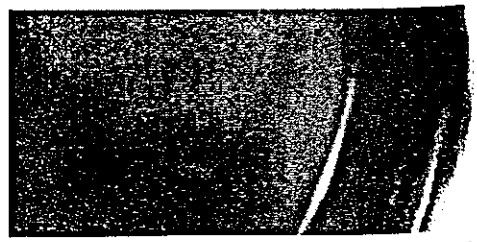

図 4. Sorin弁でのCavitation bubbles (100 bpm)

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電磁式補助人工心臓の開発：動物実験

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Development of The Direct Electromagnetic Ventricular Assist Device : Animal Experiment

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1．はじめに

臨床から研究段階のものを含め現有する拍動型補助人工心臓は，ローラーねじや油圧など何らかの運動変換機構によって拍動運動を得ている．この運動変換機構は人工心臓の部品点数を増やし，小型化と信頼性高上を妨げている．そこで本研究では，運動変換機構を用いずにリニア振動アクチュエータ（Linear Oscillatory Actuator :LOA）によって直接プッシャープレートを駆動する電磁式補助人工心臓（Direct electromagnetic Ventricular Assist Device:DEM-VAD）の開発を主目的としている．2002年に初期モデルを試作してから現在までに4次試作を終え，最大拍出量 8L/min 以上，最大効率約18%の性能を得ている[1-3]．本稿では，動物実験に向けた5次モデルの開発および動物実験結果に関して報告する．

2．電磁式補助人工心臓

LOA はステータ，ムーバ，ガイドから構成した．ステータ材には電磁軟鉄を用い，ステータ外周部にDLC（Diamond Like Carbon）コーティングを施した．ムーバには，希土類永久磁石を組み込んだ．血液ポンプハウジングは，真空注形法により硬質ポリウレタンにより作成した．ダイアフラムはセグメント化ポリウレタンを用いてディッピング法により作成した．ポンプユニットは，直径 102mm，高さ 51mm，重量 750g，容積 310ml であった．ホール素子（HW-105A/旭化成電子株式会社）を応用して，リアルタイムにプッシャープレートの位置検出を可能とした．駆動制御回路は，電圧制御型単相インバータを用いた駆動部と，A/D・D/A 変換を備えたマイクロコンピュータ（H8-3048/日立）からなる制御部で構成した．駆動制御方式として，固定拍動数駆動と完全充満完全駆出（Full-Fill/Full-Eject：以後 FFFE）駆動を可能とした．また左心室内に挿入した脱血管が，心室壁などに吸い付く現象を検出し，解除を試みる制御も組み込んだ．

3．慢性動物実験

2003年12月9日に，国立循環器病センターにて第1例目の慢性動物実験を行った．成山羊1頭（メス，56kg）を用い，左室－大動脈バイパス左心補助 *ex vivo* モデルを作成した．DEM-VAD は，主に FFFE 制御で駆動した．

4．実験結果

FFFE 制御にて，心電図などを用いずに自然心臓との心拍同期が確認された．DEM-VAD は，自然心臓の拍動数変化に追従して70～160bpm で駆動可能であった．バイパス流量は2.0～4.2L/min であった．入力電力は，動脈圧変動により 7～10W で推移した．最大効率は14%であった．

42日目にポンプ内部に血栓を認めたため，実験を終了した．ポンプ内血栓は，流入ポート延長線上のダイアフラムーハウジングジャンクション付近を基部に発生していた．LOA 周辺に磨耗粉などは認められず，アクチュエータに起因する問題は発生しなかった．解剖所見として，腸管膜動脈梗塞が広範囲に認められた．また，心尖に挿入した脱血管周辺に血栓が認められた．

5．まとめ

LOA で駆動する DEM-VAD を開発し，第1例目の慢性動物実験を行った．LOA や駆動制御回路に大きなトラブルはなく，42 日間の耐久性を確認した．血液ポンプに発生した血栓に関しては，現在原因および解決策を検討中である．

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完全埋込み型人工心臓用経皮エネルギー伝送システムの開発と評価

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The development of a transcutaneous energy transmission system for the electrohydraulic total artificial heart system

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1．緒言

完全埋込み型人工心臓(Total Artificial Heart: TAH)の実用化において、皮膚を貫通することなく体外から体内に電力を供給することができる、高効率の経皮エネルギー伝送システム(Transcutaneous Energy Transmission System: TETS)の開発[1]は極めて重要である。TETSは、体外の直流電力をスイッチング回路にて交流に変換し、体外コイルと体内コイル間の電磁誘導作用によって、体外から体内へ伝送し、体内の整流回路により直流電力に再変換するものである。開発中のTETSシステムは、TET単体にて効率82～85%で4ヶ月以上の連続伝送を行い得ることを確認している[2]。本研究では、全構成パーツを埋め込んだ慢性動物実験において、TETSおよび体内二次電池による全システムの駆動の評価を行う。

2．方法

図1にシステムの基本構成を示す。体内埋込み部分は、体内コイル、体内二次電池、体内制御回路、一体型血液ポンプ駆動ユニットから構成される。評価は、①経皮エネルギー伝送システム(TETS)による全システムの駆動及び②毎日40分の体内二次電池による全システムの駆動を行い、各部の電圧・電流・温度を測定した。計測はデータ収集ユニット(横河電機: DA100)を用い、温度センサーはT型熱電対(銅-コンスタンタン)を用いた。

3．結果と考察

10例の慢性動物実験を行い、TETS及び体内二次電池による全システムの駆動が正常に行われることを確認した。最長で27日間連続でエネルギー供給を行い得た(表1)。最近5例においては、コイル断線、パーツ故障、異常発熱、体内二次電池電圧低下や充電時間延長など認められず、安定して動作した。

経皮エネルギー伝送中の各部位の温度は、体内回路表側表面では、駆動条件によっては40℃を越える場合があり、今後、回路の改良や効率向上によって消費電力を低減し、発熱を抑える必要があると考えられる。

4．結論

全構成パーツを埋め込んだ完全埋込み型人工心臓の慢性動物実験において、経皮エネルギー伝送システム及び体内二次電池による全システムの駆動が可能であり、TAHシステムの電力伝送システムとして十分な性能を有していることが確認された。

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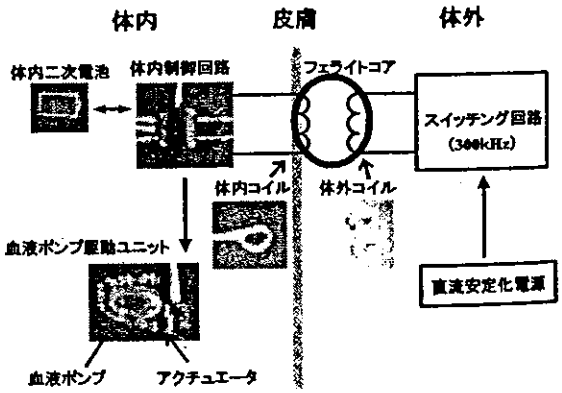

