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(54)【発明の名称】哺乳動物の関節を増強する方法およびシステム

(57)【要約】
体の中および関節部位における挿入および配置に適合した、１以上の部分的または完全に予備形成されかつ前硬化された構成成分の調製および使用を包含する、整形外科的関節の摩耗表面を創造しまたは修正する方法およびシステム。好ましい態様において、１以上の構成成分は生体外で部分的に硬化し、一般的に形成し、さらに生体内で関節部位において形成して順応を増強しかつ長期の性能を改良することができる。他の態様において、予備形成されたバルーンまたは複合物質を関節部位の中に挿入し、その場で流動性生体適合物質を充填して関節部位に順応させることができる。なお他の態様において、１以上の予備形成された構成成分を生体外で完全に硬化し、形成し、必要に応じてさらに関節部位において勘合しかつ固定することができる。予備形成された構成成分は侵襲性を最小にする侵入門を通る挿入を可能とするために十分に柔軟であり、しかも必要に応じてさらに成形される所望の形態を生体内で実質的に取るか、あるいはそれに向かう傾向を有するのに十分に弾力性であることができる。

【特許請求の範囲】
【請求項１】
１以上の部分的または完全に予備形成されたポリマーの構成成分を含んでなり、前記予備形成された構成成分は関節部位に挿入および位置決定して、支持する骨に並置される少なくとも１つの主要な表面と、対向する骨に並置される少なくとも第２表面とを有する移植片を提供するように適合されている、哺乳動物の体内の整形外科的関節の摩耗表面を創造または修正するシステム。
【請求項２】
１以上の前記ポリマーの構成成分が、使用時に、硬化性ポリマー系を使用することによって形成され、前記ポリマー系の構成成分は、自然の関節空間を再確立するときかつ整形外科的関節部位の対向する骨表面と相応して、移植された構成成分が最終的に形成するようにさせるのに適当な条件下に、少なくとも部分的に硬化させ、生体外で成形することによって部分的に形成して、生体内に挿入しかつ位置決定することができる移植可能な構成成分を提供するように適合されている、請求項１に記載のシステム。
【請求項３】
前記ポリマーの構成成分は複数の包装され、予備形成された構成成分を含んでなり、前記構成成分は侵襲性を最小にする方式で整形外科的関節部位において組立てて、整形外科的関節部位の対向する骨表面と相応する表面を有する最終プロテーゼを提供するように適合されている、請求項１に記載のシステム。
【請求項４】
生体外型をさらに含み、前記型は、関節部位における構成成分の保持および適合を改良するために十分な方法で、部分的に予備形成された構成成分に対して、粗面化、パターン化、および／または輪郭化された表面を提供するように適合されている成形表面を有する、請求項１に記載のシステム。
【請求項５】
関節部位においていったん形成されたとき構成成分を固定するために、予備形成された構成成分の中に組込むように適合されている補助的手段を前記型がさらに含む、請求項４に記載のシステム。
【請求項６】
補助的手段が軟質の組織および／または骨を関節部位に取り付けて固定を改良するように適合されている、１以上の突起をさらに含んでなる、請求項５に記載のシステム。
【請求項７】
前記輪郭化表面が、予備形成された構成成分と一体化され、生体外成形プロセス間に形成される１以上の突起を有する輪郭を含んでなる、請求項４に記載のシステム。
【請求項８】
前記突起が生体外成形プロセス間に予備形成された構成成分の中に一体化されるように適合されている、請求項６に記載のシステム。
【請求項９】
前記突起が構成成分それ自体と一体的に形成された縫合糸および／または繊維状生体適合物質から構成されている、請求項７に記載のシステム。
【請求項１０】
型それ自体に関連せず、構成成分を関節部位に固定する別の手段をさらに含んでなり、前記手段は接着剤、縫合糸、ピン、ステープル、ねじ、およびそれらの組み合わせから選択される、請求項４に記載の手段。
【請求項１１】
１以上の予備形成されたポリマーの構成成分が侵襲性を最小にする方式で関節の中に挿入するように適合されている、請求項１に記載のシステム。
【請求項１２】
外科的分野において選択しかつ使用するために複数またはある範囲のスタイルおよびサイズで、予備形成された構成成分および／または対応する型が準備されている、請求項２に

記載のシステム。
【請求項１３】
移植片が膝の脛骨表面上で使用するために適合されており、そして大腿顆および対応する中央の脛骨プラトー、側方の脛骨プラトー、または両方の形状に順応するように適合されている部分を提供する、請求項１に記載のシステム。
【請求項１４】
前記ポリマーの構成成分がポリウレタン、ポリ尿素、ヒドロゲル、ポリシロキサン、ポリアクリレート、およびエポキシ、ならびにそれらの組み合わせから成る群から選択される物質から製作されている、請求項１に記載のシステム。
【請求項１５】
前記ポリマーの構成成分がポリウレタンを含んでなる、請求項１４に記載のシステム。
【請求項１６】
ポリウレタンがポリイソシアネート、短鎖および長鎖ポリオールから製造されており、そして必要に応じての疎水性添加剤、錫および／またはアミンの触媒、ならびに酸化防止剤から成る群から選択される１以上の成分を含む、請求項１５に記載のシステム。
【請求項１７】
ポリウレタンが芳香族ポリイソシアネート、ＰＴＭＯ、および短鎖ジオールを含んでなる、請求項１６に記載のシステム。
【請求項１８】
疎水性添加剤がヒドロキシル末端ポリブタジエンを含んでなり、そして錫および／またはアミンの触媒がイソシアネートーヒドロキシル反応を優先的に促進することができ、ＵＬ２２、Ｃｏｔｉｎ ２２２、１，４－ジアザビシクロ［２．２．２］オクタン（ｄａｂｃｏ）、およびジブチル錫ジラウレート （ＤＢＴＤＬ） 、ならびにそれらの組み合わせから成る群から選択される、請求項１６に記載のシステム。
【請求項１９】
予備形成されたポリマーの構成成分がサイトカイン、成長因子、自己成長因子、ヒドロキシアパタイト、コラーゲン、およびそれらの組み合わせから成る群から選択される生物学的に活性な物質を結合して有する１以上の表面を含んでなる、請求項１４に記載のシステム。
【請求項２０】
予備形成された構成成分の表面が組織の接着を促進する反応性基を有するか、あるいは反応性基で変性されている、請求項１４に記載のシステム。
【請求項２１】
反応性基がポリマーの構成成分の製作に使用されたポリマーにより提供され、そしてアミン、ヒドロキシル基、または他の反応性もしくは水素結合性官能基から選択される、請求項２０に記載のシステム。
【請求項２２】
関節部位内に位置決定されるように適合された１以上の予備形成されたポリマーの構成成分と、予備形成された構成成分と接触させて関節鏡的に注入し、関節部位においてその場で硬化して複合移植片を提供するように適合されている、１以上の流動性生体適合物質のポリマー組成物とを含んでなる、哺乳動物の体内の整形外科的関節の摩耗表面を創造または修正するシステム。
【請求項２３】
予備形成されたポリマーの構成成分が予備形成された上部の重量支持摩耗部分を有する膨張性バルーンと、支持骨の形状に順応するように適合された予備形成された下部部分とを含んでなる、請求項２２に記載のシステム。
【請求項２４】
バルーンの１以上の部分が組織の内方成長を可能とし、かつ空気を逃がすと同時に硬化性生体適合物質を保持するのに十分に透過性である天然または合成の布帛から製作されている、請求項２３に記載のシステム。

【請求項２５】
布帛が流動性ポリマーの物理的浸透を可能とするのに十分に透過性である、請求項２４に記載のシステム。
【請求項２６】
下部部分および／または上部部分がポリウレタン、ポリエチレン、ポリプロピレン、金属、セラミック、バイオポリマーまたはその他およびそれらの組み合わせから選択される物質から構成されている、請求項２３に記載のシステム。
【請求項２７】
上部部分および下部部分がそれぞれ大腿顆および脛骨プラトーの形状に対応する形態を有する、請求項２３に記載のシステム。
【請求項２８】
バルーンが、対応する骨に向かって上部部分を押しやるのに十分な方法で、流動性生体適合物質をバルーンに充填するように適合された口をさらに含む、請求項２３に記載のシステム。
【請求項２９】
下部部分が、関節部位内の保持を改良しおよび／または関節部位内に前記部分を縫合し、ステープルで止め、ピンで止め、ピンで止め、またはねじ止めする部位を提供するのに十分な、隆起した突起を提供する、請求項２３に記載のシステム。
【請求項３０】
関節部位内に予備形成された構成成分を固定する、別の手段が設けられている、請求項２２に記載のシステム。
【請求項３１】
生ずる複合移植片の１以上の表面上に提供するように適合された１以上の生物学的に活性な物質をさらに含んでなる、請求項２２に記載のシステム。
【請求項３２】
予備形成された構成成分および／または生ずる複合物質の表面が接着を促進する反応性基を有するか、あるいは反応性基で変性されている、請求項２２に記載のシステム。
【請求項３３】
反応性基が予備形成された構成成分それ自体により提供されるか、あるいは構成成分または生ずる複合体の適当な表面処理により別々に付加され、そして反応性基がアミン、ヒドロキシル基、または他の反応性もしくは水素結合性官能基から選択される、請求項３２に記載のシステム。
【請求項３４】
１以上の予備形成された構成成分が複数またはある範囲のスタイルおよびサイズで提供される、請求項２２に記載のシステム。
【請求項３５】
１以上の流動性生体適合物質が侵襲性を最小にする手段を使用して関節の中に挿入するように適合されている、請求項２２に記載のシステム。
【請求項３６】
侵襲性を最小にする方式で整形外科的関節部位において組立てて、整形外科的関節部位の対向する骨表面に並置される相応する表面を有する最終プロテーゼを提供するように適合された、複数の包装され、予備形成された構成成分を含んでなる、哺乳動物の体内の整形外科的関節の摩耗表面を創造または修正するシステム。
【請求項３７】
１以上の予備形成された構成成分が、関節部位内に配置され、必要に応じてさらに勘合および固定されるとき、最大の接着および勘合を提供する、適切に粗面化、パターン化、または輪郭化された表面を有する、請求項３６に記載のシステム。
【請求項３８】
予備形成し、引き続いて関節部位の内側に配置され、必要に応じてさらに勘合および固定されるとき、完全に硬化するように適合された硬化性生体適合物質を使用することによっ

て、１以上の予備形成された構成成分が使用時に形成される、請求項３６に記載のシステム。
【請求項３９】
１以上の予備形成された構成成分が関節部位の中にいったん配置された構成成分をさらに固定する手段を提供する、請求項３６に記載のシステム。
【請求項４０】
構成成分を固定する保持手段が組織接着剤を使用して固定を改良することを包含する、請求項３９に記載のシステム。
【請求項４１】
保持手段が、取り囲む軟質な組織および／または骨の中に縫合、ピン止め、ステープル止め、ねじ止めまたはそれらの組み合わせまたは他の方法で取り付けられて固定を改良するように適合された１以上の突起を含んでなる、請求項３９に記載のシステム。
【請求項４２】
突起がそれら自体予備形成された構成成分と一体化されている、請求項４１に記載のシステム。
【請求項４３】
突起が予備形成された構成成分を形成するために使用する生体外成形プロセス間に流動性生体適合物質の中に一体化される、請求項４２に記載のシステム。
【請求項４４】
突起が縫合糸または繊維状物質から構成されている、請求項４３に記載のシステム。
【請求項４５】
構成成分を固定する手段が構成成分に対して外部に存在し、いったん関節部位の内部に配置されると、接着剤、縫合糸、ピン、ステープル、ねじまたはその他およびそれらの組み合わせを使用して固定して、取り囲む軟質な組織および／または骨に対する固定を改良して固定を改良する、請求項３９に記載のシステム。
【請求項４６】
１以上の予備形成された構成成分が侵襲性を最小にする方式で関節の中に挿入されるように適合されている、請求項３６に記載のシステム。
【請求項４７】
１以上の予備形成された構成成分が複数またはある範囲のスタイルおよびサイズで提供されている、請求項３６に記載のシステム。
【請求項４８】
組立てられた構成成分が大腿顆および中央の脛骨プラトー、側方の脛骨プラトー、または両方の脛骨プラトーの形状に順応する、請求項３７に記載のシステム。
【請求項４９】
１以上の予備形成された構成成分がポリウレタン、ポリエチレン、ポリ尿素、ヒドロゲル、ポリシロキサン、ポリアクリレート、およびエポキシ、ならびにそれらの組み合わせから成る群から選択される物質から製作されている、請求項３７に記載のシステム。
【請求項５０】
物質がポリウレタンを含んでなる、請求項４９に記載のシステム。
【請求項５１】
ポリウレタンが１以上のポリイソシアネート、短鎖および長鎖ポリオールから製造されており、そして必要に応じて疎水性添加剤、錫および／またはアミンの触媒、ならびに酸化防止剤から成る群から選択される１以上の成分を含む、請求項５０に記載のシステム。
【請求項５２】
ポリウレタンが芳香族ポリイソシアネート、ＰＴＭＯ、短鎖ジオールから製造されている、請求項１６に記載のシステム。
【請求項５３】
疎水性添加剤がヒドロキシル末端ポリブタジエンを含んでなり、そして錫および／またはアミンの触媒がイソシアネート－ヒドロキシル反応を優先的に促進し、ＵＬ２２、Ｃｏｔ

ｉｎ ２２２、１，４－ジアザビシクロ［２．２．２］オクタン（ｄａｂｃｏ）、およびジブチル錫ジラウレート （ＤＢＴＤＬ） 、ならびにそれらの組み合わせから成る群から選択される、請求項５２に記載のシステム。

【請求項５４】

予備形成された構成成分がサイトカイン、ヒドロキシアパタイト、成長因子、自己成長因子、コラーゲンまたはその他およびそれらの組み合わせから成る群から選択される生物学的に活性な物質を結合して有する１または２以上の表面を提供する、請求項３６に記載のシステム。

【請求項５５】

１以上の予備形成された構成成分の表面が組織の接着を促進する反応性基を有するか、あるいは反応性基で変性されている、請求項３６に記載のシステム。

【請求項５６】

反応性基が１以上のの製作に使用されたポリマーに共有結合されており、そしてアミン、ヒドロキシル基、または他の反応性もしくは水素結合性官能基から選択される、請求項５５に記載のシステム。

【請求項５７】

１以上の予備形成された構成成分が、ａ） 単一の予備形成された構成成分、ｂ） 組織部位において互いの上に層状化するように適合された複数の構成成分、ｃ） 構成成分が共同して第１および第２の主要な表面のそれぞれの部分を提供するように、インターロッキング方式で組織部位において組立てるように適合された複数の構成成分から成る群から選択される、請求項３６に記載のシステム。

【請求項５８】

ａ） 骨表面それ自体を調製し、ｂ） 骨、構成成分、および／または生理学的環境間の所望のインターフェースを提供し、および／またはｃ） １以上の構成成分を処理して、表面を提供する物質の固有の性質に比較して、異なるまたは改良された性質を構成成分に提供するように適合された、１以上の追加の物質および／または工程を使用することをさらに含んでなる、請求項１または２２または３６に記載のシステム。

【請求項５９】

物質および／または工程が接着性、潤滑性、平滑性、順応性、組織内方成長、または生物適合性から選択される表面の性質または機能を改良または提供するように適合されている、請求項５８に記載のシステム。

【請求項６０】

システムが膝の脛骨プラトー、股関節部の関節陥、肩の関節窩、肩峰突起、肩鎖関節、足根の端部脛骨表面、肘の橈骨頭、前腕の端部橈骨、足の母指の基部指節骨表面、親指の基部中手骨、および手首の菱形骨から成る群から選択されるヒト関節を包含する、種々の哺乳動物の関節の修復に使用するために適合する、請求項１または２２または３６に記載のシステム。

【請求項６１】

システムが膝の脛骨プラトーの修復に適合されている、請求項６０に記載のシステム。

【請求項６２】

システムが股関節部の関節陥の修復に適合されている、請求項６０に記載のシステム。

【発明の詳細な説明】

【０００１】

関係する出願に対する相互参照

この出願は仮米国特許出願第６０／２２８，４４４号、２０００年８月２８日提出の一部継続出願であり、その全開示は引用することによって本明細書の一部とされる。

【０００２】

技術分野

１つの面において、本発明は体内で移植および使用するための生体外で形成された生体適合物質に関する。他の面において、本発明はその場で硬化可能な生体適合物質に関する。

なお他の面において、本発明は、さらに、整形外科的移植片およびプロテーゼの分野、さらに詳しくは、整形外科的関節において使用するための移植可能な物質に関する。

【０００３】

発明の背景

出願人は以前に、なかでも、例えば、侵襲性を最小にする技術を使用して、送出し、その場で最終的に硬化することができる生体適合物質から形成された人工的移植片を記載した。例えば、下記の文献を参照のこと：米国特許第５，５５６，４２９号、米国特許第５，７９５，３５３号、米国特許第５，８８８，２２０号、米国特許第６，０７９，８６８号、米国特許第６，１４０，４５２号、米国特許第６，２２４，６３０号および米国特許第６，２４８，１３１号ならびに公開された国際出願Ｎｏ．ＷＯ ９５／３０３８８号およびＷＯ ９７／２６８４７号および国際出願ＰＣＴ／ＵＳ９７／２０８７４号、１９９７年１１月１４日出願（それらの各々の開示は引用することによって本明細書の一部とされる）。これらの出願のあるものには、なかでも、プロテアーゼの核を椎間円板内に成形する方法が記載されている。この方法は、例えば、環帯内の開口を通してそれ自体位置決定されたカニューレを通してぺしゃんこになった型装置（これは好ましい態様において「バルーン」として記載されている）を挿入し、流動性生体適合物質をバルーンに充填する工程を含み、この流動性生体適合物質は最終的にその場で硬化し、恒久的円板置換体を提供する。また、下記の特許出願を参照のこと：出願人の「多孔質生体適合物質およびバイオポリマーの表面を新しくする系」（ＰＣＴ／ＵＳ９９／１０００４号）、ならびに「移植可能な組織修復装置（ＰＣＴ／ＵＳ９９／１１７４０）、および「静的ミキサー」（ＰＣＴ／ＵＳ９９／０４４７号）。

【０００４】

下記の特許出願を参照のこと：米国特許第３，０３０，９５１号（Ｍａｎｄａｒｉｎｏ）、米国特許第４，２０３，４４４号（Ｂｏｎｎｅｌｌ他）、米国特許第４，４５６，７４５号（Ｒａｊａｎ）、米国特許第４，４６３，１４１号（Ｒｏｂｉｎｓｏｎ）、米国特許第４，４７６，２９３号（Ｒｏｂｉｎｓｏｎ）、米国特許第４，４７７，６０４号（Ｏｅｃｈｓｌｅ，ＩＩＩ）、米国特許第４，６４７，６４３号（Ｚｄｒａｈａｌａ）、米国特許第４，６５１，７３６号（Ｓａｎｄｅｒｓ）、米国特許第４，７２２，９４８号（Ｓａｎｄｅｒｓｏｎ）、米国特許第４，７４３，６３２号（Ｍａｒｉｎｏｖｉｃ他）、米国特許第４，７７２，２８７号（Ｒａｙ他）、米国特許第４，８０８，６９１号（Ｋｏｎｉｇ他）、米国特許第４，８８０，６１０号（Ｃｏｎｓｔａｎｚ）、米国特許第４，８７３，３０８号（Ｃｏｕｒｙ他）、米国特許第４，９６９，８８８号（Ｓｃｈｏｌｔｅｎ他）、米国特許第５，００７，９４０号（Ｂｅｒｇ）、米国特許第５，０６７，９６４号（Ｒｉｃｈｍｏｎｄ他）、米国特許第５，０８２，８０３号（Ｓｕｍｉｔａ）、米国特許第５，１０８，４０４号（Ｓｃｈｏｌｔｅｎ他）、米国特許第５，１０９，０７７号（Ｗｉｃｋ）、米国特許第５，１４３，９４２号（Ｂｒｏｗｎ）、米国特許第５，１６６，１１５号（Ｂｒｏｗｎ）、米国特許第５，２５４，６６２号（Ｓｚｙｃｈｅｒ他）、米国特許第５，２７８，２０１号（Ｄｕｎｎ他）、米国特許第５，５２５，４１８号（Ｈａｓｈｉｍｏｔｏ他）、米国特許第５，６２４，４６３号（Ｓｔｏｎｅ他）、米国特許第６，２０６，９２７号（Ｆｅｌｌ）、およびＥＰ ０ ３５３ ９３６号（Ｃｅｄａｒ Ｓｕｒｇｉｃａｌ）、ＥＰ ０ ５０５ ６３４号Ａ１（Ｋｙｏｃｅｒａ Ｃｏｒｐｏｒａｔｉｏｎ）、ＥＰ ５２１ ５７３号（Ｉｎｄｕｓｔｒｉａｌ Ｒｅｓ．）、およびＦＲ ２ ６３９ ８２３号（Ｇａｒｃｉａ）、ＷＯ ９３／１１７２３号（Ｒｅｇａｎ Ｃｏｒｐｏｒａｔｉｏｎ）、ＷＯ ９５３１９４６号（Ｍｉｌｎｅｒ）、ＷＯ ９５３１９４８号（Ｋｕｓｈｌｉｃｈ）。

【０００５】

出願人のＰＣＴ出願Ｎｏ．ＰＣＴ／ＵＳ９７／００４５７号（ＷＯ ９７２６８４７号Ａ１）は、型、例えば、バルーンの任意の使用を包含し、これには次のような方法が記載されている『関節内でつくられた「型」は生ずる硬化した生体適合物質が除去された繊

維軟骨の構造および機能を置換または模倣できるのに十分な形状および寸法を有することが好ましい。この型は合成および／または天然の物質から形成することができ、外因的に提供された物質および残りの天然組織により提供される物質を包含する。この型は、生体適合物質が硬化するとき、その部位から除去されるか、あるいは所定位置に止まるのに十分に生体適合性である』。

【０００６】

出願人の後のＰＣＴ出願Ｎｏ．ＰＣＴ／ＵＳ９７／２０８７４号（ＷＯ ９８２０９３９号Ａ２）には、さらに、次のような方法が記載されている『「型」は、生体適合物質をその場に送出し、硬化させる過程において、流動性生体適合物質を受け取り、拘束し、造形し、および／または保持するために使用する本発明の装置の１または２以上の部分を意味する。型はその構造、コンフォメーションまたは機能の少なくとも一部分のために天然組織（例えば、椎間円板の環状外殻）を包含するか、あるいはそれらに頼ることができる。この型は、引き続いて、少なくとも一部分、硬化した人工移植片の位置および最終寸法の決定に関係する。その型の寸法および他の物理的特性は、侵襲性を最小にする手段を使用してある部位に送出し、生体適合物質を充填し、必要に応じて、硬化した生体適合物質と天然組織との間の界面としてまたは界面に所定位置において止まる能力のような性質の最適な組み合わせを提供するように前もって決定される。特に好ましい態様において、型の物質はそれ自体硬化した生体適合物質の本体に対して一体化するようになることができる』。

【０００７】

今日までこのような型装置の出願人自身の使用は、位置決定され、その場で硬化性生体適合物質を充填するように適合された、薄い、拡張可能なバルーンの使用に主として集中した。このような型は、顕微解剖後の椎間円板の置換物として特に使用される。引き続いて、今日まで、このような型は膝のような他の関節における使用にそれほど関心がもたれてきていない。例えば、出願人のＰＣＴ出願Ｎｏ．ＷＯ ９２０９３９号Ａ２の第６図および第７図は、膝の外科手術において使用するバルーンおよび対応する穿孔テンプレートを示し、バルーンは一般的に卵形の膨張可能な部分から突起する足部分を有する。

【０００８】

最後に、米国特許第６，２０６，９２７号には、自動心合せ（ｃｅｎｔｅｒｉｎｇ）半月補形装置が記載されており、この装置は大腿顆と対応する脛骨プラトーとの間の空洞の中への、侵襲性を最小にした、装置外科的移植に適当であり、そしてこの装置の輪郭と膝の自然の関節が自由浮遊性装置に対して回復力を発揮するように、硬い、高弾性物質から構成されている。関係する方法であるように思われるものにおいて、Ｓｕｌｚｅｒは膝における骨関節炎を治療するために１区画の間置スペーサーを導入した。下記の文献を参照のこと：”Ｌｉｔｔｌｅ Ｄｅｖｉｃｅ Ｃｏｕｌｄ Ｐａｃｋ ａ Ｂｉｇ Ｐｕｎｃｈ”，Ｓｕｌｚｅｒ Ｍｅｄｉｃａ Ｊｏｕｒｎａｌ Ｅｄｉｔｉｏｎ ２／２０００（ｗｗｗ．ｓｕｌｚｅｒｍｅｄｉｃａ．ｃｏｍ／ｍｅｄｉａ／ｓｍｊ－ｆｕｌｌ－ｔｅｘｔ－６．ｈｔｍｌ）。この装置は金属の腎臓の形のインサートとして記載されており、損傷した軟骨のために大腿と脛骨との間に充填される。

【０００９】

このような金属の装置は、Ｆｅｌｌの特許および／またはＳｕｌｚｅｒの製品の文献に記載されているように、特に製品が「その位置を固定する物理的手段を欠く」硬い自動心合せ半月装置であるので、中程度～重度の軟骨軟化症の若い患者において使用するために適当であると記載されている。そのように実施するとき、Ｆｅｌｌ他の装置は有意な量の無傷の軟骨および半月を必要とする傾向がある。本明細書に記載する改良された態様を包含する、今日までの出願人自身の製品は、このような健康な軟骨を欠如する、いっそう高齢の患者に対して主として適合する。引き続いて、出願人の装置は関節表面における移植片の角度の補正および改良された固定を提供する傾向がある。

