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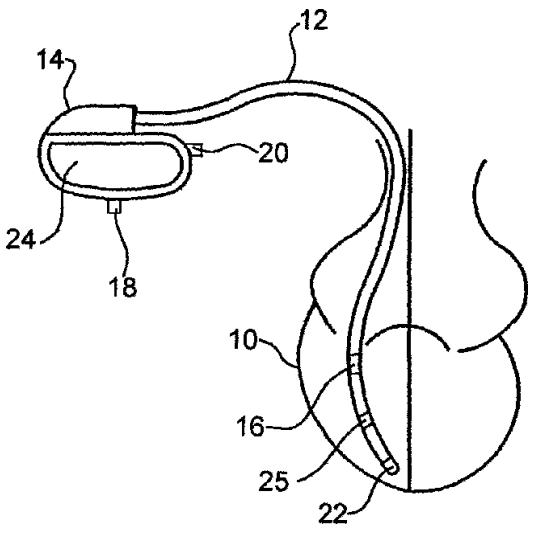
(54)【発明の名称】平均肺動脈圧を決定する方法および装置

(57)【要約】
【課題】正確な心拍間の平均測定値を提供し、臨床の場で容易に確かめられる可能性のある平均肺動脈圧（ＭＰＡＰ）を決定する改良された装置を提供する。
【解決手段】心臓の心室内に位置する圧力センサと心電図（ＥＧＭ）信号などの心臓電気活動を示す信号を用いて、平均肺動脈圧（ＭＰＡＰ）を求める。圧力は、埋め込まれた圧力センサを用いて、右心室および／または左心室内で検知することができる。検知された圧力を使用して、心室収縮期圧（ＶＳＰ）および推定肺動脈拡張期圧（ｅＰＡＤ）を求める。次に、ＶＳＰ、ｅＰＡＤ、および収縮期および拡張期に関連する時間間隔を使用して、肺動脈内に位置するセンサを使用して測定される平均肺動脈圧を精密に近似するＭＰＡＰを得る。



【特許請求の範囲】
【請求項１】
心臓の心室に位置し、それによって圧力を測定する第１センサと、
心電図（ＥＧＭ）信号を測定する第１回路と、
前記第１回路に結合して、前記圧力を示す信号および前記心電図信号を受け取り、そこから平均肺動脈圧（ＭＰＡＰ）を求める処理回路と、
を備えた患者の平均肺動脈圧を決定する装置。
【請求項２】
前記第１回路は、前記患者の心臓脈管構造内に位置する少なくとも１つの電極を備えた請求項１に記載の装置。
【請求項３】
前記第１回路は、前記患者の外部表面上に配置された少なくとも２つの電極を備えた請求項１に記載の装置。
【請求項４】
前記第１回路は、ハウジング内に収容された埋め込み可能デバイス内に位置し、前記第１回路は、前記埋め込み可能デバイスの前記ハウジングに結合する少なくとも１つの電極を備えた請求項１に記載の装置。
【請求項５】
前記第１センサは、前記心臓の第１心室内に位置しており、
前記装置は、前記心臓のもう一方の心室内に位置する第２センサを含んでおり、前記処理回路は、前記第１および第２センサの両方によって測定された圧力から前記平均肺動脈圧（ＭＰＡＰ）を推定する手段を備えた請求項１に記載の装置。
【請求項６】
前記処理回路は、埋め込み可能デバイス内に位置する請求項１に記載の装置。
【請求項７】
前記処理回路は、前記患者の外部のデバイス内に位置しており、前記装置は、前記測定された圧力の示度および前記心電図（ＥＧＭ）信号を前記処理回路に転送する通信回路をさらに備えた請求項１に記載の装置。
【請求項８】
前記処理回路は第１部分および第２部分を具備しており、前記第１部分は埋め込み可能デバイス内に位置しており、前記第２部分は、前記患者の外部のデバイス内に位置しており、前記装置は、データ信号を前記第１および第２部分の間で転送する通信回路をさらに備えた請求項１に記載の装置。
【請求項９】
前記処理回路と結合し、前記患者に治療を供給する治療送出回路をさらに備えた請求項１に記載の装置。
【請求項１０】
前記処理回路は、前記推定平均肺動脈圧（ＭＰＡＰ）に基づいて前記治療送出回路を制御する手段を備えた請求項１に記載の装置。
【請求項１１】
前記治療送出回路は、心臓再同期化治療を前記患者に供給する回路を備えた請求項１０に記載の装置。
【請求項１２】
前記治療送出回路は、生物学的に活性な薬剤を前記患者に送出する薬デリバリデバイスを備えた請求項１０に記載の装置。
【請求項１３】
（イ）心臓の心室内の圧力を検知するステップと、
（ロ）前記心臓の心電図（ＥＧＭ）信号を検知するステップと、
（ハ）平均肺動脈圧（ＭＰＡＰ）を導出するために、前記検知された圧力と前記心電図（ＥＧＭ）信号を用いるステップと、

を含む平均肺動脈圧（ＭＰＡＰ）を決定する方法。
【請求項１４】
ステップ（ハ）は、収縮期に前記心臓が費やす時間を示す収縮期時間間隔および拡張期に費やす時間を示す拡張期時間間隔を導出することを含む請求項１３に記載の方法。
【請求項１５】
ステップ（ハ）は、前記心電図（ＥＧＭ）信号のＲ波の始まりから、所定期間の間の検知圧力の変化が最大になる時点まで測定することによって、前記収縮期時間間隔を導出することを含む請求項１４に記載の方法。
【請求項１６】
ステップ（ハ）は、心室収縮期圧（ＶＳＰ）を求めるために、前記心室内からの前記検知された圧力を利用することをさらに含んでおり、前記心室収縮期圧（ＶＳＰ）は、前記心臓の心周期中の任意の時点に測定されたほぼ最大圧である請求項１５に記載の方法。
【請求項１７】
ステップ（ハ）は、推定肺動脈拡張期圧（ｅＰＡＤ）を求めるために、前記検知された圧力を利用することをさらに含んでおり、前記推定肺動脈拡張期圧（ｅＰＡＤ）は、所定期間の間の前記検知された圧力の変化が最大である、前記心周期中の時点で測定された圧力である請求項１６に記載の方法。
【請求項１８】
（ニ）前記拡張期時間間隔に前記推定肺動脈拡張期圧（ｅＰＡＤ）を乗ずること、
ホ）前記収縮期時間間隔に前記心室収縮期圧（ＶＳＰ）を乗ずること、および
へ）前記平均肺動脈圧（ＭＰＡＰ）を得るために、ステップ（ニ）および（ホ）で得られた値を加算すること、
をさらに含む請求項１７に記載の方法。
【請求項１９】
前記平均肺動脈圧（ＭＰＡＰ）に基づいて治療を送出することをさらに含む請求項１３に記載の方法。
【請求項２０】
生物学的に活性な薬剤を送出することをさらに含む請求項１９に記載の方法。
【請求項２１】
心臓再同期化治療を送出することをさらに含む請求項１９に記載の方法。
【請求項２２】
前記平均肺動脈圧（ＭＰＡＰ）に基づいて前記心臓再同期化治療のタイミングパラメータを修正することをさらに含む請求項２１に記載の方法。
【請求項２３】
心臓の心室内に位置し、圧力を測定する圧力検知手段と、
心電図（ＥＧＭ）信号を検知するＥＧＭ検知手段と、
前記測定された圧力および前記心電図（ＥＧＭ）信号に基づいて平均肺動脈圧（ＭＰＡＰ）を導出する処理手段と、
を備えた患者の平均肺動脈圧（ＭＰＡＰ）を導出する装置。
【請求項２４】
前記ＥＧＭ検知手段は、心臓の腔内に位置し、前記心電図（ＥＧＭ）信号を検知する手段を備えた請求項２３に記載の装置。
【請求項２５】
前記ＥＧＭ検知手段は、前記患者の外部にあり、前記心電図（ＥＧＭ）信号を検知する手段を備えた請求項２３に記載の装置。
【請求項２６】
前記ＥＧＭ検知手段は、前記患者の皮下に位置し、前記心電図（ＥＧＭ）信号を検知する手段を備えた請求項２３に記載の装置。
【請求項２７】
前記処理手段は、前記患者に埋め込まれる手段を備えた請求項２３に記載の装置。

【請求項２８】
前記処理手段は、前記患者の外部にある手段を備えた請求項２３に記載の装置。
【請求項２９】
前記処理手段は、前記患者に埋め込まれる手段と前記患者の外部にある手段を備えた請求項２３に記載の装置。
【請求項３０】
前記平均肺動脈圧（ＭＰＡＰ）に基づいて患者に治療を送出する治療送出手段をさらに備えた請求項２３に記載の装置。
【発明の詳細な説明】
【０００１】
［発明の分野］
本発明は、動脈圧を測定することに関し、より具体的には、歩行モニターを用いて平均動脈圧を決定する装置および方法に関する。
【０００２】
［従来技術の説明］
平均肺動脈圧（ＭＰＡＰ）は、心血管の健康状態の重要な指標である。たとえば、ある種の病気の管理は、平均肺動脈（ＰＡ）圧を用いて求められる肺血管の抵抗力の正確な示度に頼っている。ＭＰＡＰはまた、右心室の一般的な作業負荷の指標として使用され、したがって、心臓病を診断し、監視するのに使用することができる。
【０００３】
過去において、平均ＰＡ圧は、いくつかの方法を用いて求められてきた。その方法の全てが肺動脈内に位置する圧力センサを必要とする。第１の方法によれば、ＰＡ収縮期およびＰＡ拡張期の圧力測定値の両方を使用して、以下の式を用いてＭＰＡＰが求められる。
ＭＰＡＰ＝１／３（収縮期圧）＋２／３（拡張期圧）
この式は、平均心周期において、３分の１の時間が収縮期で費やされ、残りの３分の２の時間が拡張期で費やされるという前提に基づいている。しかし、この前提は、一般に、患者が安静にしている時にあてはまるだけである。運動期間中に、より正確なＭＰＡＰの推定を行なうには、上述の式を変更して、心拍数が１分当たり１００回または１２０回を超える時に、心室は、心周期の約半分の間収縮期にあり、心周期のもう半分の間拡張期にあるという事実を反映するようにしてもよい。しかし、この方法は、安静および運動の両方の期間を反映する正確な総合的なＭＰＡＰ測定値を提供しない。
【０００４】
ＭＰＡＰを測定する別の方法は、信号の脈動性を除去するために、圧力センサが生成した圧力信号をフィルタリングすることを含む。このフィルタリングは、たとえば、デジタルフィルタを用いて行なうことができる。得られる信号の値はＭＰＡＰの正確な近似値である。この方法は、拡張期圧と収縮期圧を用いて、ＭＰＡＰを計算するよりも正確であるが、フィルタリングプロセスが比較的長い時定数を必要とする。したがって、心拍間の測定値を得ることはできない。
【０００５】
さらに別の方法によれば、圧力信号が一心周期の間積分され、次に、得られた結果が、心周期内に含まれていたいくつかの所定時間間隔で除される。これは、正確な心拍ごとの平均圧を提供する。しかし、この方法は、ほとんどの医療の場ではすぐには利用できないデジタル信号処理システムを必要とするという欠点を有する。
【０００６】
したがって、必要とされているものは、正確な心拍間の平均測定値を提供し、臨床の場で容易に確かめられる可能性のあるＭＰＡＰを求める、改良された装置および方法である。好ましくは、かかる装置は、肺動脈内に位置する圧力センサの使用を必要としない。
［発明の概要］
本発明は、肺動脈内に位置するセンサを使用することなく、ＭＰＡＰを求める装置および方法を提供する。ＭＰＡＰ値は、心臓の腔内から得られる圧力測定値および心電図（ＥＧ

M）信号などの心臓電気活動を示す信号を用いて導出される。
【０００７】
本発明によれば、圧力は、埋め込まれた圧力センサを用いて、右心室および／または左心室内で検知することができる。検知圧力を使用して、心周期の間にわたる任意の時点に測定された最大圧である心室収縮期圧（ＶＳＰ）を求めるようにできる。この検知圧力をさらに使用して、所定期間の間の圧力の変化が最大である時点の圧力である、推定肺動脈拡張期圧（ｅＰＡＤ）を導出するようにできる。最後に、ＥＧＭ信号および圧力信号を使用して、心臓が、収縮期と拡張期の両方で費やす時間を求めるようにできる。ＶＳＰに収縮期で費やした時間を乗じ、さらにｅＰＡＤに拡張期で費やした時間を乗じ、次に、２つの値を加算することによって、平均肺動脈圧が正確に近似される。
【０００８】
本発明の一実施形態によれば、本装置は、ペースメーカ、カーディオバータ／ディフィブリレータ、薬デリバリデバイス、または患者に治療を送出する別のタイプのデバイスなどの、埋め込み可能デバイス内に含まれる。導出されるＭＰＡＰ値を利用して、治療デリバリを制御するようにできる。本発明の一態様によれば、心臓再同期化治療が監視され、ＭＰＡＰ値を用いて制御される。別の実施形態において、導出されたＭＰＡＰ値を使用して、生物学的に活性な薬剤の患者へのデリバリを管理するようにしてもよい。
【０００９】
本発明によって実行される処理ステップは、埋め込み可能デバイス内に位置する処理回路によって行なうことができる。別法として、１つまたは複数の処理ステップは、プログラマなど、デバイスの外部の回路によって遂行されてもよい。圧力信号およびＥＧＭ信号は通信回路を介して外部デバイスに転送され、その結果、処理の全て、または処理のある部分は、患者の外部の回路によって終了することができる。
【００１０】
一実施形態によれば、本発明は、患者の平均肺動脈圧を推定するシステムを備える。システムは、心臓の心室に位置し、圧力を測定するセンサと、心電図（ＥＧＭ）信号を測定する回路と、圧力信号およびＥＧＭ信号から平均肺動脈圧（ＭＰＡＰ）を導出する処理回路とを備える。別の実施形態によれば、本発明は、心臓の心室内の圧力を検知すること、心臓の心電図（ＥＧＭ）信号を検知すること、および、ＭＰＡＰを導出するために、検知された圧力とＥＧＭ信号を用いることよって、平均肺動脈圧（ＭＰＡＰ）を求める方法を含む。
【００１１】
本発明の他の範囲および態様は、図面およびそれに伴う説明から当業者には明らかになるであろう。
［実施例］
本発明は、心電図（ＥＧＭ）信号などの心臓電気活動信号と共に、心臓の腔内から得られる圧力測定値を用いてＭＰＡＰを決定する装置および方法を提供する。すなわち、本発明は、肺動脈内に位置する圧力センサの必要性をなくす。
【００１２】
図１は、本発明に関して使用できる埋め込み型医療デバイス（ＩＭＤ）の略図である。このＩＭＤは、患者の心臓の心室内から圧力信号を測定でき、さらに、患者の心電図（ＥＧＭ）を測定できる任意のデバイスであってよい。こうしたデバイスは、Ｍｅｄｔｒｏｎｉｃ社から市販されている「Ｃｈｒｏｎｉｃｌｅ（登録商標）」デバイスなどの血行動態モニターであってよい。「Ｃｈｒｏｎｉｃｌｅ」に含まれる回路は、同一譲受人に譲渡された米国特許第５，５３５，７５２号および第５，５６４，４３４号に記載されており、その全体が、参照によって本明細書に援用される。別法として、デバイスは、ペースメーカまたはカーディオバータ／ディフィブリレータであってよい。本発明を実施するのに使用してよい例示的なペースメーカシステムは、同一譲受人に譲渡された米国特許第５，１５８，０７８号、第５，３１８，５９３号、第５，３１２，４５３号および第５，２２６，４１３号に記載されており、その全体が、参照によって本明細書に援用される。当技術分

野で既知の任意の他のペーシングシステムが、別法において使用するようにされてもよい。付加的にまたは別法において、ＩＭＤは、同一譲受人に譲渡された米国特許第５，１９３，５３５号および第５，３１４，４３０号（その全体が参照によって本明細書に援用される）に記載されるカーディオバータ／ディフィブリレータを備える。埋め込み可能な薬デリバリデバイスなどの他のデバイスもまた、デバイスがＥＧＭおよび心室圧を測定する機能を含む限り、本発明と共に使用するようにされてもよい。

【００１３】

図１に戻ると、ＩＭＤ１４は、皮膚と肋骨の間の皮下に埋め込むことができる。適当であれば、他の埋め込み部位を使用してもよい。一実施形態において、リード線１２は、静脈を通過して心臓１０の右心室に入る。リード線またはカテーテルの遠位端は、心臓の内部に接触する先端電極２２を有してもよい。多極構成では、第２リング電極２５が先端電極２２から間隔を空けて配置されてもよい。これらの電極のそれぞれは、ＩＭＤ１４内に収容されている回路に接続されている。別法として、ＩＭＤの金属格納部すなわち「カン」の一部が電極表面２４を形成する単極モードが使用されてもよい。ＥＧＭ信号は、この表面と先端電極２２などの埋め込み型電極の間で測定される。さらに別の実施形態において、電極１８および２０などの皮下電極アレイ（ＳＥＡ）が、電気的には絶縁されているが、以下で述べられるように、米国特許第５，３３１，９６６号（その全体が参照によって本明細書に援用される）に開示されているような埋め込み可能デバイスのハウジング上に配置されてもよい。

【００１４】

右心房内に位置するリード線および／または冠状静脈洞などの冠状血管内に位置するリード線を含む付加的なリード線（図示せず）をＩＭＤに結合することができる。これらのリード線はさらに、カーディオバージョン／ディフィブリレーション治療を供給する１つまたは複数の高電圧電極を備えることができる。

【００１５】

リード線１２は、圧力センサ１６をさらに備えるように示されている。所望であれば、ＩＭＤ１４に結合される付加的なリード線が、圧力センサを保持するために備わってもよい。圧力センサは右心室内に位置するのが好ましいが、以下で述べられる方法で、左心室内に位置することもできる。圧力センサおよび本発明と共に使用することができる付属回路は、同一譲受人に譲渡された米国特許第５，３５３，７５２号、第５，３５３，８００号、第５，５６４，４３４号、第５，３３０，５０５号および第５，３６８，０４０号に記載されており、その全体が参照によって本明細書に援用される。