図1　経皮エネルギー伝送システム基本構成

表1　最近5例の慢性動物実験結果

実験No	伝送形態	伝送期間	備考
No.6	TET + BAT	(5 hours)	断線なし
No.7	TET + BAT	27 days	〃
No.8	TET + BAT	6 days	〃
No.9	TET + BAT	5 days	〃
No.10	TET + BAT	9 days	on going

国立循環器病センターにおける電気油圧駆動型人工心臓の開発

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Development of an electrohydraulic artificial heart system at the National Cardiovascular Center

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1．緒言

当施設では、平均的体格を有する邦人にも埋め込みが可能な完全体内埋め込み型電気油圧駆動式全人工心臓システム（EHTAH）の開発を行っている。現在までにアクチュエータと血液ポンプ部を仔牛に埋め込んだ慢性動物実験において87日間の国内最長生存記録を達成し、全パーツを体内に埋め込んだ慢性動物実験による評価を開始している。その現状について報告する。

2．EHTAHシステムの概要

EHTAHシステムは左右血液ポンプとアクチュエータからなる駆動ユニット、体内回路、体内電池、経皮的エネルギー伝送（TET）システム、経皮的情報伝送（TOT）システムから構成される（Fig.1）。現在までに体内埋め込みを想定した、各パーツのデザインの見直し、小型・軽量化を行ってきた。特に、駆動ユニットに関しては、従来のシステムで左右血液ポンプとアクチュエータをオイルコンデュイットで接続し、分離して設置する方式をとっていたが、オイルコンデュイットを廃止し、直接接続するようにデザインを変更したことで、容積470mL、重量1181gとなった。最終的に、ケーブル類を除くシステム全体の容積は、872mL、重量は2492ｇまで小型・軽量化できた。

3．結果と考察

一体化した駆動ユニットの性能を模擬循環回路において評価したところ、最大拍出量は12L/min、最大効率は15.4%であった。さらに、全てのパーツを10頭の仔牛（体重：63～82kg）に埋め込み、慢性動物実験によるシステムの評価を行った。駆動ユニットは胸腔内に、その他のパーツは皮下へ埋め込んだが、いずれの動物においても解剖学的な問題なく埋め込むことが可能であった。全システムを埋め込んだ動物実験においても、最長で70日間の生存記録を達成することができた（Table.1）。またTET、体内電池によるシステムの駆動、電源の切り替え動作、TOTによる皮膚を介した情報伝送を問題なく行えることを確認した。

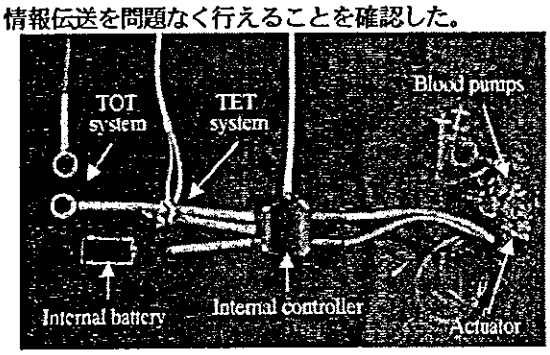

Fig.1 The EHTAH system

Table.1 Summary of EHTAH animal implantation

No.	year/ month	Body weight [kg]	Survival time [days]	Cause of death
1	03/05	63	6	Respiratory failure
2	03/07	82	14	Thromboembolism
3	03/07	70	70	Infection
4	03/07	79	1	Air embolism
5	03/09	82	4	Diaphragm breakdown
6	03/09	79	<1	Outflow valve breakdown
7	03/10	69	27	Respiratory failure
8	03/11	74	6	Respiratory failure
9	03/12	72	5	Respiratory failure
10	04/01	70	7>	Ongoing

4．結論

EHTAHシステムの開発現状について報告した。アクチュエータと血液ポンプの一体化を図り、システムの小型化と高効率化を実現し、仔牛に埋め込んだ慢性動物実験において70日間の生存を記録した。以上から、開発したEHTAHシステムは完全埋め込み型システムとして十分な性能を持っていると考えられる。

血液-ガス層連立数値流体解析による人工肺内中空糸膜充填体の血中ガス濃度分布および移動量に関する検討

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An investigation of distributions of gaseous concentration and transfer rates in the blood layer of packed beds in the oxygenator with CFD

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1. はじめに

外部灌流中空糸膜型人工肺では，中空糸の充填体が複雑な血液流れ場を形成している．さらに血液層側のガス移動が非線形なヘモグロビンとの化学反応を伴っている．このため，理論的な性能予測が困難で，特に，血液側の濃度分布や，ガス層側の影響を大きく受けると考えられる炭酸ガス移動に関して，理論的な解析がほとんど行われていない．我々は，血液ガス反応を組み込み，ガス層もモデル化して血液層と連立解析する数値流体解析手法を考案し，人工肺内のガス移動現象の数値計算を試みている．本検討では，人工肺の一部を模擬した充填体モデルにて，酸素・炭酸ガス移動量について検討した．

2. 方法

血液中のヘモグロビンと酸素・炭酸ガスとの反応式を酸素・炭酸ガスの質量濃度の関数としてモデル化した．この反応モデルを物質移動支配方程式の反応項としてプログラミングし，スーパーコンピュータを用いて数値解析を行った．参考人工肺は，内径 165 μm，外径 225 μm，長さ 95 mm の中空糸膜を，並行配糸して幅 58 mm のシート状にした後，シートを血流方向に対し直交する方向に積層配置することで厚み 30 mm 長方状の中空糸束を形成している．本検討では，人工肺内の血流は一様と仮定し，参考人工肺の中空糸充填体と同じ血流方向長さ(30 mm)と，

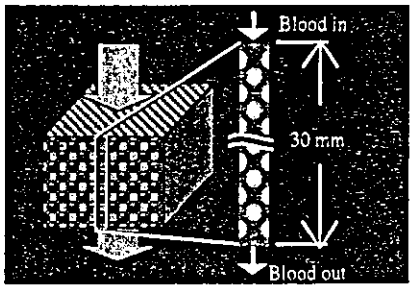

Fig.1 Referenced oxygenator was consisted of rectangular fiber bundle (Left). Packed beds model was composed of a blood passage among staggered hollow fibers (Right).