【００１０】

今日までの進展にかかわらず、製造および使用の容易さ、および体内の性能のような性質

の最適な組み合わせを提供する、関節補形システムを必要されている。
発明の概要
本発明は、整形外科的関節、特に膝のような連結する関節の摩耗表面を創造または修正する方法およびシステムを提供する。１つの好ましい態様において、この方法は、少なくとも一部分、硬化性生体適合物質の硬化の種々の段階、引き続いて、硬化したまたは硬化性の生体適合物質から構成成分を形成する種々の段階を所望の方法で相関させ、最適化することができる。引き続いて、このような方法は使用するための構成成分を一般的にかつ特異的にその場で成形する能力を提供する。
【００１１】
本発明は、種々の態様を包含し、それらの各々は好ましくは１以上の構成成分を含み、これらの構成成分は生体外で成形され、その場で最終的に形成または組立てられて、最終の人工的および接合関節表面を提供するように適合されている。種々の態様の例は、例えば、下記のものを包含する：
１） 構成成分を挿入し、最終的にその場で形成することができる方法で、各々が生体外で部分的に成形される、１以上の構成成分、
２） その場で、例えば、オーバーラップまたはインターロックする方式で、組立てるように適合された、複数の予備形成された構成成分、
３） 関節部位内に挿入し、位置決定するように適合されており、最終のプロテーゼを形成するために型と接触しおよび／または組み合わせて流動性生体適合物質を硬化させる条件下に、開放金型にその場で送出すように適合された流動性生体適合物質と組み合わせて使用される、挿入可能な開放 （例えば、ソーサー形） 金型、
４） その場で位置決定し、対応する硬化性生体適合物質を充填するように適合された、１以上の一般的に拡張性のエンベロープ （例えば、バルーンタイプの） 型、１以上の型それら自体は一般的に非拡張性の、予備形成された物質の１以上の領域を提供する。１つの態様において、例えば、複数のこのようなエンベロープ部分 （例えば、２区画の単一のエンベロープ） は、それぞれ、中央および側方の脛骨表面上に使用するように適合させることができる。
【００１２】
適当な生体適合物質、および本明細書に記載する他の特徴を選択し、使用することによって、本発明は、以前に記載された方法に比較して、利点の最適な組み合わせを提供する。このような利点は、製造および貯蔵の過程において生ずる利点 （例えば、無菌性、貯蔵安定性） 、外科的分野それ自体において生ずる利点 （例えば、使用の容易さ、適合性、予測性） 、および体内の長期使用の過程において生ずる利点 （例えば、生物適合性、湿潤硬化特性、組織適合性および順応性、保持性、摩耗特性、および物理的－機械的性質） を包含する。
【００１３】
１つの好ましい態様において、この方法およびシステムは、体の中に挿入し、配置するために、体の外側で成形することができ、かつ関節部位内でさらに成形して順応を増強することができる、部分的に硬化した構成成分の製造および使用を包含する。その場で１または２以上の構成成分を最終的に形成する能力は、種々の追加の利点、例えば、最終のプロテーゼの全体のサイズおよび形状のコントロールの増加、天然の骨を並置する表面の形状およびコンプライアンスの改善、および最終的に、対向する接合表面の形状およびコンプライアンスの改善を提供する。
【００１４】
本明細書において使用するとき、用語「硬化」およびその変化形は、本発明の構成成分を形成するために使用するとき、外科的部位における、構成成分を完全に形成する過程において考えられる物理化学的反応が何であっても、硬化性生体適合物質が、その場での長期使用間に、開始または完結する程度を意味する。引き続いて、生体適合物質は未硬化であると考えることができる （まだ混合されていない構成成分の部分またはまだ活性化されていない組成物におけるように） か、あるいはそれは部分的に硬化することができる （

例えば、構成成分が混合されているか、あるいは組成物が、硬化プロセスを開始するために適当な条件下に、活性化されるとき） か、あるいはそれは完全に硬化することができる （例えば、この場合において、起こった化学反応は何であっても実質的に終結している）。一般に、未硬化の組成物は無菌であり、貯蔵安定性であり、しばしば流動性であるが、典型的にはまだ成形されていないか、あるいは成形することができる。

【００１５】

硬化性組成物は、対照的に、一般に流動性組成物として開始するが、ゲル化または固化し始めるとき、有限の時間かかって非流動性となる。また、硬化性組成物は、例えば、体の外側で型および／または適当な造形ツールを使用することによって、および／または体内で、支持する骨上に最初に構成成分を位置決定しかつ対向する関節を形成する骨の表面を再位置決定することによって、最小限度に形成することができる。その後、本発明のある種の組成物は、例えば、長期使用の過程において関節を形成する骨の段階的作用により、経時的にさらに形成できることが考えられる。

【００１６】

また本明細書において使用するとき、用語「形成」、およびその変形語および変形は、関節部位において使用するために、一般的および／または特異的方法で、サイジングしかつ造形する方法および程度を意味する。引き続いて、このような構成成分の形成は生体外および／または生体内で、ならびに一般的方法 （例えば、生体外型またはツールを使用することによって） および／または特異的方法 （例えば、支持する骨および／または対向する関節を形成する骨の表面と並置されて最終的に硬化することによって） 、ならびにそれらの組み合わせにおいて実施することができる。

【００１７】

構成成分は、支持する骨表面および／または対向する （例えば、接合する） 骨表面の両方を包含する、その場の骨の対応する特異的形状および寸法に対して構成成分を順応させるために、この方法において「特異的に」形成することができる。このような特異的コンフォメーションは、引き続いて、快適さ、機械的性能、および／または長期安定性を包含する、最終移植片の種々の特性を改善するために使用することができる。このようなコンフォメーションは、また、１以上の構成成分、または複合プロテーゼを関節部位と相応して「順応」させる （例えば、その場で実施する最終の造形および硬化プロセスにより） 面を包含することができる。

【００１８】

また、このようなコンフォメーションは、構成成分、またはプロテーゼそれ自体を、例えば、力を加えることによって、部位内で「変形」させるように適合された面を包含することができる。例えば、実質的に完全に形成された構成成分は、関節部位の中に挿入し、通常の解剖学的力下に効果的に変形できるのに十分な機械的性質 （例えば、強さおよび弾力性） を有するように準備することができる。例えば、実質的に凸形の構成成分をその場で対応する凹形の形状にすると同時に、そのもとの凸形の形状に向かう傾向を有するのに十分な弾力性を保持することができる （例えば、ロッキング・ワッシャーを使用時に変形させるが、そのもとの形状に向かう傾向を有するようにさせる方法に類似する）。好ましくは、最終の膝構成成分は体内の使用条件下に （例えば、生理学的負荷下に） 、所望のサイズおよび脛骨適合性を維持しながら、かつ所望の角度の補正のために所望の勘合および厚さを提供する方法において、変形するように適合されている。

【００１９】

それゆえ、「予備形成された」構成成分は、一般に、例えば外科医の選択および適当なサイズの生体外型を使用することによって、生体外で少なくとも部分的に形成される構成成分を意味する。このような予備形成された構成成分は、その上、生体外方式において、例えばそれ自体意図する関節部位の特定の寸法および輪郭を反映する受注生産された型を使用することによって、特異的に形成することができる。このような受注生産された型は、例えば、外部の結像手段を使用することによって、および／または組織部位において取った陰型および／または陽型を適当に使用することによって調製することができる。必要に

応じて、かつ好ましくは、予備形成された構成成分は、全体的または部分的に、硬化プロセスが完結する前に、その場で位置決定し、支持する骨表面および対向する骨表面の両方に並置されて、特異的に形成される。いったん関節部位内に位置決定されると、任意のこのような構成成分またはプロテーゼはその場におけるその保持および／または性能を改善するように変形させる、例えば、混乱力を解放しかつ対向する骨表面を再位置決定するとき弾力的に変形するように適合させることができる。

【００２０】

例えば、予備形成された組成物を準備し、最初に硬化を生体外で開始することによって形成され、ここで組成物を硬化開始の１０秒～数日程度以内に、好ましくは約３０秒～約１０分以内に、より好ましくは約１～約５分以内に移植すると同時に、いったん体内に位置決定されたとき、表面の発熱を約５０℃より低く、より好ましくは約４５℃以内に維持することができる。

【００２１】

いったん生体内で位置決定されると、本発明の好ましい予備形成された構成成分は、約１０秒～１または２以上の時間、より好ましくは約１分～約５分の期間の間最終的に造形されるように適合される。下限は主として生体適合物質を再位置決定するか、あるいは移植片上に適当な力を他の方法で確立するために必要とする時間により定められる。上限は、引き続いて、一般にそれ以上の変形または造形に対する移植された組成物の感受性により定められる。一般に、このような最終の造形は少なくとも一部分、関節を形成する骨の表面を再位置決定することによって発生する力の下に達成される。１つの好ましい態様において、部分的に硬化した組成物は、生理学的力の下に、脛骨適合性を維持しかつ所望の角度の補正を付与しながら、約１５％より低い、好ましくは約１０％より低い、最も好ましくは約５％より低い変形を可能とする条件下に移植される。

【００２２】

それゆえ、本発明の特に好ましい予備形成された構成成分はその形成の開始の約１～約５分以内に移植することができ、そしていったん移植されると、生ずる移植片が所望の最終形態および機能を実質的に保持できる方法で、さらに約１～約５分の追加の期間の間さらに成形または形成することができる。

【００２３】

これにより、本発明のシステムは、これらの硬化および形成プロセスが相関する方法に基づいて、外科医に種々のオプションを提供する。１つの特に好ましい態様において、例えば、外科医は組成物を提供され、この組成物は生体外で部分的に硬化し、一般的に形成され、次いで体の中へ速やかに挿入し、関節部位に位置決定されるように適合されており、ここで組成物は完全に硬化するようになるの過程において最終的に、かつ特異的に形成される。

【００２４】

プロテーゼを生体外で部分的に硬化することによって、本発明のシステムは、例えば、匹敵する組成物を混合し、それが流動性である間、関節部位に送出すとき、生ずることがある潜在的問題（例えば、水分の存在下の硬化、および組織の存在下の表面の発熱）を減少させるか、あるいは回避することによって、調製プロセスをかなり簡素化する。驚くべきことには、本発明のシステムはこのようなプロテーゼの形成を可能とするばかりでなく、かつまた操作および関節の中への挿入（例えば、約１～約３ｃｍの切開を通して）を可能とする。いったん挿入されると、すべて合理的時間内に、プロテーゼを位置決定し、その場で形成することができる。実際は、この手順は外来患者の使用や局所麻酔が容易にできることが分かった。

【００２５】

その上、本発明のシステムは、下に横たわる骨の中への固定孔の形成、膝関節の破壊、靭帯の解放、脛骨プラトーの地ならし、および生体適合物質をなお流動性の形態で関節部位に典型的には直接送出することに関係する種々の他の手順のようなプロセスの使用を回避することができる。なお、本発明のプロテーゼは、下に横たわる骨との適合性の程度、摩

耗特性、骨折靭性、およびフィブリル化関節軟骨の回避のような性質の組み合わせを提供し、この性質の組み合わせは流動性の形態で送出し、主としてその場で硬化させる匹敵する生体適合物質を使用して得られる性質の組み合わせを満足させるか、あるいはそれを超える。

【００２６】

膝のような関節における中間的使用に加えて、本発明のシステムは、球およびソケットの関節、例えば、膝に適用するとき、特定の利点を提供する。１つのこのような態様において、バルーンに前述した生体適合物質を充填し、充填の前にまたは後に、脚窩内に挿入し、位置決定して、股関節部の補形部分を配置するための、柔軟で、快適な、耐久性のライニングを提供することができる。

【００２７】

それ以上の態様において、この方法およびシステムは、体の中への部位および配置のために、そして必要に応じて関節部位においてさらに勘合しかつ固定するために、体の外側で形成された１または２以上の部分的または完全に硬化された構成成分を調製しかつ使用することを包含する。典型的には、これらの予備形成された構成成分は、枕もとでの操作を少なくし、終末の滅菌、および製作部位における最終的な検査および解放の別法を提供する。

【００２８】

（詳細な説明）

本発明の方法およびシステム （例えば、１以上の予備形成された構成成分および／または硬化性生体適合物質および型） は、生体内における最終プロテーゼを調製するために使用することができる。プロテーゼは、支持する骨それ自体に並置されかつその上に保持される第１の主要な表面と、対向する （例えば、接合する） 骨のための摩耗表面を提供するように適合された第２の （一般的に実質的に並列および対向する） 主要な表面とを提供する。「上に保持される」とは、例えば、１以上の固定点を使用することによって、接着剤または他の適当な界面物質を使用することによって、縫合糸、ステープル、およびその他を使用することによって、および／または対向する関節を形成する骨の表面を再位置決定するとき達成される保持 （および必要に応じて変形を含む） 作用と一緒に、支持する骨の形状に適当に順応したまたは順応可能な骨接触表面の組み合わせにより達成される機械的ロックにより、最終プロテーゼをその意図する使用に適当な方法で支持する骨表面上で所望の位置に維持されることを意味する。

【００２９】

第１および第２の主要な表面は、任意の適当な方法、例えば、下記の方法により形成することができる：１） 単一の部分的に硬化し、一般的に予備形成された構成成分を調製し、好ましくは構成成分をさらに、かつ特異的に、生体内で形成させる条件下に、関節の中に挿入する、２） 組織部位の位置決定された初期の予備形成された構成成分 （例えば、バルーンまたは開放された型の形状の） に流動性生体適合物質を添加する、３） １以上の完全に硬化し、予備形成された構成成分を組織部位に配置し、必要に応じて要求される１以上の構成成分をさらに勘合させ、適合させ、および／または固定する、および／または４） １または２以上の構成成分をその場で組立て （例えば、表面上にインターロックする方式で並列させて） こうして組立てた構成成分が共同して第１および第２の主要な表面を提供するようにする。

【００３０】

１以上の部分的または完全に硬化した予備形成された構成成分および／または硬化性生体適合物質および関係する型に加えて、本発明の方法およびシステムは、例えば、骨表面それ自体を調製して、適当な界面 （例えば、接着剤界面および／または関節部位にさらに固定することができる突起、または必要に応じて大腿顆または脛骨プラトーの平滑化により） を提供し、１以上の表面を処理して、表面を提供する物質の固有の性質、およびその他に比較して異なるまたは改良された性質を表面に与えるために、種々の追加の物質および／または工程の任意の使用を包含する。このような物質の例は、例えば、接着剤物質

、組織内方成長刺激因子、および繊維状物質（例えば、移植片を拘束しおよび／または繊維状組織の内方成長を促進するように適合されたウェブ）の使用を包含する。

【００３１】

１以上の部分的または完全に硬化した予備形成された構成成分はそれら自体均一または不均一な性質を提供することができ、そして複数またはある範囲のスタイルまたはサイズで提供することができる。これらの構成成分は、側方または中央の区画、または両方に、および右または左の膝、または両方に順応するように設計することができる。好ましい態様において、すべての態様は侵襲性を最小にする方式で関節部位の中に挿入することができる。「侵襲性を最小にする」とは、これに関して、その場でプロテーゼをサイジングし、挿入し、位置決定し、そして形成する手順は、好ましくは、膝プロテーゼを挿入するために普通に使用されるタイプの開いた、侵襲性の切開を必要としないで達成できることを意味する。好ましい態様において、部分的に硬化した予備形成された構成成分をその場でさらに形成し、完全に硬化して、関節部位とのコンプライアンスを増強することができる。

【００３２】

また、例えば、ポリマーそれら自体を設計し、使用することによって、または完全に硬化したまたは硬化する態様を表面処理して、適当な反応性基、例えば、アミン基、ヒドロキシル基、または他の反応性または水素結合性官能基を提供することによって、１または２以上の部分的または完全に硬化した予備形成された構成成分の表面を変更して、任意の所望の性質を提供する（例えば、接着を促進する）ことができる。同様に、部分的に硬化した予備形成された構成成分または完全に硬化した構成成分、例えば、バルーンまたは複合物質に、適当な表面コーティング、例えば、生物学的に活性な物質を適用して、所望の組織の相互作用、例えば、組織または細胞の接着を促進することができる。このような生物学的に活性な物質は、例えば、サイトカイン、ヒドロキシアパタイト、コラーゲン、およびそれらの組み合わせから成る群から選択される。

【００３３】

本発明の１つの態様において、部分的に硬化した、かつ一般的に予備形成された構成成分を関節部位の中に挿入し、そこでさらに、特異的に形成してコンプライアンスを増強する。別の態様において、バルーンまたは開放された型の形態の完全に硬化した構成成分を使用して、バルーンまたは型を関節の中に挿入し、そこでそれに生体適合物質を充填し、生体適合物質をその場で硬化させ、関節部位に順応させることによって、最終の複合物質を調製することができる。他の別の態様において、１以上の完全に硬化した構成成分を準備し、単独でまたは少しずつ関節の中に挿入し、必要に応じてさらに生体内で勘合し、固定する。

【００３４】

第１のこのような態様の例として、本発明は、関節部位の所望の寸法に近似し、かつ硬化性生体適合物質を受け取るように適合された、開放生体外型を提供する。適当な型は、例えば、生体適合物質の構成成分を所望の時に容易にかつ完全に除去できるようにする慣用の物質、例えば、シリコーン物質を使用して、形成することができる。必要に応じて、型はそれ自体コーティングまたは剥離ライナー、例えば、全体的または部分的に、こうして形成された構成成分と一体化することができるコーティングを有することができる。いったん流動性生体適合物質がこの生体外型の中に送出され、部分的に硬化され、そして任意の成形または製作工程が実施されると、生体適合物質を型から取出し、それを生体内でさらにかつ最終的に形成して関節部位との順応を増強させる条件下に、関節部位の中に挿入することができる。必要に応じて、追加の生体外での形成工程または特徴は、例えば、生体内における挿入および最終的な形成前に、所望の曲率および大腿グライドパスを付与することによって、実施することができる。

【００３５】

また、構成成分を生体外で成形しおよび／またはそれを組織部位に移す過程において、種々の構造および／または物質を構成成分それ自体の中におよび／または上に組込んで、その場における配置、保持、および／または性能を増強することができる。例えば、型それ

自体は、組織部位に構成成分を提供しまたはその保持を改良するように適合された、種々の一体的構造の特徴、例えば、脛骨「タブ」を付与するために十分な形態で提供することができる。このようなタブは、例えば、型それ自体と一体でありかつ生体内で柔軟な組織および／または骨内におよび／またはそれに固定させて位置決定するように適合された１または２以上の突起の形態で提供することができる。このようなタブの例は、例えば、第１図に示されており、ここで参照番号１８は隆起した後部を描写する。

【００３６】

また、挿入可能な構成成分は、構成成分それ自体の大部分を形成するために使用されるもの以外の物質から形成された、１以上の補助的部分または突起を有することができる。例えば、その場の構成成分の初期および／または長期の保持の改良において使用するために、例えば、プロテーゼを関節部位および所望位置に拘束することによって、縫合糸または繊維状物質を大量の物質の中にまたは上に組込むことができる。生体適合物質が型を充填するとき、このような他の物質を型それ自体の中にまたは上に一時的に位置決定させるか、あるいはそうでなければ他の方法で、他の物質を生体適合物質の中に一体化させ、かつ生体外で部分的に硬化させる方法で、他の物質を準備することができる。生ずる構成成分をその場に位置させて、接着剤、縫合糸、ねじ、ピン、ステープルもしくはその他またはそれらの組み合わせを使用することによって、突起を取り囲む柔軟な組織および／または骨に固定することによって、突起を使用して移植片を拘束することができる。物質を経時的に体に吸収させ、および／または長期固定のために繊維状組織の内方成長を可能とするか、あるいは促進することによって、物質は即時の固定機能、および必要に応じてまた所望の長期機能の両方を提供することができる。

【００３７】

強化物質は任意の適当な形態で、例えば、繊維（例えば、縫合糸）として、あるいは必要に応じて１種または２種以上の強化繊維または層を含む、均一な織布または不織布として準備することができる。適当な不織布は、例えば、好ましくは商品名Ｔｒｅｖｉｒａ Ｓｐｕｎｂｏｎｄ（Ｈｏｅｃｈｓｔ Ｃｅｌａｎｅｓｅ Ｃｏｒｐｏｒａｔｉｏｎ）で商業的に入手可能な物質である。一般に、不織布は、一緒にニードルパンチしてフェルト様布帛にされた、連続的熱可塑性繊維から構成されている。Ｔｒｅｖｉｒａ Ｓｐｕｎｂｏｎｄのような布帛に加えて、他の物質、例えば、ポリエステルステープルマット、ガラス繊維のマット、ならびに他の有機および無機の繊維のマットおよび布帛を使用することができる。

【００３８】

強化用繊維を織布または不織布内に含めるか、あるいは複合体の別の層として準備することができる。このような繊維層は好ましくは有機または無機の構造強化用繊維の方向的強化用繊維層、例えば、炭素繊維、アラミド繊維（これはＤｕＰｏｎｔ Ｃｏｒｐｏｒａｔｉｏｎから商品名Ｋｅｖｌａｒで入手可能である）、線状ポリエチレンまたはポリプロピレン繊維（例えば、Ａｌｌｉｅｄ－Ｓｉｇｎａｌ，Ｉｎｃ．（現在Ｈｏｎｅｙｗｅｌｌ）から商品名Ｓｐｅｃｔｒａで入手可能である）、またはポリエステル繊維を包含することができる。「強化用繊維」という句は、自己の資質で使用するか、あるいは複合布帛物質に添加するとき、所望の構造的性質を保持するか、あるいは増強する、任意の繊維を包含することができる。繊維はランダムに配向させるか、あるいは１以上の方向に配向させることができる。強化用繊維層として使用するために多数の特定のタイプの物質が与えられてきているが、当業者は理解するように、他の同等のタイプの強化用繊維を本発明の実施において使用することができる。強化用繊維層それ自体を使用してプロテーゼを固定することができるか、あるいは多数の隙間または孔を有する織布または不織布に取り付けることができる。好ましくは、強化用繊維層または他の繊維層を、例えば、慣用の縫合、ニードルパンチ、ステープルまたはボタンにより、互いに機械的に固定する。ある種の用途の場合において、接着剤を使用することもできる。

【００３９】

同様に、例えば、関節部位との化学的相互作用を改良する表面特性を使用することによっ

て、構成成分のその場の保持を改良する適当な手段を部分的に硬化した予備形成された構成成分（および／またはその中に組込まれた補助的部分）に付加することもできる。嵩高物質の組成物それら自体を賢明に使用することによっておよび／または接着剤または他の適当な界面物質を使用することによって、このような相互作用を達成することができる。また、例えば、表面積を増加させ、引き続いて、機械的保持を改良する、粗面化、エッチングまたはクロスハッチにより、部分的に硬化した予備形成された構成成分を物理的に変更して、関節部位とのその相互作用を増加させることができる。また、例えば、接着剤、縫合糸、ねじ、ステープルまたはその他またはそれらの組み合わせを使用することによって、他の方法で取り囲む骨および／または柔軟な組織に固定される外部の手段により、部分的に硬化した予備形成された構成成分を保持することができる。関節を形成する骨に対向する主要な表面上において、部分的に硬化した予備形成された構成成分に、そのコンプライアンスおよび／または対向する骨表面との相互作用を改良するか、あるいは変更することを意図する適当な手段を取り付けることができる。

【００４０】

１つの特に好ましい態様において、システムは最初に関節部位の外側で成形され、組織部位に送出し、そこで固定位置に位置決定するように適合された、部分的に硬化した予備形成された構成成分を包含する。型は、それぞれ、一方または両方の主要な表面を予備形成するように適合された、開放または密閉された立体配置を有する（および／または１つまたは複数の成形プロセスを含む）ことができる。いったん位置決定されると、部分的に硬化した構成成分を関節部位内に最初に勘合し、位置決定し、その後生体内で関節部位の特定の寸法および／または形状（例えば、解剖学的構造）に対してよりよく順応するように適合される。必要に応じて、かつ好ましくは、型は関節部位に対して最適な接着性および順応性を有する構成成分を生ずる。また、生体外で部分的硬化プロセス間に型を加熱して、構成成分の性質を最適化するか、あるいは生体内でいっそう形成可能な構成成分を提供することができる。

【００４１】

別の好ましい態様において、この方法およびシステムは、体の中に挿入し、配置し、必要に応じて関節部位においてさらに勘合し、固定するために、１以上の完全にまたは部分的に硬化した構成成分を調製し、使用することを包含する。１つの態様において、本発明は、関節部位の中に挿入し、必要に応じて勘合または固定する単一の予備形成された構成成分を提供する。他の態様において、同一であるか、あるいは異なる物質から形成され、最終の構成成分を提供する方法で組織部位に送出し、位置決定するように適合された、複数の予備形成された構成成分を提供する。構成成分は、例えば、機械的ロックを提供することによっておよび／または界面物質、例えば、接着剤層を使用することによって、任意の適当な方式で部位において組み合わせることができる。構成成分は、例えば、骨上の層として、または組み合わせたとき、骨表面を横切るように適合された、個々の並列した構成成分として、任意の適当な方式で組み合わせることができる。１以上の予備形成された構成成分の使用において、枕もとの操作を少なくすることができ、そして終末の滅菌、および製作部位における検査および解放を実施する別法を可能とする。完全に硬化した予備形成された構成成分を使用して、本明細書に記載する部分的に硬化した予備形成された構成成分を保持する種々の手段が働くように適合させることができる。

【００４２】

本発明の方法およびシステムは、膝の脛骨プラトー、股関節部の関節陥、肩の関節窩、肩峰突起、肩鎖関節、足根の端部脛骨表面、肘の橈骨頭、前腕の端部橈骨、大足指の基部指節骨表面、親指の基部中手骨、および手首の菱形骨から成る群から選択されるヒト関節を包含する、種々の哺乳動物の関節を修復するために使用することができる。

【００４３】

骨表面と接触する予備形成された構成成分の部分または組み合わせは、調製された骨表面に、例えば、その巨視的物理的輪郭に精密に物理的に順応するように適合されることが好ましい。このようなコンフォメーションは任意の適当な方法により、例えば、下記の方法

により提供または増強することができる：１） まず生体外型中で作られ、次いで表面に対して順応するように適合されたまたは変更された （例えば、生体内でさらに形成することによって） 部分的に硬化した予備形成された構成成分を準備する、および／または２） 関節部位の中に挿入し、関節部位と順応するように生体内で硬化する流動性生体適合物質を充填する、予備形成されたバルーンまたは複合型物質を使用する、および／または３） 関節部位の中にいったん配置されると、生体適合物質のコンプライアンスのために最適な形状寸法を有する、１以上の完全に硬化した予備形成された構成成分を使用する、および／または４） 骨と予備形成された構成成分との間に適当な （例えば、薄い） 界面物質 （例えば、接着剤、充填剤、またはセメント物質） を調製し、使用する、および／または５） 構成成分それ自体中の突起に、またはそれを固定する外部の手段に取り付けられる物理的拘束手段、例えば、接着剤、ピン、ステープル、ねじ、縫合糸またはその他を使用する。