【００１６】

図２は、本発明によって使用することができるパルス発生器の例示的な実施形態の機能ブロック図である。なお、パルス発生器の機構は本発明を実施するのに必要でないことが認められるかもしれない。したがって、以下の議論は、例示としてだけ考えられるべきである。

【００１７】

図２に示す例示的装置の主要な要素は、マイクロプロセッサ（μＰ）１００、読み出し専用メモリ（ＲＯＭ）１０２、ランダムアクセスメモリ（ＲＡＭ）１０４、デジタル制御器１０６、入力増幅器回路（ＩＮ）１１０、出力回路（ＯＵＴ）１０８、および遠隔測定／プログラミングユニット（ＴＥＬＥＭ）１２０を含む。

【００１８】

本実施形態において、データ処理機能およびデバイス制御機能は、マイクロプロセッサ１００によって提供される。他のデジタル回路および／またはアナログ回路の実施形態は本発明の範囲内にあることが理解されるであろう。たとえば、Ｂｏｃｅｋ他に発行された米国特許第５，２５１，６２４号、Ｇｉｌｌｉに発行された米国特許第５，２０９，２２９号、Ｌａｎｇｅｒ他に発行された米国特許第４，４０７，２８８号、Ｈａｅｆｎｅｒ他に発行された米国特許第５，６６２，６８８号、Ｏｌｓｏｎ他に発行された米国特許第５，８５５，８９３号、Ｂａｋｅｒ他に発行された米国特許第４，８２１，７２３号、および

／またはＣａｒｒｏｌ他に発行された米国特許第４，９６７，７４７号（以上の全ての特許は、その全体が参照によって本明細書に援用される）は、本発明と共に有効に使用することができる。別法として、または付加的に、処理機構は、以下で述べられる方法で、外部処理回路によって提供することができる。

【００１９】

読み出し専用メモリは、マイクロプロセッサ１００によって実行される主命令セットを含む、ＩＭＤ用のソフトウェアおよび／またはファームウェアを記憶する。これらの命令は、本発明によって、マイクロプロセッサが行なう方法を規定する。これらの命令はまた、デバイスが行なう任意の治療機能および／または監視機能を制御することができる。付加的な記憶部は、ＲＡＭ１０４によって設けられ、ＲＡＭは、一般に、プログラムされるペーシングパラメータなどの可変制御パラメータを記憶する。ランダムアクセスメモリ１０４はまた、ＥＧＭ波形および圧力測定値、ならびにＭＰＡＰ計算中にこれらの測定信号から導出される値を示すデジタル化された信号を記憶することができる。

【００２０】

制御器１０６は、デバイスの基本的な制御およびタイミング機能の全てを行なう。制御器１０６は、少なくとも１つのプログラム可能なタイミングカウンタを備えてよく、このカウンタを使用して、本発明で使用されるＲ－Ｒ間隔などのタイミング間隔を測定するようにする。タイマカウンタもまた、当技術分野では既知の方法で、刺激パルスの送出を制御することができる。制御器はまた、アナログ・デジタル（Ａ／Ｄ）変換器を備え、アナログのＥＧＭ信号および圧力信号をデジタル化したサンプルに変換することができ、サンプルは、以下で述べるように、ＲＡＭ１０４などのメモリに記憶され、処理されることができる。

【００２１】

一実施形態において、制御器１０６を利用して、制御ライン１３２上でマイクロプロセッサ１００への対応する割り込みを発生させ、それによって、マイクロプロセッサが、ＭＰＡＰ指標の処理と関連する全ての操作を含む、必要とされる任意の数学的計算を行なうことが可能になる。別法として、制御器は、以下で述べられる方法で処理するために、測定された信号値を外部デバイスに直接転送してもよい。

【００２２】

オプションの出力回路１０８は、刺激パルスを組織に送出する機構を提供することができる。たとえば、出力回路１０８は、端子１３４および１３６に結合されているように示されており、ターミナルは、次に、患者にペーシングパルスを送出するようになっている図１の先端電極２２およびリング電極２５などの各電極に電気的に結合される。別法として、または付加的に、当技術分野で知られているように、高電圧電極は、出力回路１０８に結合されて、カーディオバージョン／ディフィブリレーションショックを患者に供給することができる。付加的な電極は、このように結合して、当技術分野で知られているように、神経組織に刺激を供給することができる。要するに、出力回路は、脊髄刺激（ＳＣＳ）または皮下刺激を含む、本発明の範囲内にあり当技術分野で知られている任意のタイプの刺激を供給するようになっていてもよい。

【００２３】

一実施形態において、出力回路１０８は、心臓の両側でペーシングする手段を備える。このタイプの治療は、心臓を再同期化し、心拍出量を最適化するために設けることができる。こうした治療は、同一譲受人に譲渡された米国特許第６，２２３，０７９号、第６，０７０，１００号、第６，０７０，１０１号、および第５，９０２，３２４号（参照によって本明細書に援用される）に記載されているが、当技術分野で知られている任意のタイプの再同期化治療を、本発明と共に使用することができる。

【００２４】

心臓再同期化治療において、心臓の右側でのペーシングは、一般に、上述したように、右心房または右心室内に１つまたは複数のリード線を置くことによって達成される。同様に、心臓の左心室のペーシングは、左心房または左心室の内部に、または隣接して、配置さ

れた１つまたは複数のリード線を用いて達成してもよい。往々にして、心臓の左側でのペーシングは、心臓の左側に近接する冠状静脈洞内に少なくとも１つのリード線を配置することによって達成される。次に、心臓の左側および右側に送出される種々のペーシングパルスに関連するタイミングは、本発明によって得られる圧力推定値に基づいて調整することができる。たとえば、右心室および左心室内に送出されるパルスに関連するＶ－Ｖタイミング間隔は、ＭＰＡＰ推定値に基づいて調整することができる。このことは以下でさらに述べられる。

【００２５】

ここで、入力回路１１０の説明に戻ると、この回路を使用して、ＥＧＭ信号などの信号を検知するようにする。この回路は、端子１３８および１４０に結合されているように示されており、端子は、次に、ＥＧＭ信号を検知する先端電極２およびリング電極２５などの電極にそれぞれ結合することができる。別法として、単極検知モードが使用される場合、信号は、埋め込まれた電極のうちの１つとデバイスハウジングまたはデバイスハウジング上の電極との間で検知されてもよい。

【００２６】

入力回路１００は、増幅器および雑音検出および保護回路を備えてよい。所望であれば、過度の雑音のある期間中、信号検知がディセーブル（消勢）されてもよい。当技術分野で知られているように、雑音除去フィルタおよび同様な回路もまた備えてよい。一実施形態において、入力回路１１０は、信号ライン１２８を介して、自然な心室収縮（ｂｅａｔｓ）およびペーシングされた心室収縮の発生の両方を示す信号を制御器１０６に供給することができる。一実施形態において、制御器１０６は、信号ライン１３２を介して、こうした心室収縮の発生を示すデジタル化された信号（割り込みの形態であってよい）をマイクロプロセッサ１００に供給する。この信号によって、マイクロプロセッサが、本発明によって、任意の必要な計算を行うか、またはＲＡＭ１０４に記憶されている値を更新することが可能になる。

【００２７】

上述したように、デバイスはまた、圧力センサ１４８を備え、心臓組織内の圧力を検知するようにする。この圧力は、ＩＭＤに結合するリード線上に配置されたセンサ１６などのセンサを用いて右心室内で検知することができる。別法として、左心室内に配置されたセンサは、以下で述べる方法で使用することができる。圧力センサ１４８は、上述したものを含む、当技術分野では既知の１つまたは複数の圧力検知回路を備えることができる。

【００２８】

Ｃｈｉｒｉｆｅに発行された米国特許第４，８６５，０３６号に開示されているインピーダンスセンサなどの血行動態センサを含む他のセンサもまた、図２のＩＭＤに結合することができる。別法として、センサ１４８は、Ｅｒｉｋｓｏｎ他に発行された米国特許第５，１７６，１３７号に開示されている酸素飽和度センサ、またはＡｎｄｅｒｓｏｎ他に発行された米国特許第４，４２８，３７８号に開示されている身体活動センサなどの心拍出量パラメータを測定するデマンド型センサであってよい。両特許は、その全体が参照によって本明細書に援用される。付加的に、または別法として、当技術分野で知られている任意の他のタイプの生理的センサを使用して、ＭＰＡＰと共に使用できる患者データを発生させて、患者の状態を診断し、治療を調整するのに役立つようにしてもよい。

【００２９】

センサ処理回路１４６は、圧力センサ１４８および任意の他の生理的センサを制御し、信号を制御器１０６に供給して、信号がデジタル表現に変換されるようにする。センサ信号はまた、後で診断に使用するためにＲＡＭ１０４に記憶することができる。

【００３０】

ＩＭＤの外部制御は、遠隔測定／プログラミングユニット１２０などの通信回路によって達成される。従来の任意の遠隔測定／プログラミング回路が、本発明の状況で使用できると思われている。情報は、外部デバイス１２１からＩＭＤ１０に提供され、制御ライン１３０を介して制御器１０６に送られることができる。同様に、ＩＭＤからの情報は、制御

ライン１３０を介して遠隔測定／プログラミングユニット１２０に提供され、その後、外部デバイスに転送されることができる。この情報は、ＥＧＭ信号などの信号データおよび圧力測定値を含むか、または、以下で述べる、導出される信号値のいずれをも含んでよい。ＭＰＡＰ指標の導出に関連する処理の一部または全ては、外部デバイス１２１内に、または別のデータ処理システム内に含まれる処理回路によって、ＩＭＤの外部で行なうことができる。

【００３１】

一実施形態において、外部デバイス１２１は、患者の状態を診断し、任意の必要な再プログラミング機能を提供するのに使用することができるプログラマである。別の実施形態において、外部デバイスは、患者へ情報を提供する、および／または、患者からコマンドを受け取るために使用される患者インタフェースであってよい。たとえば、患者インタフェースは、リストバンドなどの外部装着デバイスであってもよく、リストバンドは、本発明に関連する処理ステップの一部または全てを遂行することができる別の処理システムに生データおよび任意の導出した値を転送する。このデータの転送は、たとえば、無線通信リンクによって行なうことができる。圧力測定値、ＥＧＭ信号および／または中間段階の値やＭＰＡＰ指標などの任意の導出されたデータは、現在または将来の診断および治療の変更で使用するために、データベース内の患者ファイルに転送することができる。

【００３２】

本発明のさらに別の実施形態において、埋め込み可能デバイスは、図２に示す薬ポンプ１５０を備える。このポンプを使用して、生物学的に活性な薬剤を患者に送出するようにできる。こうした薬の送出は、さらに以下で述べるように、ＭＰＡＰ値に基づいて調整することができる。

【００３３】

先の説明は、心臓の腔内に配置した１つまたは複数のリード線を用いて、ＥＧＭ信号を得ることに的を絞っているが、同一譲受人に譲渡された米国特許第５，３３１，９６６号（その全体を参照によって本明細書に援用する）に記載されている、デバイスのハウジング上に配置した電極アレイもまたこの目的のために使用することができる。Ｍｅｄｔｒｏｎｉｃ社の「Ｍｏｄｅｌ ９５２６ Ｒｅｖｅａｌ Ｐｌｕｓ Ｉｍｐｌａｎｔａｂｌｅ Ｌｏｏｐ Ｒｅｃｏｒｄｅｒ」が提供する、このタイプのアレイは、カン上に、心臓信号を検知する少なくとも２つの検知電極を具備する。こうした全てのシステムにおいて、ハウジングの表面上の電極Ａ、Ｂ、Ｃは、適当な絶縁バンドおよび米国特許第４，３１０，０００号（参照によって本明細書に援用される）に記載されている電気フィードスルーによって、互いからまたＩＭＤハウジングの導電性表面から電気的に絶縁されていることが理解されるであろう。電極からなる３電極システムの可能な電極方向および構成の例は、図３Ａ～図３Ｅに示される。

【００３４】

図３Ａは、２つの電極がコネクタブロック１６０上に、１つの電極がパルス発生器ケース１６２上にある状態で、直角に配設された電極Ａ、ＢおよびＣの方向を示すパルス発生器の側面図である。図３Ａ～図３Ｅの図示する方向のそれぞれについて、電極Ａ、ＢおよびＣの間隔は、約１インチ程度であるが、デバイスの正確なサイズによって大きいかまたは小さい可能性がある。より小さなデバイスで、かつより近い間隔は、より大きな増幅を必要とするであろう。

【００３５】

図３Ｂは、電極の少なくとも１つが、リード線伸長部材１６４によってパルス発生器から離れるように延びて、所望であれば、より大きな電極間間隔が得られるようにしている、パルス発生器の側面図である。

【００３６】

図３Ｃは、電極１６６の少なくとも１つがリード線１６８の近位端に位置し、そのリード線が、遠位端で、皮下の電極または電極アレイに結合するリード線である、パルス発生器の側面図である。

【００３７】
図３Ｄは、複数の電極がデバイスハウジングの縁部上に位置するパルス発生器の側面図である。パルス発生器ケースの縁部上に配置した電極は、ケースの壁を貫通して延びるフィードスルーの絶縁ピンを構成するであろうことが理解されるであろう。図３Ｃおよび図３Ｄに示すように、電極の相対的な方向は、図３Ａおよび図３Ｂに示す直角方向とは幾分変わる可能性がある。
【００３８】
図３Ｅは、電極アレイを含むデバイスハウジングのさらに別の実施形態の側面図である。ここで、ＭＰＡＰを導出するのに使用される方法に議論を戻す。右心室または左心室内で測定された心臓内圧力信号およびＥＧＭ信号を含む、少なくとも２つの測定値を必要とする。これらの値を使用して、以下の値が導出される。
【００３９】
（１）心周期を通して任意の時に測定される最大圧である心室収縮期圧（ＶＳＰ）。なお、この圧力は心室内で測定することができ、右心室内で測定されるのが好ましいが、この測定は、一般的でない状態である肺動脈弁の狭窄が存在しない限り、肺動脈収縮期圧を精密に近似する。
【００４０】
（２）所定期間の間の圧力信号の変化（ｄｐ／ｄｔ）が最大である時点の心室圧の測定値である、推定肺動脈拡張期圧（ｅＰＡＤ）。ＶＳＰ測定の場合と同様に、右心室内で得られるのが好ましいこの心室測定は、肺動脈弁の狭窄が存在しない限り、肺動脈拡張期圧を精密に近似する。
【００４１】
（３）心周期（Ｒ－Ｒ間隔）における連続するＲ波間の時間は、ＥＧＭ信号を用いて求めることができる。本発明がペーシングデバイスに組み込まれている一実施形態において、この時間は、ペーシングされた収縮および／または検知された収縮の間の時間を含むであろう。
【００４２】
（４）心臓が収縮期で費やす時間であり、Ｒ波の始まりから、所定の期間の間の圧力の変化（ｄｐ／ｄｔ）が最大である時点までの時間を測定することによって推定することができる収縮期時間間隔（ＳＴＩ）。したがって、この間隔は、ＥＧＭおよび圧力信号の両方の使用を含む。
【００４３】
上述した測定値および導出された値を使用して、以下のように、収縮期および拡張期の両方で費やされる一部の時間を求めることができる。
拡張期時間間隔（ＤＴＩ）は、Ｒ－Ｒ間隔からＳＴＩを差し引くことによって得ることができる。すなわち、
ＤＴＩ＝Ｒ－Ｒ間隔－ＳＴＩ
次に、心臓が拡張期にある一部の時間は、以下のように計算することができる。すなわち、
ＤＴＩ／（Ｒ－Ｒ間隔）
同様に、収縮期で費やされる一部の時間もまた、以下のように計算することができる。すなわち、
ＳＴＩ／（Ｒ－Ｒ間隔）
最後に、これらの一部の値を使用して、以下のようにＭＰＡＰに対するより正確な値を求めることができる。
【００４４】
【数１】

$$MPAP = [(DTI/R-R間隔) \times ePAD] + [(STI/R-R間隔) \times VSP]$$

簡単に述べると、推定拡張期圧ｅＰＡＤを拡張期に費やされた時間間隔に乗じ、推定収縮期圧ＶＳＰを収縮期に費やされた時間に乗じ、２つの測定値を一緒に加算して、平均をとり、平均肺動脈圧測定値ＭＰＡＰを生成するようにする。この決定は、収縮期で費やされる時間に重み付けるために、「３分の１」のような設定分数値を単に使用した以前の推定より正確である。さらに、本発明は、肺動脈内に位置する圧力センサの使用を必要としない。さらに、本発明は、本発明を用いて、心拍間ベースで利用できる測定を提供する。

【００４５】

先に述べたことは、心臓電位信号が、患者の脈管系内に位置する電極を用いて得られることを仮定しているが、このことがあてはまる必要はない。別の実施形態において、患者の体の外部に配置した電極を使用して、ＥＣＧ信号を測定することができ、この信号は、タイムスタンプを用いて、測定された圧力信号と相関付けることができる。こうして相関付けられた測定値は、本発明による方法によって、上述した外部処理回路によって処理されるであろう。

【００４６】

図４は、本発明の一実施形態によってＭＰＡＰを求める方法ステップを要約するフロー図である。ステップの順序は、ほとんどの場合、単に例示的であることが理解されるであろう。さらに、処理を含む方法ステップは、もっぱらＩＭＤ内の処理回路によって、もっぱら生体の外部の処理回路によって、または、それらの任意の組み合わせによって実行してもよい。最後に、処理ステップは、アナログまたはデジタルハードウェア、ソフトウェア、ファームウェア、マイクロコード、または任意の他の処理手段を用いて行なうことができる。

【００４７】

まず、上述した機構のうちの任意のものを用いて、心室圧信号およびＥＧＭ信号が検知される（２００）。これらの信号値は、一般に、デジタル処理回路を用いて処理されるようにデジタル化され得るが、アナログ処理回路を使用する場合は、このことは当てはまらない。次に、ＶＳＰが、心周期にわたる任意の時に測定される最大圧として求められる（２０２）。次に、推定肺動脈拡張期圧（ｅＰＡＤ）が、所定の期間の間の圧力信号の変化（ｄｐ／ｄｔ）が最大である心室圧の測定値として求められる（２０４）。心周期内の連続するＲ波間の時間（Ｒ－Ｒ間隔）がＥＧＭ信号を用いて測定される（２０６）。Ｒ波の始まりから、所定の期間の間の圧力の変化（ｄｐ／ｄｔ）が最大である時点までの時間を測定することによって収縮期時間間隔（ＳＴＩ）を推定することができる（２０８）。拡張期時間間隔（ＤＴＩ）は、Ｒ－Ｒ間隔からＳＴＩを差し引くことによって求められる（２１０）。最後に、以下の式によって、平均肺動脈圧（ＭＰＡＰ）が求められる（２１２）。