血流断面の一部を模擬した中空糸膜充填体モデルを用いて解析を行った．形状は千鳥配置された円筒状の中空糸膜からなり，円筒内部をガス層，外部を血液層として参考人工肺の充填体構造の一部を模擬した(Fig.1)．血液およびガスの流入条件は，参考人工肺で血流量(Q)=1,3,9 L/min，血液ガス流量比(V/Q)=1 として使用した際の血液側およびガス側流速条件を与えた．流入血液性状は人静脈血値を参考にした．

3. 結果

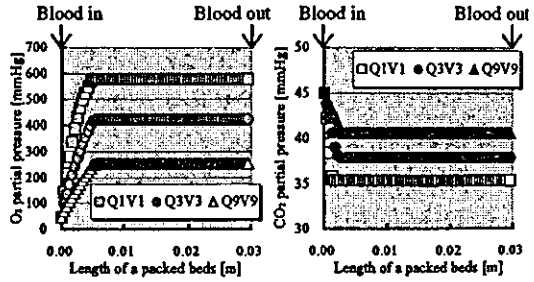

Fig.2 Both of O_2 concentration (Left) and CO_2 concentration (Right) analyzed results showed nonlinear gradients in direction of primary blood flow.

Fig.2 に示したように，血液主流方向の酸素・炭酸ガス濃度勾配はいずれも非線形な分布を示し，人工肺と同程度の充填層を形成すると，血液流出部でほぼ飽和状態に達している様子が観察された．この解析結果より，参考人工肺と同じ血流断面積に補正すると，酸素移動量および炭酸ガス移動量はそれぞれ V/Q = 1 の条件にて，Q = 1 L/min (Re = 0.4)で 71 mL/min，80 mL/min，Q = 3 L/min (Re = 1.3)で 199 mL/min，179 mL/min，Q = 9 L/min (Re = 3.9)で 540 mL/min，345 mL/min であった．

4. まとめ

本手法により，人工肺の一部分をモデル化した解析結果ではあるが，実際の人工肺のガス移動量と比較しても妥当なガス移動量の解析値が得られ，酸素および炭酸ガス移動量推定の可能性が示唆された．

補助人工心臓駆動時のダイアフラムへの負荷の軽減

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高野久輝[1]　北村惣一郎[1]　妙中義之[1]
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Reduction of overload to the diaphragm of driving ventricular assist device

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[1]Research Institute, National Cardiovascular Center, [2]Japan Association for the Advancement of Medical Equipment

1. 緒言

現在臨床で使用されているダイアフラム型補助人工心臓において，ポンプの駆動状態を認識する手段として，駆動空気圧波形を用いることが多い．ところが，完全充満，完全駆出サインである駆動空気圧波形上のピークの発生時にはダイアフラムには過剰な負荷が生じていると考えられる．ダイアフラムの耐久性を向上させるためには，この負荷がかかる状態を回避する駆動制御を行なうことが望ましい．そこで，今回は超音波センサを用いてダイアフラム位置のモニタリングを試み，ポンプ運転駆動への適用の可能性についての検討を行った．

2. 方法

ポンプ血液室外側に送信，受信を行なう２つの超音波センサを設置し，送信側センサにより発せられた超音波がダイアフラムによって反射され受信側センサによって受けとられるまでの伝播時間と作動流体の伝播速度（血液・水ともに 1540 m/s）の積により，超音波の経路を算出した．さらに，超音波センサ設置位置と超音波の経路の幾何学的な関係より，ダイアフラムの位置（血液室ハウジングからの距離）を算出した．ダイアフラムの位置計測は，モック実験および慢性動物実験で使用中の補助人工心臓を対象とした．モック実験では，ダイアフラムに過負荷が作用する状態を，空気室側と血液室側で計測を行う圧力の波形より求め，超音波センサにより求められたダイアフラムの位置との関係を求めた．動物実験では，左心バイパスを施行した慢性動物実験中の血液ポンプに超音波センサを設置し，ダイアフラムの位置のモニタリングを行なった．

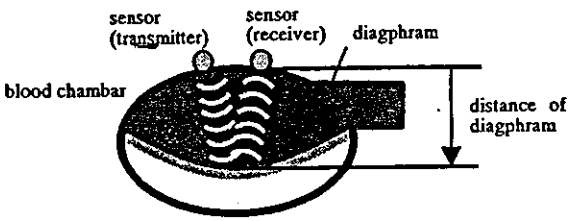

Fig. 1 Measurement method

3. 結果および考察

超音波センサで得られた伝播時間の変化からダイアフラム位置を算出した．超音波センサが示すダイアフラムの位置（血液室ハウジングからの距離）は，静的条件で完全充満，完全駆出はそれぞれ，46 mm，0 mm であった．また，空気室および血液室の圧波形から求められる過負荷状態との比較において，動的条件下でその状態を時間遅れなく認識することが可能であった．

動物実験中の血行動態と超音波センサによるダイアフラムの位置を示す．作動流体が血液の場合においても，超音波センサにより空気圧駆動型補助人工心臓内ダイアフラムの位置の同定を行なうことが可能であった．

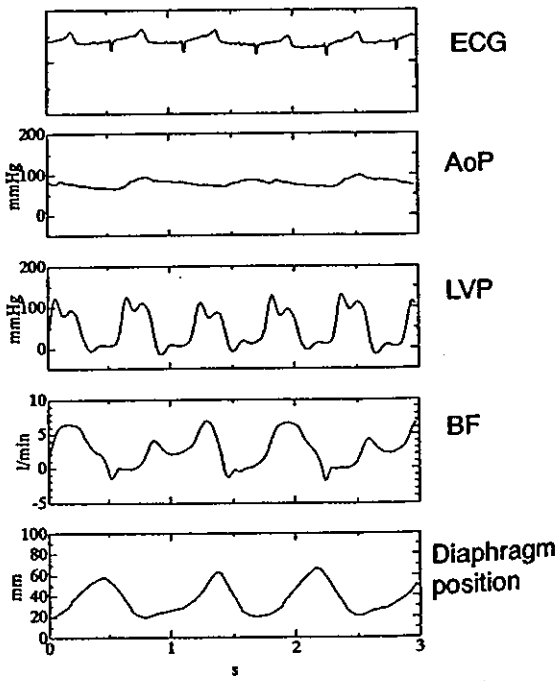

Fig. 2 Monitoring waveforms in animal experiment

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Current status of the National Cardiovascular Center totally implantable artificial heart system

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Abstract: We have been developing an electrohydraulic total artificial heart (EHTAH) system. The system consists of diaphragm-type blood pumps, an electrohydraulic energy converter, an internal control unit, a transcutaneous energy transfer (TET) system, a transcutaneous optical telemetry (TOT) system, and an internal battery. The energy converter reciprocates and delivers hydraulic silicone oil to the alternate blood pumps. The displacement volume and the weight of the system are 872 ml and 2492 g, respectively. The maximum flow rate was 12 L/min and the maximum efficiency was 15.4 %. The system performance was examined in a series of in vivo experiments. The system was successfully implanted in 16 calves in the range of 60 kg or more. Four of the 16 calves survived for more than 1 month approximately. One of them lived for 70 days. The system was basically driven by the TET system, and was driven by the internal battery for 40 minutes everyday. The internal battery was fully charged within 3 hours after usage. DC-DC transmission efficiency of around 80 % was maintained during operation with the TET system. These results indicate that EHTAH has the potential to be a totally implantable system.