【００４４】

図面を参照して、本発明の方法およびシステムをさらに説明する。

【００４５】

図１は、本発明に従い生体外型を使用して製造された好ましい予備形成された膝移植片（１０） の平面および側面の斜視図を示す。この移植片は、脛骨表面上に位置決定されるように適合された第１の主要な表面 （１２） と、大腿顆に対して位置決定されるように適合された一般的に平らな第２の主要な表面 （１４） とを提供する。典型的な態様において、第２の主要な表面は、引き続いて、その場の動作を促進する大腿グライドパス（１６）を有することが好ましい。この大腿グライドパス （１６） は一般に中央の卵形のくぼみの形態であり、その最低点における深さが約１ ｍｍ～約５ ｍｍ （示されているように２ ｍｍ） 、長さが約３０ ｍｍ～約５０ ｍｍ、そして幅が１０ ｍｍ～３０ ｍｍ （示されているように４０ ｍｍ×２０ ｍｍ） である。当業者は、この説明が与えられると、絶対的用語および相対的用語期間の両方において、実際の関節のサイズおよび所望の結果 （例えば、角度の補正） のような因子に依存して、最適な使用のために実際の寸法を容易に決定するであろう。示されているように、移植片は、また、脛骨プラトーの後部をつかむように適合された、隆起した脛骨突起（１８）を有する。移植片は約４０～約６０ ｍｍ程度の前後の寸法、約３０ ｍｍ～約４０ ｍｍ程度の中央－側方の寸法、および約１０ ｍｍ～約２０ ｍｍ程度の後部リップにおける最大厚さを有する。

【００４６】

図２は、その場で挿入し、組立てて最終移植片 （２０） を形成するように、複数の予備形成された構成成分が適合されている態様を示す。図２ａは、予備形成された構成成分（それぞれ２２～２５） を並列する方法で順次に、かつその場で、かつ脛骨表面上で組立てる、態様を示す。かみ合わせ可能な予備形成された切片の各々は、生ずる骨接触表面および摩耗表面の少なくとも一部分、ならびに１または２以上のそれぞれ他の部分との機械的ロックを提供するように適合された１または２以上の部分を提供する。機械的ロックは、任意の適当な手段において、例えば、それぞれ対応する雄部分および雌部分を準備することによって達成することができる。これらの部分は、その場で、例えば、押込嵌め法または滑り法でかみ合わせてそれぞれの構成成分を取り付けることができる。同一態様の隆起した透視図、および第２ｂ図において見ることができるように、生ずるアセンブリーにおいて、組み合わされた構成成分は共同して脛骨接触表面 （２８） および摩耗表面（２６） の両方を提供する。

【００４７】

図３の選択的態様において、骨表面を横切って並列方式で （図２におけるように） 位置決定するよりむしろ、例えば、その場で予備形成された構成成分を互いに上に層状にするか、あるいは滑らせ、表面上に位置決定することによって、それらを互いに積み重ねることができる形態で挿入された、インターロックする予備形成された構成成分（この場合では、それぞれ、部分３１～３３）を使用して、最終移植片を準備する。これらの部分を任意の適当な方式で、例えば、完全に組織部位上に、完全に生体外で、または必要に応じて

変化する組み合わせで組立てることができる。必要に応じて、一般的に平らな部分は、例えば、溝およびタブの形態で、対応するかみ合わせ可能な部分を有して滑り勘合を提供するか、あるいはくぼみおよび対応する突起を有して、横方向の変位を所望の程度に防止するために十分なプレス嵌め、スナップ嵌め、または他の適当な勘合を提供する。生ずる形成されたプロテーゼ移植片は、本明細書に記載する種々の特徴、例えば、よりすぐれた勘合または性能を提供するように適合された所望の成形された部分を有することができる。部分（３１）は望ましい摩耗表面を提供するために特に十分に適しているが、１または２以上の中間的部分（要素３２で示されているように）は厚さ、クッション、および角度の補正のような性質の最適な組み合わせを提供するように適合されている。示されているように、一番下の部分（３３）は骨それ自体の中に形成された対応する固定孔または適当なくぼみ内に保持されるように適合された突起（３４）を有する。図３ｂおよび図３ｃは一般にそれぞれ底面図および上面図を提供し、部分を層状の方式で組み合わせることができる方法を示す。

【００４８】

図３の態様において、コンパクトな積み重ねを形成するように、各下に横たわる層（または骨）内の対応するくぼみの中に位置決定ように適合された突起を有する、予備形成された層が示されている。このような態様において、典型的には、対応するシステムは、初期の骨接触構成成分と摩耗表面を提供する最終の構成成分とを包含する、少なくとも２つ予備形成された構成成分を含むであろう。このシステムは１種以上の中間的層を提供することができ、例えば、それらの数および／または選択を使用して、最終の所望の高さを全体の複合体に提供し、および／または異なる性質（例えば、圧縮性、弾力性、組織の内方成長に関する）を提供し、および／または最初の構成成分と最終の構成成分との間の改良された保持を提供することができる。

【００４９】

図４ａは、実質的に開放された（ソーサー形）型（４０）を関節部位の中に挿入し、その場で対応する硬化性生体適合物質で充填する態様を示す。型の上部（４２）は開放されていて生体適合物質（図示せず）を受け取るが、下部（４４）は骨に接触するように適合された下の主要な表面（４６）を提供し、骨それ自体の中に空けられた対応する固定点内に位置決定されるように適合された充填された突起（４８）において終わる。カップの前部へり（５０）はカップそれ自体の平面に対して実質的に垂直であるが、後部へり（５２）は先細であって（かつ必要に応じて隆起して）脛骨脊椎の対応する形状を収容する。

【００５０】

示されているように、かつ成人のヒトにおいて使用するために、生体外型は約５ｍｌ～約１５ｍｌ程度の前もって決定した体積を収容する。本発明のそれ以上の利点として、生体適合物質の量は生体外型の体積に対応するように前もって決定し、コントロールすることができる。さらに、生体外型はサイジングおよび関節部位に対する順応性を最適にするように設計され、そしてＭＲＩソフトウェアを使用して関節部位のために最良の型を選択することができる。移植片の厚さ、それゆえ角度の補正をこの方法においてコントロールすることができる。

【００５１】

図４ｂは、図４ａの型装置の底面斜視図を示し、充填された突起（４８）を示す。後部へり部分は、再び対応する脛骨脊椎の典型的な形状を収容する、溝またはくぼみ（５４）を提供すると見ることができる。全体的に、型は脛骨表面に対応するように適合された、一般的に腎臓形の立体配置を取ると見ることができる。このような型は複数のサイズおよび形状で準備することができ、使用時に特定の患者の要求および外科医の望みを満足するように選択される。

【００５２】

図５ａおよび図５ｂは骨表面上に位置決定されている図４ａの型（図５ａ）を示し、突起は対応する固定点内に位置決定されており、そして（図５ｂにおいて）生体適合物質

送出しカニューレ（５６）の先端はその上に位置決定されており、そして流動性生体適合物質（５８）が送出過程にあることが示されている。

【００５３】

図６は、１または２以上の予備形成された構成成分を含む種々の選択的態様を示す。図６ａは単一のくさび形態様（６０）を示し、ここで後部（６２）は前部（６４）に比較してサイズが有意に増加している。図６ｂは異なる摩耗特性を有する部分（ここでは層）を提供するように成形された移植片（６６）を示し、別々に形成された下部（７０）に比較して改良された摩耗を有する予備形成された上部を含む。対照的に、図６ｃは外科手術時にその場で位置決定し、組立てるように適合された複数の構成成分（７２）を示す。これらは他のものに比較して改良された摩耗特性を有する上部（７４）を含み、下部（７８）は患者の形状寸法および所望の角度の補正に対して適当に形成されており、そして１（または２以上の）中央部分（７６）は上部と下部との間に位置決定されて所望の性質、例えば、全体の厚さ、角度、および／または物理化学的性質（例えば、モジュラス）を達成するように適合されている。

【００５４】

図６ｄは外科手術時に予備形成された物質から切断できる単一の片（８０）を示すが、図７は予備形成された構成成分、例えば、図６ｄに示す構成成分を固定する、種々の選択的手段を示す。これらは図７ａに示すようなグラウト（８２）または他の適当な界面物質の使用；図７ｂに示すような別々の外部の保持装置（８４）の使用；図７ｃにおけるような体それ自体を一般に横切る要素（８６）により例示されるような、外部に準備されたピン、ねじ、縫合糸、およびその他の使用；および図７ｄに示すような１または２以上の適当な表面に沿って位置決定された１以上の固定部分（８８）の使用を包含する。

【００５５】

図８は、図８ａにおけるような粗面化表面（９０）；またはそれぞれ図８ｂおよび図８ｃの要素９２および９４として示すタブ（例えば、布帛または縫合糸のような物質により提供される）を包含する、補助的部分および／または表面テキスチャーを使用することによって予備形成された部分を固定または安定化する種々の変形を示す。実際には、予備形成された構成成分は本明細書に記載または示した種々の特徴および態様の任意の組み合わせから利益を得ることができる。

【００５６】

図９は実質的に密閉された（バルーンのような）型の種々の態様を示し、これらは関節部位の中に挿入し、対応する硬化性生体適合物質を充填するように適合されており、型それ自体は予備形成された接合性の摩耗表面を提供し、一体的な予備形成された摩耗表面および部分（９８）を含む膨張可能なバルーン部分（９６）、ならびに膨張可能な部分に流動性生体適合物質を充填するように適合されたルーメン（１００）を示す図９ａを包含する。図９ｂは対応するバルーン（１０２）を示し、これは予備形成された部分をもたないが、その生体適合物質のルーメン（１０４）を含む。示されていないが、このバルーンまたは任意の態様は種々の内部および／または外部の表面コーティングを含むことができ、そして異なる所望の物理化学的性質（例えば、多孔度）を有する領域および／または層を有することができる。図９ｃは２区画の閉じたバルーン様型（１０６）を示し、ここで各区画はそれぞれの中央または側方の脛骨表面に順応するように適合されている。

【００５７】

図１０は、生体適合物質を充填するとき、股関節部中の接合性の表面の配置と関連して脚窩型（１１０）として使用するために適合した型を示し、この型は対応する大腿頭部を保持するように適合された凹形部分を形成する。この型は型を形成する内側密閉層と外側密閉層（それぞれ、１１６および１１４）との間の空間に取り付けられた、任意の適当な形態で充填するように適合された（例えば、除去可能な導管（図示せず）を使用する）、薄い一般的にカップ形の型を提供することが示されている。

【００５８】

図１１は、本発明の方法およびシステムと組み合わせて使用するために適当な膝蓋骨関節の形態を示す。図１１ａ～図１１ｃに示すように、この形態はアルミニウムまたは他の適当な支柱部分（１２４）を有するシリコーンまたは他の適当なパッド物質（１２２）と、末端のハンドルまたは握り部分（１２６）とを有する。使用において、膝を一般に４５度の角度にして、この片を大腿骨表面に対して形成し、アルミニウム支柱を曲げることによって、その形態を維持する。必要に応じて、大腿骨の中に切断して形成された固定点を使用して、骨から離れて保持された上のハンドルで型を骨に対して緊密に保持して、型と骨との間に硬化性生体適合物質を送出すことができるようにする。ポリマーが骨上に（かつ任意の固定点の中に）配置されたとき、ポリマーを適切に形成するのに十分な時間の間、型を維持し、次いで型を除去することができる。

【００５９】

出願人の同時係属仮米国特許出願第６０／２２８，４４４号に記載されているように、摩耗表面を創造するか、あるいは変更する方法およびシステムは、哺乳動物におけるもとの摩耗表面の形状に一般に順応するように、もとの摩耗表面の支持構造物に固定された移植物質を使用する。骨表面の末端が回転する、滑るか、あるいはローリングする表面、例えば、膝、指、股関節部、足指、脊椎、手首、肘、肩、足根、またはＴＭＪ関節における表面である方法またはシステム。移植片は下記のものとして機能するであろう：

ａ） スペーサー、

ｂ） 緩衝材、

ｃ） 改良された摩擦係数を有する表面（疾患を有する表面に比較して）、および／または

ｄ） 重量を支持する面積を増加させ、かつ関節部位の適合性を改良する（疾患状態に比較して）。

【００６０】

本発明の方法およびシステムは、無菌的壊死、例えば、手首における舟状骨の領域に適用することができる。移植すべき物質は、複数の物質、例えば、ポリマー、例えば、ポリウレタン、ポリエチレン、ポリ尿素、ポリアクリレート、ポリウレタンアクリレート、ヒドロゲル、エポキシおよび／または上記の任意のハイブリッドから成る。

【００６１】

別の態様において、表面は１連の金属、例えば、チタン、ステンレス鋼、コバルトクロムミリチウム合金およびタンタルで形成することができる。他の表面物質は種々のセラミックおよび生物学的ポリマーを包含することができる。

【００６２】

再表面形成のための移植可能な物質は、成形された形状に硬化する、注射可能な物質として、生体外および／または生体内で形成することができる。状態を液体から固体に変化させる方法は、冷却または加熱、状態の変化を可能とする時間経過、または異なる反応物間の化学反応を包含する。この反応は発熱性または吸熱性であることができる。硬化は光活性化または化学的に触媒することができるか、あるいは加熱活性化することができる。このようなシステムの例は、２またはそれ以上の成分の流動性ポリマー、光活性化ポリマー、および触媒または熱、例えば、体の熱により硬化されたポリマーを包含する。型はバルーン、ダムまたは保持装置の形態で使用することができる。型は局所的解剖と組み合わせて使用して、所望の形状および形状寸法を生成することができる。型は保持されかつ移植片の一部分となるか、あるいは生体適合物質の成分の硬化後に除去できる物質から構成することができる。

【００６３】

別の態様において、物質は半固体であり、成形し、次いで生体内で硬化することができる。これは関節鏡の侵入門を通して、または小さいミニ関節切開を通して、侵襲性を最小にする適用を可能とする。それ以上の態様として、物質を生体外で合成し、次いで移植片の所望の形状寸法およびサイズを前もって決定するために映像を使用して、勘合するように機械加工することができる。それ以上の別法として、ある範囲の移植片サイズを準備し、

手順の間にサイジングを達成することができる。成形物質を使用して生体外型を勘合し、移植直前に部位上で移植片を成形することができる。

【００６４】

移植片の固定法は、移植片を下に横たわる表面に接着させる生物学的接着剤、機械的固定を引き起こす表面上の穴の中への移植片の捕捉、下に横たわる構造物に対する種々のアンカーの使用、およびその表面への移植片の固定または型保持装置および／またはねじ、ステープル、縫合糸またはピンの使用を包含する。他の態様において、下に横たわる構造物中のアンカーはその表面に移植片を固定するために使用することができ、また、固定を確保するために組織内方成長システムを使用することができる。

【００６５】

好ましい態様において、患者は骨関節炎の診断を有し、関節を形成する表面上の軟骨を喪失している。関節の正常の角度を再達成するために必要な補正量を決定する。靭帯をバランスさせて、移植片を所定位置にしてある範囲の運動の喪失が存在しないようにし、かつ究極的に生ずる表面の形状寸法がもとの関節表面と同一平面および配向を再確立するような位置に表面を配置させる。

【００６６】

部位へのアクセスは侵襲性を最小にする方法で達成される。好ましい態様において、これは関節鏡侵入門を使用する関節鏡手段により実施される。別の態様において、関節を取り囲む神経、血管、筋肉または靭帯を犠牲にしないで、関節へのアクセスを可能とする小さい切開を使用するミニ関節切開により、アクセスは達成される。好ましい態様において、変性したフィブリル化した関節を形成する軟骨を軟骨下表面まで除去する。この表面を乾燥させ、適当な固定のために調製する。これは機械的固定を与えるか、あるいは代りに単純に水平および側方の安定性を提供する固定点を含むことができる。組織の接着を必要とする場合、乾燥および粗面化により、この表面を調製することができる。前もって作ったアンカーを設置することができる。これらは種々の金属物質またはポリマーから作ることができ、そして移植片を通して延びてそれを下に横たわる表面に固定するくぎから成ることができる。この取り囲む軟骨下骨を粗面化して、組織の内方成長または移植片接着を増強することができる。その場で硬化する技術を使用して移植片を設置する場合（出願人の仮親出願の図１および図４に示す方法において）、物質を移植するとき、関節上に配置されるダムまたは型により移植片の最終の寸法を決定する。

【００６７】

型内の外科的部位に形成された前もって作られた物質について、安定化の種々の形態、例えば、定着ピンまたはチタンねじを使用することができる。選択的に、前もって作られた物質は、患者の関節表面の映像化から開発された規格に対して工場（ｏｆｆ ｓｉｔｅ）で作ることができる。第３の態様において、複数のサイズを工場製とし、外科手術時に適当な移植片のサイズを選択することができる。この仮出願の図２に示されている２つの別法は、侵入門を通して設置できる単一のセグメントまたは侵入門を通して設置し、いったん関節の中に入ると固定することができる１連のセグメントを含む。セグメントを順次に配置し、次いで骨の中にカットされた固定点によるか、あるいはねじまたは組織の内方成長により骨に固定させることができる。最終的に、ロボット、ジャグまたは他のカッティングジグを使用して、固定点の固定された形状寸法に対して前もって作られた移植片のために骨表面を調製することができる。

【００６８】

予備形成された構成成分および、生体適合物質（使用する場合）の両方は、任意の適当な物質から製造することができる。典型的には、物質は生物適合性、物理的強さおよび耐久性のような性質、および最終の複合体において使用する他の成分（および／または生体適合物質）との適合性を有するポリマー物質を包含する。１または２以上の予備形成された構成成分の製造において使用するために適当な物質の例は、その場で硬化する生体適合物質と同一であるか、あるいは異なることができ、そしてポリウレタン、ポリエチレン、ポリプロピレン、ダクロン（Ｄａｃｒｏｎｓ）、ポリ尿素、ヒドロゲル、金属、セラ

ミック、エポキシ、ポリシロキサン、ポリアクリレート、ならびにバイオポリマー、例えば、コラーゲン、コラーゲンをベースとする物質またはその他およびそれらの組み合わせを包含する。

【００６９】

使用する場合、流動性物質の製造において使用するために適当な物質の例は、ポリウレタン、ポリ尿素、ヒドロゲル、エポキシ、ポリシロキサン、ポリアクリレート、およびそれらの組み合わせを包含する。

【００７０】

現在好ましい態様において、予備形成された構成成分および、流動性生体適合物質（使用する場合）の各々は、生物適合性ポリウレタンを含んでなる。同一であるか、あるいは異なるポリウレタン配合物を使用して、例えば、射出成形技術により、予備形成された構成成分、ならびに、流動性生体適合物質（存在する場合）の両方を形成することができる。

【００７１】

予備形成された構成成分または生体適合物質として使用するために適当なポリウレタンは、（１） １以上のポリオール、および１以上のジイソシアネート、および必要に応じて、１以上の疎水性添加剤の反応生成物を含んでなる擬プレポリマー、および （２） １以上のポリオール、１以上の連鎖延長剤、１以上の触媒、および必要に応じて、他の成分、例えば、酸化防止剤、および疎水性添加剤を組み合わせることによって製造することができる。

【００７２】

その場で硬化性のポリマーを使用する態様において、本発明は、好ましくは、使用時に混合して流動性組成物を形成し、硬化を開始することができる複数の部分を含んでなり、硬化性ポリウレタン組成物を提供し、その部分は下記のものを包含する： （１） １以上のポリオール、および１以上のジイソシアネート、必要に応じて、１以上の疎水性添加剤を含んでなる擬プレポリマー、および （２） １以上のポリオール、１以上の連鎖延長剤、１以上の触媒、および必要に応じて、他の成分、例えば、酸化防止剤、疎水性添加剤および色素。混合すると、組成物は十分に流動性であって体に送出すことができ、そしてそこで生理学的条件下に完全に硬化する。好ましくは、構成成分の部分はそれ自体流動性であるか、あるいは流動性として、それらの混合および使用を促進することができる。

【００７３】

本発明において使用する流動性生体適合物質は、好ましくは生体外またはその場で反応して固体のポリウレタン （「ＰＵ」） を生成するポリウレタンプレポリマー成分を包含する。生成したＰＵは、引き続いて、硬質セグメントおよび軟質セグメントの両方を包含する。硬質セグメントは典型的にはジイソシアネートおよび連鎖延長剤から形成した剛性オリゴウレタン単位から構成されるが、軟質セグメントは典型的には１以上の柔軟なポリオール単位から構成される。これらの２タイプのセグメントは互いに不相溶性である傾向があるので、一般に相分離して硬質および軟質のセグメントドメインを形成する。当業者は、この教示が与えられると、形成したポリウレタン中の硬質および軟質のセグメントの相対量、ならびに相分離の程度がポリマーの最終の物理的および機械的性質に対して有意な衝撃を与える方法を理解するであろう。引き続いて、当業者は、このようなポリマー組成物を操作して、本発明の範囲内に入る性質の所望の組み合わせを有する硬化したおよび硬化するポリマーを製造する方法を理解するであろう。

【００７４】

ジイソシアネートまたは多官能性イソシアネートと連鎖延長剤との間の反応により、ポリマーの硬質セグメントを形成できる。本発明の硬質セグメントの製造に適当なイソシアネートのいくつかの例は、芳香族ジイソシアネートおよびそれらのポリマーの形態または異性体の混合物またはそれらの組み合わせ、例えば、トルエンジイソシアネート、ナフタレンジイソシアネート、フェニレンジイソシアネート、キシリレンジイソシアネート、およびジフェニルメタンジイソシアネート、およびこの分野において知られている他の芳香族ポリイソシアネートを包含する。本発明の硬質セグメントの製造に適当なポリイソシアネ

ートの他の例は、脂肪族および脂環族イソシアネートおよびそれらのポリマーまたは混合物またはそれらの組み合わせ、例えば、シクロヘキサンジイソシアネート、シクロヘキシル－ビスメチレンジイソシアネート、イソホロンジイソシアネートおよびヘキサメチレンジイソシアネートおよび他の脂肪族ポリイソシアネートを包含する。芳香族および脂肪族またはアリールアルキルジイソシアネートの組み合わせを使用することもできる。

【００７５】

イソシアネート成分は任意の適当な形態で準備することができ、それらの例は２，４’－ジフェニルメタンジイソシアネート、４，４’－ジフェニルメタンジイソシアネート、およびそれらの異性体の混合物または組み合わせ、および必要に応じて少量の２，２’－ジフェニルメタンジイソシアネート（典型的には商業的に入手可能なジフェニルメタンジイソシアネート）を包含する。他の例は芳香族ポリイソシアネートおよびそれらの混合物または組み合わせ、例えば、アニリンおよびホルムアルデヒドの縮合生成物のホスゲン化から誘導されたものを包含する。より揮発性の物質、例えば、トルエンジイソシアネートよりむしろ、低い揮発性を有するイソシアネート、例えば、ジフェニルメタンジイソシアネートを使用することは適当である。特に適当なイソシアネート成分の例は、４，４’－ジフェニルメタンジイソシアネート（「ＭＤＩ」）である。選択的に、それはＭＤＩの２，２’－、２，４’－および４，４’異性体の組み合わせとして液体の形態で提供される。好ましい態様において、イソシアネートはＭＤＩおよびなおより好ましくは４，４’－ジフェニルメタンジイソシアネートである。

【００７６】

本発明の硬質セグメントを製造するための連鎖延長剤のいくつかの例は下記のものを包含するが、これらに限定されない：短鎖ジオールまたはトリオールおよびそれらの混合またはそれらの組み合わせ、例えば、１，４－ブタンジオール、２－メチル－１，３－プロパンジオール、１，３－プロパンジオールエチレングリコール、ジエチレングリコール、グリセロール、シクロヘキサンジメタノール、トリエタノールアミン、およびメチルジエタノールアミン。本発明の硬質セグメントを製造するための連鎖延長剤の他の例は下記のものを包含するが、これらに限定されない：短鎖ジアミンおよびそれらの混合またはそれらの組み合わせ、例えば、ジアニリン、トルエンジアミン、シクロヘキシルジアミン、およびこの分野において知られている他の短鎖ジアミン。

【００７７】

軟質セグメントは、ポリイソシアネートまたはジイソシアネートまたはポリマーのジイソシアネートおよびポリオールの間の反応により形成した、ウレタン末端ポリオール部分から成る。適当なジイソシアネートの例は上に記載したとおりである。本発明の軟質セグメントを製造するためのポリオールのいくつかの例は下記のものを包含するが、これらに限定されない：アルキレンオキシド（例えば、エチレンオキシド、プロピレンオキシド、およびそれらのブレンド）、ならびにテトラヒドロフランをベースとするポリテトラメチレンエーテルグリコール、ポリカプロラクトンジオール、ポリカーボネートジオールおよびポリエステルジオールならびにそれらの組み合わせの縮合から誘導されたポリアルキレンオキシドエーテル。好ましい態様において、ポリオールはポリテトラヒドロフランポリオール（「ＰＴＨＦ」）であり、これらはまたポリテトラメチレンオキシド（「ＰＴＭＯ」）またはポリテトラメチレンエーテルグリコール（「ＰＴＭＥＧ」）として知られている。なおより好ましくは、２５０、６５０、１０００、１４００、１８００、２０００および２９００から成る商業的に入手可能な群から選択される異なる分子量を有する２種またはそれ以上のＰＴＭＯを使用する。

【００７８】

異なる分子量の２種以上のＰＴＭＯジオールは、ブレンドとしてまたは別々に、かつ２部系の異なる部間のような独立の方式で使用することができる。ＰＴＭＯジオールの固化温度は一般にそれらの分子量に比例する。ＰＴＭＯジオールと連鎖延長剤、例えば、１，４－ブタンジオールとの適合性はジオールの分子量に逆比例する。したがって、「硬化剤」（Ｂ部分）成分中の低分子量ＰＴＭＯジオール、およびプレポリマー（Ａ部分）成分

中の高分子量ＰＴＭＯジオールの混入は、比較的低温において使用できる２部系を提供することができる。引き続いて、低分子量ＰＴＭＯジオールと連鎖延長剤、例えば、１，４－ブタンジオールとのすぐれた適合性は、より高い（プレポリマー／硬化剤）容積比の２部系の製造を可能とする。また、アミン末端ポリエーテルおよび／またはポリカーボネートをベースとするジオールを軟質セグメントの構築に使用することができる。