【００４８】

【数２】

$$MPAP = [(DTI / R\text{-}R\text{間隔}) \times ePAD] + [(STI / R\text{-}R\text{間隔}) \times VSP]$$

ＭＰＡＰが導出された後、この値を使用して治療を始動し、終了させ、調整することができる。たとえば、ＭＰＡＰが許容可能な範囲外にあると判断されると、薬などの生物学的に活性な薬剤が、制御器１０６およびマイクロプロセッサ１００の制御下で薬ポンプ１５０（図２）によって自動的に送出されることができる。たとえば、圧力が高過ぎ、肺高血圧症が存在することを示している場合、「Ｆｌｏｌａｎ」などの薬の投与によって動脈拡張を行なうことができる。別法として、または付加的に、電気刺激パラメータが調整されてもよい。

【００４９】

一実施形態において、推定ＭＰＡＰ値を使用して、心臓再同期化治療に関連するパラメータを調整することができる。心臓再同期化治療の使用は、同一譲受人に譲渡された米国特許第６，２２３，０７９号に詳細に記載されており、その全体を参照により本明細書に援

用する。このタイプの治療は、左心室および右心室の両方をペーシングすることを含み、それによって、心臓病患者の心臓機能の効率を改善する。Ａ－Ｖ間隔または心室のそれぞれに送出されるペーシングパルスの間のＶ－Ｖ間隔などのペーシングパラメータを調整することによって、肺圧を調整することができる。一般に、心臓病患者において、このことは、動脈圧を下げるためにパラメータを調整することを含むであろうが、動脈圧はまた、必要である場合には、同じ方法で、上昇させられてもよい。

【００５０】

本発明のさらに別の用途において、ＭＰＡＰ値を使用して、睡眠時無呼吸を治療してもよい。このタイプの睡眠障害を病む患者は、ＭＰＡＰを用いて検出することができる肺動脈圧の降下を経験する。この圧力降下を妨げるために、応答して、埋め込み可能ペースメーカを有する患者に対してペーシングレートを上昇させることができる。

【００５１】

上述の例は、右心室内に位置する圧力センサの使用を議論しているが、そうである必要はない。上述した実施形態の任意の実施形態において、右心室内のセンサに付加して、またはその別法として、圧力センサが左心室内に位置してもよい。これは、センサを、右心室内に導いて、中隔壁を通って、左心室内に導くことによって行なうことができる。別法として、左心室が露出される侵襲的手法の間に、リード線が、左心室壁を通って左心室腔内に直接挿入されてもよい。いずれの場合も、このタイプのセンサ配置は、別の目的で左心室リード線配置をすでに指示されている患者に望ましいだけであろう。その理由は、こうしたリード線配置は、凝血によって生ずる発作の見込みを増やすからである。さらに、こうしたリード線配置は、一般に、凝固を防ぐために、抗凝固薬物療法を施すことを伴う。

【００５２】

図５は、左心室および右心室のそれぞれに位置する圧力センサを示す例示的な図である。リード線２５２の遠位端の圧力センサ２５０は、中隔壁２５４を通して配置され、左心室２５６内に位置する。第２圧力センサ２６０は、右心室２６６内でリード線２５２上の圧力センサに近接して位置する。リード線はＩＭＤ２７０に結合される。この構成を用いると、心臓の両側からの圧力測定値を用いて、ＭＰＡＰ推定値を導出することができる。所望であれば、圧力センサのうちの１つだけを、ＩＭＤ内の切換えロジックを用いて所定時点に作動する必要がある。左心室圧と右心室圧を用いて導出した２つのＭＰＡＰ値を、たとえば、平均値を得ることによるように、さらに処理することができる。別の実施形態において、図５に示すセンサが個別のリード線に保持されることができる。さらに別の実施形態において、ただ１つの圧力センサ２５０が左心室圧を測定するために設けられる。

【００５３】

本発明によって求めたＭＰＡＰを、患者の肺動脈内に位置する圧力センサを用いて測定した平均動脈圧と比較する調査を行なった。データは、種々の血行動態ストレッサを受けている被検者について収集された。これらの調査が結論付けていることは、本発明のシステムおよび方法が、肺動脈内に位置する圧力センサを用いて測定されるであろう圧力値を精密に近似するＭＰＡＰ測定値を提供するということである。

【００５４】

図６は、本発明を用いて得たＭＰＡＰ推定値を平均動脈圧測定値と比較する一調査の結果を示すグラフである。測定された肺動脈圧は、上述した積分法を用いて処理されている。ＭＰＡＰ推定値は、Ｙ軸上に示されており、測定された肺動脈圧値は「ＰＡ平均」と表示したＸ軸上に示されている。得られる線について「１」の傾斜は、ＭＰＡＰとＰＡ平均の間に十分な相関があることを示すことに留意されてよい。グラフは、推定ＭＰＡＰと実際に測定された平均動脈圧ＰＡの間に密接な相関があることを示している。

【００５５】

本発明の他の範囲および態様は、本発明のシステムおよび方法の先の説明、ならびに添付図面から当業者には理解されるであろう。

【図面の簡単な説明】

【図１】

図１は、本発明と共に使用することができる埋め込み可能医療デバイス（ＩＭＤ）の略図である。

【図２】

図２は、本発明によって使用することができるパルス発生器の例示的な実施形態のブロック機能図である。

【図３】

図３Ａは、本発明と共に使用することができる皮下電極アレイを示すパルス発生器の側面図である。

図３Ｂは、電極のうちの少なくとも１つがリード線伸長部材によってパルス発生器から離れるように延びる電極アレイを有するパルス発生器の側面図である。

図３Ｃは、電極のうちの少なくとも１つ、または電極アレイが、リード線の近位端に位置する、パルス発生器の側面図である。

図３Ｄは、電極アレイの複数の電極が、デバイスハウジングの縁部上に位置するパルス発生器の側面図である。

図３Ｅは、電極アレイを含むデバイスハウジングのさらに別の実施形態の側面図である。

【図４】

図４は、本発明の一実施形態による、ＭＰＡＰを求める方法ステップを要約するフロー図である。

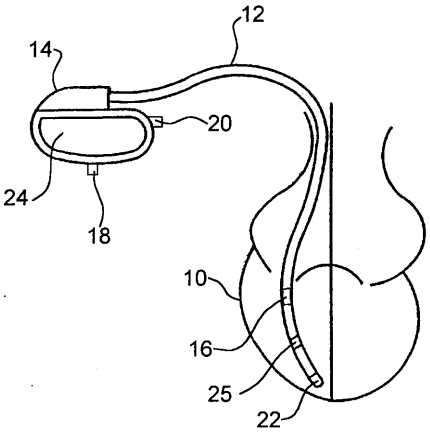
【図５】

図５は、圧力センサが左心室および右心室のそれぞれに位置する例示的な実施形態の図である。

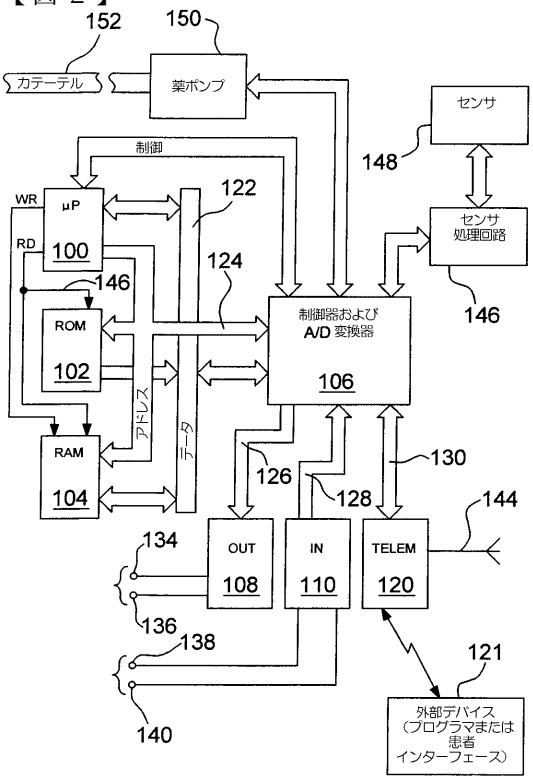
【図６】

図６は、動脈内に位置する圧力センサを用いて得た圧力測定値と本発明の方法を用いて得た圧力推定値を比較するグラフである。

【図１】



【図２】



【図３】

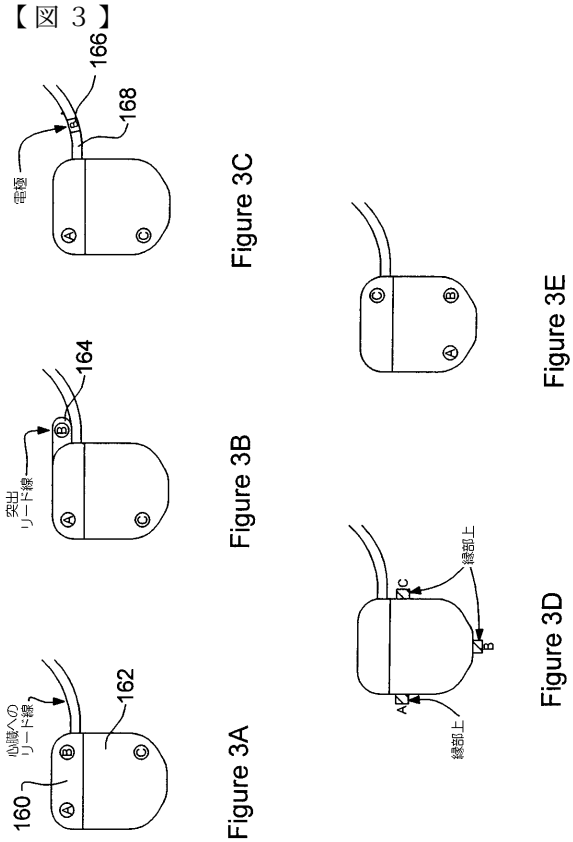


Figure 3C

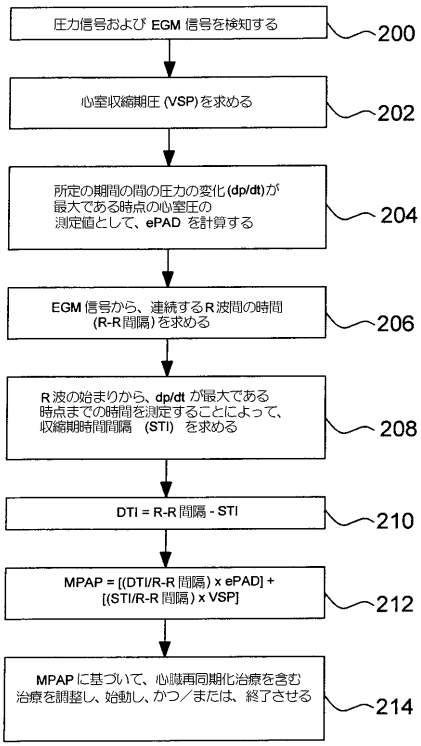
Figure 3B

Figure 3A

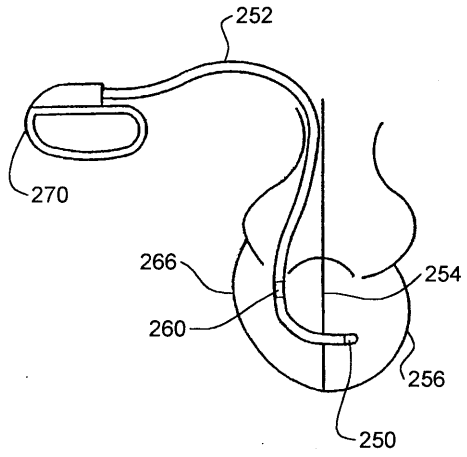
Figure 3E

Figure 3D

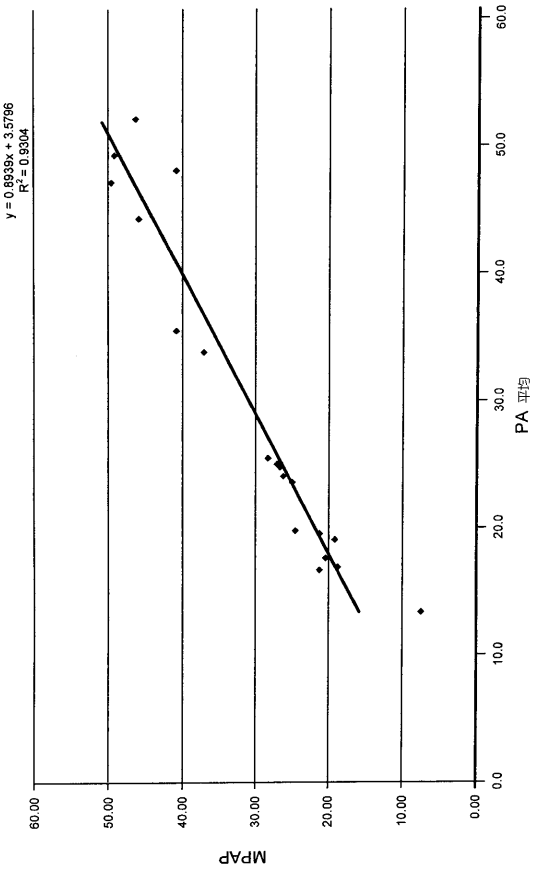
【図４】



【図５】



【図６】



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(54) Title: METHOD AND APPARATUS FOR MEASUREMENT OF MEAN PULMONARY ARTERY PRESSURE FORM A VENTRICLE IN AN AMBULATORY MONITOR

(57) Abstract: A system and method for determining mean pulmonary arterial pressure (MPAP) using a pressure sensor located within a ventricle of a heart, and a signal indicative of cardiac electrical activity such as an electrocardiogram (EGM) signal. The pressure may be sensed within the right and/or left ventricle using an implanted pressure sensor. The sensed pressure may be used to determine the Ventricular Systolic Pressure (VSP) and an estimated Pulmonary Arterial diastolic pressure (ePAD). The VSP, ePAD, and time intervals associated with systole and diastole may then be used to obtain an MPAP that closely approximates mean pulmonary arterial measured using a sensor located in the pulmonary artery.

METHOD AND APPARATUS FOR MEASUREMENT OF MEAN PULMONARY ARTERY PRESSURE FROM A VENTRICLE IN AN AMBULATORY MONITOR

FIELD OF THE INVENTION

This invention relates to measuring arterial pressure; and more specifically, relates to system and method for measuring mean arterial pressure using an ambulatory monitor.

DESCRIPTION OF THE PRIOR ART

Mean Pulmonary Artery Pressure (MPAP) is an important indicator of cardiovascular health. For example, the management of some diseases depends upon an accurate indication of pulmonary vascular resistance, which is determined using mean Pulmonary Arterial (PA) pressure. MPAP is also used as a general indicator of the work load of the right ventricle, and can therefore be used to diagnose and monitor heart failure.

In the past, mean PA pressure has been determined using several methods, all of which require a pressure sensor that is located within the pulmonary artery. According to a first method, both the PA systolic and PA diastolic pressure measurement values are used to determined MPAP using the following equation:

MPAP = 1/3(Systolic Pressure + 2/3(Diastolic Pressure)

This equation is based on the premise that in an average cardiac cycle, one-third of the time is spent in systole, and the remaining two-thirds of the time is spent in diastole. This is generally only true, however, when a patient is at rest. To provide a more accurate estimation of MPAP during a period of exercise, the above-described equation may be altered to reflect the fact that when a heart rate is above 100 or 120 beats-per-minute, the ventricles are in systole during approximately half of the cardiac cycle, and in diastole the other half of the cycle. This method does not, however, provide an accurate overall MPAP measurement that reflects both periods of rest and exercise.

Another method of measuring MPAP involves filtering the pressure signal as generated by the pressure sensor to remove signal pulsatility. This may be accomplished using a digital filter, for example. The resulting signal value is a close approximation of

the MPAP. Although this is more accurate than using diastolic and systolic pressures to calculate MPAP, the filtering process requires a relatively long time constant. Therefore, beat-to-beat measurements cannot be obtained.

According to yet another method, the pressure signal is integrated over a cardiac cycle, and then the resulting sum is divided by a number of predetermined time increments that were included in the cycle. This provides an accurate beat-by-beat average pressure. This method has the disadvantage, however, of requiring a digital signal processing system that is not readily available in most clinical settings.

What is needed, therefore, is an improved system and method for determined MPAP, which provides accurate beat-to-beat average measurements, and can be readily ascertained in a clinical setting. Preferably, such a device does not require the use of a pressure sensor located within the pulmonary artery.

SUMMARY OF THE INVENTION

The current invention provides a system and method for determining MPAP without the use of a sensor located within the pulmonary artery. The MPAP value is derived using a pressure measurement obtained from within a heart chamber, and a signal indicative of cardiac electrical activity such as an electrocardiogram (EGM) signal.

According to the current invention, pressure may be sensed within the right and/or left ventricle using an implanted pressure sensor. The sensed pressure may be used to determine the Ventricular Systolic Pressure (VSP), which is the maximum pressure measured at any time throughout the cardiac cycle. This sensed pressure may further be used to derive an estimated Pulmonary Arterial Diastolic pressure (ePAD), which is the pressure at the time the change in pressure over time is at a maximum. Finally, the EGM and pressure signals may be used to determine the time the heart spends both in systole and diastole. By multiplying the VSP by the time spent in systole, further multiplying the ePAD by the time spent in diastole, then adding the two values, mean pulmonary arterial pressure is closely approximated.

According to one embodiment of the invention, the system is included within an implantable device such as a pacemaker, cardioverter/defibrillator, drug delivery device, or another type of device for delivering therapy to a patient. The derived MPAP value

may be utilized to control therapy delivery. According to one aspect of the invention, cardiac resynchronization therapy is monitored and controlled using the MPAP value. In another embodiment, the derived MPAP value may be used to control the delivery of a biologically-active agent to the patient.