Keywords: Total artificial heart (TAH), Electrohydrauric TAH (EHTAH), Energy converter, Transcutaneous energy transfer (TET) system, Transcutaneous optical information transfer (TOT) system

1. Introduction

Several types of totally implantable artificial hearts are being developed at various institutes [1]-[4]. We started the development of a totally implantable electrohydraulic total artificial heart (EHTAH) system in 1987[5]-[14]. The totally implantable EHTAH system has been developed and evaluated by in vitro study and long-term in vivo animal experiments. This paper describes the present status of our research development and the results of evaluation of the EHTAH system.

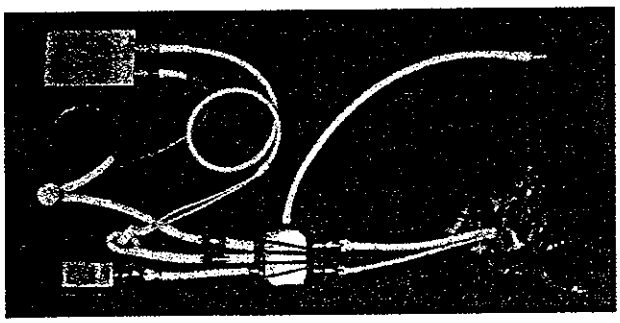

Fig.1 System configuration of EHTAH system

2. Material and Methods

2.1 System configuration

The system consists of diaphragm blood pumps, a electrohydraulic energy converter with a regenerative oil pump, an internal controller, a transcutaneous energy transfer (TET) system, a transcutaneous optical telemetry (TOT) system, internal battery and an external controller. System configuration of EHTAH system is shown in Fig.1.

2.2 Blood pumps

The EHTAH system uses polyurethane diaphragm-type ellipsoidal blood pumps. The blood pumps consist of a blood chamber, an oil chamber and a diaphragm. The total volume of the left and right pumps is 390 ml. Dynamic stroke volume of each pump is 75 to 80 ml and static volume is 90 ml. Housings of the blood pumps are formed by a vacuum injection molding method and made of polyurethane resin (CR330, Vantico K.K., Hyogo, Japan) and polyurethane elastomer (Miractran E980, Nippon Miractran Co., Ltd., Kanagawa, Japan). Mechanical heart valves (Hall Valve (Aortic), 25[mm]

PR0002/04/0000-0436 ¥400

(inlet), 23[mm] (outlet), Medtronic Japan Co., Ltd., Kawasaki, Japan) are set at the inlet and outlet ports of both pumps, respectively [15]-[16]. A composite atrial cuff made of antithrombogenic polyurethane (TM3, Toyobo, Shiga, Japan) reinforced velour texture and an aortic and a pulmonary artery graft made of a woven dacron graft (Cooley low-porosity, 24[mm], Meadox Medicals, NJ, USA).

2.3 Energy converter

The energy converter consists of a brushless DC motor (SPK0513-16A, Shinmeiwa Kogyo, Co., Kanagawa, Japan) and a regenerative oil pump. A pair of oil ports for the energy converter is connected to the left and right blood pumps. Silicone oil (SH200、kinematic viscosity: 1.5 cSt, specific gravity: 0.853, Toray Silicone Co., Ltd., Tokyo, Japan) fills the oil chambers of blood pumps. The left and right blood pumps are alternately driven by the bidirectional rotation of a disk impeller in the energy converter. The thickness and weight of the energy converter are 52.8 mm and 600 g, respectively.

2.4 Pumping unit

The pumping unit is composed of diaphragm type blood pumps and an electrohydraulic energy converter. In the previous system, the energy converter was designed to be placed outside the pericardial space using oil conduits [17]-[18]. In the new system, the blood pumps are directly combined with the energy converter without the need for oil conduits. The weight and the displacement volume of the pumping unit are 1181 g and 470 mL respectively.

2.5 Internal controller

The internal controller consists of 4 parts; the driver circuit, the CPU circuit, the TET circuit and the TOT circuit. The 16-bit microprocessor manages all internal components and communicates with an external computer through the TOT system. These electrical circuits are packed into a titanium case. The weight and the displacement volume of the internal controller are 974 g and 252 mL respectively.

2.6 Internal Battery

The internal battery consists of seven series lithium-ion rechargeable batteries [19]. Seven cells with terminal voltage of 3.5 volts and 0.8 mAh of storage capacity each are packed into a titanium case to yield 24 volts of electric power. The internal battery can drive the system for more than 70 min and can be recharged more than 600 times. The weight and the displacement volume of the internal battery are 332 g and 150 mL respectively.

2.7 TET system

An external coupling method is being developed for the TET system [20]-[21]. The internal coil (external major axis: 55 mm; external minor axis: 42 mm; internal major axis 39 mm; internal minor axis 26 mm) is implanted in such a manner that a half portion of the annular coil is extruded from the body surface to make an arch and is wrapped by a skin flap to be completely concealed. A semicircular ferrite core (external diameter: 38 mm; internal diameter 22 mm; thickness: 14 mm) , wound by an external coil, is inserted into the arch shaped aperture of the internal coil and coupled with another coil to make a ring shaped core. The coupling method, using semicircular ferrite cores to make a ring shape, prevents the external coil from falling off or coming loose. DC-DC energy transmission efficiency and maximum power transmission are 86 % and 60 W, respectively.

2.8 TOT system

Transcutaneous optical coupler (diameter: 37 mm; thickness: 11 mm), consisting of an infrared laser diode and phototransistors, is used in the TOT system [22]. Internal and external optical couplers are placed face to face to transmit information across the skin. The transmission rate is as high as 9,600 bps. The maximum permissible eccentric deviation is 11 mm.

2.9 In vitro evaluation of the EHTAH pumping unit

Pump performance of the EHTAH system was examined in a mock circulation. The EHTAH system was driven by an afterload of 100 mm Hg for the left pump, an afterload of 20 mm Hg for the right pump, and a preload 10 mm Hg for both pumps. Systolic ratio was fixed at 50 % and rotation speeds of the oil pump impeller were regulated to maintain the full-fill and full-eject condition. The efficiency of the pumping unit was calculated by input power and output work of EHTAH obtained by multiplying mean head and cardiac output. The input power into the EHTAH was measured by a power meter. Head was calculated by subtracting preload from afterload, and cardiac output was determined by measuring the amount of water overflow from the overflow tanks for a constant period.