【００７９】

ＰＵは、例えば、多官能性もしくは分枝鎖状ＯＨ末端架橋剤または連鎖延長剤、または多官能価イソシアネートを添加することによって、化学的に架橋することができる。適当な架橋剤のいくつかの例は下記のものを包含するが、これらに限定されない：トリメチロールプロパン（「ＴＭＰ」）、グリセロール、ヒドロキシル末端ポリブタジエン、ヒドロキシル末端ポリブタジエン（ＨＯＰＢ）、トリマーアルコール、ヒマシ油ポリエチレンオキシド（ＰＥＯ）、ポリプロピレンオキシド（ＰＰＯ）およびＰＥＯ－ＰＰＯトリオール。好ましい態様において、ＨＯＰＢを架橋剤として使用する。

【００８０】

化学的架橋剤は、適用温度においてガラス状態である硬質セグメントドメインによるポリマーの物理的または「事実上の」架橋を増強する。最適レベルの化学的架橋は物質の圧縮永久歪を改良し、抽出可能な成分の量を減少し、そしてＰＵの生物耐久性を改良する。これは比較的柔軟性のポリウレタン、例えば、損傷した軟骨の修復に適当であるポリウレタンにおいて特に有用であることがある。事実上の架橋単独による強化は、ある種の用途における生体内性能のために十分な強度を発生しない。より高い官能性のポリオールの使用による潜在的に発生した、軟質セグメントからの追加の架橋を使用して、より剛性の、より少ないエラストマーの物質を提供することができる。この方法において、硬質セグメントおよび軟質セグメントのバランス、および全体の性質に対するそれらの相対的寄与を達成することができる。

【００８１】

さらに、本発明のポリマーシステムは好ましくは少なくとも１以上の生物適合性触媒を含有し、これらの触媒は下記の期間を含む、硬化プロセスのコントロールを促進することができる：（１）誘導期間および（２）生体適合物質の硬化期間。絶対的長さおよび比較的長さを包含する、これらの２つの期間、および各期間内の加速または硬化の速度は、一緒になって、組成物の硬化反応速度またはプロファイルを決定する。本発明の形成したＰＵを製造するために適当な触媒のいくつかの例は下記のものを包含するが、これらに限定されない：錫および第三級アミン化合物またはそれらの組み合わせ、例えば、ジブチル錫ジラウレート、および錫または混合錫触媒、例えば、商品名「Ｃｏｔｉｎ ２２２」で入手可能な触媒、「Ｆｏｒｍｒｅｚ ＵＫ－２２」（Ｗｉｔｃｏ）、「ｄａｂｃｏ」（Ｓｉｇｍａ－Ａｌｄｒｉｃｈからのトリエチレンジアミン）、オクタン酸第一錫、トリメチルアミン、およびトリエチルアミン。好ましい態様において、触媒はＦｏｒｍｒｅｚ ＵＫ－２２（Ｗｉｔｃｏ）である。別の好ましい態様において、触媒はＣｏｔｉｎ ２２（ＣａｓＣｈｅｍ）とｄａｂｃｏ（Ｓｉｇｍａ－Ａｌｄｒｉｃｈ）との組み合わせである。

【００８２】

本発明の生体内および生体外硬化したポリウレタンは、２部分の反応による形成することができる。その部分Ｉ（選択的に部分Ａと呼ばれる）は、１以上のＯＨ末端化合物と、１以上のイソシアネートとの反応生成物である、２または多官能性イソシアネートまたは擬プレポリマーを包含する。ポリウレタンの部分ＩＩ（ここにおいて選択的に部分Ｂと呼ばれる）は、１以上の連鎖延長剤および１以上のポリオール、および１以上の触媒、および他の添加剤、例えば、酸化防止剤および色素を含む硬化剤成分である。適当な形成したＰＵについて、部分Ｉ（擬プレポリマー）とＩＩ（硬化剤成分）との間の化学量論は、イソシアネート末端プレポリマー（部分Ｉ）／硬化剤成分（部分ＩＩ）のＮＣＯ：ＯＨのモル比で表して、好ましくは約０．８／１．０～１．２／１．０、より好ましくは約０．９／１～約１．１／１．０の範囲内である。

【００８３】
必要に応じて、反応性ポリマー添加剤を添加することができ、そしてこのような添加剤はポリブタジエン、ポリイソプレン、ポリイソブチレン、シリコーン、ポリエチレン－プロピレンジエン、ブタジエンとアクリロニトリルとのコポリマー、ブタジエンとスチレンとのコポリマー、イソプレンとアクリロニトリルとのコポリマー、イソプレンとスチレンとのコポリマー、およびそれらの混合物から成る群から選択される。ヒドロキシルまたはアミン末端化合物からなる群から選択される。
【００８４】
本発明において使用するために適当な組成物は、それらの製造、適用、および生体内使用に関する性質の最適な組み合わせを提供するポリマー物質である。未硬化の状態において、このような性質は成分の混和性または適合性、加工性、適切に滅菌できるまたは無菌的に加工および貯蔵できる能力を包含する。このような組成物を適用する過程において、適当な物質は流動性、成形性、および生体内硬化性のような性質の最適な組み合わせを示す。硬化した状態において、適当な組成物は強度（例えば、引張り強さおよび圧縮強さ）、モジュラス、生物適合性および生物安定性のような性質の最適な組み合わせを示す。
【００８５】
硬化したとき、組成物は、特にコンフォメーションの安定性および物理的形状の保持、生物適合性、および物理的性能、ならびに機械的性質、例えば、負荷を支持する強さ、剪断強さ、剪断疲労抵抗、緩衝性、摩耗抵抗、および表面磨耗抵抗のような性質の最適な組み合わせを示す。このような性能は、天然の組織および関節の評価、ならびに一般に物質およびポリマーの評価について普通に受け入れられている手順を使用して評価することができる。特に、好ましい組成物は、硬化した形態で、提供または置換しようとする天然組織の機械的性質に近似するか、あるいはそれらを超える機械的性質を示す。
【００８６】
これらの所望の未硬化および送出特性を達成するために、「ポリマー系」は、本明細書において使用するとき、本発明のポリマー組成物を製造するために使用する１または２以上の成分を意味する。好ましい態様において、ポリマー系は２つの部分を形成するために必要な成分を含んでなる：部分ＩはＮＣＯ末端プレポリマー（必要に応じて「イソシアネート擬ポリマー」と呼ぶ）である。典型的には、部分Ｉの擬ポリマーは、必要に応じて疎水性添加成分、および過剰のイソシアネート成分と組み合わせて、ポリオール成分を含む。２成分系の部分ＩＩは、１つの長鎖ポリオール、連鎖延長剤および／または架橋剤、ならびに他の成分（例えば、触媒、安定剤、可塑剤、酸化防止剤、色素およびその他）を包含することができる。このようなアジュバントまたは成分は、混合、送出、および／または硬化の前にまたは時に任意の他の成分に添加するか、あるいはそれと組み合わせることができる。
【００８７】
特に好ましい態様において、本発明のポリマー系は複数の成分の部として提供され、そして１以上の触媒を使用する。触媒を包含する、成分の部分を混合して硬化を開始し、次いで送出し、所望の目的に十分な条件（例えば、時間および発熱）下に固化し、完全に硬化させることができる。硬化が完結すると、生ずる組成物は障害または損傷した組織の修復または置換において使用するために最適な性質の組み合わせを提供する。特に好ましい態様において、配合物は生体適合物質部分の適合性および安定性、生体外または生体内の硬化能力および特性（例えば、抽出可能なレベル、生物適合性、熱的／機械的性質）、機械的性質（例えば、引張り、引裂きおよび疲労性質）、および生物安定性のような性質の最適な組み合わせを包含する。
【００８８】
また、部分の容積比を使用して、未硬化および硬化の性質を改良し、影響を与えることができる。２以上の部分を有する組成物は好ましい。２部分を使用するとき、相対的容積は、例えば、１：１０～１０：１（擬プレポリマー／硬化剤成分、容積に基づく）である。現在好ましい範囲は２：１～１：２である。本発明の説明が与えられると、当業者は理

解するように、最適な容積比は主として部分Ａおよび部分Ｂの適合性および安定性により決定される。

【００８９】

所定の配合物について最適な容積比を選抜するとき、本発明の説明が与えられると、当業者は下記の考察を処理することができる方法を理解するであろう。予備形成された構成成分を射出成形するために、またはその場の硬化のために使用する温度において、反応性部分の粘度は、カートリッジ、静止ミキサー、ガンおよび他の構成成分を含む送出システムの任意の構成成分の機械的破損を引き起こさないで、許容される程度の混合および流れ速度を提供すべきである。

【００９０】

好ましくは、生体適合物質は十分に流動性であって、型または組織部位の中にそれを送出（例えば、注入）することができるべきである。両方の反応性部分の組成は、これらの部が適用の温度範囲において均質性であり、かつ相安定性であるような組成であるべきである。一般に、反応の発熱の最高温度は混合したポリマー中の反応性基の濃度に対して比例する。高濃度の反応性基は高過ぎる反応発熱エネルギーを発生させ、したがって取り囲む組織に熱的損傷を引き起こすことがある。反応性部分は好ましくは混合の間は実質的に液体の形態に止まるであろう。

【００９１】

成分の所望の安定な容積比は、任意の方法において、例えば、一定の容積比を有し、二重区画のカートリッジを使用するか、あるいは各成分について独立的に可変の送出速度を有し、注入装置を使用することによって達成することができる。

【００９２】

また、さらに他の方法で、例えば、ポリマーの適用前に成分を予熱することによって、組成物の適合性に影響を与える（かつ改良する）ことができる。組成物の均質性を増強するために、本発明の好ましい組成物の成分を、混合および送出し前に、例えば、使用前に約６０℃～約８０℃に約２～約６時間加熱することによって、予熱することが好ましい。

【００９３】

本発明の組成物を形成するとき使用するために適当な、完全に硬化したポリマー（例えば、ポリウレタン）の生体適合物質は、クリープおよび磨耗抵抗のような性質の最適な組み合わせを提供する。好ましくは、例えば、ＡＳＴＭ試験法Ｄ５９６３－９６（“Ｓｔａｎｄａｒｄ Ｔｅｓｔ Ｍｅｔｈｏｄｓ ｆｏｒ Ｒｕｂｂｅｒ Ｐｒｏｐｅｒｔｙ Ａｂｒａｓｉｏｎ Ｒｅｓｉｓｔａｎｃｅ Ｒｏｔａｒｙ Ｄｒｕｍ Ａｂｒａｄｅｒ”）により測定して、生体適合物質は約１００ mm^3 より低い、より好ましくは約８０ mm^3 より低い、最も好ましくは６０ mm^3 より低いＤＩＮ磨耗値を提供する。

【図面の簡単な説明】

【図１】

図１は、本発明に従い製造された好ましい予備形成された膝移植片の平面および側面の斜視図を示す。

【図２】

図２は、予備形成された構成成分が挿入され、その場で組立てるように適合されている態様を示す。

【図３】

図３は、予備形成された構成成分を使用する、別の態様を示す。

【図４】

図４は、実質的に開放された（ソーサー形）型を関節部位の中に挿入し、その場で対応する硬化性生体適合物質で充填する態様を示す。

【図５】

図５は、実質的に開いた（ソーサ形）型を関節部位の中に挿入し、その場で対応する硬化性生物物質で充填する態様を示す。

【図６】
図６は、１または２以上の予備形成された構成成分を含む、種々の選択的態様を示す。
【図７】
図７は、図６ｄに示すような予備形成された構成成分を固定する種々の選択的手段を示す。
【図８】
図８は、補助的部分および／または表面テキスチャーの使用により予備形成された部分を固定または安定化するための他の変法を示す。
【図９】
図９は、実質的に密閉された（バルーン様）型を関節部位の中に挿入し、対応する治癒性生体適合物質で充填するように適合されている、種々の態様を示す。
【図１０】
図１０は、股関節部における関節表面の置換と組み合わせて脚窩型として使用するように適合されている型を示す。
【図１１】
図１１は、本発明の法およびシステムと組み合わせて使用するために適当な膝蓋骨大腿関節の形態を示す。

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(54) **Title:** METHOD AND SYSTEM FOR MAMMALIAN JOINT RESURFACING

(57) **Abstract:** A method and system for the creation or modification of the wear surface of orthopedic joints, involving the preparation and use of one or more partially or fully preformed and procured components, adapted for insertion and placement into the body and at the joint site. In a preferred embodiment, component(s) can be partially cured and generally formed *ex vivo* and further and further formed *in vivo* at the joint site to enhance conformance and improve long term performance. In another embodiment, a preformed balloon or composite material can be inserted into the joint site and filled with a flowable biomaterial in situ to conform to the joint site. In yet another embodiment, the performed component(s) can be fully cured and formed *ex vivo* and optionally further fitted and secured at the joint site. Preformed components can be sufficiently pliant to permit insertion through a minimally invasive portal, yet resilient enough to substantially assume, or tend towards, the desired form *in vivo* with additional forming there as needed.

METHOD AND SYSTEM FOR MAMMALIAN JOINT RESURFACING

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of Provisional US Application Serial No. 60/228,444, filed August 28, 2000, the entire disclosure of which is incorporated herein by reference.

TECHNICAL FIELD

In one aspect, this invention relates to biomaterials formed *ex vivo* for implantation and use within the body. In another aspect, the invention relates to *in situ* curable biomaterials. In yet another aspect, this invention further relates to the field of orthopedic implants and prostheses, and more particularly, for implantable materials for use in orthopedic joints.

BACKGROUND OF THE INVENTION

Applicant has previously described, *inter alia*, prosthetic implants formed of biomaterials that can be delivered and finally cured *in situ*, e.g., using minimally invasive techniques. See for instance, U.S. Patent Nos. 5,556,429, 5,795,353, 5,888,220, 6,079,868, 6,140,452, 6,224,630 and 6,248,131 as well as published International Application Nos. WO 95/30388 and WO 97/26847 and International Application PCT/US97/20874 filed 11/14/97 (the disclosures of each of which are incorporated herein by reference). Certain of these applications describe, *inter alia*, the formation of a prosthetic nucleus within an intervertebral disc by a method that includes, for instance, the steps of inserting a collapsed mold apparatus (which in a preferred embodiment is described as a "balloon") through a cannula that is itself positioned through an opening within the annulus, and filling the balloon with a flowable biomaterial that is adapted to finally cure *in situ* and provide a permanent disc replacement. See also, Applicant's "Porous Biomaterial and Biopolymer

Resurfacing System" (PCT/US99/10004), as well as "Implantable Tissue Repair Device (PCT/US99/11740), and "Static Mixer" (PCT/US99/04407) applications.

See also, US Patent Nos. 3,030,951 (Mandarino), 4,203,444 (Bonnell et al.), 4,456,745 (Rajan), 4,463,141 (Robinson), 4,476,293 (Robinson), 4,477,604 (Oechsle, III), 4,647,643 (Zdrahala), 4,651,736 (Sanders), 4,722,948 (Sanderson), 4,743,632 (Marinovic et al.), 4,772,287 (Ray et al.), 4,808,691 (König et al.), 4,880,610 (Constanz), 4,873,308 (Coury et al.), 4,969,888 (Scholten et al.), 5,007,940 (Berg), 5,067,964 (Richmond et al.), 5,082,803 (Sumita), 5,108,404 (Scholten et al.), 5,109,077 (Wick), 5,143,942 (Brown), 5,166,115 (Brown), 5,254,662 (Szycher et al.), 5,278,201 (Dunn et al.), 5,525,418 (Hashimoto et al.), 5,624,463 (Stone et al.), 6,206,927 (Fell), and EP 0 353 936 (Cedar Surgical), EP 0 505 634 A1 (Kyocera Corporation), EP 0 521 573 (Industrial Res.), and FR 2 639 823 (Garcia) , WO 93/11723 (Regen Corporation), WO 9531946 (Milner), WO 9531948 (Kuslich).

Applicant's PCT Application No. PCT/US97/00457 (WO 9726847A1) includes the optional use of a mold, such as a balloon, and describes the manner in which "[t]he mold created within the joint is preferably of sufficient shape and dimensions to allow the resulting cured biomaterial to replace or mimic the structure and function of the removed fibrocartilage. The mold can be formed of synthetic and/or natural materials, including those that are provided exogenously and those provided by the remaining natural tissues. The mold can either be removed from the site, upon curing of the biomaterial, or is sufficiently biocompatible to allow it to remain in position."

Applicant's later PCT Application No. PCT/US97/20874 (WO 9820939A2) further describes the manner in which " 'mold' will refer to the portion or portions of an apparatus of the invention used to receive, constrain, shape and/or retain a flowable biomaterial in the course of delivering and curing the biomaterial *in situ*. A mold may include or rely upon natural tissues (such as the annular shell of an intervertebral disc) for at least a portion of its structure, conformation or function. The mold, in turn, is responsible, at least in part, for determining the position and final dimensions of the cured prosthetic implant. As such, its dimensions and other physical characteristics can be predetermined to provide an optimal combination of such properties as the ability to be delivered to a site using minimally invasive means,

filled with biomaterial, and optionally, then remain in place as or at the interface between cured biomaterial and natural tissue. In a particularly preferred embodiment the mold material can itself become integral to the body of the cured biomaterial."

Applicant's own use of such mold apparatuses to date has concentrated largely on the use of thin, extensible balloons adapted to be positioned and then filled *in situ* with curable biomaterial, with particular use as a replacement for the intervertebral disc following microdiscetomy. In turn, there has been considerably less focus, to date, on the use of any such molds in other joints, such as the knee. Figures 6 and 7 of Applicant's PCT Publication No. WO 920939 A2, for instance, shows a balloon and corresponding drilling template for use in knee surgery, the balloon having foot portions protruding from a generally ovoid inflatable portion.

Finally, US Patent No. 6,206,927 describes a self-centering meniscal prosthesis device suitable for minimally invasive, surgical implantation into the cavity between a femoral condyle and the corresponding tibial plateau is composed of a hard, high modulus material shaped such that the contour of the device and the natural articulation of the knee exerts a restoring force on the free-floating device. In what appears to be a related manner, Sulzer has introduced a unicompartmental interpositional spacer to treat osteoarthritis in the knee. See "Little Device Could Pack a Big Punch", Sulzer Medica Journal Edition 2/2000 (www.sulzermedica.com/media/smj-full-tex/2000/0002-full-text-6.html). The device is described as a metallic kidney-shaped insert which fills in for the damaged cartilage between the femur and the tibia.

Such a metallic device, as described in either the Fell patent and/or Sulzer's product literature, is described as appropriate for use in younger patients with moderate to severe chondromalacia, particularly since the product provides a hard, self-centering meniscal device that is "devoid of physical means that fix its location". In so doing, the device of Fell et al. tends to require a significant amount of intact cartilage and meniscus. Applicant's own products to date, including those improved embodiments described herein, have been largely geared toward more elderly patients, where such healthy cartilage is lacking. In turn, Applicant's devices tend to provide angular correction and improved anchoring of the implant at the joint surface.

In spite of developments to date, there remains a need for a joint prosthesis system that provides an optimal combination of properties such as ease of preparation and use, and performance within the body.

BRIEF DESCRIPTION OF THE DRAWING

In the Drawing:

Figure 1 shows top and side perspectives of a preferred preformed knee implant prepared according to the present invention.

Figure 2 shows an embodiment in which preformed components adapted to be inserted and assembled *in situ*.

Figure 3 shows an alternative embodiment in which preformed components are employed.

Figures 4 and 5 show an embodiment in which a substantially open (saucer-shaped) mold is inserted into the joint site, to be filled with a corresponding curable biomateral *in situ*.

Figure 6 shows a variety of alternative embodiments that include one or more preformed component.

Figure 7 shows a variety of alternative means for anchoring a preformed component such as that shown in Fig. 6d.

Figure 8 shows a further variety for anchoring or stabilizing a preformed portion by the use of ancillary portions and/or surface texture.

Figure 9 shows a variety of embodiments in a substantially closed (balloon like) mold is adapted to be inserted into the joint site and filled with a corresponding curable biomaterial.

Figure 10 shows a mold adapted for use as an acetabular mold in connection with the replacement of the articulating surface in a hip.

Figure 11 shows a patella femoral joint form suitable for use in combination with the method and system of this invention.

SUMMARY OF THE INVENTION

The present invention provides a method and system for the creation or modification of the wear surface of orthopedic joints, and particularly articulating

joints such as the knee. In one preferred embodiment, the method relies, at least in part, upon the manner in which the various stages of curing a curable biomaterial, and in turn, the various stages of forming a component from the cured or curing biomaterial, can be correlated and optimized in a desired manner. In turn, such a method provides the ability to both generally and specifically form the component for use *in situ*.

The present invention includes a variety of embodiments, each of which preferably includes one or more components that are formed *ex vivo*, and that are adapted to be inserted and finally formed or assembled *in situ* in order to provide a final prosthesis and articulating joint surface. Examples of the various embodiments include, for instance,

1) one or more components that are each partially molded *ex vivo*, in a manner that permits the component to be inserted and finally formed *in situ*,

2) a plurality of preformed components adapted to be assembled *in situ*, for instance in an overlapping or interlocking fashion,

3) an insertable open (e.g., saucer shaped) mold, adapted to be inserted and positioned within the joint site, and there used in combination with a flowable biomaterial adapted to be delivered to the open mold *in situ*, under conditions that permit the flowable biomaterial to cure in contact and/or combination with the mold in order to form a final prosthesis,

4) one or more generally extensible envelope (e.g., balloon- type) molds, adapted to be positioned and filled *in situ* with corresponding curable biomaterials, one or more of the molds themselves providing one or more regions of generally non-extensible, preformed material. In one embodiment, for instance, a plurality of such envelope portions (e.g., a bi-compartmental single envelope) can be adapted for use on both the medial and lateral tibial surfaces, respectively.

By the selection and use of a suitable biomaterial, and other features as described herein, the present invention provides an optimal combination of benefits, as compared to methods previously described. Such benefits include those that arise in the course of preparation and storage (e.g., sterility, storage stability), those that arise in the surgical field itself (e.g., ease of use, adaptability, predictability), and those that arise in the course of long term use within the body (e.g., biocompatibility,

moisture cure characteristics, tissue congruity and conformability, retention, wear characteristics, and physical-mechanical properties).

In one preferred embodiment, the method and system involve the preparation and use of partially cured components that can be formed outside the body, for insertion and placement into the body, and that can then be further formed within the joint site in order to enhance conformance. The ability to finally form one or more components *in situ* provides various additional benefits, such as increased control over the overall size and shape of the final prosthesis, improved shape and compliance of the surface apposing natural bone, and finally, improved shape and compliance of the opposite, articulating surface.

As used herein, the word "cure", and inflections thereof, will refer to the extent to which a curable biomaterial, as used to form a component of this invention, has begun or completed whatever physical- chemical reactions may be contemplated in the course of fully forming the component, at the surgical site, for long term use *in situ*. In turn, the biomaterial can be considered as uncured (as in component parts that have not yet been mixed or compositions that have not yet been activated), or it can be partially cured (e.g., wherein the components have been mixed, or compositions activated, under conditions suitable to begin the curing process), or it can be fully cured (e.g., in which case, whatever chemical reactions may have occurred have substantially subsided). Generally, uncured compositions are sterile, storage stable, and often flowable, though are typically not yet formed or capable of being formed.

Curing compositions, by contrast, generally begin as flowable compositions, but become nonflowable over a finite time period as they begin to gel or set. Curing compositions can also be minimally formed, e.g., outside the body by the use of molds and/or suitable shaping tools, and/or within the body, as by the initial positioning of the component on supporting bone and by the repositioning of opposing, articulating bone surfaces. Thereafter, it is contemplated that certain compositions of this invention can be further formed, over time, as by the gradual effect of articulating bone in the course of long term use.

As also used herein, the word "form", and inflections and variations thereof, will refer to the manner and extent to which a component has been sized and shaped, in either a general and/or specific manner, for use at a joint site. In turn, the forming

of such a component can occur either *ex vivo* and/or *in vivo*, as well as in a general manner (e.g., by the use of an *ex vivo* mold or tools) and/or a specific manner (e.g., by final curing in apposition to supporting bone and/or opposing articulating bone surfaces), as well as combinations thereof.

A component can be "specifically" formed in this manner in order to conform the component (and particularly its surfaces) to the corresponding specific shapes and dimensions of bone *in situ*, including both supporting bone surfaces and/or opposing (e.g., articulating) bone surfaces. Such specific conformation, in turn, can be used to improve a variety of characteristics of the final implant, including comfort, mechanical performance, and/or long term stability. Such conformation can also include aspects in which one or more components, or the composite prosthesis, are "conformed" in correspondence with the joint site (e.g., by final shaping and curing processes that occur *in situ*).

Such conformation can also include aspects in which the components, or prosthesis itself, are adapted to be "deformed" within the site, as by the application of force. For instance, a substantially fully formed component can be provided to have sufficient mechanical properties (e.g., strength and resilience) to permit it to be inserted into a joint site and effectively deformed under normal anatomic forces For instance, a substantially convex component can be deformed to assume the corresponding concave shape *in situ*, in , while retaining sufficient resilient strength to tend towards its original convex shape (e.g., analogous to the manner in which a locking washer can be deformed in use, while tending toward its original shape). Preferably, a final knee component is adapted to be deformed under conditions of use within the body (e.g., under physiologic load), while maintaining desired size and tibial congruency, and in a manner that provides desired fit and thickness for desired angular correction.

Hence a "preformed" component will generally refer to a component that is at least partially formed *ex vivo*, as by the surgeon's selection and use of an appropriately sized *ex vivo* mold. Such a preformed component can be specifically formed as well, including in an *ex vivo* fashion, as by the use of a customized mold that is itself reflective of the particular dimensions and contours of the intended joint site. Such customized molds can be prepared, for instance, by the use of external

imaging means, and/or by the appropriate use of negative and/or positive molds taken at the tissue site. Optionally, and preferably, the preformed component is specifically formed, in whole or in part, by being positioned *in situ*, prior to the completion of the curing process, and in apposition to both supporting bone and opposing bone surfaces. Once positioned within the joint site, any such component or prosthesis can be adapted to be deformed in order to improve its retention and/or performance *in situ*, e.g., resiliently deformed upon release of distracting forces and repositioning of the opposing bone surface.

For instance, a preformed composition is provided, formed initially by the *ex vivo* onset of cure, in which the composition can be implanted within on the order of 10 seconds to several days of the onset of cure, preferably within about 30 seconds to about 10 minutes, and more preferably within about one to about five minutes, while maintaining a surface exotherm of less than about 50C, and more preferably less than about 45C once positioned within the body.