Processing steps performed according to the current invention may be carried out by a processing circuit located within an implantable device. Alternatively, one or more processing steps may be accomplished by a circuit external to the device, such as a programmer. The pressure and EGM signals may be transferred via a communication circuit to an external device so that all, or some, of the processing is completed by a circuit external to the patient.

According to one embodiment, the invention includes a system for estimating mean pulmonary arterial pressure of a patient. The system comprises a sensor located in a ventricle of a heart to measure pressure, a circuit to measure electrocardiogram (EGM) signals, and a processing circuit to derive mean pulmonary arterial pressure (MPAP) from the pressure and the EGM signals. According to another embodiment, the invention comprises a method for determining mean pulmonary arterial pressure (MPAP), by sensing pressure within a ventricle of a heart, sensing an electrocardiogram (EGM) signal of the heart, and using the sensed pressure and the EGM signal to derive the MPAP.

Other scopes and aspects of the invention will become apparent to those skilled in the art from the drawings and the accompanying description.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a schematic representation of an implanted medical device (IMD) as may be used with the current invention.

Figure 2 is a block functional diagram of an illustrative embodiment of a pulse generator that may be employed according to the present invention.

Figure 3A is a side view of a pulse generator illustrating a subcutaneous electrode array as may be used with the current invention.

Figure 3B is a side view of a pulse generator having an electrode array wherein at least one of the electrodes extends away from the pulse generator by a lead extension member.

Figure 3C is a side view of a pulse generator wherein at least one of the electrodes or an electrode array is located at a proximal end of a lead.

Figure 3D is a side view of a pulse generator wherein multiple electrodes of an electrode array are located on an edge of a device housing.

Figure 3E is a side view of yet another embodiment of a device housing including an array of electrodes.

Figure 4 is a flow diagram summarizing the method steps for determining the MPAP according to one embodiment of the invention.

Figure 5 is an exemplary embodiment wherein a pressure sensor is located in each of the left and right ventricles.

Figure 6 is a graph comparing pressure measurements obtained with a pressure sensor located within an arterial and pressure estimates obtained using the method of the current invention.

DETAIL DESCRIPTION OF THE DRAWINGS

The current invention provides a system and method for determining MPAP using a pressure measurement obtained from within a heart chamber in conjunction with a signal of cardiac electrical activity such as an electrocardiogram (EGM) signal. Thus, the current invention eliminates the need for a pressure sensor located in the pulmonary artery.

Figure 1 is a schematic representation of an implanted medical device (IMD) as may be used with the current invention. This IMD may be any device that is capable of measuring pressure signals from within a ventricle of a patient's heart, and which is further capable of measuring the patient's electrocardiogram (EGM). Such a device may be a hemodynamic monitor such as the Chronicle ™ device commercially available from the Medtronic Corporation. Circuitry included in the Chronicle is described in commonly-assigned U.S. Patents 5,535,752 and 5,564,434 which are incorporated herein by reference in their entireties. Alternatively, the device may be a pacemaker, or a cardioverter/defibrillator. Exemplary pacemaker systems that may be used to practice the current invention are described in commonly-assigned U.S. Patent Numbers 5,158,078, 5,318,593, 5,312,453, and 5,226,413, which are incorporated herein by reference in their entireties. Any other pacing system known in the art may be adapted for use in the

alternative. The IMD may additionally, or in the alternative, include cardioversion/defibrillation circuitry as described in commonly-assigned U.S. Patent Numbers 5,193,535, and 5,314,430, which are incorporated herein by reference in their entireties. Other devices such as implantable drug delivery devices may also be adapted for use with the current invention so long as the device includes the capability to measure an EGM and ventricular pressure.

Returning to Figure 1, the IMD 14 may be implanted subcutaneously, between the skin and the ribs. Other implantation sites may be used if appropriate. In one embodiment, a lead 12 is passed through a vein into the right ventricle of the heart 10. The distal end of the lead or catheter may have a tip electrode 22 contacting the interior of the heart. In a multi-polar configuration, a second ring electrode 25 may be spaced from the tip electrode 22. Each of these electrodes is connected to the circuitry contained in the IMD 14. Alternatively, a uni-polar mode made be used wherein a portion of the metallic enclosure or "can" of the IMD may form an electrode surface 24. The EGM signal is measured between this surface and an implanted electrode such as the tip electrode 22. In yet another embodiment, a Subcutaneous Electrode Array (SEA) such as electrodes18 and 20 may be located on, but electrically isolated from, the housing of the implantable device such as disclosed in U.S. Patent Number 5,331,966, incorporated herein by reference in its entirety, as is discussed below.

Additional leads (not shown) may be coupled to IMD, including a lead located within the right atrium, and/or a lead located within a coronary vessel such as the coronary sinus. These leads may further include one or more high-voltage electrodes for provide cardioversion/defibrillation therapy.

Lead 12 is shown to further include a pressure sensor 16. If desired, an additional lead coupled to IMD 14 may be provided to carry the pressure sensor. The pressure sensor is preferably located within the right ventricle, although it may also be located within the left ventricle in a manner to be discussed below. Pressure sensors and accompanying circuitry as may be adapted for use with the current invention are described in commonly-assigned U.S. Patent Numbers 5,353,752, 5,353,800, 5,564,434, 5,330,505, and 5,368,040 which are incorporated herein by reference in their entireties.

Figure 2 is a block functional diagram of an illustrative embodiment of a pulse generator that may be employed according to the present invention. It may be noted that pulse generation capabilities are not necessary for practicing the current invention, and the following discussion is therefore to be considered exemplary only.

The primary elements of the exemplary apparatus illustrated in Figure 2 include a microprocessor 100, read-only memory (ROM) 102, random-access memory (RAM) 104, a digital controller 106, an input amplifier circuit 110, two output circuits 108 and 109, and a telemetry/programming unit 120.

Within the current embodiment, data processing capabilities and device control functions are provided by microprocessor 100. It will be understood that other digital and/or analog circuitry embodiments are within the scope of the invention. For example, the configurations illustrated in U.S. Pat. No. 5,251,624 issued to Bocek et al., U.S. Pat. No. 5,209,229 issued to Gilli, U.S. Pat. No. 4,407,288, issued to Langer et al, U.S. Pat. No. 5,662,688, issued to Haefner et al., U.S. Pat. No. 5,855,893, issued to Olson et al., U.S. Pat. No. 4,821,723, issued to Baker et al., and/or U.S. Pat. No. 4,967,747, issued to Carroll et al., all incorporated herein by reference in their entireties, may be usefully employed in conjunction with the present invention. Alternatively, or additionally, processing capabilities may be provided by an external processing circuit in a manner to be discussed below.

Read-only memory stores software and/or firmware for the IMD, including the primary instruction set executed by microprocessor 100. These instructions define the methods performed by the microprocessor according to the current invention. These instructions may also control any therapy and/or monitoring functions performed by the device. Additional storage is provided by RAM 104, which generally stores variable control parameters, such as programmed pacing parameters. Random-access memory 104 may also store digitized signals indicative of EGM waveforms and pressure measurements, as well as values that are derived from these measured signals during calculation of the MPAP.

Controller 106 performs all of the basic control and timing functions of the device. Controller 106 may include at least one programmable timing counter, which is used to measure timing intervals such as R-R intervals used in the current invention. The timer

counter may also control delivery of stimulation pulses in a manner known in the art. Controller may also include an analog-to-digital conversion (A/D) circuit to transform analog EGM and pressure signals to digitized samples that may be stored in memory such as RAM 104 and processed as described below.

In one embodiment, controller 106 may be utilized to generate corresponding interrupts on control lines 132 to microprocessor 100, allowing the microprocessor to perform any required mathematical calculations, including all operations associated with processing of the MPAP indicator. Alternatively, controller may directly transfer measured signal values to an external device for processing in a manner to be discussed below.

Optional output stage 108 may provide the ability to deliver stimulation pulses to tissue. For example, output stage 108 is shown coupled to terminals 134 and 136, which may, in turn, be electrically coupled to respective electrodes such as tip electrode 22 and ring electrode 25 of Figure 1 adapted to deliver pacing pulses to a patient. Alternatively, or in addition, high-voltage electrodes may be coupled to output stage 108 as is known in the art to provide cardioversion/defibrillation shocks to a patient. Additional electrodes may be so coupled to provide stimulate to nervous tissue as is known in the art. In sum, output stage may be adapted to provide any type of stimulation known in the art within the scope of the present invention, including spinal cord stimulation (SCS) or subcutaneous stimulation.

In one embodiment, output stage 108 includes means for pacing on both sides of the heart. This type of therapy may be provided to resynchronize the heart and optimize cardiac output. Such therapy is described in commonly-assigned U.S. Patent Nos. 6,223,079, 6,070,100, 6,070,101, and 5,902,324 incorporated herein by reference, although any type of resynchronization therapy known in the art may be used in conjunction with the current invention.

In cardiac resynchronization therapy, pacing on the right side of the heart is generally accomplished by locating one or more leads in the right atrium or ventricle, as set forth above. Similarly, pacing of the left side of the heart may be accomplished using one or more leads positioned within, or adjacent to, the left atrium or ventricle. Often,

pacing on the left side of the heart is accomplished by positioning at least one lead within the coronary sinus in proximity to the left side of the heart. The timing associated with the various pacing pulses delivered on the left and right sides of the heart may then be adjusted based on pressure estimates obtained according to the current invention. For example, the V-V timing interval associated with pulses delivered in the right and left ventricles may be adjusted based on MPAP estimates. This is discussed further below.

Turning now to a discussion of the input circuit 110, this circuit is used to sense signals such as the EGM signals. This circuit is shown coupled to terminals 138 and 140, which, in turn, may be respectively coupled to electrodes such as tip electrode 22 and ring electrode 25 to sense EGM signals. Alternatively, if a unipolar mode of sensing is employed, signals may be sensed between one of the implanted electrodes and the device housing, or an electrode on the device housing.

Input circuit 100 may include amplification, and noise detection and protection circuitry. Signal sensing may be disabled during periods of excessive noise, if desired. Noise rejection filters and similar circuitry may also be included, as is known in the art. In one embodiment, input circuit 110 may provide signals indicating both the occurrence of natural ventricular beats and paced ventricular beats to the controller 106 via signal lines 128. In one embodiment, controller 106 provides digitized signals indicative of the occurrence of such ventricular beats to microprocessor 100 via signal lines 132, which may be in the form of interrupts. This allows the microprocessor to perform any necessary calculations or to update values stored in RAM 104 according to the current invention.

As discussed above, the device also includes a pressure sensor 148 to sense pressure within the cardiac system. This pressure may be sensed within the right ventricle using a sensor such as sensor 16 positioned on a lead coupled to the IMD. Alternatively, a sensor placed within the left ventricle may be used in a manner discussed below. The pressure sensor 148 may include one or more of the pressure sensing circuits known in the art, including those discussed above.

It may be noted that other sensors may also be coupled to the IMD of Figure 2, including a hemodynamic sensor such as an impedance sensor disclosed in U.S. Pat. No. 4,865,036 issued to Chirife. Alternatively, sensor 148 may be a demand sensor for measuring cardiac output parameters, such as an oxygen saturation sensor disclosed in

U.S. Pat. No. 5,176,137, issued to Erickson et al. or a physical activity sensor as disclosed in U.S. Pat. No. 4,428,378, issued to Anderson et al., both of which are incorporated herein by reference in their entireties. Any other types of physiological sensors known in the art may be used in addition, or in the alternative, to develop patient data that may be used in conjunction with the MPAP to diagnose patient conditions and aid in adjusting therapy.

Sensor processing circuitry 146 controls pressure sensor 148 and any other physiological sensors, and provides the signals to the controller 106 so that the signals may be transformed into digital representations. Sensor signals may also be stored in RAM 104 for later diagnostic use.

External control of the IMD is accomplished via a communication circuit such as telemetry/control block 120. Any conventional programming/telemetry circuitry is believed workable in the context of the present invention. Information may be provided to the IMD 10 from an external device 121 and passed to controller 106 via control lines 130. Similarly, information from the IMD may be provided to the telemetry block 120 via control lines 130 and thereafter transferred to the external device. This information may include signal data such as EGM signals and pressure measurements, or may include any of the derived signal values discussed below. Some, or all, of the processing associated with derivation of the MPAP indicator may be performed outside of the IMD by a processing circuit included within external device 121 or within another data processing system.

In one embodiment, the external device 121 is a programmer that may be utilized to diagnose patient conditions and to provide any necessary re-programming functions. In another embodiment, the external device may be a patient interface used to provide information to, and/or receive commands from, the patient. For example, the patient interface may be an externally-worn device such as a wrist band that transfers raw data and any derived values to another processing system which may complete some or all of the processing steps associated with the current invention. This transfer of data may be accomplished via a wireless communication link, for example. Pressure measurements, the EGM signals, and/or any derived data such as intermediate values and the MPAP

indicator may be transferred to a patient file within a database for use with current or future diagnosis and therapy modifications.

In yet another embodiment of the invention, the implantable device includes a drug pump 150 as shown in Figure 2. This pump may be used to deliver a biologically-active agent to the patient. Such drug delivery may be adjusted based on the MPAP value, as will be discussed further below.

Although the above description focuses on obtaining the EGM signals using one or more leads positioned within heart chambers, electrode arrays positioned on the housing of a device may also be used for this purpose as described in commonly-assigned U.S. Pat. No. 5,331,966, which is incorporated herein by reference in its entirety. This type of array, which is provided by the Medtronic Model 9526 Reveal Plus Implantable Loop Recorder, includes at least two sensing electrodes on the can for sensing of cardiac signals. In all such systems, it will be understood that the electrodes A, B, C on the surface of the housing are electrically isolated from one another and the conductive surface of the IMD housing through suitable insulating bands and electrical feedthroughs as described in U.S. Pat. No. 4,310,000, incorporated herein by reference. Examples of possible electrode orientations and configurations of a three electrode system comprising the electrodes are set forth in Figures 3A through 3E.

Figure 3A is a side view of a pulse generator illustrating the orientation of orthogonally-disposed electrodes A, B and C with two electrodes on the connector block 160 and one electrode on the pulse generator case 162. The spacing of the electrodes A, B and C on each of the illustrated orientations of Figure 3A through 3E may be on the order of about one inch but can be larger or smaller depending on the exact size of the device. Smaller devices and closer spacing will require greater amplification.

Figure 3B is a side view of a pulse generator wherein at least one of the electrodes extends away from the pulse generator by a lead extension member 164 to achieve a greater inter-electrode spacing, if desirable.

Figure 3C is a side view of a pulse generator wherein at least one of the electrodes 166 is located at a proximal end of a lead 168, which may be a lead coupled at a distal end to a subcutaneous electrode or electrode array.

Figure 3D is a side view of a pulse generator wherein multiple electrodes are located on an edge of a device housing. It will be understood that the electrodes placed on the edge of the pulse generator case could constitute insulated pins of feedthroughs extending through the wall of the case. As illustrated in Figures 3C and 3D, the relative orientation of the electrodes may vary somewhat from the orthogonal orientation depicted in Figures 3A and 3B.

Figure 3E is a side view of yet another embodiment of a device housing including an array of electrodes.

Discussion may now turn to the method used to derive the MPAP. At least two measurements are required including an intercardiac pressure signal measured within the right or left ventricle, and an EGM signal. These values are used to derive the following values:

1.) The Ventricular Systolic Pressure (VSP), which is the maximum pressure that is measured at any time throughout the cardiac cycle. It may be noted that although this pressure may be measured within a ventricle, and is preferably measured within the right ventricle, this measurement closely approximates the pulmonary arterial systolic pressure unless stenosis of the pulmonic valve is present, which is an uncommon condition.

2.) The estimated Pulmonary Artery Diastolic pressure (ePAD), which is a measure of the ventricular pressure at the time the change in the pressure signal over time (dp/dt) is at a maximum. As is similar to the case of the VSP measurement, this ventricular measurement, which is preferably obtained in the right ventricle, closely approximates the pulmonary arterial diastolic pressure unless stenosis of the pulmonic valve is present.

3.) The time between successive R waves in the cardiac cycle (R-R interval) may be determined using the EGM signal. In one embodiment wherein the invention is incorporated into a pacing device, this could include a time between paced and/or sensed beats.

4.) The Systolic Time Interval (STI), which is the time the heart is spent in systole, may be estimated by measuring the time from the start of an R wave to the time when the change in pressure over time (dp/dt) is at a maximum. Thus, this involves use of both the EGM and the pressure signal.

The foregoing measurements and derived values may be used to determine the fractional portion of the time spent in both systole and diastole, as follows:

The Diastolic Time Interval (DTI) may be obtained by subtracting the STI from the R-R interval:

DTI = R-R Interval - STI.

The fractional portion of the time the heart is in diastole may then be calculated as follows:

DTI/(R-R Interval).

Similarly, the fractional portion of the time spent in systole may also be calculated as follows:

STI/(R-R Interval).

Finally, these fractional values may be used to determine a more accurate value for MPAP as follows:

MPAP = [(DTI/R-R Interval) x ePAD] + [(STI/R-R Interval) x VSP].

Simply put, the estimated diastolic pressure ePAD is multiplied by the time spent in diastole, the estimated systolic pressure VSP is multiplied by the time spent in diastole, and the two measurements are added together to create an average Mean Pulmonary Arterial Pressure measurement. This determination is more accurate than the previous estimate that merely used a set fractional value such as "one-third" to weight time spent in systole. Moreover, the current invention does not require use of a pressure sensor located within the pulmonary artery. Additionally, the invention provides a measurement that is available on a beat-to-beat basis using the current invention.

Although the above description assumes that cardiac potential signals are obtained using an electrode located within the vasculature of the patient, this need not be the case. In another embodiment, electrodes placed externally on the patient's body may be used to measure an ECG signal and this signal may be correlated with the measured pressure

signals using timestamps. Such correlated measurements could be processed by an external processing circuit as discussed above according to the current inventive method.

Figure 4 is a flow diagram summarizing the method steps for determining the MPAP according to one embodiment of the invention. It will be appreciated that the ordering of the steps is, in most cases, purely exemplary. Additionally, the method steps involving processing may be performed either entirely by a processing circuit within an IMD, entirely by a processing circuit external to a living body, or by any combination thereof. Finally, the processing steps may be accomplished using any combination of analogue or digital hardware, software, firmware, microcode, or any other processing means.