2.10 In vivo evaluation of the EHTAH system

The EHTAH systems were implanted in 16 Holstein calves weighing from 63-87 kg to examine the performance through in vivo experiments. Anatomic compatibility, pumping function in vivo, and heat generation level on each part of the system were evaluated. The pumping unit was implanted in the pericardial space and the internal controller, the internal battery, the TET system and the TOT system were placed in the subcutaneous pocket in the right thoracic region. An interatrial shunt (IAS) was used in the EHTAH system to compensate for the left-right output imbalance [23]-[24]. The IAS was formed by punching 5 mm diameter hole on orifice at the site of the fossa ovalis in the native atrial seprum.

3. Result

3.1 In vitro evaluation of the EHTAH pumping unit

The EHTAH system was tested in a mock circulation. Fig.2 shows the flow rate plot of the system. The flow rate of the left pump increase up to 150 bpm linearly. The maximum flow rate is 12 L/min at 150 bpm. Fig.3 shows the efficiency plot of the system. The efficiency of the system at 5 L/min of a cardiac output is 15.1 % and the maximum efficiency is 15.4 % at 50 bpm.

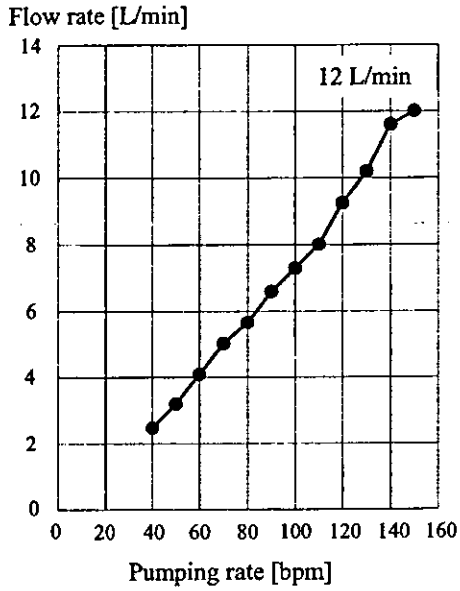

Fig.2 Flow rate plot of the system

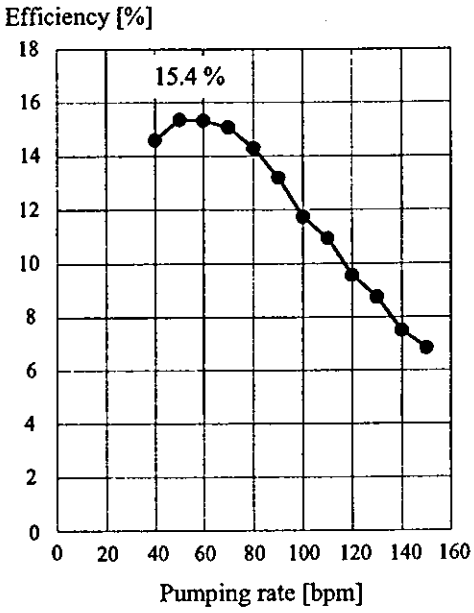

Fig.3 Efficiency plot of the system

3.2 In vivo evaluation of the EHTAH system

The pumping units were implanted easily in the pericardial space of the calves and anatomically fitted well. The internal controller, the internal battery, the TET system and the TOT system were placed in the subcutaneous pocket in the right thoracic region successfully. Four of 16 calves survived for more than about a month (Table.1). Major causes of termination were respiratory failure and device failure.

Table.1 Summary of EHTAH animal implantation

No.	Year /month	Body weight [Kg]	Survival time [days]	Cause of death
1	2003/05	63	6	Respiratory failure
2	2003/07	82	14	Thromboembolism
3	2003/07	70	70	Infection
4	2003/07	79	1	Air embolism
5	2003/09	82	4	Diaphragm breakdown
6	2003/09	79	<1	Left outflow valve fail-away
7	2003/10	69	27	Respiratory failure
8	2003/11	74	6	Respiratory failure
9	2003/12	72	5	Respiratory failure
10	2004/01	70	30	Respiratory failure
11	2004/01	76	0	System failure
12	2004/02	77	6	Convulsion
13	2004/02	86	2	Hemorriage
14	2004/03	77	31	Infection
15	2004/04	71	20	System failure
16	2004/05	87	11	Pneumonia