Once positioned *in vivo*, preferred preformed components of this invention are adapted to be finally shaped, for a period of between about 10 seconds and one or more hours, and more preferably between about one minute and about five minutes. The lower limit is defined largely by the time it takes to effectively reposition bone, or otherwise re-establish suitable force on the implant. The upper limit, in turn, is generally defined by the susceptibility of the implanted composition to further deformation or shaping. Such final shaping is generally accomplished, at least in part, under the force brought about by repositioning articulating bone surfaces. In one preferred embodiment, the partially cured composition is implanted under conditions that permit it to deform less than about 15%, preferably less than about 10%, and most preferably less than about 5%, under physiologic forces, while maintaining tibial congruency and imparting desired angular correction.

Hence, a particularly preferred preformed component of this invention can be implanted within an initial about one to about five minutes of the onset of its formation, and once implanted can be further molded or formed for a further period of about one to about five additional minutes, in a manner that permits the resultant implant to substantially retain a desired final form and function.

The system of the present invention thereby provides the surgeon with a variety of options, based on the manner in which these curing and forming processes are correlated. In one particularly preferred embodiment, for instance, the surgeon is provided with a composition adapted to be partially cured and generally formed *ex vivo*, and then promptly inserted into the body and positioned at the joint site, where it can be finally, and specifically, formed in the course of becoming fully cured.

By partially curing the prosthesis *ex vivo*, the present system simplifies the preparation process considerably, e.g., by lessening or avoiding potential problems (such as curing in the presence of moisture, and surface exotherm in the presence of tissue) that can arise when a comparable composition is mixed and delivered to the joint site while it is still flowable. Surprisingly, the present system permits such prostheses to be not only formed, but also manipulated and inserted into the joint (e.g., through an incision of between about 1 cm and about 3 cm). Once inserted, the prosthesis can be positioned, and further formed *in situ*, all within a reasonable time frame. In fact, it has been found that the procedure is amenable to outpatient use and even regional anesthesia.

Moreover, the present system can avoid the use of such processes as the drilling anchor holes into the underlying bone, distraction of the knee joint, ligament release, leveling of the tibial plateau, and the various other procedures typically involved with delivering the biomaterial directly to the joint site in still flowable form. Yet, the prosthesis of the present invention provides a combination of properties such as the extent of congruence with underlying bone, wear characteristics, fracture toughness, and avoidance of fibrillated articular cartilage, that meets or exceeds the combination of properties obtained using a comparable biomaterial in flowable form, delivered and largely cured *in situ*.

In addition to its immediate use in such joints as the knee, the system of the present invention provides particular advantages when applied to ball and socket joints, such as the hip. In one such embodiment, a balloon can be filled with a biomaterial as described herein, and inserted and positioned within the acetabulum, prior to or following filling, to provide a soft, conformable, durable lining for the placement of a hip prosthetic portion.

In a further embodiment, the method and system involve the preparation and use of one or more partially or fully cured component(s) formed outside the body, for insertion and placement into the body and optionally further fitting and securing at the joint site. These preformed component(s) typically require less manipulation at the bedside and allow for alternative methods of terminal sterilization, and final inspection and release at the manufacturing site.

DETAILED DESCRIPTION

The method and system (e.g., preformed component(s) and/or curable biomaterial and mold) can be used to prepare a final prosthesis, *in vivo*, that provides a first major surface in apposition to and retained upon the supporting bone itself, and a second (generally substantially parallel and opposite) major surface adapted to provide a wear surface for opposing (e.g., articulating) bone. By "retained upon" it is meant that the final prosthesis is maintained in a desired position upon the supporting bone surface in a manner suitable for its intended use, e.g., by the use of one or more anchor points, by the use of adhesive or other suitable interface materials, by the use of sutures, staples, and the like, and/or by a mechanical lock achieved by the combination of a bone-contacting surface suitably conformed or conformable to the terrain of supporting bone, together with the retaining (and optionally including deforming) effect achieved upon repositioning opposing articulating bone surface.

The first and second major surfaces can be provided in any suitable manner, for instance, 1) by the preparation and insertion of a single partially cured and generally preformed component into the joint, preferably under conditions that permit the component to become further, and specifically, formed *in vivo*, 2) by adding a flowable biomaterial to an initial preformed component (e.g., in the shape of a balloon or open mold) positioned at the tissue site, 3) by placing one or more fully cured and preformed components at the tissue site and optionally further fitting, adapting and/or securing the component(s) as needed, and/or 4) by assembling one or more preformed components *in situ* (e.g., side by side in an interlocking fashion upon the surface) such that the assembled components cooperate to provide the first and second major surfaces.

In addition to the partially or fully cured preformed component(s) and/or curable biomaterial and related molds, the method and system of this invention include the optional use of various additional materials and/or steps, e.g., to prepare the bone surface itself, to provide suitable interfaces (e.g., adhesive interfaces and/or protrusions that can be further secured to the joint site or by smoothing of the femoral condyle or tibial plateau as needed), to treat one or more surfaces in order to provide them with different or improved properties as compared to the inherent properties of the material providing the surface, and the like. Examples of such materials include, for instance, the use of adhesive materials, tissue in-growth stimulators, and fibrous materials (e.g., webs adapted to tether the implant and/or to facilitate fibrous tissue ingrowth).

The partially or fully cured preformed component(s) can themselves each provide uniform or non-uniform properties, and can be provided in a plurality or range of styles and sizes. These components can be designed to conform to lateral or medial compartments, or both, and to right or left knees, or both. In a preferred embodiment, all embodiments can be inserted into the joint site in a minimally invasive fashion. By "minimally invasive", in this context, it is meant that the procedure of sizing, inserting, positioning and forming the prosthesis, *in situ*, can preferably be accomplished without the need for open, invasive incisions of the type conventionally used for inserting total knee prostheses. In a preferred embodiment, the partially cured preformed components can be further formed and fully cured *in vivo* to enhance compliance with the joint site.

The surface of the partially or fully cured preformed component(s) can also be modified to provide any desired properties (e.g., promote adhesion), such as by the design and use of polymers themselves or by surface treatment of the fully cured or curing embodiments to provide suitable reactive groups such as amines, hydroxyl groups, or other reactive or hydrogen bonding functionalities. Similarly, the partially cured preformed component or fully cured component, including balloons or composite materials, can be provided with appropriate surface coatings, e.g., biologically active agents to promote desired tissue interactions, including tissue or cellular adhesion, such as those selected from the group consisting of cytokines, hydroxyapatite, collagen, and combinations thereof.

In one embodiment of this invention, partially cured, and generally preformed components are inserted into the joint site, and there further and specifically formed to enhance compliance. In an alternative embodiment, fully cured components in the shape of a balloon or open mold are employed to provide a final composite material by inserting the balloon or mold into the joint and there filling it with a biomaterial that cures *in situ* and conforms with the joint site. In another alternative embodiment, the fully cured component(s) are provided and inserted into the joint either singly or piecemeal and optionally further fitted and secured *in vivo*.

As an example of the first such embodiment, the invention provides an open *ex vivo* mold, adapted to approximate the desired dimensions of the joint site, and to receive a curable biomaterial. A suitable mold can be formed, for instance, from the use of conventional materials such as silicone materials, that permit the curing biomaterial component to be easily and entirely removed at the desired time. Optionally, the mold can itself be provided with a coating or release liner, including those that can be integrated, in whole or in part, with the component thus formed. Once the flowable biomaterial has been delivered and partially cured in this *ex vivo* mold, and any optional molding or fabricating steps have occurred, the biomaterial can be removed from the mold and inserted into the joint site, under conditions suitable to permit it to be further and finally formed *in vivo* to enhance conformance with the joint site. Optionally, additional *ex vivo* forming steps or features can be performed, e.g., by imparting desired curvature and femoral glide paths, prior to inserting and final forming *in vivo*.

Also, in the course of molding the component *ex vivo*, and/or transferring it to the tissue site, various structures and/or materials can be incorporated into and/or onto the component itself, to enhance its placement, retention and/or performance *in situ*. For instance, the mold itself can be provided in a form sufficient to impart various integral structural features, such as tibial "tabs", adapted to provide or improve the retention of the component at the tissue site. Such tabs, for instance, can be provided in the form of one or more protrusions integral with the mold itself and adapted to be positioned within and/or affixed to the soft tissue and/or bone *in vivo*. Examples of such tabs are shown, for instance, in Figure 1, where reference number 18 depicts a raised posterior portion.

An insertable component can also be provided with one or more ancillary portions or protrusions formed of materials other than that used to form the bulk of the component itself. For instance, sutures or fibrous materials can be incorporated into or onto the bulk material, for use in improving the initial and/or long term retention of the component *in situ*, e.g, by tethering the prosthesis at the joint site and in a desired position. Such other materials can be temporarily positioned into or upon the mold itself, for instance, or otherwise provided, in a manner that permits them to become integrated into the biomaterial as it fills the mold and becomes partially cured *ex vivo*. With the resulting component positioned *in situ*, the protrusions can be used to tether the implant, by securing them to the surrounding soft tissue and/or bone by use of adhesives, sutures, screws, pins, staples or the like or combinations thereof. The materials can provide both an immediate fixation function, and optionally also a desired long term function, by permitting them to be either absorbed by the body over time, and/or to permit or encourage fibrous tissue ingrowth for long term fixation.

The reinforcing material can be provided in any suitable form, e.g., as fibers (e.g., sutures) or as a uniform woven or non-woven fabric, optionally including one or more reinforcing fibers or layers. A suitable non-woven fabric, for instance, is preferably a material such as is commercially available under the trade name Trevira Spunbond from Hoechst Celanese Corporation. The non-woven fabric is generally composed of continuous thermoplastic fiber, needle punched together to yield a felt-like fabric. In addition to fabrics like Trivira Spunbond, other materials such as polyester staple mat, glass fiber mat, as well as other organic and inorganic fiber mats and fabrics can be employed.

Reinforcing fibers can be included within the woven or non-woven fabric, or provided as separate layers of a composite. Such fiber layers can preferably include a directional reinforcing fiber layer of organic or inorganic structural reinforcing fibers such as fiberglass, carbon fibers, aramid fibers which is available from DuPont Corporation under the trade name Kevlar, linear polyethylene or polypropylene fibers such as is commercially available from Allied-Signal, Inc. (now Honeywell) under the trade name Spectra, or polyester fibers. The phrase "reinforcing fiber" can include any fiber which, when used in its own right or added to a composite fabric material, retains or enhances desired structural properties. The fibers can be randomly oriented,

or preferentially, they can be oriented in one or more directions. While a number of specific types of materials have been given for use as the reinforcing fiber layer, it will be appreciated by those of ordinary skill in the art that other equivalent-type reinforcing fiber layers can be employed in the practice of the invention. A reinforcing fiber layer can be itself used to secure the prosthesis, or can be attached to a woven or non-woven fiber layer having a number of interstices or pores. Preferably, the reinforcing fiber layer and other fiber layers are secured to each other mechanically, as by conventional stitching, needle punching, stapling or buttons. In the case of certain applications, adhesives can also be used.

Similarly, a partially cured preformed component (and/or ancillary portions incorporated therein) can also be provided with suitable means to improve its ability to retain the component *in situ*, e.g., by the use of surface characteristics that provide improved chemical interactions with the joint site. Such interactions can be achieved by the judicious use of bulk material compositions themselves and/or the use of adhesives or other suitable interface materials. The partially cured, preformed, component can also be physically modified to increase its interactions with joint site, as by surface roughening, etching or cross-hatching, which would tend to provide increased surface area, and in turn, improved mechanical retention. A partially cured, preformed, component can also be retained by external means that are otherwise secured to the surrounding bone and/or soft tissue by use of adhesives, sutures, screws, pins, staples or the like or combinations thereof. On the major surface opposing articulating bone, the partially cured preformed component can be provided with suitable means as well, intended to improve or alter either its compliance and/or interactions with the opposing bone surface.

In one particularly preferred embodiment, the system includes a partially cured preformed component that is first molded outside of the joint site and adapted to be delivered to a tissue site and there positioned in a fixed position. The mold can be of an open or closed configuration (and/or can involve a one- or multi-step molding process), adapted to preform one or both major surfaces, respectively. Once positioned, the partially cured component is adapted to be initially fit and positioned within the joint site, and to thereafter become better conformed to the specific dimensions and/or terrain (e.g., anatomic structure) of the joint site *in vivo*.

Optionally, and preferably, the molds are designed to yield components that have optimum adhesion and conformance to the joint sites. The molds may also be heated during the *ex vivo* partial curing process to optimize component properties or to provide a component that is more formable *in vivo*.

In an alternative preferred embodiment, the method and system involve the preparation and use of one or more fully or partially cured component(s) formed outside the body, for insertion and placement into the body and optionally further fitting and securing at the joint site. In one embodiment, the invention provides a single preformed component that is inserted into the joint site and optionally further fitted or secured as needed. In another embodiment, the invention provides a plurality of preformed components, formed of the same or different materials, and adapted to be delivered and positioned at the tissue site in a manner that provides a final composite. The components can be combined at the site in any suitable fashion, e.g., by providing a mechanical lock and/or by the use of interfacial materials such as adhesive layers. The components can be combined in any suitable fashion, e.g., as layers upon the bone, or as individual side-by-side components adapted to traverse the bone surface when combined. The use of preformed component(s) can require less manipulation at the bedside and allow for alternative methods of terminal sterilization, and final inspection and release at the manufacturing site. The various means of retaining partially cured preformed components, discussed herein, can be adapted to work with fully cured preformed components.

The method and system of this invention can be used for repairing a variety of mammalian joints, including human joints selected from the group consisting of the tibial plateau of the knee, the acetabulum of the hip, the glenoid of the shoulder, the acromion process of the shoulder, the acromio-clavicular joint of the shoulder, the distal tibial surface of the ankle, the radial head of the elbow, the distal radius of the forearm, the proximal phalanx surface of the great toe, the proximal metacarpal surface of the thumb, and the trapezium of the wrist.

Those portions or combinations of preformed component(s) that contact the bone surface are preferably adapted to physically conform closely to the prepared bone surface, e.g., to its macroscopic physical contours. Such conformation can be provided or enhanced in any suitable manner, e.g., 1) by providing a partially cured

preformed component that is first made in an *ex vivo* mold and then adapted or modified to conform to the surface (e.g., by further forming *in vivo*), and/or 2) by use of a preformed balloon or composite mold material that is inserted into the joint site and filled with a flowable biomaterial that cures *in vivo* so that it conforms with the joint site and/or 3) by the use of fully cured preformed component(s) that has optimum geometry for biomaterial compliance once placed in the joint site and/or 4) by the preparation and use of a suitable (e.g., thin) interface material between bone and preformed component (e.g., adhesive, filler, or cement material), and/or 5) by the use of physical restraining means, such as adhesives, pins, staples screws, sutures or the like that are attached to protrusions in the component itself or to an external means of securing it.

The method and system of this invention will be further described with reference to the Drawing, wherein

Figure 1 shows a top and side perspective of a preferred preformed knee implant (10) prepared using an *ex vivo* mold according to the present invention. The implant provides a first major surface (12) adapted to be positioned upon the tibial surface, and a generally planar second major surface (14) adapted to be positioned against the femoral condyle. In a typical embodiment, the second major surface, in turn, is preferably provided with a femoral glide path (16) to facilitate its performance *in situ*, in the form of a generally central oval depression about 1 mm to about 5mm deep at its lowest point (2 mm as shown) and about 30 mm to about 50 mm in length by 10 mm to 30 mm in width (40 mm by 20 mm as shown). Those skilled in the art, given the present description, will readily determine the actual dimensions for optimal use, in both absolute and relative terms, depending on such factors as the actual joint size and desired results (e.g., angular correction). As shown, the implant is also provided with a raised tibial projection (18), adapted to catch the posterior portion of the tibial plateau. The implant can have dimensions on the order of between about 40 to about 60 mm in the anterior-posterior dimension, between about 30 mm to about 40 mm in the medial-lateral dimension, and a maximum thickness (at the posterior lip of between about 10 mm and about 20 mm.

Figure 2 shows an embodiments in which a plurality of preformed components are adapted to be inserted and assembled *in situ* to provide the final implant (20)

Figure 2a shows an embodiment, in which preformed components (22 through 25, respectively) are assembled in a side-by-side manner sequentially, and *in situ*, and upon the tibial surface. The matable preformed sections each provide at least a portion of the resultant bone-contacting surface and wear surface, as well as one or more portions adapted to provide a mechanical lock with one or more respective other portions. The mechanical lock can be achieved in any suitable manner, as by the provision of corresponding male and female portions, respectively. The portions can be mated, *in situ*, e.g., in a press fit or sliding manner, in order to attach the respective components. As can be seen in the raised perspective of the same embodiment, and Figure 2b, in the resultant assembly, the combined components cooperate to provide both a tibial bone-contacting surface (28) and a wear surface (26).

In the alternative embodiment of Figure 3, rather than being positioned in a side-by-side fashion across the bone surface (as in Figure 2), a final implant is provided using interlocking preformed components (show in this case as portions 31 through 33, respectively) are instead provided in a form that permits them to be stacked upon each other, e.g., by layering or sliding them onto each other, and positioned upon the surface, *in situ*. The portions can be assembled in any suitable fashion, e.g., entirely on the tissue site, entirely *ex vivo*, or in varying combinations as desired. Optionally, and preferably, the generally planar portions are provided with corresponding matable portions, e.g., in the form of grooves and tabs to provide a sliding fit, or a depression and corresponding projection to provide either a press fit, snap fit, or other suitable fit sufficient to prevent lateral displacement to the extent desired. The resultant formed prosthetic implant can be provided with various features as described herein, including desired molded portions adapted to provide better fit or performance. Top portion (31) is particularly well suited to provide a desirable wear surface, while one or more intermediate portions (as shown by element 32) are adapted to provide an optimal combination of such properties as thickness, cushioning, and angular correction. As shown the lowermost portion (33) is shown with a projection (34) adapted to be retained within a corresponding anchor hole or suitable depression formed into the bone itself. Figures 3b and 3c provide generally bottom and top views, respectively, showing the manner in which the portions can be combined in a layered fashion.

In the embodiment of Figure 3, preformed layers are shown having protrusions adapted to be positioned in a corresponding indentation within each underlying layer (or bone), in order to form a compact stack. In such an embodiment, the corresponding system will typically include at least two preformed components, including the initial, bone-contacting component, and final component providing the wear surface. The system can provide one or more intermediate layers, e.g., the number and/or selection of which can be used to provide a final desired height to the overall composite, and/or to provide differing properties (e.g., with respect to compressibility, resilience, tissue ingrowth), and/or to provide improved retention between the first and final components.

Figure 4a shows an embodiment in which a substantially open (saucer-shaped) mold (40) is inserted into the joint site, to be filled with a corresponding curable biomateral *in situ*. The top (42) of the mold is open to receive biomaterial (not show), while the bottom (44) provides a lower major surface (46) adapted to contact bone and terminates in a filled protrusion (48) adapted to be positioned within a corresponding anchor point drilled in the bone itself. The anterior edge (50) of the cup is substantially perpendicular to the plane of the cup itself, while the posterior edge (52) is tapered (and optionally raised) to accommodate the corresponding shape of the tibial spine.

As shown, and for use in an adult human, the *ex vivo* mold accommodates a predetermined volume of biomaterial of on the order of about 5 ml to about 15 ml. As a further advantage of this invention, the amount of biomaterial actually can be predetermined and controlled to correspond with the *ex vivo* mold volume. In addition the *ex vivo* molds are designed for optimum sizing and conformance to the joint site and MRI software may be used to chose best mold for joint site. Implant thickness and hence angular correction can be controlled in this way.

Figure 4b shows a bottom perspective view of the mold apparatus of Figure 4a, showing the filled protrusion (48). The posterior edge portion can be seen as provided with a groove or indentation (54), again to accommodate the typical shape of the corresponding tibial spine. Overall, the mold can be seen as assuming a generally kidney-shaped configuration, adapted to correspond with the tibial surface. Such a

mold can be provided in a plurality of sizes, and shapes, to be selected at the time of use to accommodate the particular patient's needs and surgeon's desires.

Figures 5a and 5b show the mold of Figure 4a being positioned upon a tibial surface (Fig. 5a), with the protrusion positioned within a corresponding anchor point, and (in Fig. 5b) with the tip of a biomaterial delivery cannula (56) positioned upon it, and with flowable biomaterial (58) being shown in the course of delivery.

Figure 6 shows a variety of alternative embodiments that include one or more preformed component. Fig. 6a shows a simple wedge shaped embodiment (60), in which the posterior portion (62) is significantly increased in size as compared to the anterior (64). Fig. 6b shows an implant (66) molded to provide portions (here, layers) having differing wear characteristics, including a preformed top having improved wear as compared to the separately formed bottom portion (70). Fig. 6c, by comparison, shows a plurality of components (72) adapted to be positioned and assembled in situ at the time of surgery. These include an upper portion (74) having improved wear characteristics as compared to the others, a bottom portion (78) being suitably formed to the patient's geometry and desired angular correction, and one (or more) central portions (76) adapted to be positioned between the top and bottom portions to achieve desired properties such as overall thickness, angles, and/or physical chemical properties (such as moduli).

The embodiment of Figure 6d shows a single piece (80) as might be cut from preformed material at the time of surgery, while Figure 7 shows a variety of alternative means for anchoring a preformed component such as that shown in Fig. 6d. These include the use of a grout (82) or other suitable interface material as shown in Fig. 7a; the use of a separate external retaining device (84) as shown in Fig. 7b; the use of externally provided pins, screws, sutures, etc. as exemplified by elements (86) which generally traverse the body itself as in Fig. 7c; and the use of one or more anchor portions (88) positioned along one or more suitable surfaces as shown in Fig. 7d.

Figure 8 shows a further variety for anchoring or stabilizing a preformed portion by the use of ancillary portions and/or surface texture, including a roughened surface (90) as in Fig. 8a; or tabs (e.g., provided by fabric or suture like materials) as shown as elements 92 and 94 of Figs. 8b and 8c, respectively. In practice, the

preformed components can benefit from any suitable combination of the various features and embodiments described or shown herein.

Figure 9 shows a variety of embodiments in a substantially closed (balloon like) mold is adapted to be inserted into the joint site and filled with a corresponding curable biomaterial, the mold itself providing a preformed articulating wear surface, including Fig. 9a which shows an inflatable balloon portion (96) that includes an integral preformed wear surface and portion (98), as well as a lumen (100) adapted to fill the inflatable portion with flowable biomaterial. Fig. 9b shows a corresponding balloon (102) though without a preformed portion, and including its biomaterial lumen (104). Although not shown, the balloon of this or any embodiment can include various interior and/or exterior surface coatings, and can have regions and/or layers having different desired physical-chemical properties (such as porosity). Fig. 9c shows a bi-compartmental closed balloon-like mold (106), wherein each compartment is adapted to conform to a respective medial or lateral tibial surface.

Figure 10 shows a mold adapted for use as an acetabular mold (110) in connection with the replacement of the articulating surface in a hip, when filled with biomaterial, the mold forming a concave portion adapted to retain a corresponding femoral head. The mold is shown providing a thin generally cup-shaped mold adapted to be filled in any suitable form (e.g., using a removable conduit (not shown) attached to the space between inner and outer sealed layers (116 and 114, respectively) forming the mold.

Figure 11 shows a patella-femoral joint form suitable for use in combination with the method and system of this invention. As shown in the views of 11a through 11c, the form includes a silicone or other suitable pad material (122) having aluminum or other suitable stay portions (124) and terminal handle or grasping portions (126). In use, with the knee at a generally 45 degree angle, the piece is formed to the femoral bone surface, with its form maintained by bending the aluminum stays. With anchor points cut into the femoral bone, if desired, the form is held tight against the bone with the upper handle held away from bone to permit the delivery of curable biopolymer between the form and the bone. As polymer is placed onto the bone (and into any anchor points) the form is maintained for a time sufficient to suitably form the polymer, whereafter it can be removed.

As described in Applicant's co-pending US provisional application 60/228,444, the present application describes a method and system for the creation or modification of the wear surface using an implanted material fixed to the support structure of the original wear surface, to generally conform to the shape of the original surface in a mammal. A method or system where the end of the bony surface is a rotating, sliding or rolling surface, such as in the knee, finger, hip, toe, spine, wrist, elbow, shoulder, ankle, or TMJ joint. The implant will function:

a) as a spacer,

b) as an impact absorber

c) as a surface with improved coefficient of friction (as compared to the diseased surface), and/or

d) to increase the weight bearing area and improve congruency of the joint surface (as compared to the diseased condition).

The method and system of this invention can be applied to areas of aseptic necrosis, such as the nevecular bone in the wrist. The material to be implanted consists of a plurality of materials, such as polymers, including polyurethane, polyethyelenes, polyureas, polyacrylates, polyurethane acrylates, hydrogels, epoxies and/or hybrids of any of the above.

In an alternative embodiment, the surface can be provided by any of a series of metals, including titanium, stainless steel, cobalt chrome millithium alloys and tantalum. Other surface materials can include various ceramics and biologic polymers.

The implantable material for the resurfacing can be formed ex vivo and/or in vivo as an injectable material that sets up to the molded shape. The methods for changing state from liquid to solid state include cooling or heating, the passage of time, which allows for a change of state, or a chemical reaction between different reactants. The reaction can be exothermic or endothermic. The set-up can be light activated or chemically catalyzed or it could be heat activated. Examples of such systems include flowable polymers of two or more components, light activated polymers, and polymers cured either by catalysts or by heat, including body heat. Molds can be used in the form of balloons, dams or retainers. They can be used in combination with the local anatomy to produce the desired shape and geometry.

Molds can be of materials that are retained and becomes part of the implant or could be removed after curing of the biomaterial component.

In an alternative embodiment, the material would be semi-solid and could be shaped and then set up in vivo. This would allow for the minimally invasive application, either through an arthroscopic portal or through a small mini arthrotomy. As a further embodiment, the material could be synthesized ex vivo and then machined to fit using imaging to pre-determine the desired geometry and size of the implant. As a further alternative, a range of implant sizes could be provided and sizing could be accomplished during the procedure. An ex vivo mold could be fit using molding materials and the implant could be molded on site just prior to implantation.

Fixation methods for the implant would include biologic glues to glue the implant to the underlying surface, trapping of the implant into a cavity on the surface that causes a mechanical lock, using various anchors to the underlying structure and fixing the implant to that surface or using mold retainers and/or screws, staples, sutures or pins. In alternative embodiment, anchors in the underlying structure may be used for fixing the implant to that surface and we may also use a tissue ingrowth system to secure anchoring.