First, ventricular pressure and EGM signals are sensed using any of the mechanisms discussed above (200). These signal values are generally digitized so that they may be processed using a digital processing circuit, but if an analog processing circuit is used, this need not be the case. Next, the VSP is determined as the maximum pressure that is measured at any time throughout the cardiac cycle (202). The estimated Pulmonary Artery Diastolic pressure (ePAD) is then determined as a measure of the ventricular pressure at the time the change in the pressure signal over time (dp/dt) is at a maximum (204). The time between successive R waves in the cardiac cycle (R-R interval) is measured using the EGM signal (206). The Systolic Time Interval (STI) may be estimated by measuring the time from the start of an R wave to the time when the change in pressure over time (dp/dt) is at a maximum (208). The Diastolic Time Interval (DTI) is determined by subtracting STI from R-R Interval (210). Finally, Mean Pulmonary Arterial Pressure (MPAP) is determined (212) according to the following equation:

$$MPAP = [\,(DTI/R\text{-}R\ Interval) \times ePAD\,] + [\,(STI/R\text{-}R\ Interval) \times VSP\,].$$

After MPAP is derived, this value may be used to initiate, terminate, or adjust therapy. For example, if the MPAP is determined to be outside of an acceptable range, biologically-active agents such as drugs may be delivered automatically by drug pump 150 (Figure 2) under the control of controller 106 and microprocessor 100. For example, if the pressure is too high, indicating pulmonary hypertension exists, arterial dilation may be

accomplished by administration of a drug such as Flolan. Alternatively, or additionally, electrical stimulation parameters may be adjusted.

In one embodiment, the estimated MPAP value may be used to adjust parameters associated with cardiac resynchronization therapy. The use of cardiac resynchronization therapy is described in detail in commonly-assigned U.S. Patent No. 6,223,079, incorporated herein by reference in its entirety. This type of therapy involves pacing both the left and right ventricles to improve the efficiency of cardiac operation in heart failure patients. By adjusting pacing parameters such as A-V intervals or the V-V intervals between pacing pulses delivered in each of the ventricles, pulmonary pressure may be adjusted. Generally, in heart failure patients, this will involve adjusting parameters to lower arterial pressure, although arterial pressure may also be raised in the same manner if necessary.

In yet another application of the invention, the MPAP value may be used to treat sleep apnea. Patients suffering from this type of sleep disorder experience a drop in pulmonary arterial pressure which may be detected using the MPAP. In response, pacing rate may be increased for patient's having an implantable pacemaker to counteract this drop in pressure.

The foregoing examples discuss use of a pressure sensor located within the right ventricle, although this need not be the case. In any of the above-described embodiments, a pressure sensor may be located in the left ventricle in addition to, or as an alternative to, a sensor in the right ventricle. This may be accomplished by guiding the sensor into the right ventricle, through the septal wall, and into the left ventricle. Alternatively, during an invasive procedure wherein the left ventricle is exposed, a lead may be directly inserted through the left ventricular wall into the left ventricular chamber. In either situation, this type of sensor placement is probably only desirable in patients that are already indicated for left ventricular lead placement for another purpose, since such lead placement increases the probability of stroke caused by blood clots. Additionally, such lead placement is generally accompanied by the administration of anticoagulation medication to prevent clotting.

Figure 5 is an exemplary embodiment illustrating a pressure sensor located in each of the left and right ventricles. A pressure sensor 250 at the distal end of the lead 252 is

positioned through the septal wall 254 and located within the left ventricle 256. A second pressure sensor 260 is located proximal pressure sensor 250 on lead 252 within the right ventricle 266. The lead is coupled to IMD 270. Using this configuration, MPAP estimates may be derived using pressure measurements from both sides of the heart. If desired, only one of the pressure sensors need be activated at a given time using switching logic within the IMD. The two MPAP values derived using left and right ventricular pressures may be further processed, as by obtaining an average value, for example. In an alternative embodiment, the sensors shown in Figure 5 may be carried on separate leads. In yet another embodiment, only pressure sensor 250 is provided to measure the left ventricular pressure.

Studies were conducted to compare the MPAP as determined by the current invention against mean arterial pressure measured using a pressure sensor located in the patient's pulmonary artery. Data was collected for subjects undergoing various hemodynamic stressors. These studies conclude that the inventive system and method provides a MPAP measurement that closely approximates pressure values that would be measured using a pressure sensor located within the pulmonary artery.

Figure 6 is a graph illustrating the results of one study comparing MPAP estimates obtained using the current invention to mean arterial pressure measurements. The measured pulmonary artery pressure is processed using the integration method discussed above. The MPAP estimates are shown on the Y axis, whereas the measured pulmonary arterial pressure values are illustrated on the X axis labeled as "PA mean". It may be noted that a slope of "one" for the resulting line indicates a perfect correlation between the MPAP and the PA mean. The graph shows the close correlation between the estimated MPAP and the actual measured mean pulmonary arterial pressure PA.

Other scopes and aspects of the current invention will be appreciated by one skilled in the art from the above description of the inventive system and method, and the attached drawings.

CLAIMS

What is Claimed is:

1. A system for determine mean pulmonary arterial pressure of a patient, comprising:
a first sensor located in a ventricle of a heart to measure pressure;
a first circuit to measure electrocardiogram (EGM) signals; and
a processing circuit coupled to receive signals indicative of the pressure and the EGM signals, and to determine mean pulmonary arterial pressure (MPAP) therefrom.

2. The system of Claim 1, wherein the first circuit includes at least one electrode located within the cardiac vasculature of the patient.

3. The system of Claim 1, wherein the first circuit includes at least two electrodes placed on an external surface of the patient.

4. The system of Claim 1, wherein the first circuit is located within an implantable device contained within a housing, and wherein the first circuit includes at least one electrode coupled to the housing of the implantable device.

5. The system of Claim 1, wherein the first sensor is located within a first ventricle of the heart, and wherein the system includes a second sensor located within the other ventricle of the heart, and wherein the processing circuit includes means to estimate the MPAP from pressure measured by both the first and second sensors.

6. The system of Claim 1, wherein the processing circuit is located within an implantable device.

7. The system of Claim 1, wherein the processing circuit is located in a device external to the patient, and wherein the system further includes a communication circuit to

transfer indications of the measured pressure and the EGM signals to the processing circuit.

8. The system of Claim 1, wherein the processing circuit includes first and second portions, wherein the first portion is located within an implantable device, wherein the second portion is located within a device external to the patient, and wherein the system further includes a communication circuit to transfer data signals between the first and second portions.

9. The system of Claim 1, and further including a therapy delivery circuit coupled to the processing circuit to provide therapy to the patient.

10. The system of Claim 1, wherein the processing circuit includes means for controlling the therapy delivery circuit based on the estimated MPAP.

11. The system of Claim 10, wherein the therapy delivery circuit includes a circuit to provide cardiac resynchronization therapy to the patient.

12. The system of Claim 10, wherein the therapy delivery circuit includes a drug delivery device to deliver a biologically-active agent to the patient.

13. A method of determining mean pulmonary arterial pressure (MPAP), comprising:
a.) sensing pressure within a ventricle of a heart;
b.) sensing an electrocardiogram (EGM) signal of the heart; and
c.) using the sensed pressure and the EGM signal to derive the MPAP.

14. The method of Claim 13, wherein step c.) includes deriving a systolic time interval indicative of time spent by the heart in systole, and a diastolic time interval indicative of time spent in diastole.

15. The method of Claim 14, wherein step c.) includes deriving the systolic time interval by measuring from a start of an R-wave of the EGM signal to a time when a change in sensed pressure over time is at a maximum.

16. The method of Claim 15, wherein step c.) further includes utilizing the sensed pressure from within the ventricle to determine a Ventricular Systolic Pressure (VSP), wherein the VSP is substantially a maximum pressure measured at any time during a cardiac cycle of the heart.

17. The method of Claim 16, wherein step c.) further includes utilizing the sensed pressure to determine an estimated Pulmonary Arterial Diastolic pressure (ePAD), wherein the ePAD is a pressure measured substantially at a time in the cardiac cycle wherein the change in the sensed pressure over time is at a maximum.

18. The method of Claim 17, and further including:
c.) multiplying the diastolic time interval by the ePAD;
d.) multiplying the systolic time interval by the VSP; and
e.) adding the values obtained in steps c.) and d.) to obtain the MPAP.

19. The method of Claim 13, and further comprising delivering therapy based on the MPAP.

20. The method of Claim 19, and further comprising delivering a biologically-active agent.

21. The method of Claim 19, and further comprising delivering cardiac resynchronization therapy.

22. The method of Claim 21, and further comprising modifying timing parameters of the cardiac resynchronization therapy based on the MPAP.

23. A system for deriving mean pulmonary arterial pressure (MPAP) of a patient, comprising:

pressure sensing means located in a ventricle of a heart for measuring pressure;

EGM sensing means for sensing an electrocardiogram (EGM) signal; and

processing means for deriving the (MPAP) based on the measured pressure and the EGM signal.

24. The system of Claim 23, wherein the EGM sensing means includes means located within a chamber of a heart for sensing the EGM signal.

25. The system of Claim 23, wherein the EGM sensing means includes means external to the patient for sensing the EGM signal.

26. The system of Claim 23, wherein the EGM sensing means includes means located subcutaneously on the patient for sensing the EGM signal.

27. The system of Claim 23, wherein the processing means include means implanted within the patient.

28. The system of Claim 23, wherein the processing means includes means external to the patient.

29. The system of Claim 23, wherein the processing means includes means implanted within the patient and means external to the patient.

30. The system of Claim 23, and further including therapy delivery means for delivering therapy to a patient based on the MPAP.

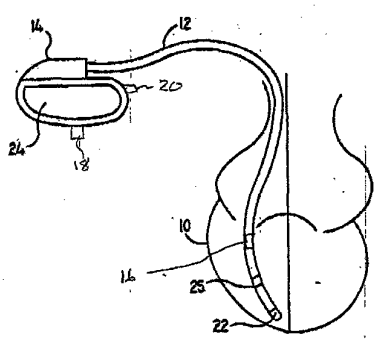
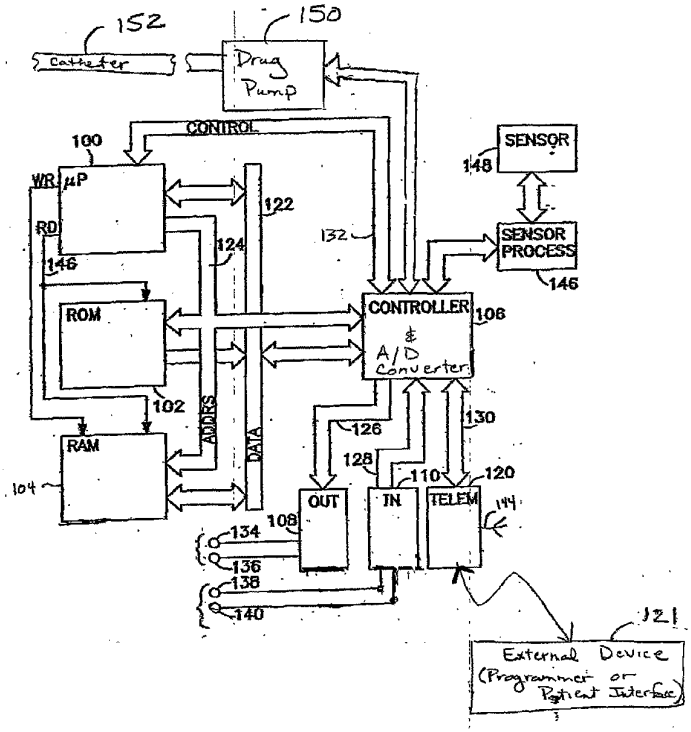


FIG. 1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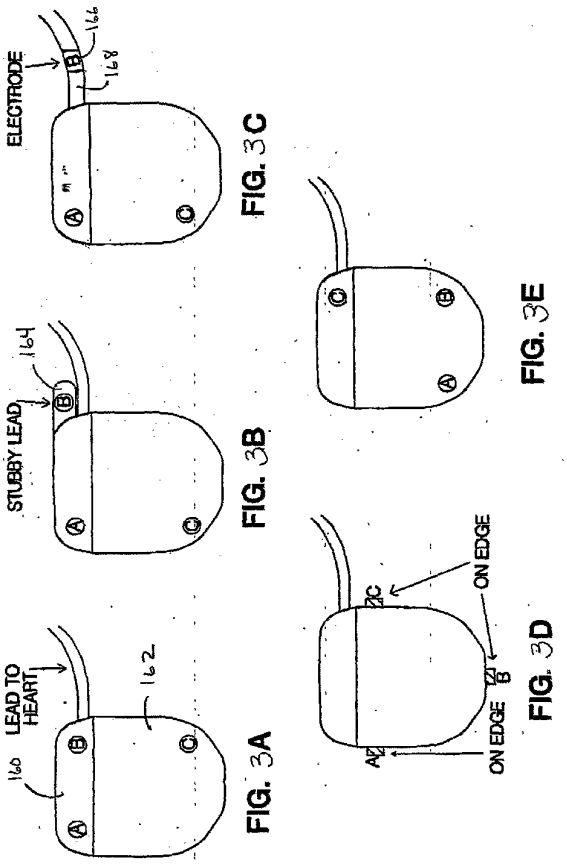
SENSOR PROCESS
146
ROM
102
CONTROLLER
&
A/D Converter
106
RAM
104
ADDRS
DATA
126
128
130
110
120
OUT
IN
TELEM
114
108
134
136
138
140
121
External Device
(Programmer or Patient Interface)

Figure 2


ELECTRODE
166
168
B
A
C
FIG. 3C
STUBBY LEAD
164
B
A
C
FIG. 3B
LEAD TO HEART
160
162
B
A
C
FIG. 3A
ON EDGE
C
B
A
ON EDGE
FIG. 3D
FIG. 3E

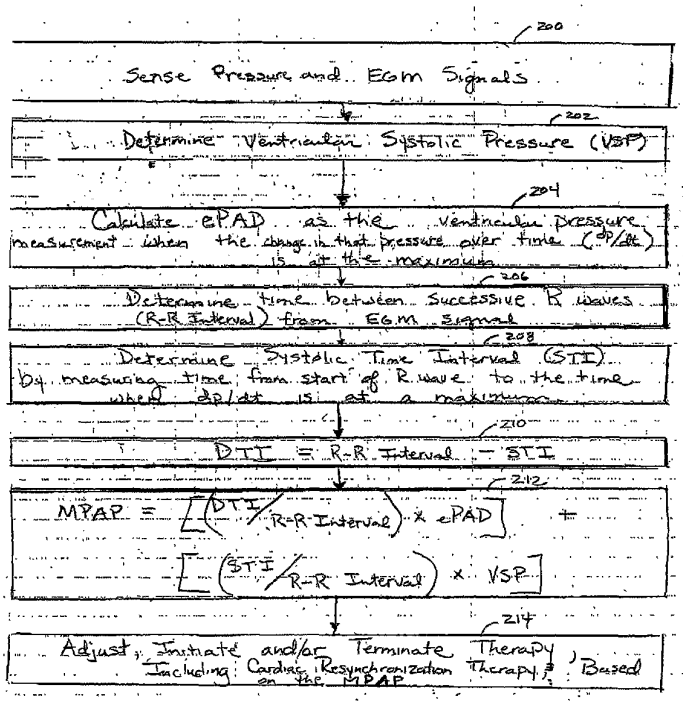

200
Sense Pressure and EGM Signals
202
Determine Ventricular Systolic Pressure (VSP)
204
Calculate ePAD as the ventricular pressure measurement when the change in that pressure over time (dP/dt) is at the maximum
206
Determine time between successive R waves (R-R Interval) from EGM signal
208
Determine Systolic Time Interval (STI) by measuring time from start of R wave to the time when dP/dt is at a maximum
210
DTI = R-R Interval − STI
212
MPAP = [(DTI / R-R Interval) x ePAD] + [(STI / R-R Interval) x VSP]
214
Adjust, Initiate and/or Terminate Therapy, Including Cardiac Resynchronization Therapy, Based on the MPAP

Figure 4

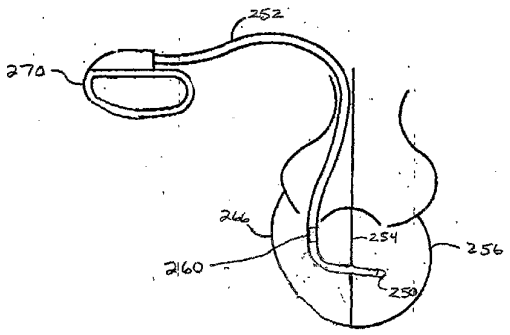


FIG. 5

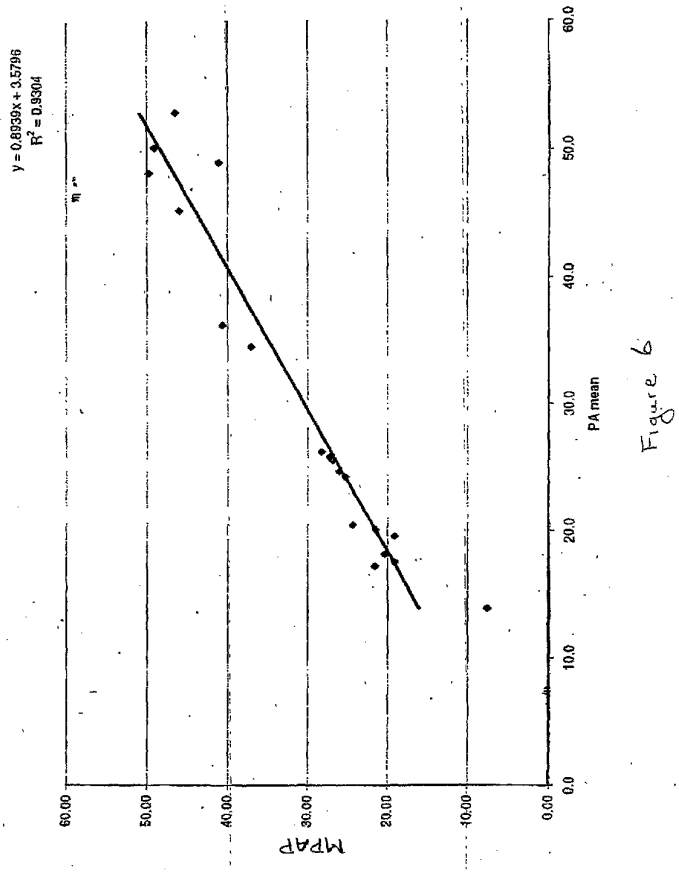

y = 0.8939x + 0.5796
R² = 0.9304
MPAP
PA mean
60.00
50.00
40.00
30.00
20.00
10.00
0.00
60.0
50.0
40.0
30.0
20.0
10.0
0.0

Figure 6

【国際公開パンフレット（コレクトバージョン）】

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(81) Designated States (national): CA, JP.