Fig.4 The longest surviving calf with the EHTAH system

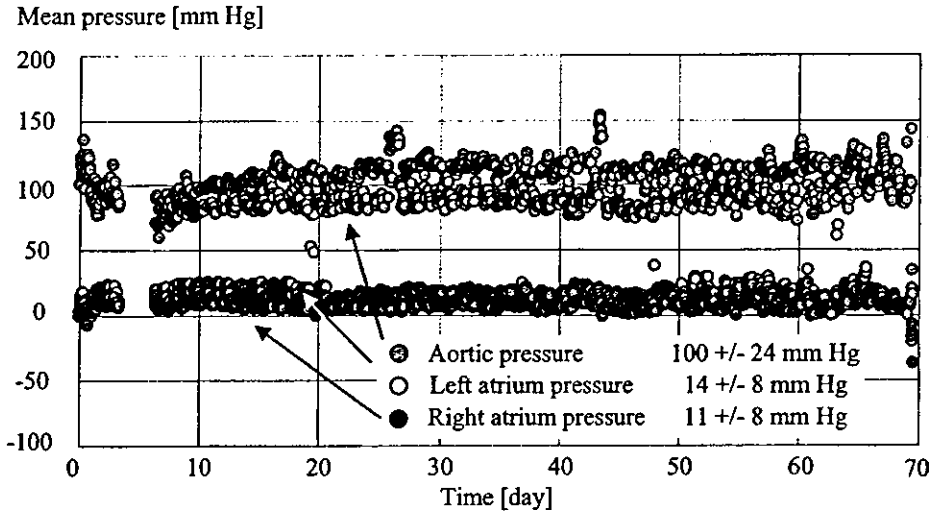

Fig.5 Changes in Aop, LAP, RAP

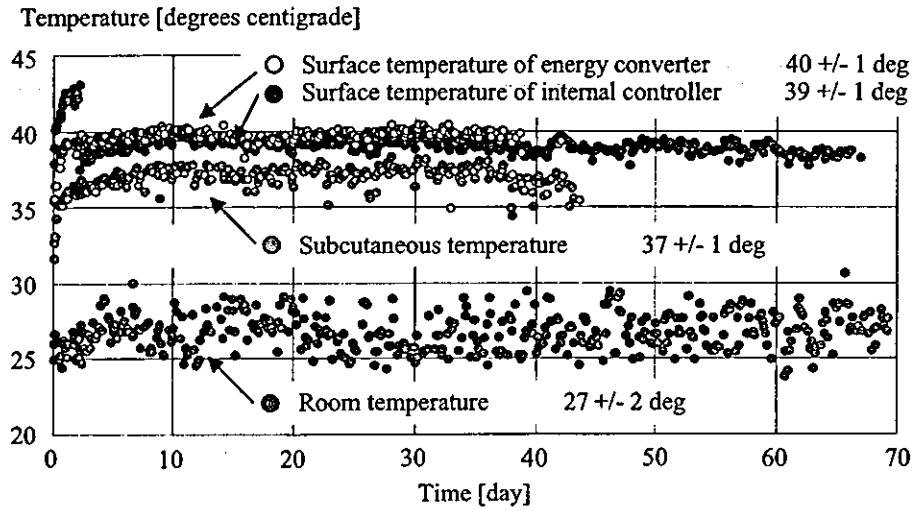

Fig.6 Changes in temperature

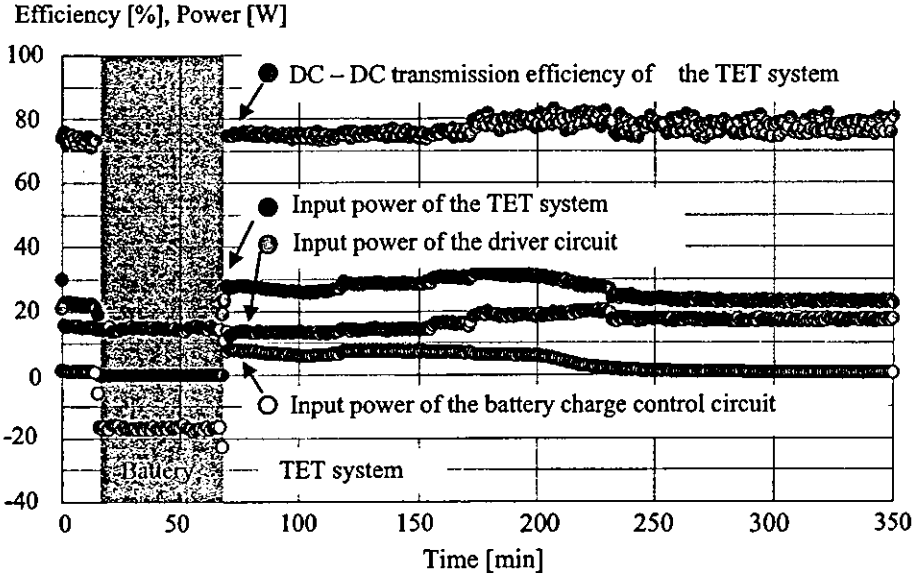

Fig.7 Changes in efficiency and input power

The longest survivor lasted for 70 days and remained in good general condition until termination due to infection (Fig.4). In the longest-surviving animal, the pumping unit was driven at 120 bpm throughout the experimental period. The average values of mean right atrial pressure, mean left atrial pressure and mean arterial pressure were maintained at 11 ± 8 mm Hg, 14 ± 8 mm Hg, and 100 ± 24 mm Hg, respectively (Fig.5). The cardiac output was estimated to be about 6-8 l/min. The temperature on the surface of the energy converter and the internal controller were 40 ± 1 deg and 39 ± 1 deg, respectively (Fig.6).

The system was basically driven with the TET system, and the internal battery for 40 minutes everyday. The EHTAH systems were controlled by an external controller through the TOT system.

Fig.7 shows the example of changes in efficiency and input power of the system. The system was driven with battery for nearly 60 minutes. The internal battery was fully charged about 3 hours later. The efficiency and the input power of the TET system were maintained at nearly 80 % and 23 W during operation with the TET system.

4. Discussion

In the present study, the pumping unit demonstrated a sufficient in vivo output of 6-8 L/min under a fixed driving condition throughout most of the experimental period. The EHTAH system stabilized animal's circulation for as long as 70 days. The current EHTAH system with 6-8 L/min in vivo output provided animals an acceptable quality of life in terms of moderate exercise ability. However, control methods of cardiac output are required to increase the pumping performance up to 12 L/min in vitro maximum output. A fill to empty control method using driving pressure or ultrasound transducer is being developed and a physiological control method using mixed venous oxygen saturation sensor signal is being developed [25]-[26] for this purpose.

In the longest surviving animal the efficiency and the input power of the TET system were maintained at nearly 80 % and 23 W during operation with the TET system, which acceptable in terms of energy consumption.

The device surface temperatures always remained around 39-40 degrees centigrade. It seemed permissible in chronic implantation given that tissue necrosis did not occur. In the EHTAH system, heater electric components, such as FET, were located on the energy converter. The heat generation by the energy converter and FET was efficiently dissipated into the blood through the driving fluid and across the diaphragms of the blood pump. As a result, temperature rise was controlled.

Chronic studies of TET system showed a stable power supply for as long as 70 days. The internal battery had an ability to supply around 20W of power to the system for approximately 40 minutes everyday. Initially wire breakdown of the internal coil in the TET system occurred. Strength of the internal coil was improved by using spiral wire and reinforcing material.

The TOT system demonstrated good transmission performance with a speed of 9600 bps through the skin. Initially low transmission performance with communication errors occurred. Transmission performance was improved by eliminating electromagnetic noise.

5. Conclusion

The totally implantable EHTAH system has been developed. The system has been downsized as small as 2492 g of weight. The Pump performance of the EHTAH system was examined within in vitro experimentation. The maximum cardiac output and the efficiency of the pumping unit were improved to 12 L/min and 15.4 %, respectively. The durability of the EHTAH system was confirmed within in vivo animal experiments. The system was successfully implanted in 16 calves of more than 60 kg range. Four of 16 calves survived for more than about 1 month. The longest surviving calf lived for 70 days and remained in good general condition until termination. The feasibility of the TET and TOT systems within human patients was confirmed within in vivo animal experiments and demonstrated long-term working performance. These findings indicate that the EHTAH has the potential to be a totally implantable cardiac replacement for human hearts.

6. Acknowledgment

This work was supported financially, in part, by the Health and Labor Science Research Grants for Translational-research and for Cardiovascular Diseases (13C-3) from the Ministry of Health, Labour and Welfare of Japan, a Grant-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (No.14370369, No.14658300), and The New Energy and Industrial Technology Development Organization (NEDO).

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ADDITIONAL REGENERATION THERAPY TO SEVERE FAILING HEART SUPPORTED WITH VAD FOR BRIDGE TO RECOVERY

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Aim: Improvement of myocardial contractility during ventricular assist device (VAD) support is important to increase the possibility of bridging to recovery. In the last few years cardiac regeneration therapy was attempted for recovering heart failure. However it is not clear whether such a therapy is effective to severe failing heart supported with VAD. We examined two types of regeneration therapy: one is gene therapy of angiogenesis factor to acute myocardial infarction (AMI) and another is cell transplantation to cardiomyopathy in goats with VAD support.
Methods: AMI was provoked in six adult goats weighing 57.4+/-1.5 kg by ligation of the left anterior descending coronary artery, and installed pulsatile bi-VADs. Three of them were infused with a gene of an angiogenesis factor (Hepatocyte Growth Factor c-DNA-plasmid), and the rest was not infused (control group). Heart failure was provoked in two adult goats weighing 55.7+/-3.2 kg by infusing adriamycin chronically, installed pulsatile left VAD and infused bone marrow-derived stem cells (BMSC) which were cultured *in vitro*.
Results: The goats which were infused with HGF recovered better cardiac function and were more suppressed LV dilatation than control group.
The number of BMSC was increased to 10^9, which was necessary to increase cardiac contractility in cell transplantation.
Conclusion: Additional regeneration therapy to severe failing heart supported VAD may contribute to recover cardiac function and increase the possibility of bridging to recovery.