In the preferred embodiment, the patient will have a diagnosis of osteoarthritis and have loss of cartilage on the articulating surface. A determination will be made of the amount of correction needed for the reestablishment of a normal angle of articulation. The ligaments will be balanced so that there is no loss of range of motion with the implant in place and the surface will be placed in such a position that the eventual resulting surface geometry reestablishes the same plane and orientation of the original articular surface.

Access to the site is obtained in a minimally invasive way. In a preferred embodiment, this is accomplished through arthroscopic means with arthroscopic portals. In an alternative embodiment, the access is accomplished by a mini arthrotomy with a small incision that allows access to the joint without sacrificing nerves, vessels, muscles or ligaments surrounding the joint. In the preferred embodiment fibrillated articulating cartilage that is degenerated is removed down to the subchondral surface. The surface is dried and prepared for appropriate anchoring.

This may include anchor points that give a mechanical lock or that alternatively simply supply horizontal and lateral stability. The surface may be prepared by drying and roughening in case a tissue adhesive is used. Pre-made anchors may be installed. These may be made of various metallic materials or of polymers and may consist of pegs that would extend up through the implant to anchor it to the underlying surface. This surrounding subchondral bone may be roughened to enhance tissue ingrowth or implant adhesion. The final geometry of the implant may be determined by a dam or mold that is placed on the joint at the time the material is implanted, when the implant is installed using an *in situ* cured technique (in the manner shown in Figures 1 and 4 of Applicant's provisional parent application).

For pre-made material formed at the surgical site within a mold, various forms of stabilization could be used, including anchor points or titanium screws. Alternatively, the pre-made material could be made off site to the specs developed from imaging of the patient's joint surface. In a third embodiment, multiple sizes could be made off site and the selection of the appropriate implant size could be chosen at the time of surgery. Two alternatives shown in Figure 2 of the parent provisional application include a single segment that can be installed through a portal or a series of segments that can be installed through a portal and locked together once inside the joint. They would be placed sequentially and then anchored to the bone by anchor points cut in the bone or by screws or tissue ingrowth. Finally, a robot, a jag or other cutting fixture could be used to prepare the bony surface for the pre-made implant to a fixed geometry of the anchor point.

Both the preformed component(s) and flowable biomaterial, if used, can be prepared from any suitable material. Typically, the materials include polymeric materials, having an optimal combination of such properties as biocompatibility, physical strength and durability, and compatibility with other components (and/or biomaterials) used in the assembly of a final composite. Examples of suitable materials for use in preparing the preformed component(s) may be the same or different from the *in situ* curing biomaterial, and include polyurethanes, polyethylenes, polypropylenes, Dacrons, polyureas, hydrogels, metals, ceramics, epoxies, polysiloxanes, polyacrylates, as well as biopolymers, such as collagen or collagen-based materials or the like and combinations thereof.

Examples of suitable materials for use in preparing the flowable biomaterial, if used, include polyurethanes, polyureas, hydrogels, epoxies, polysiloxanes, polyacrylates, and combinations thereof.

In a presently preferred embodiment, the preformed component(s) and the flowable biomaterial, if included, each comprise a biocompatible polyurethane. The same or different polyurethane formulations can be used to form both the preformed component(s), e.g., by an injection molding technique, as well as for the flowable biomaterial, if present.

Suitable polyurethanes for use as either the preformed component or biomaterial can be prepared by combining: (1) a quasi-prepolymer component comprising the reaction product of one or more polyols, and one or more diisocyanates, and optionally, one or more hydrophobic additives, and (2) a curative component comprising one or more polyols, one or more chain extenders, one or more catalysts, and optionally, other ingredients such as an antioxidant, and hydrophobic additive.

In the embodiment in which an *in situ* curing polymer is used, the present invention preferably provides a biomaterial in the form of a curable polyurethane composition comprising a plurality of parts capable of being mixed at the time of use in order to provide a flowable composition and initiate cure, the parts including: (1) a quasi-prepolymer component comprising the reaction product of one or more polyols, and one or more diisocyanates, optionally, one or more hydrophobic additives, and (2) a curative component comprising one or more polyols, one or more chain extenders, one or more catalysts, and optionally, other ingredients such as an antioxidant, hydrophobic additive and dye. Upon mixing, the composition is sufficiently flowable to permit it to be delivered to the body, and there be fully cured under physiological conditions. Preferably, the component parts are themselves flowable, or can be rendered flowable, in order to facilitate their mixing and use.

The flowable biomaterial used in this invention preferably includes polyurethane prepolymer components that react either *ex vivo* or *in situ* to form solid polyurethane ("PU"). The formed PU, in turn, includes both hard and soft segments. The hard segments are typically comprised of stiffer oligourethane units formed from diisocyanate and chain extender, while the soft segments are typically comprised of

one or more flexible polyol units. These two types of segments will generally phase separate to form hard and soft segment domains, since they tend to be incompatible with one another. Those skilled in the relevant art, given the present teaching, will appreciate the manner in which the relative amounts of the hard and soft segments in the formed polyurethane, as well as the degree of phase segregation, can have a significant impact on the final physical and mechanical properties of the polymer. Those skilled in the art will, in turn, appreciate the manner in which such polymer compositions can be manipulated to produce cured and curing polymers with desired combination of properties within the scope of this invention.

The hard segments of the polymer can be formed by a reaction between the diisocyanate or multifunctional isocyanate and chain extender. Some examples of suitable isocyanates for preparation of the hard segment of this invention include aromatic diisocyanates and their polymeric form or mixtures of isomers or combinations thereof, such as toluene diisocyanates, naphthalene diisocyanates, phenylene diisocyanates, xylylene diisocyanates, and diphenylmethane diisocyanates, and other aromatic polyisocyanates known in the art. Other examples of suitable polyisocyanates for preparation of the hard segment of this invention include aliphatic and cycloaliphatic isocyanates and their polymers or mixtures or combinations thereof, such as cyclohexane diisocyanates, cyclohexyl-bis methylene diisocyanates, isophorone diisocyanates and hexamethylene diisocyanates and other aliphatic polyisocyanates. Combinations of aromatic and aliphatic or arylakyl diisocyanates can also be used.

The isocyanate component can be provided in any suitable form, examples of which include 2,4'-diphenylmethane diisocyanate, 4,4'-diphenylmethane diisocyanate, and mixtures or combinations of these isomers, optionally together with small quantities of 2,2'-diphenylmethane diisocyanate (typical of commercially available diphenylmethane diisocyanates). Other examples include aromatic polyisocyanates and their mixtures or combinations, such as are derived from phosgenation of the condensation product of aniline and formaldehyde. It is suitable to use an isocyanate that has low volatility, such as diphenylmethane diisocyanate, rather than more volatile materials such as toluene diisocyanate. An example of a particularly suitable isocyanate component is the 4,4'-diphenylmethane diisocyanate

("MDI"). Alternatively, it can be provided in liquid form as a combination of 2,2'-, 2,4'- and 4,4'- isomers of MDI. In a preferred embodiment, the isocyanate is MDI and even more preferably 4,4'-diphenylmethane diisocyanate.

Some examples of chain extenders for preparation of the hard segment of this invention include, but are not limited, to short chain diols or triols and their mixtures or combinations thereof, such as 1,4-butane diol, 2-methyl-1,3-propane diol, 1,3-propane-diol ethylene glycol, diethylene glycol, glycerol, cyclohexane dimethanol, triethanol amine, and methyldiethanol amine. Other examples of chain extenders for preparation of the hard segment of this invention include, but are not limited to, short chain diamines and their mixtures or combinations thereof, such as dianiline, toluene diamine, cyclohexyl diamine, and other short chain diamines known in the art.

The soft segment consists of urethane terminated polyol moieties, which are formed by a reaction between the polyisocyanate or diisocyanate or polymeric diisocyanate and polyol. Examples of suitable diisocyanates are denoted above. Some examples of polyols for preparation of the soft segment of this invention include but are not limited to polyalkylene oxide ethers derived form the condensation of alkylene oxides (e.g. ethylene oxide, propylene oxide, and blends thereof), as well as tetrahyrofuran based polytetramethylene ether glycols, polycaprolactone diols, polycarbonate diols and polyester diols and combinations thereof. In a preferred embodiment, the polyols are polytetrahydrofuran polyols ("PTHF"), also known as polytetramethylene oxide ("PTMO") or polytetramethylene ether glycols ("PTMEG"). Even more preferably, the use of two or more of PTMO diols with different molecular weights selected from the commercially available group consisting of 250, 650,1000, 1400, 1800, 2000 and 2900.

Two or more PTMO diols of different molecular weight can be used as a blend or separately, and in an independent fashion as between the different parts of the two part system. The solidification temperature(s) of PTMO diols is generally proportional to their molecular weights. The compatibility of the PTMO diols with such chain extenders as 1,4-butanediol is generally in the reverse proportion to molecular weight of the diol(s). Therefore the incorporation of the low molecular weight PTMO diols in the "curative" (part B) component, and higher molecular weight PTMO diols in the prepolymer (part A) component, can provide a two-part

system that can be used at relatively low temperature. In turn, good compatibility of the low molecular weight PTMO diols with such chain extenders as 1,4-butanediol permits the preparation of two part systems with higher (prepolymer to curative) volume ratio. Amine terminated polyethers and/or polycarbonate-based diols can also be used for building of the soft segment.

The PU can be chemically crosslinked, e.g., by the addition of multifunctional or branched OH-terminated crosslinking agents or chain extenders, or multifunctional isocyanates. Some examples of suitable crosslinking agents include, but are not limited to, trimethylol propane ("TMP"), glycerol, hydroxyl terminated polybutadienes, hydroxyl terminated polybutadienes (HOPB), trimer alcohols, Castor oil polyethyleneoxide (PEO), polypropyleneoxide (PPO) and PEO-PPO triols. In a preferred embodiment, HOPB is used as the crosslinking agent.

This chemical crosslinking augments the physical or "virtual" crosslinking of the polymer by hard segment domains that are in the glassy state at the temperature of the application. The optimal level of chemical cross-linking improves the compression set of the material, reduces the amount of the extractable components, and improves the biodurability of the PU. This can be particularly useful in relatively soft polyurethanes, such as those suitable for the repair of damaged cartilage. Reinforcement by virtual cross-links alone may not generate sufficient strength for *in vivo* performance in certain applications. Additional cross-linking from the soft segment, potentially generated by the use of higher functional polyols can be used to provide stiffer and less elastomeric materials. In this manner a balancing of hard and soft segments, and their relative contributions to overall properties can be achieved.

Additionally, a polymer system of the present invention preferably contains at least one or more, biocompatible catalysts that can assist in controlling the curing process, including the following periods: (1) the induction period, and (2) the curing period of the biomaterial. Together these two periods, including their absolute and relative lengths, and the rate of acceleration or cure within each period, determines the cure kinetics or profile for the composition. Some examples of suitable catalysts for preparation of the formed PU of this invention include, but are not limited to, tin and tertiary amine compounds or combinations thereof such as dibutyl tin dilaurate, and tin or mixed tin catalysts including those available under the tradenames "Cotin 222",

"Formrez UL-22" (Witco), "dabco" (a triethylene diamine from Sigma-Aldrich), stannous octanoate, trimethyl amine, and triethyl amine. In a preferred embodiment, the catalyst is Formrez UL-22 (Witco). In an alternative preferred embodiment, the catalyst is a combination Cotin 222 (CasChem) and dabco (Sigma-Aldrich).

The *in vivo* and *ex vivo* cured polyurethanes of this invention can be formed by the reaction of two parts. Part I of which (alternatively referred to as Part A) includes a di- or multifunctional isocyanate or quasi-prepolymer which is the reaction product of one or more OH-terminated components, and one or more isocyanates. Part II of the polyurethane (alternatively referred to as Part B herein) is a curative component that includes of one or more chain extenders and one or more polyols, and one or more catalysts, and other additives such as antioxidants and dyes. For a suitable formed PU, the stoichiometry between Parts I (quasi-prepolymer) and II (curative component), expressed in terms of NCO:OH molar ratio of the isocyanate terminated pre-polymer (Part I) and the curative component (Part II) is preferably within the range of about 0.8 to 1.0 to 1.2 to 1.0, and more preferably from about 0.9 to 1 to about 1.1 to 1.0.

Optionally, a reactive polymer additive can be included and is selected from the group consisting of hydroxyl- or amine-terminated compounds selected from the group consisting of poybutadiene, polyisoprene, polyisobutylene, silicones, polyethylene-propylenediene, copolymers of butadiene with acryolnitrile, copolymers of butadiene with styrene, copolymers of isoprene with acrylonitrile, copolymers of isoprene with styrene, and mixtures of the above.

Suitable compositions for use in the present invention are those polymeric materials that provide an optimal combination of properties relating to their manufacture, application, and *in vivo* use. In the uncured state, such properties include component miscibility or compatibility, processability, and the ability to be adequately sterilized or aseptically processed and stored. In the course of applying such compositions, suitable materials exhibit an optimal combination of such properties as flowability, moldability, and *in vivo* curability. In the cured state, suitable compositions exhibit an optimal combination of such properties as strength (e.g., tensile and compressive), modulus, biocompatibility and biostability.

When cured, the compositions demonstrate an optimal combination of properties, particularly in terms of their conformational stability and retention of physical shape, dissolution stability, biocompatibility, and physical performance, as well mechanical properties such as load-bearing strength, tensile strength, shear strength, shear fatigue resistance, impact absorption, wear resistance, and surface abrasion resistance. Such performance can be evaluated using procedures commonly accepted for the evaluation of natural tissue and joints, as well as the evaluation of materials and polymers in general. In particular, a preferred composition, in its cured form, exhibits mechanical properties that approximate or exceed those of the natural tissue it is intended to provide or replace.

To achieve these desirable uncured and delivery properties, a "polymer system", as used herein refers to the component or components used to prepare a polymeric composition of the present invention. In a preferred embodiment, a polymer system comprises the components necessary to form two parts: Part I being an NCO terminated pre-polymer (optionally referred to as an "isocyanate quasi-polymer"). The quasi-polymer of Part I typically includes a polyol component, optionally in combination with a hydrophobic additive component, and an excess of an isocyanate component. Part II of the two component system can include one long-chain polyols, chain extenders and/or cross-linkers, together with other ingredients (e.g., catalysts, stabilizers, plasticizers, antioxidants, dyes and the like). Such adjuvants or ingredients can be added to or combined with any other component thereof either prior to or at the time of mixing, delivery, and/or curing.

In a particularly preferred embodiment, a polymer system of this invention is provided as a plurality of component parts and employs one or more catalysts. The component parts, including catalyst, can be mixed to initiate cure, and then delivered, set and fully cured under conditions (e.g., time and exotherm) sufficient for its desired purpose. Upon the completion of cure, the resultant composition provides an optimal combination of properties for use in repairing or replacing injured or damaged tissue. In a particularly preferred embodiment, the formulation provides an optimal combination of such properties as compatibility and stability of the biomaterial parts, ex vivo or *in situ* cure capability and characteristics (e.g., extractable levels,

biocompatibility, thermal/ mechanical properties), mechanical properties (e.g., tensile, tear and fatigue properties), and biostability.

The volume ratio of the parts can also be used to improve and affect the uncured and curing properties Compositions having two or more parts, are preferred. Where two parts are used, the relative volumes can range, for instance, from 1:10 to 10:1 (quasi-prepolymer to curative components, based on volume). A presently preferred range is between 2:1 and 1:2. As those skilled in the art will appreciate, given the present description, the optimal volume ratio is largely determined by the compatibility and the stability of part A and B.

In choosing an optimal volume ratio for a given formulation, those skilled in the art, given the present description, will appreciate the manner in which the following considerations can be addressed. The viscosity of the reactive parts, at the temperature used for either injection-molding preformed components, or for *in situ* cure, should provide an acceptable degree of mixing and flow rate, without causing mechanical failure of any component of the delivery system including cartridge, static mixer, gun and other components.

Preferably, the biomaterial is sufficiently flowable to permit it to be delivered (e.g., injected) into the mold or tissue site. The composition of both reactive parts must be such that these parts are homogeneous and phase stable in the temperature range of the application. Generally, the maximum temperature of the reaction exotherm is proportional to the concentration of the reactive groups in the mixed polymer. A high concentration of the reactive groups might evolve too high reaction exothermal energy and therefore cause thermal damage to the surrounding tissues. The reactive parts will preferably remain substantially liquid in form during mixing.

A desired and stable volume ratio of the components can be achieved in any suitable manner, e.g., by the use of dual-compartment cartridges with constant volume ratio or by using the injectors with delivery rates independently variable for each component.

Compatibility of the composition can also be affected (and improved) in other ways as well, e.g., by pre-heating the components prior to polymer application. To enhance the homogeneity of the components, the components of a preferred composition of this invention are preferably preheated before mixing and delivery,

e.g., by heating to about 60 C to about 80 C for about 2 to about 6 hours prior to use. Preferably, the composition parts are cooled back to about 35 C to 37 C before use in injection.

Fully cured polymeric (e.g., polyurethane) biomaterials suitable for use in forming components of this invention provide an optimal combination of such properties as creep and abrasion resistance. Preferably, for instance, the biomaterial provides DIN abrasion values of less than about 100 mm^3, more preferably less than about 80 mm^3 and most preferably less than about 60 mm^3, as determined by ASTM Test Method D5963-96 ("Standard Test Method for Rubber Property Abrasion Resistance Rotary Drum Abrader").

CLAIMS

What is claimed is:

1. A system for the creation or modification of the wear surface of an orthopedic joint within a mammalian body, the system comprising one or more partially or fully preformed polymeric components, adapted to be inserted and positioned at a joint site to provide an implant having at least one major surface in apposition to supporting bone, and at least a second major surface in apposition to opposing bone.

2. A system according to claim 1 wherein one or more of the polymeric components are formed at the time of use, by the use of a curable polymer system adapted to be at least partially cured and partially formed by *ex vivo* molding in order to provide an implantable component adapted to be inserted and positioned *in vivo*, under conditions suitable to permit the implanted component to become finally formed upon reestablishing the natural joint space and in conformance with the opposing bone surfaces of the orthopedic joint site.

3. A system according to claim 1 wherein the polymeric components comprise a plurality of packaged, preformed components adapted to be assembled at the orthopedic joint site in a minimally invasive fashion to provide a final prosthesis having surfaces in conformance with the opposing bone surfaces of the orthopedic joint site.

4. A system according to claim 1 further comprising an *ex vivo* mold having a molding surface adapted to provide a roughened, patterned, and/or contoured surface to the partially preformed component, in a manner sufficient to provide improved retention and fit of the component at the joint site.

5. A system according to claim 4 wherein the mold further provides ancillary means adapted to be incorporated into the preformed component for securing the component once formed in the joint site.

6. A system according to claim 5 wherein the ancillary means comprise one or more protrusions adapted to be attached to either soft tissue and/or bone at the joint site to improve fixation.

7. A system according to claim 4 wherein the contoured surface comprises a contour having one or more protrusions, integral with the preformed component, and formed during the *ex vivo* molding process.

8. A system according to claim 6 wherein the protrusions are adapted to be integrated into the preformed component during the *ex vivo* molding process.

9. A system according to claim 7 wherein the protrusions are comprised of sutures and/or fibrous biomaterials integrally formed with the component itself.

10. A system according to claim 4 further comprising separate means, not associated with the mold itself, for securing the component to the joint site, selected from the group consisting of adhesives, sutures, pins, staples, screws, and combinations thereof.

11. A system according to claim 1 wherein the one or more preformed polymeric component(s) are adapted to be inserted into a joint in a minimally invasive fashion.

12. A system according to claim 2 in which the preformed component(s) and/or corresponding mold(s) are provided in a plurality or range of styles and sizes for selection and use in the surgical field.

13. A system according to claim 1 wherein the implant is adapted for use on the tibial surface of the knee, and provides portions adapted to conform to the shape of the femoral condyle and corresponding medial tibial plateau, lateral tibial plateau, or both.

14. A system according to claim 1 wherein the polymeric component is fabricated from a material selected from the group consisting of polyurethanes, polyureas, hydrogels, polysiloxanes, polyacrylates, and epoxies, and combinations thereof.

15. A system according to claim 14 wherein the polymeric component comprises a polyurethane.

16. A system according to claim 15 wherein the polyurethane is prepared from polyisocyanate(s), short and long chain polyols, and optionally including one or more ingredients selected from the group hydrophobic additive(s), tin and/or amine catalyst(s), and antioxidant(s).

17. A system according to claim 16 wherein the polyurethane comprises aromatic polyisocyanates, PTMO's, and short chain diols.

18. A system according to claim 16 wherein the hydrophobic additive comprises hydroxyl-terminated polybutadiene, and the tin and/or amine catalyst(s) are adapted to promote the isocyanate - hydroxyl reaction preferentially and are selected from the group consisting of UL22, Cotin 222, 1,4-diazabicyclo[2.2.2]octane (dabco), and dibutyltin dilaurate (DBTDL), and combinations thereof.

19. A system according to claim 14, wherein the preformed polymeric component comprises one or more surfaces having attached thereto a biologically active agent selected from the group cytokines, growth factors, autologous growth factors, hydroxyapatite, collagen, and combinations thereof.

20. A system according to claim 14 wherein the surface of the preformed component is provided or modified with reactive groups to promote tissue adhesion.

21. A system according to claim 20 wherein the reactive groups are provided by the polymers used to fabricate the polymeric component, and are selected from amines, hydroxyl groups, or other reactive or hydrogen bonding functionalities.

22. A system for the creation or modification of the wear surface of an orthopedic joint within a mammalian body, the system comprising one or more preformed polymeric components adapted to be positioned within the joint site and one or more flowable biomaterial polymer compositions adapted to be arthroscopically injected into contact with a preformed component and cured *in situ* at the joint site in order to provide a composite implant.

23. A system according to claim 22 wherein the preformed polymeric components comprise an inflatable balloon having a preformed top weight-bearing wear portion and a preformed bottom portion adapted to conform to the shape of supporting bone.

24. A system according to claim 23 wherein the one or more portions of the balloon are fabricated from a natural or synthetic fabric adapted to permit tissue in-growth, and sufficiently permeable to permit air to escape while retaining the curable biomaterial.

25. A system according to claim 24 wherein the fabric is of sufficient permeability to permit physical interpenetration of the flowable polymer.

26. A system according to claim 23 wherein the bottom and/or top portions comprise materials selected from polyurethanes, polyethylenes, polypropylenes, metals, ceramics, biopolymers or the like and combinations thereof.

27. A system according to claim 23 wherein the top and bottom portions are provided with forms corresponding to the shape of a femoral condyle and tibial plateau, respectively.

28. A system according to claim 23 wherein the balloon further comprises a port adapted to fill the balloon with flowable biomaterial *in situ*, in a manner sufficient to force the top portion toward corresponding bone.

29. A system according to claim 23 wherein the bottom portion provides a raised protrusion sufficient to improve retention within the joint site and/or to provide a site for suturing, stapling, pinning, or screwing the portion within the joint site.

30. A system according to claim 22 wherein separate means are provided for securing the preformed component within the joint site.

31. A system according to claim 22, further comprising one or more biologically active agents adapted to be provided on one or more surfaces of the resultant composite implant.

32. A system according to claim 22 wherein the surface of the preformed component and/or resultant composite material are provided or modified with reactive groups to promote adhesion.

33. A system according to claim 32 wherein the reactive groups are either provided by the preformed component itself, or are separately added by suitable surface treatment of the component or resultant composite, and the reactive groups are selected from amines, hydroxyl groups, or other reactive or hydrogen bonding functionalities.

34. A system according to claim 22 in which one or more of the preformed components are provided in a plurality or range of styles and sizes.

35. A system according to claim 22 wherein the one or more flowable biomaterial(s) are adapted to be inserted into a joint using minimally invasive means.

36. A system for the creation or modification of the wear surface of an orthopedic joint within a mammalian body, the system comprising a plurality of packaged, preformed components adapted to be assembled at the orthopedic joint site in a minimally invasive fashion to provide a final prosthesis having surfaces in apposition to and conformance with the opposing bone surfaces of the orthopedic joint site.

37. A system according to claim 36 wherein one or more of the preformed components are provided with surfaces suitably roughened, patterned, or contoured to provide maximum adhesion and fit when placed, and optionally further fitted and secured, within the joint site.

38. A system according to claim 36, wherein one or more of the preformed components are formed at the time of use by the use of a curable bomaterial adapted to completely cure when preformed and then placed and optionally further fitted or secured inside the joint site.

39. A system according to claim 36 wherein one or more of the preformed components provide means for further securing the component once placed in the joint site.

40. A system according to claim 39 wherein the retention means to secure the component includes the use of tissue adhesives to improve fixation.

41. A system according to claim 39 wherein the retention means comprise one or more protrusions adapted to be sutured, pinned, stapled, screwed or combinations thereof or otherwise mechanically attached into the surrounding soft tissue and/or bone to improve fixation.

42. A system according to claim 41 wherein the protrusions are themselves integral with the preformed component.

43. A system according to claim 42 wherein the protrusions are integrated into a flowable biomaterial during the *ex vivo* molding process used to form the preformed component.

44. A system according to claim 43 wherein the protrusions are comprised of sutures or fibrous materials.

45. A system according to claim 39 wherein means to secure the component are external to it and secured once inside the joint site by the use of adhesives, sutures, pins, staples, screws or the like and combinations thereof to improve fixation to the surrounding soft tissue and/or bone to improve fixation.

46. A system according to claim 36 wherein the one or more preformed component(s) are adapted to be inserted into a joint in a minimally invasive fashion.

47. A system according to claim 36 in which the one or more preformed component(s) are provided in a plurality or range of styles and sizes.

48. A system according to claim 37 wherein the assembled components conform to the shape of the femoral condyle and tibial plateau, medial, lateral or both.

49. A system according to claim 37 wherein the preformed component(s) are fabricated from materials selected from the group consisting of polyurethanes, polyethylenes, polyureas, hydrogels, polysiloxanes, polyacrylates, epoxies, and combinations thereof.

50. A system according to claim 49 wherein the material comprises a polyurethane.

51. A system according to claim 50 wherein polyurethane is prepared from polyisocyanate(s), short and long chain polyols, and optionally including one or more ingredients selected from the group hydrophobic additive(s), tin and/or amine catalyst(s), and antioxidant(s).