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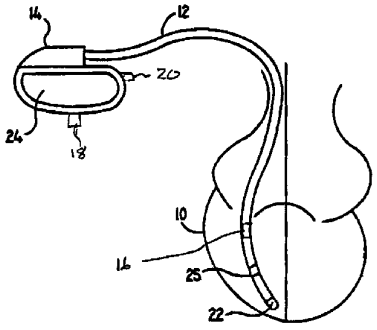
For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: METHOD AND APPARATUS FOR MEASUREMENT OF MEAN PULMONARY ARTERY PRESSURE FORM A VENTRICLE IN AN AMBULATORY MONITOR



(57) Abstract: A system and method for determining mean pulmonary arterial pressure (MPAP) using a pressure sensor (16) located within a ventricle of a heart, and a signal indicative of cardiac electrical activity such as an electrocardiogram (EGM) signal. The pressure may be sensed within the right and/or left ventricle using an implanted pressure sensor (16). The sensed pressure may be used to determine the Ventricular Systolic Pressure (VSP) and an estimated Pulmonary Arterial diastolic pressure (ePAD). The VSP, ePAD, and time intervals associated with systole and diastole may then be used to obtain an MPAP that closely approximates mean pulmonary arterial measured using a sensor located in the pulmonary artery.

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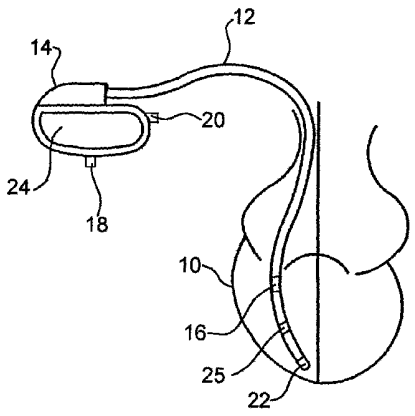

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METHOD AND APPARATUS FOR MEASUREMENT OF MEAN PULMONARY ARTERY PRESSURE FROM A VENTRICLE IN AN AMBULATORY MONITOR

FIELD OF THE INVENTION

This invention relates to measuring arterial pressure; and more specifically, relates to system and method for measuring mean arterial pressure using an ambulatory monitor.

DESCRIPTION OF THE PRIOR ART

Mean Pulmonary Artery Pressure (MPAP) is an important indicator of cardiovascular health. For example, the management of some diseases depends upon an accurate indication of pulmonary vascular resistance, which is determined using mean Pulmonary Arterial (PA) pressure. MPAP is also used as a general indicator of the work load of the right ventricle, and can therefore be used to diagnose and monitor heart failure.

In the past, mean PA pressure has been determined using several methods, all of which require a pressure sensor that is located within the pulmonary artery. According to a first method, both the PA systolic and PA diastolic pressure measurement values are used to determined MPAP using the following equation:

MPAP = 1/3(Systolic Pressure + 2/3(Diastolic Pressure)

This equation is based on the premise that in an average cardiac cycle, one-third of the time is spent in systole, and the remaining two-thirds of the time is spent in diastole. This is generally only true, however, when a patient is at rest. To provide a more accurate estimation of MPAP during a period of exercise, the above-described equation may be altered to reflect the fact that when a heart rate is above 100 or 120 beats-per-minute, the ventricles are in systole during approximately half of the cardiac cycle, and in diastole the other half of the cycle. This method does not, however, provide an accurate overall MPAP measurement that reflects both periods of rest and exercise.

Another method of measuring MPAP involves filtering the pressure signal as generated by the pressure sensor to remove signal pulsatility. This may be accomplished using a digital filter, for example. The resulting signal value is a close approximation of

the MPAP. Although this is more accurate than using diastolic and systolic pressures to calculate MPAP, the filtering process requires a relatively long time constant. Therefore, beat-to-beat measurements cannot be obtained.

According to yet another method, the pressure signal is integrated over a cardiac cycle, and then the resulting sum is divided by a number of predetermined time increments that were included in the cycle. This provides an accurate beat-by-beat average pressure. This method has the disadvantage, however, of requiring a digital signal processing system that is not readily available in most clinical settings.

What is needed, therefore, is an improved system and method for determined MPAP, which provides accurate beat-to-beat average measurements, and can be readily ascertained in a clinical setting. Preferably, such a device does not require the use of a pressure sensor located within the pulmonary artery.

SUMMARY OF THE INVENTION

The current invention provides a system and method for determining MPAP without the use of a sensor located within the pulmonary artery. The MPAP value is derived using a pressure measurement obtained from within a heart chamber, and a signal indicative of cardiac electrical activity such as an electrocardiogram (EGM) signal.

According to the current invention, pressure may be sensed within the right and/or left ventricle using an implanted pressure sensor. The sensed pressure may be used to determine the Ventricular Systolic Pressure (VSP), which is the maximum pressure measured at any time throughout the cardiac cycle. This sensed pressure may further be used to derive an estimated Pulmonary Arterial Diastolic pressure (ePAD), which is the pressure at the time the change in pressure over time is at a maximum. Finally, the EGM and pressure signals may be used to determine the time the heart spends both in systole and diastole. By multiplying the VSP by the time spent in systole, further multiplying the ePAD by the time spent in diastole, then adding the two values, mean pulmonary arterial pressure is closely approximated.

According to one embodiment of the invention, the system is included within an implantable device such as a pacemaker, cardioverter/defibrillator, drug delivery device, or another type of device for delivering therapy to a patient. The derived MPAP value

may be utilized to control therapy delivery. According to one aspect of the invention, cardiac resynchronization therapy is monitored and controlled using the MPAP value. In another embodiment, the derived MPAP value may be used to control the delivery of a biologically-active agent to the patient.

Processing steps performed according to the current invention may be carried out by a processing circuit located within an implantable device. Alternatively, one or more processing steps may be accomplished by a circuit external to the device, such as a programmer. The pressure and EGM signals may be transferred via a communication circuit to an external device so that all, or some, of the processing is completed by a circuit external to the patient.

According to one embodiment, the invention includes a system for estimating mean pulmonary arterial pressure of a patient. The system comprises a sensor located in a ventricle of a heart to measure pressure, a circuit to measure electrocardiogram (EGM) signals, and a processing circuit to derive mean pulmonary arterial pressure (MPAP) from the pressure and the EGM signals. According to another embodiment, the invention comprises a method for determining mean pulmonary arterial pressure (MPAP), by sensing pressure within a ventricle of a heart, sensing an electrocardiogram (EGM) signal of the heart, and using the sensed pressure and the EGM signal to derive the MPAP.

Other scopes and aspects of the invention will become apparent to those skilled in the art from the drawings and the accompanying description.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 is a schematic representation of an implanted medical device (IMD) as may be used with the current invention.

Figure 2 is a block functional diagram of an illustrative embodiment of a pulse generator that may be employed according to the present invention.

Figure 3A is a side view of a pulse generator illustrating a subcutaneous electrode array as may be used with the current invention.

Figure 3B is a side view of a pulse generator having an electrode array wherein at least one of the electrodes extends away from the pulse generator by a lead extension member.

Figure 3C is a side view of a pulse generator wherein at least one of the electrodes or an electrode array is located at a proximal end of a lead.

Figure 3D is a side view of a pulse generator wherein multiple electrodes of an electrode array are located on an edge of a device housing.

Figure 3E is a side view of yet another embodiment of a device housing including an array of electrodes.

Figure 4 is a flow diagram summarizing the method steps for determining the MPAP according to one embodiment of the invention.

Figure 5 is an exemplary embodiment wherein a pressure sensor is located in each of the left and right ventricles.

Figure 6 is a graph comparing pressure measurements obtained with a pressure sensor located within an arterial and pressure estimates obtained using the method of the current invention.

DETAIL DESCRIPTION OF THE DRAWINGS

The current invention provides a system and method for determining MPAP using a pressure measurement obtained from within a heart chamber in conjunction with a signal of cardiac electrical activity such as an electrocardiogram (EGM) signal. Thus, the current invention eliminates the need for a pressure sensor located in the pulmonary artery.

Figure 1 is a schematic representation of an implanted medical device (IMD) as may be used with the current invention. This IMD may be any device that is capable of measuring pressure signals from within a ventricle of a patient's heart, and which is further capable of measuring the patient's electrocardiogram (EGM). Such a device may be a hemodynamic monitor such as the Chronicle ™ device commercially available from the Medtronic Corporation. Circuitry included in the Chronicle is described in commonly-assigned U.S. Patents 5,535,752 and 5,564,434 which are incorporated herein by reference in their entireties. Alternatively, the device may be a pacemaker, or a cardioverter/defibrillator. Exemplary pacemaker systems that may be used to practice the current invention are described in commonly-assigned U.S. Patent Numbers 5,158,078, 5,318,593, 5,312,453, and 5,226,413, which are incorporated herein by reference in their entireties. Any other pacing system known in the art may be adapted for use in the

alternative. The IMD may additionally, or in the alternative, include cardioversion/defibrillation circuitry as described in commonly-assigned U.S. Patent Numbers 5,193,535, and 5,314,430, which are incorporated herein by reference in their entireties. Other devices such as implantable drug delivery devices may also be adapted for use with the current invention so long as the device includes the capability to measure an EGM and ventricular pressure.

Returning to Figure 1, the IMD 14 may be implanted subcutaneously, between the skin and the ribs. Other implantation sites may be used if appropriate. In one embodiment, a lead 12 is passed through a vein into the right ventricle of the heart 10. The distal end of the lead or catheter may have a tip electrode 22 contacting the interior of the heart. In a multi-polar configuration, a second ring electrode 25 may be spaced from the tip electrode 22. Each of these electrodes is connected to the circuitry contained in the IMD 14. Alternatively, a uni-polar mode made be used wherein a portion of the metallic enclosure or "can" of the IMD may form an electrode surface 24. The EGM signal is measured between this surface and an implanted electrode such as the tip electrode 22. In yet another embodiment, a Subcutaneous Electrode Array (SEA) such as electrodes18 and 20 may be located on, but electrically isolated from, the housing of the implantable device such as disclosed in U.S. Patent Number 5,331,966, incorporated herein by reference in its entirety, as is discussed below.

Additional leads (not shown) may be coupled to IMD, including a lead located within the right atrium, and/or a lead located within a coronary vessel such as the coronary sinus. These leads may further include one or more high-voltage electrodes for provide cardioversion/defibrillation therapy.

Lead 12 is shown to further include a pressure sensor 16. If desired, an additional lead coupled to IMD 14 may be provided to carry the pressure sensor. The pressure sensor is preferably located within the right ventricle, although it may also be located within the left ventricle in a manner to be discussed below. Pressure sensors and accompanying circuitry as may be adapted for use with the current invention are described in commonly-assigned U.S. Patent Numbers 5,353,752, 5,353,800, 5,564,434, 5,330,505, and 5,368,040 which are incorporated herein by reference in their entireties.

Figure 2 is a block functional diagram of an illustrative embodiment of a pulse generator that may be employed according to the present invention. It may be noted that pulse generation capabilities are not necessary for practicing the current invention, and the following discussion is therefore to be considered exemplary only.

The primary elements of the exemplary apparatus illustrated in Figure 2 include a microprocessor 100, read-only memory (ROM) 102, random-access memory (RAM) 104, a digital controller 106, an input amplifier circuit 110, two output circuits 108 and 109, and a telemetry/programming unit 120.

Within the current embodiment, data processing capabilities and device control functions are provided by microprocessor 100. It will be understood that other digital and/or analog circuitry embodiments are within the scope of the invention. For example, the configurations illustrated in U.S. Pat. No. 5,251,624 issued to Bocek et al., U.S. Pat. No. 5,209,229 issued to Gilli, U.S. Pat. No. 4,407,288, issued to Langer et al, U.S. Pat. No. 5,662,688, issued to Haefner et al., U.S. Pat. No. 5,855,893, issued to Olson et al., U.S. Pat. No. 4,821,723, issued to Baker et al., and/or U.S. Pat. No. 4,967,747, issued to Carroll et al., all incorporated herein by reference in their entireties, may be usefully employed in conjunction with the present invention. Alternatively, or additionally, processing capabilities may be provided by an external processing circuit in a manner to be discussed below.

Read-only memory stores software and/or firmware for the IMD, including the primary instruction set executed by microprocessor 100. These instructions define the methods performed by the microprocessor according to the current invention. These instructions may also control any therapy and/or monitoring functions performed by the device. Additional storage is provided by RAM 104, which generally stores variable control parameters, such as programmed pacing parameters. Random-access memory 104 may also store digitized signals indicative of EGM waveforms and pressure measurements, as well as values that are derived from these measured signals during calculation of the MPAP.

Controller 106 performs all of the basic control and timing functions of the device. Controller 106 may include at least one programmable timing counter, which is used to measure timing intervals such as R-R intervals used in the current invention. The timer

counter may also control delivery of stimulation pulses in a manner known in the art. Controller may also include an analog-to-digital conversion (A/D) circuit to transform analog EGM and pressure signals to digitized samples that may be stored in memory such as RAM 104 and processed as described below.

In one embodiment, controller 106 may be utilized to generate corresponding interrupts on control lines 132 to microprocessor 100, allowing the microprocessor to perform any required mathematical calculations, including all operations associated with processing of the MPAP indicator. Alternatively, controller may directly transfer measured signal values to an external device for processing in a manner to be discussed below.

Optional output stage 108 may provide the ability to deliver stimulation pulses to tissue. For example, output stage 108 is shown coupled to terminals 134 and 136, which may, in turn, be electrically coupled to respective electrodes such as tip electrode 22 and ring electrode 25 of Figure 1 adapted to deliver pacing pulses to a patient. Alternatively, or in addition, high-voltage electrodes may be coupled to output stage 108 as is known in the art to provide cardioversion/defibrillation shocks to a patient. Additional electrodes may be so coupled to provide stimulate to nervous tissue as is known in the art. In sum, output stage may be adapted to provide any type of stimulation known in the art within the scope of the present invention, including spinal cord stimulation (SCS) or subcutaneous stimulation.

In one embodiment, output stage 108 includes means for pacing on both sides of the heart. This type of therapy may be provided to resynchronize the heart and optimize cardiac output. Such therapy is described in commonly-assigned U.S. Patent Nos. 6,223,079, 6,070,100, 6,070,101, and 5,902,324 incorporated herein by reference, although any type of resynchronization therapy known in the art may be used in conjunction with the current invention.

In cardiac resynchronization therapy, pacing on the right side of the heart is generally accomplished by locating one or more leads in the right atrium or ventricle, as set forth above. Similarly, pacing of the left side of the heart may be accomplished using one or more leads positioned within, or adjacent to, the left atrium or ventricle. Often,

pacing on the left side of the heart is accomplished by positioning at least one lead within the coronary sinus in proximity to the left side of the heart. The timing associated with the various pacing pulses delivered on the left and right sides of the heart may then be adjusted based on pressure estimates obtained according to the current invention. For example, the V-V timing interval associated with pulses delivered in the right and left ventricles may be adjusted based on MPAP estimates. This is discussed further below.

Turning now to a discussion of the input circuit 110, this circuit is used to sense signals such as the EGM signals. This circuit is shown coupled to terminals 138 and 140, which, in turn, may be respectively coupled to electrodes such as tip electrode 22 and ring electrode 25 to sense EGM signals. Alternatively, if a unipolar mode of sensing is employed, signals may be sensed between one of the implanted electrodes and the device housing, or an electrode on the device housing.

Input circuit 100 may include amplification, and noise detection and protection circuitry. Signal sensing may be disabled during periods of excessive noise, if desired. Noise rejection filters and similar circuitry may also be included, as is known in the art. In one embodiment, input circuit 110 may provide signals indicating both the occurrence of natural ventricular beats and paced ventricular beats to the controller 106 via signal lines 128. In one embodiment, controller 106 provides digitized signals indicative of the occurrence of such ventricular beats to microprocessor 100 via signal lines 132, which may be in the form of interrupts. This allows the microprocessor to perform any necessary calculations or to update values stored in RAM 104 according to the current invention.

As discussed above, the device also includes a pressure sensor 148 to sense pressure within the cardiac system. This pressure may be sensed within the right ventricle using a sensor such as sensor 16 positioned on a lead coupled to the IMD. Alternatively, a sensor placed within the left ventricle may be used in a manner discussed below. The pressure sensor 148 may include one or more of the pressure sensing circuits known in the art, including those discussed above.

It may be noted that other sensors may also be coupled to the IMD of Figure 2, including a hemodynamic sensor such as an impedance sensor disclosed in U.S. Pat. No. 4,865,036 issued to Chirife. Alternatively, sensor 148 may be a demand sensor for measuring cardiac output parameters, such as an oxygen saturation sensor disclosed in

U.S. Pat. No. 5,176,137, issued to Erickson et al. or a physical activity sensor as disclosed in U.S. Pat. No. 4,428,378, issued to Anderson et al., both of which are incorporated herein by reference in their entireties. Any other types of physiological sensors known in the art may be used in addition, or in the alternative, to develop patient data that may be used in conjunction with the MPAP to diagnose patient conditions and aid in adjusting therapy.

Sensor processing circuitry 146 controls pressure sensor 148 and any other physiological sensors, and provides the signals to the controller 106 so that the signals may be transformed into digital representations. Sensor signals may also be stored in RAM 104 for later diagnostic use.