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DEVELOPMENT OF A COMPLETELY DECELLULARIZED AND PRE-CELLULARIZED FUNCTIONAL PORCINE AORTIC VALVE

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Aim: The final goal of this study is to develop a tissue-engineered functional aortic heart valve. Xenogeneic porcine aortic valves were employed as tissue scaffolds. In this study, a novel technology to completely decellularize thick aortic tissues, and also a pulsatile bioreactor for pre-seeding recipient cells were developed, respectively.
Methods: An innovative decellularization device can perform microwave irradiation under pulsatile circulation, which is expected to enhance immersion of the detergent into tissues by vibration effect and pressure effect. On the other hand, a novel pulsatile bioreactor, which can simulate physiologic pressure and flow waveforms, was developed for pre-seeding recipient cells. Porcine and human endothelial cells (ECs) were, respectively, seeded and cultivated under aortic pressure of 110/70 mmHg and mean aortic flow of 5 l/min for 1 hour–48 hours.
Results: The novel decellularization treatment successfully enabled complete removal of cell components from both cusps and aortic wall. Moreover, the time required was only for 48 hours, On the contrary, 80% of residual cells were observed in the valves decellularized by static immersion even for 1 month. Mechanical tensile tests and micro-structural analysis demonstrated that the novel treatment induced no tissue damages. Besides, cell cultivation seeded on valves under pulsatile environments significantly enhanced cell proliferations, and the entire valve surfaces were covered with ECs in 48 hours. Moreover, the ECs were highly stimulated and oriented as observed *in vivo*.
Conclusion: A hybrid tissue-engineered aortic heart valve was successfully developed via innovative dynamic bioreactor technologies.

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TISSUE ENGINEERING OF HEART VALVES: ELIMINATION OF THE ALPHA-GAL-EPITOPE IN DECELLULARIZED PORCINE PULMONARY CONDUITS

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Aim: The porcine endothelial cell specific alpha-Gal epitope is known to be responsible for hyperacute rejection in xeno-transplantation. We recently described various methods of decellularization procedures and their efficacy. We have also reported the early failure of the first commercially available tissue engineered decellularized porcine graft (Synergraft®, Cryolife Inc.,USA). The objective of this study was to compare the decellularization results of porcine conduits after treatment with non-ionic, non-enzymatic detergents and nucleases and the Synergraft® with respect to removal of cells and elimination of the alpha-Gal.
Method: Porcine pulmonary conduits were decellularized using Triton-X 100 Na-deoxycholate and Igepal 630®. After further treatment with ribonuclease, these specimens and specimens of the Synergraft® grafts were processed for scanning-electron-microscopy (SEM) and for laser-scanning-microscopy (LSM). Cryostat sections were stained for von Willebrand factor (vWf), TO-PRO®3 (nuclear staining), collagen type I & III, elastin and alpha-Gal (BS isolectin B4).
Results: SEM revealed complete removal of endothelial cells on the surface of all specimens. LSM showed complete cell removal and elimination of the alpha-Gal only in the conduit treated with Triton-X 100 Na-deoxycholate and Igepal 630® and ribonuclease. In contrast in the Synergraft® graft walls alpha-Gal was present due to incomplete decellularization.
Conclusion: The decellularization procedure developed by us lead to complete removal of cells and elimination of the alpha-Gal. Elimination of the alpha-Gal epitope is crucial in tissue engineering using the decellularized porcine matrix as scaffold. Remaining alpha-Gal may induce severe inflammatory response in humans and may lead to rapid graft failure.

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GENE THERAPY OF ADVANCED CORONARY ARTERY DISEASE WITH phVEGF165 IN "NO OPTION PATIENTS"

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Aim: We initiated clinical study to determine safety and activity of gene encoding vascular endothelial growth factor (VEGF)165 administered directly into the myocardium as the only treatment. Our trials with the plasmid encoding VEGF165 show that intramyocardial application is safe and patients have benefited with the therapy.
Methods: VEGF gene transfer was performed in 16 patients (14 male, 2 female, ages from 51 to 73 years old). 400 µg of the plasmid encoding VEGF165 was injected into the ischemic, viable myocardium that could not be revascularized in any other way. There was no possibility of CABG because of surgical limitations and the application of genes encoding VEGF165 was the only solution. Patients with ejection fraction (%EF) < 30%, fertile females, acute myocardial infarction (MI), retinopathy and neoplasms were excluded from the study. %EF, myocardial perfusion, ECHO, angiogram, ventriculography, quality of life and nitroglycerin consumption were evaluated pre- and post-operatively.
Results: Most of the patients tolerated surgery uneventfully. One death occurred. In two cases the evidence of myocardial infarction and in one case recurrent unstable angina were noted. Most of the patients were angina free at 6 months after surgery. %EF improvement hasn't been noticed so far. Patients reported much better quality of life and reduction of nitroglycerin use. A reduction in ischemic defects on SPECT scans were observed, particularly on rest SPECT scans. Some of the patients' agiographies revealed improved collateral filling.
Conclusions: Direct myocardial administration of genes encoding VEGF165 can be an effective method of treatment in patients with chronic and advanced coronary artery disease especially in "no option cases".

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Total Artificial Heart

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DEVELOPMENT OF THE NATIONAL CARDIOVASCULAR CENTER ELECTRO-HYDRAULIC TOTALLY IMPLANTABLE ARTIFICIAL HEART

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Aim: The purpose of this work is to develop an electrohydraulic total artificial heart (EHTAH) system.
Methods: The system consists of polyurethane-made diaphragm-type blood pumps, an electrohydraulic energy converter, an internal control unit, a transcutaneous energy transfer (TET) system, a transcutaneous optical telemetry (TOT) system, and an internal battery. The energy converter reciprocates and delivers hydraulic silicone oil to the alternate blood pumps. The displacement volume and the weight of the system were 872 ml and 2492 g, respectively. The maximum flow rate was 12 l/min and the maximum efficiency was 15.4 %. The system performance was examined in a series of *in vivo* experiments.
Results: The system was successfully implanted in 15 calves weighing 63 to 86 kg without any fitting problems. Three of 15 calves survived for about 1 month. One of these lived for 70 days in good general condition. The system was basically driven with the TET system, and was driven with the internal battery for 40 minutes everyday. The internal battery was fully charged within 3 hours later. DC-DC transmission efficiency of around 80 % was maintained during operation with the TET system. Driving parameters were transmitted through the skin with the TOT system at 9600 bps without any transmitting error.
Conclusion: The durability of the EHTAH system was confirmed *in vivo* animal experiments. These results indicate that developed EHTAH has the potential to be a totally implantable system.