52. A system according to claim 51 wherein the polyurethanes are prepared from aromatic polyisocyanates, PTMO's, short chain diols.

53. A system according to claim 52 wherein the hydrophobic additive comprises hydroxyl-terminated polybutadiene, and the tin and/or amine catalyst(s) used promote the isocyanate - hydroxyl reaction preferentially and are selected from the group consisting of UL22, Cotin 222, 1,4-diazabicyclo[2.2.2]octane (dabco), and dibutyltin dilaurate (DBTDL) or the like and combinations thereof.

54. A system according to claim 36 wherein the preformed components provide one or more surfaces having attached thereto a biologically active agent selected from the group cytokines, hydroxyapatite, growth factors, autologous growth factors, collagen or the like and combinations thereof.

55. A system according to claim 36 wherein the surface of one or more preformed component(s) is provided or modified with reactive groups to promote tissue adhesion.

56. A system according to claim 55 wherein the reactive groups are covalently attached to the polymers used to fabricate the preformed component(s), and are selected from amines, hydroxyl groups, or other reactive or hydrogen bonding functionalities.

57. A system according to claim 36 wherein the preformed component(s) are selected from the group consisting of a) a single preformed component, b) a plurality of components adapted to be layered upon each other at the tissue site, c) a plurality of components adapted to be assembled at the tissue site in an interlocking fashion, such that the components cooperate to provide a respective portion of the first and second major surfaces.

58. A system according to claims 1 or 22 or 36 further comprising the use of one or more additional materials and/or steps adapted to a) prepare the bone surface itself, b) provide a desired interface between bone, component(s), and/or the physiologic environment, and/or c) treat one or more surfaces of the component(s) in order to provide them with different or improved properties as compared to the inherent properties of the material providing the surface.

59. A system according to claim 58 wherein the materials and/or steps are adapted to affect, improve or provide a surface property or function selected from adhesion, lubricity, smoothness, conformance, tissue in-growth, or biocompatibility.

60. A system according to claims 1 or 22 or 36 wherein the system is adapted to be used for repairing a variety of mammalian joints, including human joints selected from the group consisting of the tibial plateau of the knee, the acetabulum of the hip, the glenoid of the shoulder, the acromion process of the shoulder, the acromio-clavicular joint of the shoulder, the distal tibial surface of the ankle, the radial head of the elbow, the distal radius of the forearm, the proximal phalanx surface of the great toe, the proximal metacarpal surface of the thumb, and the trapezium of the wrist.

61. A system according to claim 60 wherein the system is adapted to be used for repairing the tibial plateau of the knee.

62. A system according to claim 60 wherein the system is adapted to be used for repairing the acetabulum of the hip.

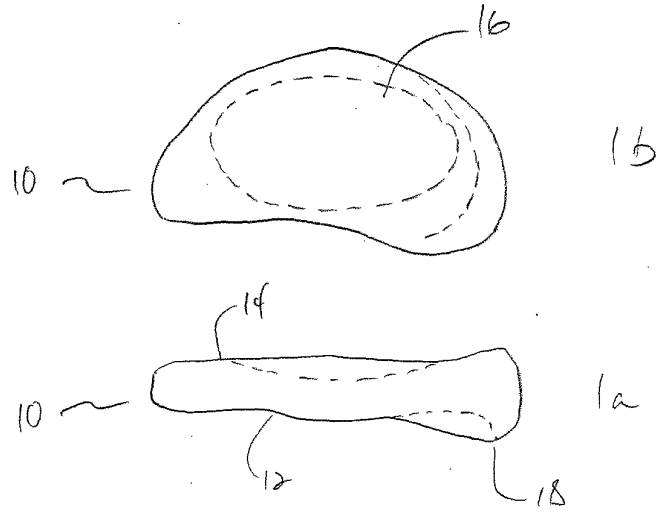

FIG 1

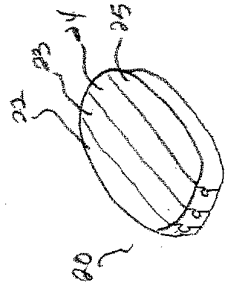

Fig 2b

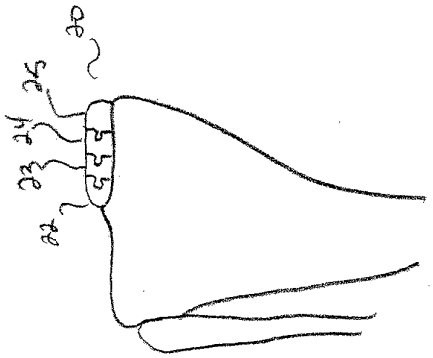

Fig 2a

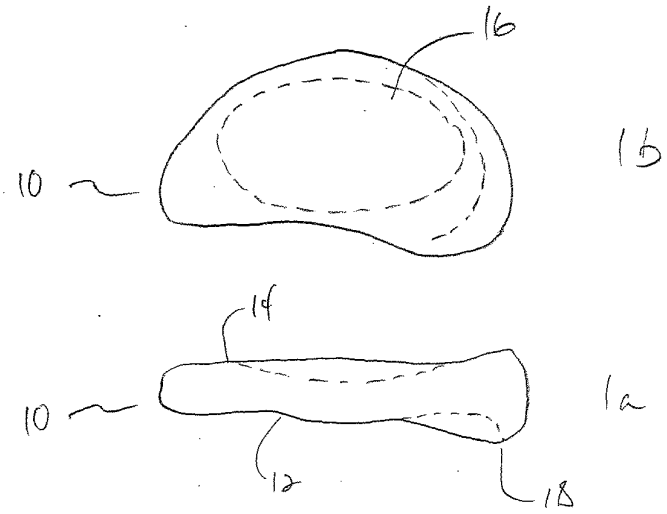

FIG 1

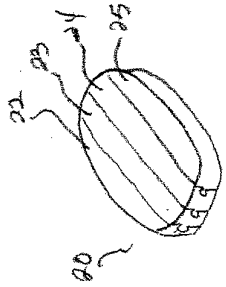

FIG 2b

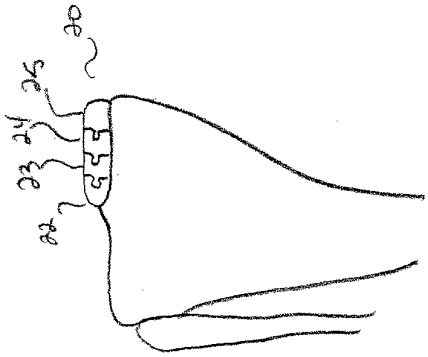

FIG 2a

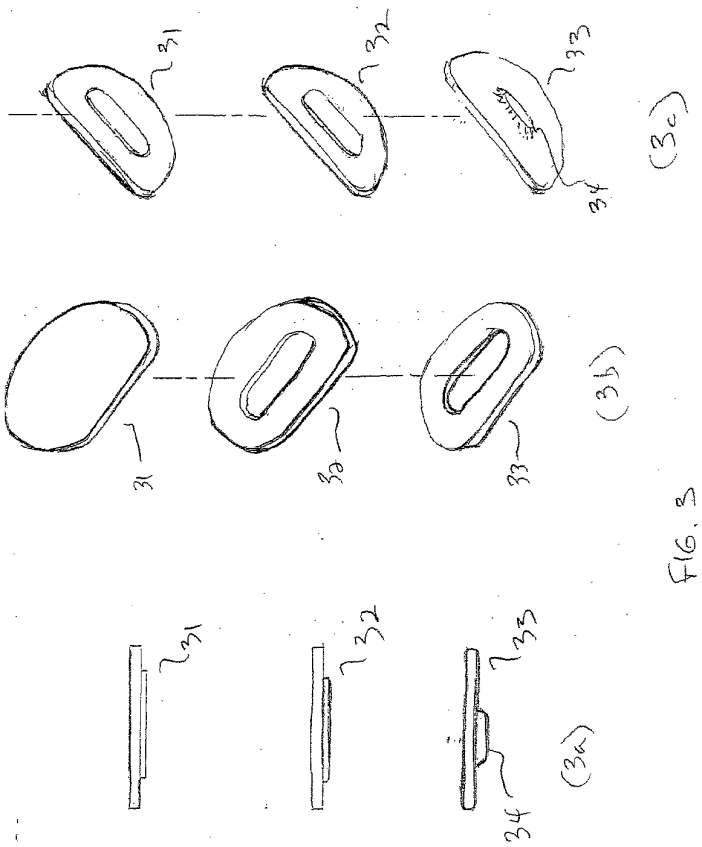

FIG. 3

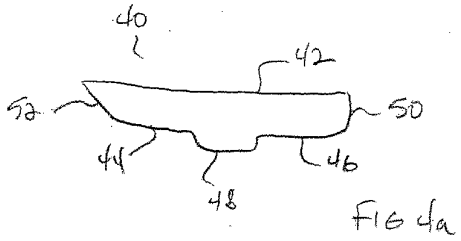

Fig 4a

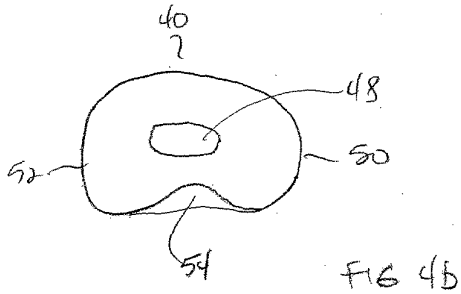

Fig 4b

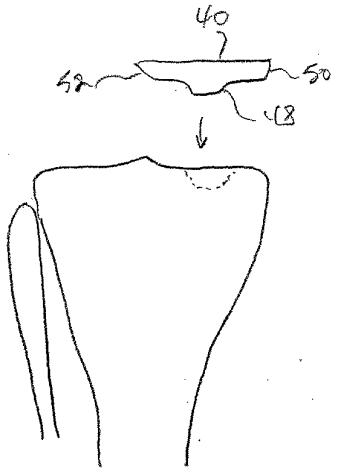

Fig 5a

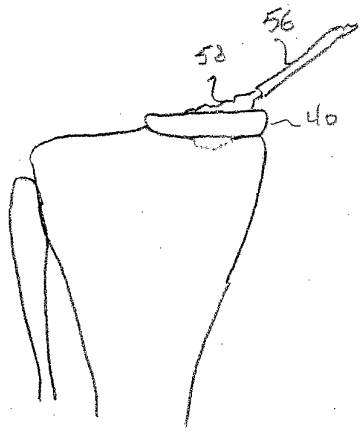

Fig 5b

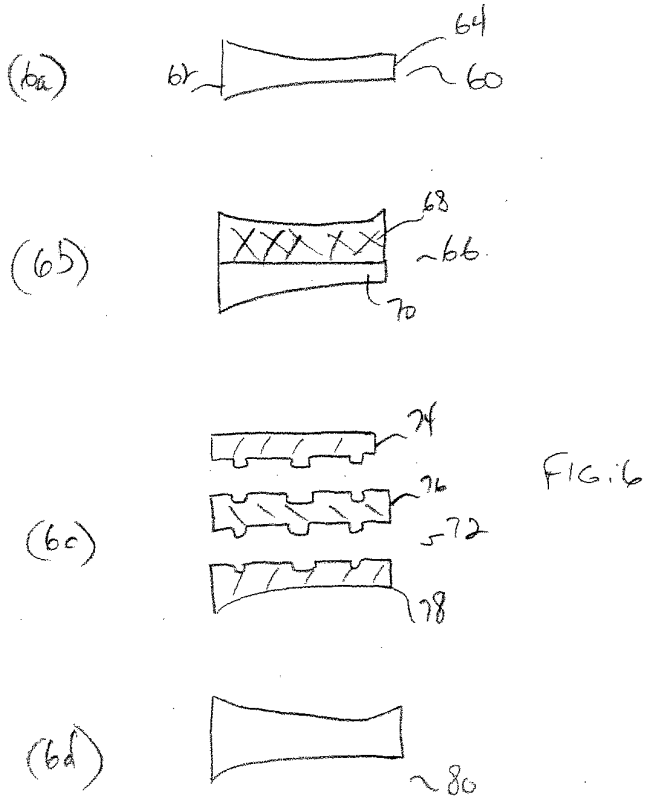

FIG. 6

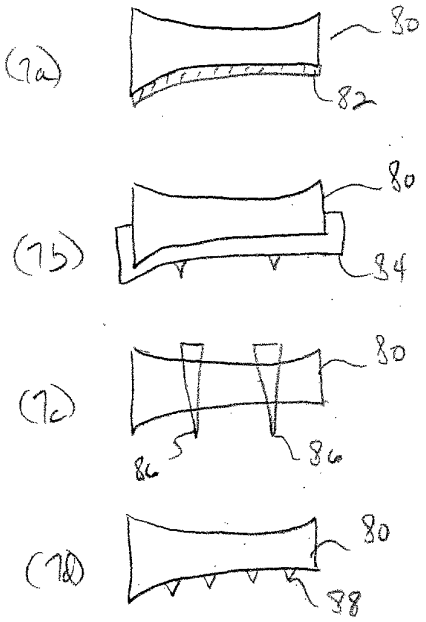

FIG. 7

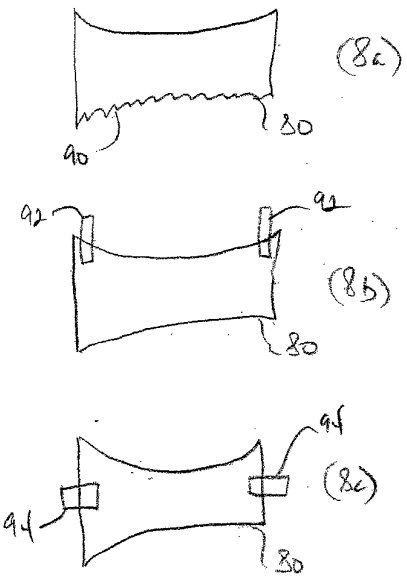

FIG. 8

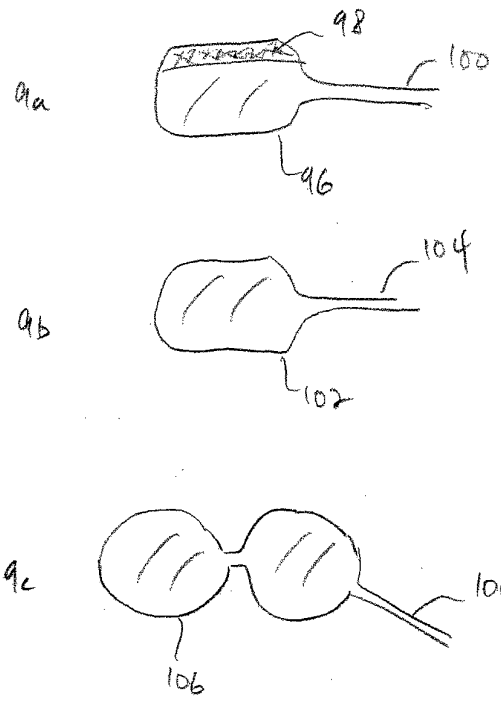

Fig. 9

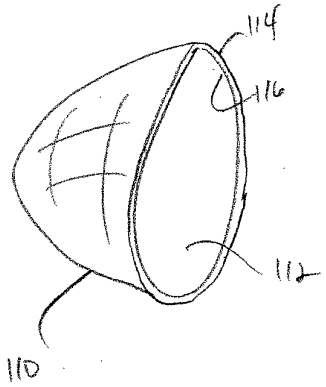

Fig. 10

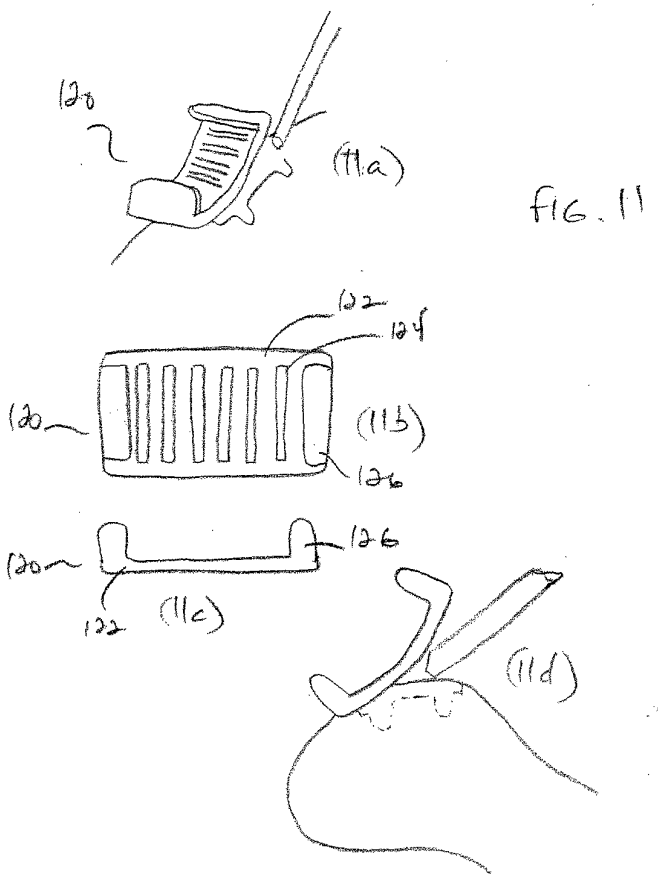

FIG. 11

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(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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21 November 2002

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(54) Title: METHOD FOR MAMMALIAN JOINT RESURFACING

(57) Abstract: A method and system for the creation or modification of the wear surface of orthopedic joints, involving the preparation and use of one or more partially or fully preformed and procured components, adapted for insertion and placement into the body and at the joint site. In a preferred embodiment, component(s) can be partially cured and generally formed *ex vivo* and further and further formed *in vivo* at the joint site to enhance conformance and improve long term performance. In another embodiment, a preformed balloon or composite material can be inserted into the joint site and filled with a flowable biomaterial in situ to conform to the joint site. In yet another embodiment, the performed component(s) can be fully cured and formed *ex vivo* and optionally further fitted and secured at the joint site. Preformed components can be sufficiently pliant to permit insertion through a minimally invasive portal, yet resilient enough to substantially assume, or tend towards, the desired form *in vivo* with additional forming there as needed.

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(54) Title: METHOD FOR MAMMALIAN JOINT RESURFACING

(57) Abstract: A method and system for the creation or modification of the wear surface of orthopedic joints, involving the preparation and use of one or more partially or fully preformed and procured components, adapted for insertion and placement into the body and at the joint site. In a preferred embodiment, component(s) can be partially cured and generally formed *ex vivo* and further and further formed *in vivo* at the joint site to enhance conformance and improve long term performance. In another embodiment, a preformed balloon or composite material can be inserted into the joint site and filled with a flowable biomaterial in situ to conform to the joint site. In yet another embodiment, the performed component(s) can be fully cured and formed *ex vivo* and optionally further fitted and secured at the joint site. Preformed components can be sufficiently pliant to permit insertion through a minimally invasive portal, yet resilient enough to substantially assume, or tend towards, the desired form *in vivo* with additional forming there as needed.

METHOD FOR MAMMALIAN JOINT RESURFACING

METHOD AND SYSTEM FOR MAMMALIAN JOINT RESURFACING

CROSS REFERENCE TO RELATED APPLICATIONS

This application is a continuation-in-part of Provisional US Application Serial No. 60/228,444, filed August 28, 2000, the entire disclosure of which is incorporated herein by reference.

TECHNICAL FIELD

In one aspect, this invention relates to biomaterials formed *ex vivo* for implantation and use within the body. In another aspect, the invention relates to *in situ* curable biomaterials. In yet another aspect, this invention further relates to the field of orthopedic implants and prostheses, and more particularly, for implantable materials for use in orthopedic joints.

BACKGROUND OF THE INVENTION

Applicant has previously described, *inter alia*, prosthetic implants formed of biomaterials that can be delivered and finally cured *in situ*, e.g., using minimally invasive techniques. See for instance, U.S. Patent Nos. 5,556,429, 5,795,353, 5,888,220, 6,079,868, 6,140,452, 6,224,630 and 6,248,131 as well as published International Application Nos. WO 95/30388 and WO 97/26847 and International Application PCT/US97/20874 filed 11/14/97 (the disclosures of each of which are incorporated herein by reference). Certain of these applications describe, *inter alia*, the formation of a prosthetic nucleus within an intervertebral disc by a method that includes, for instance, the steps of inserting a collapsed mold apparatus (which in a preferred embodiment is described as a "balloon") through a cannula that is itself positioned through an opening within the annulus, and filling the balloon with a flowable biomaterial that is adapted to finally cure *in situ* and provide a permanent disc replacement. See also, Applicant's "Porous Biomaterial and Biopolymer

Resurfacing System" (PCT/US99/10004), as well as "Implantable Tissue Repair Device (PCT/US99/11740), and "Static Mixer" (PCT/US99/04407) applications.

See also, US Patent Nos. 3,030,951 (Mandarino), 4,203,444 (Bonnell et al.), 4,456,745 (Rajan), 4,463,141 (Robinson), 4,476,293 (Robinson), 4,477,604 (Oechsle, III), 4,647,643 (Zdrahala), 4,651,736 (Sanders), 4,722,948 (Sanderson), 4,743,632 (Marinovic et al.), 4,772,287 (Ray et al.), 4,808,691 (Kōnig et al.), 4,880,610 (Constanz), 4,873,308 (Coury et al.), 4,969,888 (Scholten et al.), 5,007,940 (Berg), 5,067,964 (Richmond et al.), 5,082,803 (Sumita), 5,108,404 (Scholten et al.), 5,109,077 (Wick), 5,143,942 (Brown), 5,166,115 (Brown), 5,254,662 (Szycher et al.), 5,278,201 (Dunn et al.), 5,525,418 (Hashimoto et al.), 5,624,463 (Stone et al.), 6,206,927 (Fell), and EP 0 353 936 (Cedar Surgical), EP 0 505 634 A1 (Kyocera Corporation), EP 0 521 573 (Industrial Res.), and FR 2 639 823 (Garcia) , WO 93/11723 (Regen Corporation), WO 9531946 (Milner), WO 9531948 (Kuslich).

Applicant's PCT Application No. PCT/US97/00457 (WO 9726847A1) includes the optional use of a mold, such as a balloon, and describes the manner in which "[t]he mold created within the joint is preferably of sufficient shape and dimensions to allow the resulting cured biomaterial to replace or mimic the structure and function of the removed fibrocartilage. The mold can be formed of synthetic and/or natural materials, including those that are provided exogenously and those provided by the remaining natural tissues. The mold can either be removed from the site, upon curing of the biomaterial, or is sufficiently biocompatible to allow it to remain in position."

Applicant's later PCT Application No. PCT/US97/20874 (WO 9820939A2) further describes the manner in which " 'mold' will refer to the portion or portions of an apparatus of the invention used to receive, constrain, shape and/or retain a flowable biomaterial in the course of delivering and curing the biomaterial *in situ*. A mold may include or rely upon natural tissues (such as the annular shell of an intervertebral disc) for at least a portion of its structure, conformation or function. The mold, in turn, is responsible, at least in part, for determining the position and final dimensions of the cured prosthetic implant. As such, its dimensions and other physical characteristics can be predetermined to provide an optimal combination of such properties as the ability to be delivered to a site using minimally invasive means,

filled with biomaterial, and optionally, then remain in place as or at the interface between cured biomaterial and natural tissue. In a particularly preferred embodiment the mold material can itself become integral to the body of the cured biomaterial."

Applicant's own use of such mold apparatuses to date has concentrated largely on the use of thin, extensible balloons adapted to be positioned and then filled *in situ* with curable biomaterial, with particular use as a replacement for the intervertebral disc following microdiscetomy. In turn, there has been considerably less focus, to date, on the use of any such molds in other joints, such as the knee. Figures 6 and 7 of Applicant's PCT Publication No. WO 920939 A2, for instance, shows a balloon and corresponding drilling template for use in knee surgery, the balloon having foot portions protruding from a generally ovoid inflatable portion.

Finally, US Patent No. 6,206,927 describes a self-centering meniscal prosthesis device suitable for minimally invasive, surgical implantation into the cavity between a femoral condyle and the corresponding tibial plateau is composed of a hard, high modulus material shaped such that the contour of the device and the natural articulation of the knee exerts a restoring force on the free-floating device. In what appears to be a related manner, Sulzer has introduced a unicompartmental interpositional spacer to treat osteoarthritis in the knee. See "Little Device Could Pack a Big Punch", Sulzer Medica Journal Edition 2/2000 (www.sulzermedica.com/media/smj-full-tex/2000/0002-full-text-6.html). The device is described as a metallic kidney-shaped insert which fills in for the damaged cartilage between the femur and the tibia.

Such a metallic device, as described in either the Fell patent and/or Sulzer's product literature, is described as appropriate for use in younger patients with moderate to severe chondromalacia, particularly since the product provides a hard, self-centering meniscal device that is "devoid of physical means that fix its location". In so doing, the device of Fell et al. tends to require a significant amount of intact cartilage and meniscus. Applicant's own products to date, including those improved embodiments described herein, have been largely geared toward more elderly patients, where such healthy cartilage is lacking. In turn, Applicant's devices tend to provide angular correction and improved anchoring of the implant at the joint surface.

In spite of developments to date, there remains a need for a joint prosthesis system that provides an optimal combination of properties such as ease of preparation and use, and performance within the body.

BRIEF DESCRIPTION OF THE DRAWING

In the Drawing:

Figure 1 shows top and side perspectives of a preferred preformed knee implant prepared according to the present invention.

Figure 2 shows an embodiment in which preformed components adapted to be inserted and assembled *in situ*.

Figure 3 shows an alternative embodiment in which preformed components are employed.

Figures 4 and 5 show an embodiment in which a substantially open (saucer-shaped) mold is inserted into the joint site, to be filled with a corresponding curable biomateral *in situ*.

Figure 6 shows a variety of alternative embodiments that include one or more preformed component.

Figure 7 shows a variety of alternative means for anchoring a preformed component such as that shown in Fig. 6d.

Figure 8 shows a further variety for anchoring or stabilizing a preformed portion by the use of ancillary portions and/or surface texture.

Figure 9 shows a variety of embodiments in a substantially closed (balloon like) mold is adapted to be inserted into the joint site and filled with a corresponding curable biomaterial.

Figure 10 shows a mold adapted for use as an acetabular mold in connection with the replacement of the articulating surface in a hip.

Figure 11 shows a patella femoral joint form suitable for use in combination with the method and system of this invention.