External control of the IMD is accomplished via a communication circuit such as telemetry/control block 120. Any conventional programming/telemetry circuitry is believed workable in the context of the present invention. Information may be provided to the IMD 10 from an external device 121 and passed to controller 106 via control lines 130. Similarly, information from the IMD may be provided to the telemetry block 120 via control lines 130 and thereafter transferred to the external device. This information may include signal data such as EGM signals and pressure measurements, or may include any of the derived signal values discussed below. Some, or all, of the processing associated with derivation of the MPAP indicator may be performed outside of the IMD by a processing circuit included within external device 121 or within another data processing system.

In one embodiment, the external device 121 is a programmer that may be utilized to diagnose patient conditions and to provide any necessary re-programming functions. In another embodiment, the external device may be a patient interface used to provide information to, and/or receive commands from, the patient. For example, the patient interface may be an externally-worn device such as a wrist band that transfers raw data and any derived values to another processing system which may complete some or all of the processing steps associated with the current invention. This transfer of data may be accomplished via a wireless communication link, for example. Pressure measurements, the EGM signals, and/or any derived data such as intermediate values and the MPAP

indicator may be transferred to a patient file within a database for use with current or future diagnosis and therapy modifications.

In yet another embodiment of the invention, the implantable device includes a drug pump 150 as shown in Figure 2. This pump may be used to deliver a biologically-active agent to the patient. Such drug delivery may be adjusted based on the MPAP value, as will be discussed further below.

Although the above description focuses on obtaining the EGM signals using one or more leads positioned within heart chambers, electrode arrays positioned on the housing of a device may also be used for this purpose as described in commonly-assigned U.S. Pat. No. 5,331,966, which is incorporated herein by reference in its entirety. This type of array, which is provided by the Medtronic Model 9526 Reveal Plus Implantable Loop Recorder, includes at least two sensing electrodes on the can for sensing of cardiac signals. In all such systems, it will be understood that the electrodes A, B, C on the surface of the housing are electrically isolated from one another and the conductive surface of the IMD housing through suitable insulating bands and electrical feedthroughs as described in U.S. Pat. No. 4,310,000, incorporated herein by reference. Examples of possible electrode orientations and configurations of a three electrode system comprising the electrodes are set forth in Figures 3A through 3E.

Figure 3A is a side view of a pulse generator illustrating the orientation of orthogonally-disposed electrodes A, B and C with two electrodes on the connector block 160 and one electrode on the pulse generator case 162. The spacing of the electrodes A, B and C on each of the illustrated orientations of Figure 3A through 3E may be on the order of about one inch but can be larger or smaller depending on the exact size of the device. Smaller devices and closer spacing will require greater amplification.

Figure 3B is a side view of a pulse generator wherein at least one of the electrodes extends away from the pulse generator by a lead extension member 164 to achieve a greater inter-electrode spacing, if desirable.

Figure 3C is a side view of a pulse generator wherein at least one of the electrodes 166 is located at a proximal end of a lead 168, which may be a lead coupled at a distal end to a subcutaneous electrode or electrode array.

Figure 3D is a side view of a pulse generator wherein multiple electrodes are located on an edge of a device housing. It will be understood that the electrodes placed on the edge of the pulse generator case could constitute insulated pins of feedthroughs extending through the wall of the case. As illustrated in Figures 3C and 3D, the relative orientation of the electrodes may vary somewhat from the orthogonal orientation depicted in Figures 3A and 3B.

Figure 3E is a side view of yet another embodiment of a device housing including an array of electrodes.

Discussion may now turn to the method used to derive the MPAP. At least two measurements are required including an intercardiac pressure signal measured within the right or left ventricle, and an EGM signal. These values are used to derive the following values:

1.) The Ventricular Systolic Pressure (VSP), which is the maximum pressure that is measured at any time throughout the cardiac cycle. It may be noted that although this pressure may be measured within a ventricle, and is preferably measured within the right ventricle, this measurement closely approximates the pulmonary arterial systolic pressure unless stenosis of the pulmonic valve is present, which is an uncommon condition.

2.) The estimated Pulmonary Artery Diastolic pressure (ePAD), which is a measure of the ventricular pressure at the time the change in the pressure signal over time (dp/dt) is at a maximum. As is similar to the case of the VSP measurement, this ventricular measurement, which is preferably obtained in the right ventricle, closely approximates the pulmonary arterial diastolic pressure unless stenosis of the pulmonic valve is present.

3.) The time between successive R waves in the cardiac cycle (R-R interval) may be determined using the EGM signal. In one embodiment wherein the invention is incorporated into a pacing device, this could include a time between paced and/or sensed beats.

4.) The Systolic Time Interval (STI), which is the time the heart is spent in systole, may be estimated by measuring the time from the start of an R wave to the time when the change in pressure over time (dp/dt) is at a maximum. Thus, this involves use of both the EGM and the pressure signal.

The foregoing measurements and derived values may be used to determine the fractional portion of the time spent in both systole and diastole, as follows:

The Diastolic Time Interval (DTI) may be obtained by subtracting the STI from the R-R interval:

DTI = R-R Interval - STI.

The fractional portion of the time the heart is in diastole may then be calculated as follows:

DTI/(R-R Interval).

Similarly, the fractional portion of the time spent in systole may also be calculated as follows:

STI/(R-R Interval).

Finally, these fractional values may be used to determine a more accurate value for MPAP as follows:

MPAP = [(DTI/R-R Interval) x ePAD] + [(STI/R-R Interval) x VSP].

Simply put, the estimated diastolic pressure ePAD is multiplied by the time spent in diastole, the estimated systolic pressure VSP is multiplied by the time spent in diastole, and the two measurements are added together to create an average Mean Pulmonary Arterial Pressure measurement. This determination is more accurate than the previous estimate that merely used a set fractional value such as "one-third" to weight time spent in systole. Moreover, the current invention does not require use of a pressure sensor located within the pulmonary artery. Additionally, the invention provides a measurement that is available on a beat-to-beat basis using the current invention.

Although the above description assumes that cardiac potential signals are obtained using an electrode located within the vasculature of the patient, this need not be the case. In another embodiment, electrodes placed externally on the patient's body may be used to measure an ECG signal and this signal may be correlated with the measured pressure

signals using timestamps. Such correlated measurements could be processed by an external processing circuit as discussed above according to the current inventive method.

Figure 4 is a flow diagram summarizing the method steps for determining the MPAP according to one embodiment of the invention. It will be appreciated that the ordering of the steps is, in most cases, purely exemplary. Additionally, the method steps involving processing may be performed either entirely by a processing circuit within an IMD, entirely by a processing circuit external to a living body, or by any combination thereof. Finally, the processing steps may be accomplished using any combination of analogue or digital hardware, software, firmware, microcode, or any other processing means.

First, ventricular pressure and EGM signals are sensed using any of the mechanisms discussed above (200). These signal values are generally digitized so that they may be processed using a digital processing circuit, but if an analog processing circuit is used, this need not be the case. Next, the VSP is determined as the maximum pressure that is measured at any time throughout the cardiac cycle (202). The estimated Pulmonary Artery Diastolic pressure (ePAD) is then determined as a measure of the ventricular pressure at the time the change in the pressure signal over time (dp/dt) is at a maximum (204). The time between successive R waves in the cardiac cycle (R-R interval) is measured using the EGM signal (206). The Systolic Time Interval (STI) may be estimated by measuring the time from the start of an R wave to the time when the change in pressure over time (dp/dt) is at a maximum (208). The Diastolic Time Interval (DTI) is determined by subtracting STI from R-R Interval (210). Finally, Mean Pulmonary Arterial Pressure (MPAP) is determined (212) according to the following equation:

$$MPAP = [\,(DTI/R\text{-}R\ Interval) \times ePAD\,] + [\,(STI/R\text{-}R\ Interval) \times VSP\,].$$

After MPAP is derived, this value may be used to initiate, terminate, or adjust therapy. For example, if the MPAP is determined to be outside of an acceptable range, biologically-active agents such as drugs may be delivered automatically by drug pump 150 (Figure 2) under the control of controller 106 and microprocessor 100. For example, if the pressure is too high, indicating pulmonary hypertension exists, arterial dilation may be

accomplished by administration of a drug such as Flolan. Alternatively, or additionally, electrical stimulation parameters may be adjusted.

In one embodiment, the estimated MPAP value may be used to adjust parameters associated with cardiac resynchronization therapy. The use of cardiac resynchronization therapy is described in detail in commonly-assigned U.S. Patent No. 6,223,079, incorporated herein by reference in its entirety. This type of therapy involves pacing both the left and right ventricles to improve the efficiency of cardiac operation in heart failure patients. By adjusting pacing parameters such as A-V intervals or the V-V intervals between pacing pulses delivered in each of the ventricles, pulmonary pressure may be adjusted. Generally, in heart failure patients, this will involve adjusting parameters to lower arterial pressure, although arterial pressure may also be raised in the same manner if necessary.

In yet another application of the invention, the MPAP value may be used to treat sleep apnea. Patients suffering from this type of sleep disorder experience a drop in pulmonary arterial pressure which may be detected using the MPAP. In response, pacing rate may be increased for patient's having an implantable pacemaker to counteract this drop in pressure.

The foregoing examples discuss use of a pressure sensor located within the right ventricle, although this need not be the case. In any of the above-described embodiments, a pressure sensor may be located in the left ventricle in addition to, or as an alternative to, a sensor in the right ventricle. This may be accomplished by guiding the sensor into the right ventricle, through the septal wall, and into the left ventricle. Alternatively, during an invasive procedure wherein the left ventricle is exposed, a lead may be directly inserted through the left ventricular wall into the left ventricular chamber. In either situation, this type of sensor placement is probably only desirable in patients that are already indicated for left ventricular lead placement for another purpose, since such lead placement increases the probability of stroke caused by blood clots. Additionally, such lead placement is generally accompanied by the administration of anticoagulation medication to prevent clotting.

Figure 5 is an exemplary embodiment illustrating a pressure sensor located in each of the left and right ventricles. A pressure sensor 250 at the distal end of the lead 252 is

positioned through the septal wall 254 and located within the left ventricle 256. A second pressure sensor 260 is located proximal pressure sensor 250 on lead 252 within the right ventricle 266. The lead is coupled to IMD 270. Using this configuration, MPAP estimates may be derived using pressure measurements from both sides of the heart. If desired, only one of the pressure sensors need be activated at a given time using switching logic within the IMD. The two MPAP values derived using left and right ventricular pressures may be further processed, as by obtaining an average value, for example. In an alternative embodiment, the sensors shown in Figure 5 may be carried on separate leads. In yet another embodiment, only pressure sensor 250 is provided to measure the left ventricular pressure.

Studies were conducted to compare the MPAP as determined by the current invention against mean arterial pressure measured using a pressure sensor located in the patient's pulmonary artery. Data was collected for subjects undergoing various hemodynamic stressors. These studies conclude that the inventive system and method provides a MPAP measurement that closely approximates pressure values that would be measured using a pressure sensor located within the pulmonary artery.

Figure 6 is a graph illustrating the results of one study comparing MPAP estimates obtained using the current invention to mean arterial pressure measurements. The measured pulmonary artery pressure is processed using the integration method discussed above. The MPAP estimates are shown on the Y axis, whereas the measured pulmonary arterial pressure values are illustrated on the X axis labeled as "PA mean". It may be noted that a slope of "one" for the resulting line indicates a perfect correlation between the MPAP and the PA mean. The graph shows the close correlation between the estimated MPAP and the actual measured mean pulmonary arterial pressure PA.

Other scopes and aspects of the current invention will be appreciated by one skilled in the art from the above description of the inventive system and method, and the attached drawings.

CLAIMS

What is Claimed is:

1. A system for determine mean pulmonary arterial pressure of a patient, comprising:
a first sensor located in a ventricle of a heart to measure pressure;
a first circuit to measure electrocardiogram (EGM) signals; and
a processing circuit coupled to receive signals indicative of the pressure and the EGM signals, and to determine mean pulmonary arterial pressure (MPAP) therefrom.

2. The system of Claim 1, wherein the first circuit includes at least one electrode located within the cardiac vasculature of the patient.

3. The system of Claim 1, wherein the first circuit includes at least two electrodes placed on an external surface of the patient.

4. The system of Claim 1, wherein the first circuit is located within an implantable device contained within a housing, and wherein the first circuit includes at least one electrode coupled to the housing of the implantable device.

5. The system of Claim 1, wherein the first sensor is located within a first ventricle of the heart, and wherein the system includes a second sensor located within the other ventricle of the heart, and wherein the processing circuit includes means to estimate the MPAP from pressure measured by both the first and second sensors.

6. The system of Claim 1, wherein the processing circuit is located within an implantable device.

7. The system of Claim 1, wherein the processing circuit is located in a device external to the patient, and wherein the system further includes a communication circuit to

transfer indications of the measured pressure and the EGM signals to the processing circuit.

8. The system of Claim 1, wherein the processing circuit includes first and second portions, wherein the first portion is located within an implantable device, wherein the second portion is located within a device external to the patient, and wherein the system further includes a communication circuit to transfer data signals between the first and second portions.

9. The system of Claim 1, and further including a therapy delivery circuit coupled to the processing circuit to provide therapy to the patient.

10. The system of Claim 1, wherein the processing circuit includes means for controlling the therapy delivery circuit based on the estimated MPAP.

11. The system of Claim 10, wherein the therapy delivery circuit includes a circuit to provide cardiac resynchronization therapy to the patient.

12. The system of Claim 10, wherein the therapy delivery circuit includes a drug delivery device to deliver a biologically-active agent to the patient.

13. A method of determining mean pulmonary arterial pressure (MPAP), comprising:
a.) sensing pressure within a ventricle of a heart;
b.) sensing an electrocardiogram (EGM) signal of the heart; and
c.) using the sensed pressure and the EGM signal to derive the MPAP.

14. The method of Claim 13, wherein step c.) includes deriving a systolic time interval indicative of time spent by the heart in systole, and a diastolic time interval indicative of time spent in diastole.

15. The method of Claim 14, wherein step c.) includes deriving the systolic time interval by measuring from a start of an R-wave of the EGM signal to a time when a change in sensed pressure over time is at a maximum.

16. The method of Claim 15, wherein step c.) further includes utilizing the sensed pressure from within the ventricle to determine a Ventricular Systolic Pressure (VSP), wherein the VSP is substantially a maximum pressure measured at any time during a cardiac cycle of the heart.

17. The method of Claim 16, wherein step c.) further includes utilizing the sensed pressure to determine an estimated Pulmonary Arterial Diastolic pressure (ePAD), wherein the ePAD is a pressure measured substantially at a time in the cardiac cycle wherein the change in the sensed pressure over time is at a maximum.

18. The method of Claim 17, and further including:
c.) multiplying the diastolic time interval by the ePAD;
d.) multiplying the systolic time interval by the VSP; and
e.) adding the values obtained in steps c.) and d.) to obtain the MPAP.

19. The method of Claim 13, and further comprising delivering therapy based on the MPAP.

20. The method of Claim 19, and further comprising delivering a biologically-active agent.

21. The method of Claim 19, and further comprising delivering cardiac resynchronization therapy.

22. The method of Claim 21, and further comprising modifying timing parameters of the cardiac resynchronization therapy based on the MPAP.

23. A system for deriving mean pulmonary arterial pressure (MPAP) of a patient, comprising:

pressure sensing means located in a ventricle of a heart for measuring pressure;

EGM sensing means for sensing an electrocardiogram (EGM) signal; and

processing means for deriving the (MPAP) based on the measured pressure and the EGM signal.

24. The system of Claim 23, wherein the EGM sensing means includes means located within a chamber of a heart for sensing the EGM signal.

25. The system of Claim 23, wherein the EGM sensing means includes means external to the patient for sensing the EGM signal.

26. The system of Claim 23, wherein the EGM sensing means includes means located subcutaneously on the patient for sensing the EGM signal.

27. The system of Claim 23, wherein the processing means include means implanted within the patient.

28. The system of Claim 23, wherein the processing means includes means external to the patient.

29. The system of Claim 23, wherein the processing means includes means implanted within the patient and means external to the patient.

30. The system of Claim 23, and further including therapy delivery means for delivering therapy to a patient based on the MPAP.