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THROMBUS FORMATION AND RENAL EMBOLISATION ARE DEPENDENT ON PLACEMENT OF ATRIAL CANNULA IN A SHEEP MODEL OF ATRIO-AORTAL LEFT VENTRICULAR ASSIST DEVICE

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Aim: We aimed to analyse the relation of renal embolisation to the location of thrombus formation of a left ventricular assist device in a sheep model.
Methods: In five sheep the paracorporeal MEDOS® left ventricular assist device pumped for seven days atrio-aortal. Creatinine was measured twice a day and the sheep were post-mortem analysed for thrombus formation and pathologic changes.
Results: Major thrombus formation occurred in two sheep at the atrial cannula related to wall contact and renal infarction and slight increases in creatinine (up to 2.3 mg/dL at day one) were observed. In the three other sheep major thrombus formation and subsequent renal embolisation could be omitted by careful placement of the cannula. In these sheep no relevant renal infarction was seen and creatinine remained normal within seven days.
Conclusion: Renal embolisation is directly connected with atrial thrombus formation and not pump housing. Thrombus formation can be prevented when avoiding cannula contact to atrial wall.

P103

DESIGN OF TRANSCUTANEOUS INFORMATION TRANSMISSION SYSTEM FOR IMPROVEMENT OF PRODUCTIVITY

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Aim: A transcutaneous information transmission system is essential for an implantable artificial heart because monitor of the artificial heart condition is required in order to secure patient's safety. We have improved a transcutaneous bi-directional information transmission system in order to produce automatically by means of CAD/CAM technology for practical usage.
Methods: The transcutaneous information transmission system mainly consists of an ASK (Amplitude Shift Keying) circuit with carrier electromagnetic wave frequencies of 4 MHz and 10 MHz, and corresponding demodulation circuit, loop coil antennas for transmission and receiving, and an one-chip microcomputer (Microchip technology co., PIC16F84, USA) for alarm system to indicate misalignment of antennas outside transmittable range to ensure error free data transmission. The electric circuit and board layout were designed by means of circuit design CAD/CAM software, also loop coil antennas were formed using printed wiring created on the circuit board like a radio frequency identification technology. Size of the transcutaneous information transmission system board was 42 mm of diameter and thickness of 9 mm.
Results: The transcutaneous information transmission system was evaluated in *in vitro* and *in vivo* experiments. The *in vitro* experiments showed that the transcutaneous information transmission system could transmit data through a tissue within an area of axial direction of 5 cm and a radial direction of 4 cm under data transmission speed of 56kbps. An animal experiment showed that the transcutaneous information transmission system worn on a goat implanted an undulation pump LVAD had stable operation and excellent fitting and biocompatibility during over 2 weeks.
Conclusion: Above results showed that the developed transcutaneous information transmission system is promising for practical usage due to its performance and improvement of productivity.

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TRANSCUTANEOUS ENERGY SYSTEM FOR IMPLANTABLE ARTIFICIAL HEARTS

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Aim: An abdominal, transcutaneous energy system is to be developed. The system will adapt the transmitted energy to the actual requirement of the implant.
Methods: For transmission, two flexible coils are used. One of them is implanted underneath the skin, the other is embedded in an extra-corporal belt. The implanted electronics consist of a charger and a battery with a capacity of 0.7 Ah, voltage 24V and a total weight of 306 g. A user-programmable processor and a controller for brushless DC motors are included. The implantable coil is a flexible ring made of braided copper with a diameter of 150 mm, a thickness of 8 mm and a weight of 120 g. Infrared sensors are embedded for transcutaneous data transfer. The coil is placed at a depth of up to 20 mm underneath the skin. The extra-corporal coil is placed vis-a-vis, a display indicates the quality of transmission.
Results: During the first *in vitro* test, the system was able to transmit up to approx. 40 Watt, where the distance of the coils was 30 mm. During the experiment, no significant warming between the coils was measured.
Conclusion(s): The transcutaneous energy system is able to transmit energy in an allowable frequency range for medical devices. The transmitted energy is automatically adapted to the requirement of the implant as well as to the load of the implanted battery. In future, the warming of single components, especially the condensers, will be balanced through an optimised distribution of the parts.

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Development of artificial internal organs at National Cardiovascular Center

Akihiko Homma*, Member, Yoshiyuki Taenaka*, Non-member, Eisuke Tatsumi*, Non-member, Yoshiaki Takewa*, Non-member, Tadayuki Kamimura*, Non-member, Toshihide Mizuno*, Non-member, Kyoko Shioya**, Non-member, Hwan Sung Lee*, Non-member, Tomonori Tsukiya*, Non-member, Yukihide Kakuta*, Non-member, Nobumasa Katagiri*, Non-member, Hisateru Takano*, Non-member, Soichiro Kitamura*, Non-member, Kohji Koshiji***, Non-member, Kenji Shiba****, Member, Hideki Wakui**, Non-member, Katsuya Tsuchimoto**, Non-member, Hiroaki Fukuda**, Non-member, Hideaki Yamaguchi**, Non-member, Kiniji Tsukahara**, Non-member,

We have been developing an electrohydraulic total artificial heart (EHTAH) system. The system consists of diaphragm-type blood pumps, an electrohydraulic energy converter, an internal control unit, a transcutaneous energy transfer (TET) system, a transcutaneous optical telemetry (TOT) system, and an internal battery. The energy converter reciprocates and delivers hydraulic silicone oil to the alternate blood pumps. The displacement volume and the weight of the system are 872 ml and 2492 g, respectively. The maximum flow rate was 12 L/min and the maximum efficiency was 15.4 %. The system performance was examined in a series of in vivo experiments. The system was successfully implanted in 16 calves in the range of 60 kg or more. Four of the 16 calves survived for more than 1 month approximately. One of them lived for 70 days. The system was basically driven by the TET system, and was driven by the internal battery for 40 minutes everyday. The internal battery was fully charged within 3 hours after usage. DC-DC transmission efficiency of around 80 % was maintained during operation with the TET system. These results indicate that EHTAH has the potential to be a totally implantable system.

キーワード：電気油圧駆動式全人工心臓、血液ポンプ、ブラシレスDCモータ、経皮エネルギ伝送システム、経皮光伝送システム
Keywords : Electrohydrauric total artificial heart, Blood pump, Brushless DC motor, Transcutaneous energy transfer (TET) system, Transcutaneous optical information transfer (TOT) system