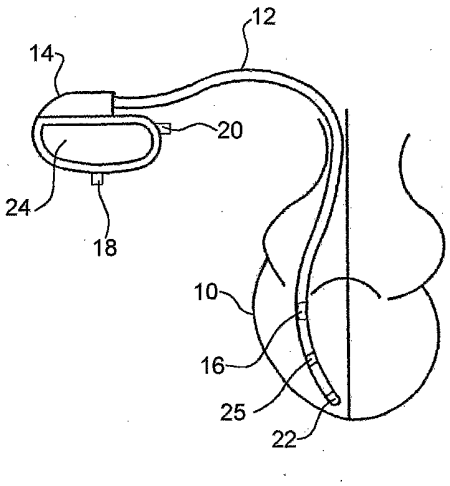

Figure 1

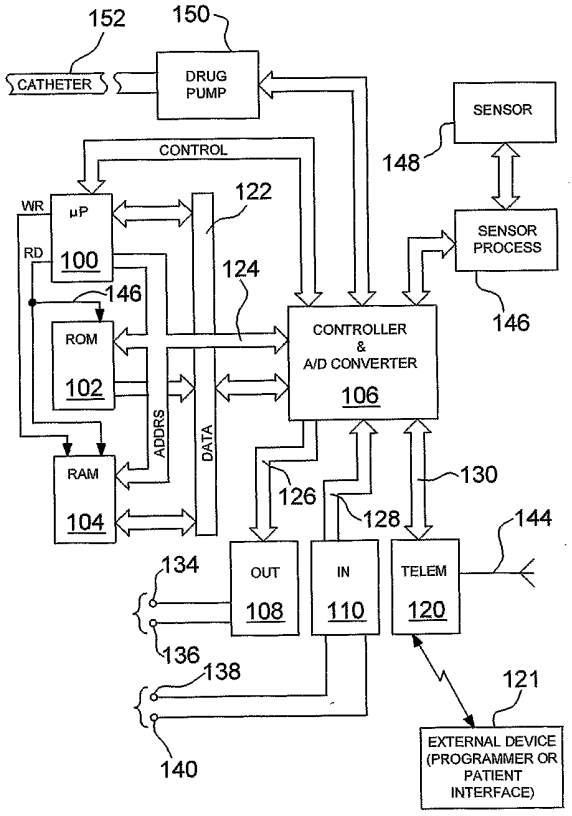
152
150
CATHETER
DRUG PUMP
SENSOR
148
CONTROL
122
WR
μP
RD
100
124
SENSOR PROCESS
146
146
ROM
102
CONTROLLER & A/D CONVERTER
106
ADDRS
DATA
RAM
104
126
130
128
144
134
OUT
108
IN
110
TELEM
120
136
138
121
140
EXTERNAL DEVICE (PROGRAMMER OR PATIENT INTERFACE)

Figure 2

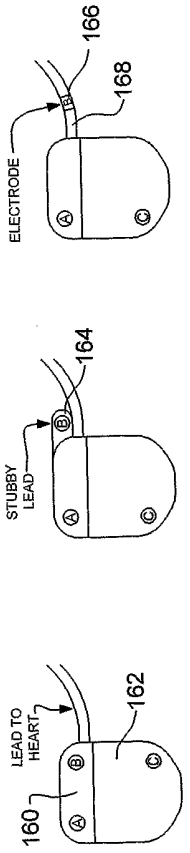

Figure 3C

Figure 3B

Figure 3A

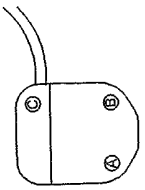

Figure 3E

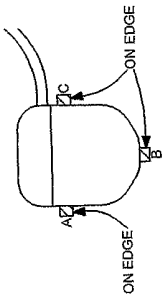

Figure 3D

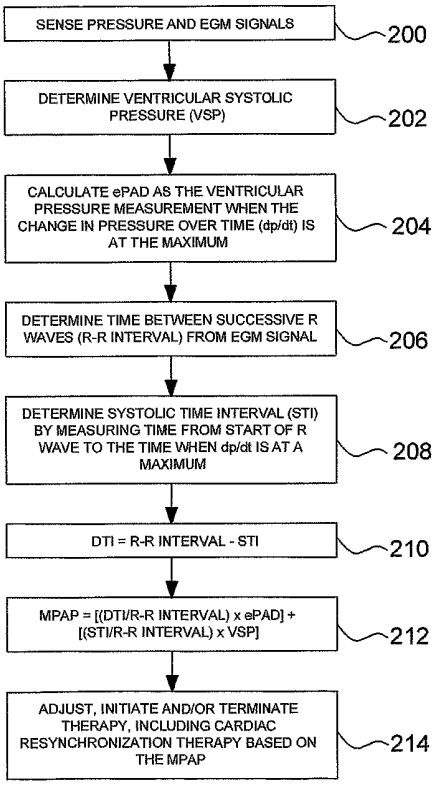
SENSE PRESSURE AND EGM SIGNALS
200
DETERMINE VENTRICULAR SYSTOLIC PRESSURE (VSP)
202
CALCULATE ePAD AS THE VENTRICULAR PRESSURE MEASUREMENT WHEN THE CHANGE IN PRESSURE OVER TIME (dp/dt) IS AT THE MAXIMUM
204
DETERMINE TIME BETWEEN SUCCESSIVE R WAVES (R-R INTERVAL) FROM EGM SIGNAL
206
DETERMINE SYSTOLIC TIME INTERVAL (STI) BY MEASURING TIME FROM START OF R WAVE TO THE TIME WHEN dp/dt IS AT A MAXIMUM
208
DTI = R-R INTERVAL - STI
210
MPAP = [(DTI/R-R INTERVAL) x ePAD] + [(STI/R-R INTERVAL) x VSP]
212
ADJUST, INITIATE AND/OR TERMINATE THERAPY, INCLUDING CARDIAC RESYNCHRONIZATION THERAPY BASED ON THE MPAP
214

Figure 4

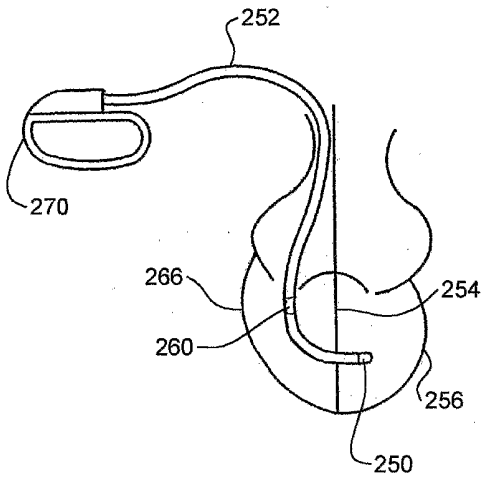

Figure 5

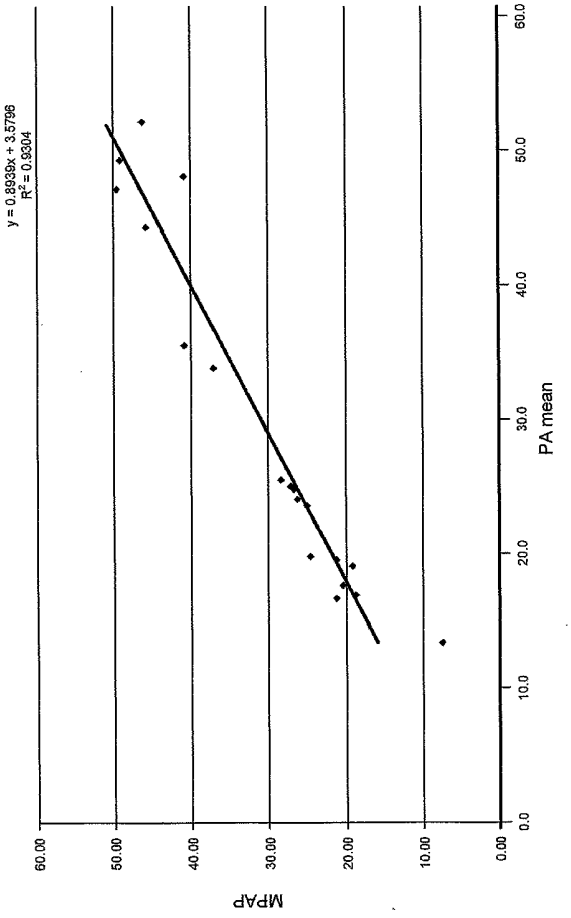
y = 0.8939x + 3.5796
R² = 0.9304
60.00
50.00
40.00
30.00
20.00
10.00
0.00
MPAP
60.0
50.0
40.0
30.0
20.0
10.0
0.0
PA mean

Figure 6

【手続補正書】
【提出日】平成14年10月8日(2002.10.8)
【手続補正１】
【補正対象書類名】明細書
【補正対象項目名】特許請求の範囲
【補正方法】変更
【補正の内容】
【特許請求の範囲】
【請求項１】
心室圧を測定して、心室圧力信号を形成するために、心臓の心室に位置する第１センサと、
心周期に対応する心電図（ＥＧＭ）信号を測定する第１回路と、
前記第１回路に結合して、前記心室圧力信号および前記心電図（ＥＧＭ）信号を受ける処理回路であって、前記心周期の間、前記第１センサが測定する最大圧力に基づいて心室収縮期圧（ＶＳＰ）を求め、所定期間の間の前記心室圧力信号の変化が最初に最大となる時点に対応する前記心室圧力信号に基づいて推定肺動脈拡張期（ｅＰＡＤ）圧を求め、前記心電図（ＥＧＭ）信号を用いてＲ－Ｒ間隔を求め、Ｒ波の始まりから、所定期間の間の前記心室圧力信号の変化が２番目に最大となる時点までに対応する時間枠に基づいて推定収縮期時間間隔（ＳＴＩ）を求め、前記Ｒ－Ｒ間隔から前記推定収縮期時間間隔（ＳＴＩ）を差し引くことによって拡張期時間間隔（ＤＴＩ）を求め、前記拡張期時間間隔（ＤＴＩ）を前記Ｒ－Ｒ間隔で割ったものと前記推定肺動脈拡張期（ｅＰＡＤ）圧の積と、前記推定収縮期時間間隔（ＳＴＩ）を前記Ｒ－Ｒ間隔で割ったものと前記心室収縮期圧（ＶＳＰ）の積との和に基づいて推定の平均肺動脈圧（ＭＰＡＰ）を求める、前記処理回路と、
を備えたこと特徴とする患者の平均肺動脈圧を決定する装置。
【請求項２】
前記第１回路は、前記患者の心臓脈管構造内に位置する少なくとも１つの電極を備えたことを特徴とする請求項１に記載の装置。
【請求項３】
前記第１回路は、前記患者の外部表面上に配置された少なくとも２つの電極を備えたことを特徴とする請求項１に記載の装置。
【請求項４】
前記第１回路は、ハウジング内に収容された埋め込み可能デバイス内に位置しており、前記第１回路は、前記埋め込み可能デバイスの前記ハウジングに結合する少なくとも１つの電極を備えたことをさらに特徴とする請求項１に記載の装置。
【請求項５】
前記心臓のもう一方の心室内に位置する第２センサを含んでおり、前記第１センサは、前記心臓の第１心室内に位置しており、前記処理回路は、前記第１および第２センサの両方によって測定された圧力から前記推定の平均肺動脈圧（ＭＰＡＰ）を求める手段を備えたことを特徴とする請求項１に記載の装置。
【請求項６】
前記処理回路は、埋め込み可能デバイス内に位置することを特徴とする請求項１に記載の装置。
【請求項７】
前記処理回路は、前記患者の外部のデバイス内に位置していること、および
前記測定された圧力の示度および前記心電図（ＥＧＭ）信号を前記処理回路に転送する通信回路をさらに備えたこと、
を特徴とする請求項１に記載の装置。
【請求項８】
前記処理回路は第１部分および第２部分を備えており、前記第１部分は、埋め込み可能デバイス内に位置しており、前記第２部分は、前記患者の外部のデバイス内に位置している

こと、
データ信号を前記第１および第２部分の間で転送する通信回路をさらに備えたこと、
を特徴とする請求項１に記載の装置。
【請求項９】
前記処理回路と結合し、前記患者に治療を供給する治療送出回路をさらに備えたことを特徴とする請求項１に記載の装置。
【請求項１０】
前記処理回路は、前記推定平均肺動脈圧（ＭＰＡＰ）に基づいて前記治療送出回路を制御する手段を備えたことを特徴とする請求項１に記載の装置。
【請求項１１】
前記治療送出回路は、心臓再同期化治療を前記患者に供給する回路を備えたことを特徴とする請求項１０に記載の装置。
【請求項１２】
前記治療送出回路は、生物学的に活性な薬剤を前記患者に送出する薬デリバリデバイスを備えたことを特徴とする請求項１０に記載の装置。
【請求項１３】
（イ）心臓の心室内の圧力を検知すること、
（ロ）前記心臓の心電図（ＥＧＭ）信号を検知すること、および
（ハ）平均肺動脈圧（ＭＰＡＰ）を導出するために、前記検知された圧力と前記心電図（ＥＧＭ）信号を用いること、
を含む平均肺動脈圧（ＭＰＡＰ）を決定する方法。
【請求項１４】
ステップ（ハ）は、収縮期に前記心臓が費やす時間を示す収縮期時間間隔および拡張期に費やす時間を示す拡張期時間間隔を導出することを含む請求項１３に記載の方法。
【請求項１５】
ステップ（ハ）は、前記心電図（ＥＧＭ）信号のＲ波の始まりから、所定期間の間の検知圧力の変化が最大になる時点まで測定することによって、前記収縮期時間間隔を導出することを含む請求項１４に記載の方法。
【請求項１６】
ステップ（ハ）は、心室収縮期圧（ＶＳＰ）を求めるために、前記検知された圧力を利用することをさらに含んでおり、前記心室収縮期圧（ＶＳＰ）は、前記心臓の心周期中の任意の時点に測定されたほぼ最大圧である請求項１５に記載の方法。
【請求項１７】
ステップ（ハ）は、推定肺動脈拡張期圧（ｅＰＡＤ）を求めるために、前記検知された圧力を利用することをさらに含んでおり、前記推定肺動脈拡張期圧（ｅＰＡＤ）は、前記心周期中の、所定期間の間の前記検知された圧力の変化が最大である、およその時点に測定された圧力である請求項１６に記載の方法。
【請求項１８】
（ニ）前記拡張期時間間隔に前記推定肺動脈拡張期圧（ｅＰＡＤ）を乗ずること、
（ホ）前記収縮期時間間隔に前記心室収縮期圧（ＶＳＰ）を乗ずること、および
（ヘ）前記平均肺動脈圧（ＭＰＡＰ）を得るために、ステップ（ニ）および（ホ）で得られた値を加算すること、
をさらに含む請求項１７に記載の方法。
【請求項１９】
前記平均肺動脈圧（ＭＰＡＰ）に基づいて治療を送出することをさらに含む請求項１３に記載の方法。
【請求項２０】
前記平均肺動脈圧（ＭＰＡＰ）に基づいて前記患者に生物学的に活性な薬剤を送出することをさらに含む請求項１９に記載の方法。
【請求項２１】

前記平均肺動脈圧（ＭＰＡＰ）に基づいて前記患者に心臓再同期化治療を送出することをさらに含む請求項１９に記載の方法。
【請求項２２】
前記平均肺動脈圧（ＭＰＡＰ）に基づいて前記心臓再同期化治療のタイミングパラメータを修正することをさらに含む請求項２１に記載の方法。
【請求項２３】
心臓の心室内に位置し、心室圧を測定して、心室圧力信号を形成するようにする圧力検知手段と、
心周期に対応する心電図（ＥＧＭ）信号を検知するＥＧＭ検知手段と、
前記測定された圧力信号および前記心電図（ＥＧＭ）信号に基づいて平均肺動脈圧（ＭＰＡＰ）を導出する処理手段であって、前記心周期の間、前記第１センサが測定する最大圧力に基づいて心室収縮期圧（ＶＳＰ）を求め、所定期間の間の前記心室圧力信号の変化が最初に最大となる時点に対応する前記心室圧力信号に基づいて推定肺動脈拡張期（ｅＰＡＤ）圧を求め、前記心電図（ＥＧＭ）信号を用いてＲ－Ｒ間隔を求め、Ｒ波の始まりから、所定期間の間の前記心室圧力信号の変化が２番目に最大となる時点までに対応する時間枠に基づいて推定収縮期時間間隔（ＳＴＩ）を求め、前記Ｒ－Ｒ間隔から前記推定収縮期時間間隔（ＳＴＩ）を差し引くことによって拡張期時間間隔（ＤＴＩ）を求め、前記拡張期時間間隔（ＤＴＩ）を前記Ｒ－Ｒ間隔で割ったものと前記推定肺動脈拡張期（ｅＰＡＤ）圧の積と、前記推定収縮期時間間隔（ＳＴＩ）を前記Ｒ－Ｒ間隔で割ったものと前記心室収縮期圧（ＶＳＰ）の積との和に基づいて推定平均肺動脈圧（ＭＰＡＰ）を求める、前記処理手段と、
を備えた患者の平均肺動脈圧（ＭＰＡＰ）を導出する装置。
【請求項２４】
前記ＥＧＭ検知手段は、心臓の腔内に位置し、前記心電図（ＥＧＭ）信号を検知する手段を備えたことを特徴とする請求項２３に記載の装置。
【請求項２５】
前記ＥＧＭ検知手段は、前記患者の外部にあり、前記心電図（ＥＧＭ）信号を検知する手段を備えたことを特徴とする請求項２３に記載の装置。
【請求項２６】
前記ＥＧＭ検知手段は、前記患者の皮下に位置し、前記心電図（ＥＧＭ）信号を検知する手段を備えたことを特徴とする請求項２３に記載の装置。
【請求項２７】
前記処理手段は、前記患者に埋め込まれる手段を備えたことを特徴とする請求項２３に記載の装置。
【請求項２８】
前記処理手段は、前記患者の外部にある手段を備えたことを特徴とする請求項２３に記載の装置。
【請求項２９】
前記処理手段は、前記患者に埋め込まれる手段と前記患者の外部にある手段を備えたことを特徴とする請求項２３に記載の装置。
【請求項３０】
前記平均肺動脈圧（ＭＰＡＰ）に基づいて患者に治療を送出する治療送出手段をさらに備えたことを特徴とする請求項２３に記載の装置。

【国際調査報告】

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/44978

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B5/02 A61B5/021

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61B A61N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 984 572 A (COHEN TODD J) 15 January 1991 (1991-01-15) column 8, line 20 -column 9, line 41; figures 1-5	1-3, 23-25
Y		4
Y	US 4 532 931 A (MILLS PERRY A) 6 August 1985 (1985-08-06) column 4, line 64 -column 5, line 4; figure 1	4
A	US 4 667 680 A (ELLIS DAVID M) 26 May 1987 (1987-05-26)	
A	US 6 113 548 A (BELL GLENN B ET AL) 5 September 2000 (2000-09-05)	

☐ Further documents are listed in the continuation of box C. ☒ Patent family members are listed in annex.

° Special categories of cited documents :

'A' document defining the general state of the art which is not considered to be of particular relevance
'E' earlier document but published on or after the international filing date
'L' document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
'O' document referring to an oral disclosure, use, exhibition or other means
'P' document published prior to the international filing date but later than the priority date claimed
'T' later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
'X' document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
'Y' document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
'&' document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
17 July 2002	09/08/2002
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Muller, G

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 01/44978

Box I ***Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)***

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 13-22
because they relate to subject matter not required to be searched by this Authority, namely:

Subject-matter relates to methods for treatment of the human or animal body by surgery or therapy. Rule 39(iv) PCT.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US 01/44978

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
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フロントページの続き

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摘要(译)

要解决的问题：提供一种改进的装置，以在心跳之间提供准确的平均值，并确定在临床环境中容易确定的平均肺动脉压（MPAP）。 平均肺动脉压力（MPAP）使用位于心脏心室的压力传感器和指示心脏电活动的信号（例如心电图（EGM）信号）确定。 可以使用植入的压力传感器感测右心室和/或左心室中的压力。 感测到的压力用于确定心室收缩压（VSP）和估计的肺舒张压（ePAD）。 然后使用与VSP，ePAD以及心脏收缩和舒张相关的时间间隔来获得MPAP，该MPAP可以非常接近使用位于肺动脉内的传感器测得的平均肺动脉压。