SUMMARY OF THE INVENTION

The present invention provides a method and system for the creation or modification of the wear surface of orthopedic joints, and particularly articulating

joints such as the knee. In one preferred embodiment, the method relies, at least in part, upon the manner in which the various stages of curing a curable biomaterial, and in turn, the various stages of forming a component from the cured or curing biomaterial, can be correlated and optimized in a desired manner. In turn, such a method provides the ability to both generally and specifically form the component for use *in situ*.

The present invention includes a variety of embodiments, each of which preferably includes one or more components that are formed *ex vivo*, and that are adapted to be inserted and finally formed or assembled *in situ* in order to provide a final prosthesis and articulating joint surface. Examples of the various embodiments include, for instance,

1) one or more components that are each partially molded *ex vivo*, in a manner that permits the component to be inserted and finally formed *in situ*,

2) a plurality of preformed components adapted to be assembled *in situ*, for instance in an overlapping or interlocking fashion,

3) an insertable open (e.g., saucer shaped) mold, adapted to be inserted and positioned within the joint site, and there used in combination with a flowable biomaterial adapted to be delivered to the open mold *in situ*, under conditions that permit the flowable biomaterial to cure in contact and/or combination with the mold in order to form a final prosthesis,

4) one or more generally extensible envelope (e.g., balloon- type) molds, adapted to be positioned and filled *in situ* with corresponding curable biomaterials, one or more of the molds themselves providing one or more regions of generally non-extensible, preformed material. In one embodiment, for instance, a plurality of such envelope portions (e.g., a bi-compartmental single envelope) can be adapted for use on both the medial and lateral tibial surfaces, respectively.

By the selection and use of a suitable biomaterial, and other features as described herein, the present invention provides an optimal combination of benefits, as compared to methods previously described. Such benefits include those that arise in the course of preparation and storage (e.g., sterility, storage stability), those that arise in the surgical field itself (e.g., ease of use, adaptability, predictability), and those that arise in the course of long term use within the body (e.g., biocompatibility,

moisture cure characteristics, tissue congruity and conformability, retention, wear characteristics, and physical-mechanical properties).

In one preferred embodiment, the method and system involve the preparation and use of partially cured components that can be formed outside the body, for insertion and placement into the body, and that can then be further formed within the joint site in order to enhance conformance. The ability to finally form one or more components *in situ* provides various additional benefits, such as increased control over the overall size and shape of the final prosthesis, improved shape and compliance of the surface apposing natural bone, and finally, improved shape and compliance of the opposite, articulating surface.

As used herein, the word "cure", and inflections thereof, will refer to the extent to which a curable biomaterial, as used to form a component of this invention, has begun or completed whatever physical- chemical reactions may be contemplated in the course of fully forming the component, at the surgical site, for long term use *in situ*. In turn, the biomaterial can be considered as uncured (as in component parts that have not yet been mixed or compositions that have not yet been activated), or it can be partially cured (e.g., wherein the components have been mixed, or compositions activated, under conditions suitable to begin the curing process), or it can be fully cured (e.g., in which case, whatever chemical reactions may have occurred have substantially subsided). Generally, uncured compositions are sterile, storage stable, and often flowable, though are typically not yet formed or capable of being formed.

Curing compositions, by contrast, generally begin as flowable compositions, but become nonflowable over a finite time period as they begin to gel or set. Curing compositions can also be minimally formed, e.g., outside the body by the use of molds and/or suitable shaping tools, and/or within the body, as by the initial positioning of the component on supporting bone and by the repositioning of opposing, articulating bone surfaces. Thereafter, it is contemplated that certain compositions of this invention can be further formed, over time, as by the gradual effect of articulating bone in the course of long term use.

As also used herein, the word "form", and inflections and variations thereof, will refer to the manner and extent to which a component has been sized and shaped, in either a general and/or specific manner, for use at a joint site. In turn, the forming

of such a component can occur either *ex vivo* and/or *in vivo*, as well as in a general manner (e.g., by the use of an *ex vivo* mold or tools) and/or a specific manner (e.g., by final curing in apposition to supporting bone and/or opposing articulating bone surfaces), as well as combinations thereof.

A component can be "specifically" formed in this manner in order to conform the component (and particularly its surfaces) to the corresponding specific shapes and dimensions of bone *in situ*, including both supporting bone surfaces and/or opposing (e.g., articulating) bone surfaces. Such specific conformation, in turn, can be used to improve a variety of characteristics of the final implant, including comfort, mechanical performance, and/or long term stability. Such conformation can also include aspects in which one or more components, or the composite prosthesis, are "conformed" in correspondence with the joint site (e.g., by final shaping and curing processes that occur *in situ*).

Such conformation can also include aspects in which the components, or prosthesis itself, are adapted to be "deformed" within the site, as by the application of force. For instance, a substantially fully formed component can be provided to have sufficient mechanical properties (e.g., strength and resilience) to permit it to be inserted into a joint site and effectively deformed under normal anatomic forces For instance, a substantially convex component can be deformed to assume the corresponding concave shape *in situ*, in , while retaining sufficient resilient strength to tend towards its original convex shape (e.g., analogous to the manner in which a locking washer can be deformed in use, while tending toward its original shape). Preferably, a final knee component is adapted to be deformed under conditions of use within the body (e.g., under physiologic load), while maintaining desired size and tibial congruency, and in a manner that provides desired fit and thickness for desired angular correction.

Hence a "preformed" component will generally refer to a component that is at least partially formed *ex vivo*, as by the surgeon's selection and use of an appropriately sized *ex vivo* mold. Such a preformed component can be specifically formed as well, including in an *ex vivo* fashion, as by the use of a customized mold that is itself reflective of the particular dimensions and contours of the intended joint site. Such customized molds can be prepared, for instance, by the use of external

imaging means, and/or by the appropriate use of negative and/or positive molds taken at the tissue site. Optionally, and preferably, the preformed component is specifically formed, in whole or in part, by being positioned *in situ*, prior to the completion of the curing process, and in apposition to both supporting bone and opposing bone surfaces. Once positioned within the joint site, any such component or prosthesis can be adapted to be deformed in order to improve its retention and/or performance *in situ*, e.g., resiliently deformed upon release of distracting forces and repositioning of the opposing bone surface.

For instance, a preformed composition is provided, formed initially by the *ex vivo* onset of cure, in which the composition can be implanted within on the order of 10 seconds to several days of the onset of cure, preferably within about 30 seconds to about 10 minutes, and more preferably within about one to about five minutes, while maintaining a surface exotherm of less than about 50C, and more preferably less than about 45C once positioned within the body.

Once positioned *in vivo*, preferred preformed components of this invention are adapted to be finally shaped, for a period of between about 10 seconds and one or more hours, and more preferably between about one minute and about five minutes. The lower limit is defined largely by the time it takes to effectively reposition bone, or otherwise re-establish suitable force on the implant. The upper limit, in turn, is generally defined by the susceptibility of the implanted composition to further deformation or shaping. Such final shaping is generally accomplished, at least in part, under the force brought about by repositioning articulating bone surfaces. In one preferred embodiment, the partially cured composition is implanted under conditions that permit it to deform less than about 15%, preferably less than about 10%, and most preferably less than about 5%, under physiologic forces, while maintaining tibial congruency and imparting desired angular correction.

Hence, a particularly preferred preformed component of this invention can be implanted within an initial about one to about five minutes of the onset of its formation, and once implanted can be further molded or formed for a further period of about one to about five additional minutes, in a manner that permits the resultant implant to substantially retain a desired final form and function.

The system of the present invention thereby provides the surgeon with a variety of options, based on the manner in which these curing and forming processes are correlated. In one particularly preferred embodiment, for instance, the surgeon is provided with a composition adapted to be partially cured and generally formed *ex vivo*, and then promptly inserted into the body and positioned at the joint site, where it can be finally, and specifically, formed in the course of becoming fully cured.

By partially curing the prosthesis *ex vivo*, the present system simplifies the preparation process considerably, e.g., by lessening or avoiding potential problems (such as curing in the presence of moisture, and surface exotherm in the presence of tissue) that can arise when a comparable composition is mixed and delivered to the joint site while it is still flowable. Surprisingly, the present system permits such prostheses to be not only formed, but also manipulated and inserted into the joint (e.g., through an incision of between about 1 cm and about 3 cm). Once inserted, the prosthesis can be positioned, and further formed *in situ*, all within a reasonable time frame. In fact, it has been found that the procedure is amenable to outpatient use and even regional anesthesia.

Moreover, the present system can avoid the use of such processes as the drilling anchor holes into the underlying bone, distraction of the knee joint, ligament release, leveling of the tibial plateau, and the various other procedures typically involved with delivering the biomaterial directly to the joint site in still flowable form. Yet, the prosthesis of the present invention provides a combination of properties such as the extent of congruence with underlying bone, wear characteristics, fracture toughness, and avoidance of fibrillated articular cartilage, that meets or exceeds the combination of properties obtained using a comparable biomaterial in flowable form, delivered and largely cured *in situ*.

In addition to its immediate use in such joints as the knee, the system of the present invention provides particular advantages when applied to ball and socket joints, such as the hip. In one such embodiment, a balloon can be filled with a biomaterial as described herein, and inserted and positioned within the acetabulum, prior to or following filling, to provide a soft, conformable, durable lining for the placement of a hip prosthetic portion.

In a further embodiment, the method and system involve the preparation and use of one or more partially or fully cured component(s) formed outside the body, for insertion and placement into the body and optionally further fitting and securing at the joint site. These preformed component(s) typically require less manipulation at the bedside and allow for alternative methods of terminal sterilization, and final inspection and release at the manufacturing site.

DETAILED DESCRIPTION

The method and system (e.g., preformed component(s) and/or curable biomaterial and mold) can be used to prepare a final prosthesis, *in vivo*, that provides a first major surface in apposition to and retained upon the supporting bone itself, and a second (generally substantially parallel and opposite) major surface adapted to provide a wear surface for opposing (e.g., articulating) bone. By "retained upon" it is meant that the final prosthesis is maintained in a desired position upon the supporting bone surface in a manner suitable for its intended use, e.g., by the use of one or more anchor points, by the use of adhesive or other suitable interface materials, by the use of sutures, staples, and the like, and/or by a mechanical lock achieved by the combination of a bone-contacting surface suitably conformed or conformable to the terrain of supporting bone, together with the retaining (and optionally including deforming) effect achieved upon repositioning opposing articulating bone surface.

The first and second major surfaces can be provided in any suitable manner, for instance, 1) by the preparation and insertion of a single partially cured and generally preformed component into the joint, preferably under conditions that permit the component to become further, and specifically, formed *in vivo*, 2) by adding a flowable biomaterial to an initial preformed component (e.g., in the shape of a balloon or open mold) positioned at the tissue site, 3) by placing one or more fully cured and preformed components at the tissue site and optionally further fitting, adapting and/or securing the component(s) as needed, and/or 4) by assembling one or more preformed components *in situ* (e.g., side by side in an interlocking fashion upon the surface) such that the assembled components cooperate to provide the first and second major surfaces.

In addition to the partially or fully cured preformed component(s) and/or curable biomaterial and related molds, the method and system of this invention include the optional use of various additional materials and/or steps, e.g., to prepare the bone surface itself, to provide suitable interfaces (e.g., adhesive interfaces and/or protrusions that can be further secured to the joint site or by smoothing of the femoral condyle or tibial plateau as needed), to treat one or more surfaces in order to provide them with different or improved properties as compared to the inherent properties of the material providing the surface, and the like. Examples of such materials include, for instance, the use of adhesive materials, tissue in-growth stimulators, and fibrous materials (e.g., webs adapted to tether the implant and/or to facilitate fibrous tissue ingrowth).

The partially or fully cured preformed component(s) can themselves each provide uniform or non-uniform properties, and can be provided in a plurality or range of styles and sizes. These components can be designed to conform to lateral or medial compartments, or both, and to right or left knees, or both. In a preferred embodiment, all embodiments can be inserted into the joint site in a minimally invasive fashion. By "minimally invasive", in this context, it is meant that the procedure of sizing, inserting, positioning and forming the prosthesis, *in situ*, can preferably be accomplished without the need for open, invasive incisions of the type conventionally used for inserting total knee prostheses. In a preferred embodiment, the partially cured preformed components can be further formed and fully cured *in vivo* to enhance compliance with the joint site.

The surface of the partially or fully cured preformed component(s) can also be modified to provide any desired properties (e.g., promote adhesion), such as by the design and use of polymers themselves or by surface treatment of the fully cured or curing embodiments to provide suitable reactive groups such as amines, hydroxyl groups, or other reactive or hydrogen bonding functionalities. Similarly, the partially cured preformed component or fully cured component, including balloons or composite materials, can be provided with appropriate surface coatings, e.g., biologically active agents to promote desired tissue interactions, including tissue or cellular adhesion, such as those selected from the group consisting of cytokines, hydroxyapatite, collagen, and combinations thereof.

In one embodiment of this invention, partially cured, and generally preformed components are inserted into the joint site, and there further and specifically formed to enhance compliance. In an alternative embodiment, fully cured components in the shape of a balloon or open mold are employed to provide a final composite material by inserting the balloon or mold into the joint and there filling it with a biomaterial that cures *in situ* and conforms with the joint site. In another alternative embodiment, the fully cured component(s) are provided and inserted into the joint either singly or piecemeal and optionally further fitted and secured *in vivo*.

As an example of the first such embodiment, the invention provides an open *ex vivo* mold, adapted to approximate the desired dimensions of the joint site, and to receive a curable biomaterial. A suitable mold can be formed, for instance, from the use of conventional materials such as silicone materials, that permit the curing biomaterial component to be easily and entirely removed at the desired time. Optionally, the mold can itself be provided with a coating or release liner, including those that can be integrated, in whole or in part, with the component thus formed. Once the flowable biomaterial has been delivered and partially cured in this *ex vivo* mold, and any optional molding or fabricating steps have occurred, the biomaterial can be removed from the mold and inserted into the joint site, under conditions suitable to permit it to be further and finally formed *in vivo* to enhance conformance with the joint site. Optionally, additional *ex vivo* forming steps or features can be performed, e.g., by imparting desired curvature and femoral glide paths, prior to inserting and final forming *in vivo*.

Also, in the course of molding the component *ex vivo*, and/or transferring it to the tissue site, various structures and/or materials can be incorporated into and/or onto the component itself, to enhance its placement, retention and/or performance *in situ*. For instance, the mold itself can be provided in a form sufficient to impart various integral structural features, such as tibial "tabs", adapted to provide or improve the retention of the component at the tissue site. Such tabs, for instance, can be provided in the form of one or more protrusions integral with the mold itself and adapted to be positioned within and/or affixed to the soft tissue and/or bone *in vivo*. Examples of such tabs are shown, for instance, in Figure 1, where reference number 18 depicts a raised posterior portion.

An insertable component can also be provided with one or more ancillary portions or protrusions formed of materials other than that used to form the bulk of the component itself. For instance, sutures or fibrous materials can be incorporated into or onto the bulk material, for use in improving the initial and/or long term retention of the component *in situ*, e.g, by tethering the prosthesis at the joint site and in a desired position. Such other materials can be temporarily positioned into or upon the mold itself, for instance, or otherwise provided, in a manner that permits them to become integrated into the biomaterial as it fills the mold and becomes partially cured *ex vivo*. With the resulting component positioned *in situ*, the protrusions can be used to tether the implant, by securing them to the surrounding soft tissue and/or bone by use of adhesives, sutures, screws, pins, staples or the like or combinations thereof. The materials can provide both an immediate fixation function, and optionally also a desired long term function, by permitting them to be either absorbed by the body over time, and/or to permit or encourage fibrous tissue ingrowth for long term fixation.

The reinforcing material can be provided in any suitable form, e.g., as fibers (e.g., sutures) or as a uniform woven or non-woven fabric, optionally including one or more reinforcing fibers or layers. A suitable non-woven fabric, for instance, is preferably a material such as is commercially available under the trade name Trevira Spunbond from Hoechst Celanese Corporation. The non-woven fabric is generally composed of continuous thermoplastic fiber, needle punched together to yield a felt-like fabric. In addition to fabrics like Trivira Spunbond, other materials such as polyester staple mat, glass fiber mat, as well as other organic and inorganic fiber mats and fabrics can be employed.

Reinforcing fibers can be included within the woven or non-woven fabric, or provided as separate layers of a composite. Such fiber layers can preferably include a directional reinforcing fiber layer of organic or inorganic structural reinforcing fibers such as fiberglass, carbon fibers, aramid fibers which is available from DuPont Corporation under the trade name Kevlar, linear polyethylene or polypropylene fibers such as is commercially available from Allied-Signal, Inc. (now Honeywell) under the trade name Spectra, or polyester fibers. The phrase "reinforcing fiber" can include any fiber which, when used in its own right or added to a composite fabric material, retains or enhances desired structural properties. The fibers can be randomly oriented,

or preferentially, they can be oriented in one or more directions. While a number of specific types of materials have been given for use as the reinforcing fiber layer, it will be appreciated by those of ordinary skill in the art that other equivalent-type reinforcing fiber layers can be employed in the practice of the invention. A reinforcing fiber layer can be itself used to secure the prosthesis, or can be attached to a woven or non-woven fiber layer having a number of interstices or pores. Preferably, the reinforcing fiber layer and other fiber layers are secured to each other mechanically, as by conventional stitching, needle punching, stapling or buttons. In the case of certain applications, adhesives can also be used.

Similarly, a partially cured preformed component (and/or ancillary portions incorporated therein) can also be provided with suitable means to improve its ability to retain the component *in situ*, e.g., by the use of surface characteristics that provide improved chemical interactions with the joint site. Such interactions can be achieved by the judicious use of bulk material compositions themselves and/or the use of adhesives or other suitable interface materials. The partially cured, preformed, component can also be physically modified to increase its interactions with joint site, as by surface roughening, etching or cross-hatching, which would tend to provide increased surface area, and in turn, improved mechanical retention. A partially cured, preformed, component can also be retained by external means that are otherwise secured to the surrounding bone and/or soft tissue by use of adhesives, sutures, screws, pins, staples or the like or combinations thereof. On the major surface opposing articulating bone, the partially cured preformed component can be provided with suitable means as well, intended to improve or alter either its compliance and/or interactions with the opposing bone surface.

In one particularly preferred embodiment, the system includes a partially cured preformed component that is first molded outside of the joint site and adapted to be delivered to a tissue site and there positioned in a fixed position. The mold can be of an open or closed configuration (and/or can involve a one- or multi-step molding process), adapted to preform one or both major surfaces, respectively. Once positioned, the partially cured component is adapted to be initially fit and positioned within the joint site, and to thereafter become better conformed to the specific dimensions and/or terrain (e.g., anatomic structure) of the joint site *in vivo*.

Optionally, and preferably, the molds are designed to yield components that have optimum adhesion and conformance to the joint sites. The molds may also be heated during the *ex vivo* partial curing process to optimize component properties or to provide a component that is more formable *in vivo*.

In an alternative preferred embodiment, the method and system involve the preparation and use of one or more fully or partially cured component(s) formed outside the body, for insertion and placement into the body and optionally further fitting and securing at the joint site. In one embodiment, the invention provides a single preformed component that is inserted into the joint site and optionally further fitted or secured as needed. In another embodiment, the invention provides a plurality of preformed components, formed of the same or different materials, and adapted to be delivered and positioned at the tissue site in a manner that provides a final composite. The components can be combined at the site in any suitable fashion, e.g., by providing a mechanical lock and/or by the use of interfacial materials such as adhesive layers. The components can be combined in any suitable fashion, e.g., as layers upon the bone, or as individual side-by-side components adapted to traverse the bone surface when combined. The use of preformed component(s) can require less manipulation at the bedside and allow for alternative methods of terminal sterilization, and final inspection and release at the manufacturing site. The various means of retaining partially cured preformed components, discussed herein, can be adapted to work with fully cured preformed components.

The method and system of this invention can be used for repairing a variety of mammalian joints, including human joints selected from the group consisting of the tibial plateau of the knee, the acetabulum of the hip, the glenoid of the shoulder, the acromion process of the shoulder, the acromio-clavicular joint of the shoulder, the distal tibial surface of the ankle, the radial head of the elbow, the distal radius of the forearm, the proximal phalanx surface of the great toe, the proximal metacarpal surface of the thumb, and the trapezium of the wrist.

Those portions or combinations of preformed component(s) that contact the bone surface are preferably adapted to physically conform closely to the prepared bone surface, e.g., to its macroscopic physical contours. Such conformation can be provided or enhanced in any suitable manner, e.g., 1) by providing a partially cured

preformed component that is first made in an *ex vivo* mold and then adapted or modified to conform to the surface (e.g., by further forming *in vivo*), and/or 2) by use of a preformed balloon or composite mold material that is inserted into the joint site and filled with a flowable biomaterial that cures *in vivo* so that it conforms with the joint site and/or 3) by the use of fully cured preformed component(s) that has optimum geometry for biomaterial compliance once placed in the joint site and/or 4) by the preparation and use of a suitable (e.g., thin) interface material between bone and preformed component (e.g., adhesive, filler, or cement material), and/or 5) by the use of physical restraining means, such as adhesives, pins, staples screws, sutures or the like that are attached to protrusions in the component itself or to an external means of securing it.

The method and system of this invention will be further described with reference to the Drawing, wherein

Figure 1 shows a top and side perspective of a preferred preformed knee implant (10) prepared using an *ex vivo* mold according to the present invention. The implant provides a first major surface (12) adapted to be positioned upon the tibial surface, and a generally planar second major surface (14) adapted to be positioned against the femoral condyle. In a typical embodiment, the second major surface, in turn, is preferably provided with a femoral glide path (16) to facilitate its performance *in situ*, in the form of a generally central oval depression about 1 mm to about 5mm deep at its lowest point (2 mm as shown) and about 30 mm to about 50 mm in length by 10 mm to 30 mm in width (40 mm by 20 mm as shown). Those skilled in the art, given the present description, will readily determine the actual dimensions for optimal use, in both absolute and relative terms, depending on such factors as the actual joint size and desired results (e.g., angular correction). As shown, the implant is also provided with a raised tibial projection (18), adapted to catch the posterior portion of the tibial plateau. The implant can have dimensions on the order of between about 40 to about 60 mm in the anterior-posterior dimension, between about 30 mm to about 40 mm in the medial-lateral dimension, and a maximum thickness (at the posterior lip of between about 10 mm and about 20 mm.

Figure 2 shows an embodiments in which a plurality of preformed components are adapted to be inserted and assembled *in situ* to provide the final implant (20)

Figure 2a shows an embodiment, in which preformed components (22 through 25, respectively) are assembled in a side-by-side manner sequentially, and *in situ*, and upon the tibial surface. The matable preformed sections each provide at least a portion of the resultant bone-contacting surface and wear surface, as well as one or more portions adapted to provide a mechanical lock with one or more respective other portions. The mechanical lock can be achieved in any suitable manner, as by the provision of corresponding male and female portions, respectively. The portions can be mated, *in situ*, e.g., in a press fit or sliding manner, in order to attach the respective components. As can be seen in the raised perspective of the same embodiment, and Figure 2b, in the resultant assembly, the combined components cooperate to provide both a tibial bone-contacting surface (28) and a wear surface (26).

In the alternative embodiment of Figure 3, rather than being positioned in a side-by-side fashion across the bone surface (as in Figure 2), a final implant is provided using interlocking preformed components (show in this case as portions 31 through 33, respectively) are instead provided in a form that permits them to be stacked upon each other, e.g., by layering or sliding them onto each other, and positioned upon the surface, *in situ*. The portions can be assembled in any suitable fashion, e.g., entirely on the tissue site, entirely *ex vivo*, or in varying combinations as desired. Optionally, and preferably, the generally planar portions are provided with corresponding matable portions, e.g., in the form of grooves and tabs to provide a sliding fit, or a depression and corresponding projection to provide either a press fit, snap fit, or other suitable fit sufficient to prevent lateral displacement to the extent desired. The resultant formed prosthetic implant can be provided with various features as described herein, including desired molded portions adapted to provide better fit or performance. Top portion (31) is particularly well suited to provide a desirable wear surface, while one or more intermediate portions (as shown by element 32) are adapted to provide an optimal combination of such properties as thickness, cushioning, and angular correction. As shown the lowermost portion (33) is shown with a projection (34) adapted to be retained within a corresponding anchor hole or suitable depression formed into the bone itself. Figures 3b and 3c provide generally bottom and top views, respectively, showing the manner in which the portions can be combined in a layered fashion.

In the embodiment of Figure 3, preformed layers are shown having protrusions adapted to be positioned in a corresponding indentation within each underlying layer (or bone), in order to form a compact stack. In such an embodiment, the corresponding system will typically include at least two preformed components, including the initial, bone-contacting component, and final component providing the wear surface. The system can provide one or more intermediate layers, e.g., the number and/or selection of which can be used to provide a final desired height to the overall composite, and/or to provide differing properties (e.g., with respect to compressibility, resilience, tissue ingrowth), and/or to provide improved retention between the first and final components.

Figure 4a shows an embodiment in which a substantially open (saucer-shaped) mold (40) is inserted into the joint site, to be filled with a corresponding curable biomateral *in situ*. The top (42) of the mold is open to receive biomaterial (not show), while the bottom (44) provides a lower major surface (46) adapted to contact bone and terminates in a filled protrusion (48) adapted to be positioned within a corresponding anchor point drilled in the bone itself. The anterior edge (50) of the cup is substantially perpendicular to the plane of the cup itself, while the posterior edge (52) is tapered (and optionally raised) to accommodate the corresponding shape of the tibial spine.

As shown, and for use in an adult human, the *ex vivo* mold accommodates a predetermined volume of biomaterial of on the order of about 5 ml to about 15 ml. As a further advantage of this invention, the amount of biomaterial actually can be predetermined and controlled to correspond with the *ex vivo* mold volume. In addition the *ex vivo* molds are designed for optimum sizing and conformance to the joint site and MRI software may be used to chose best mold for joint site. Implant thickness and hence angular correction can be controlled in this way.

Figure 4b shows a bottom perspective view of the mold apparatus of Figure 4a, showing the filled protrusion (48). The posterior edge portion can be seen as provided with a groove or indentation (54), again to accommodate the typical shape of the corresponding tibial spine. Overall, the mold can be seen as assuming a generally kidney-shaped configuration, adapted to correspond with the tibial surface. Such a

mold can be provided in a plurality of sizes, and shapes, to be selected at the time of use to accommodate the particular patient's needs and surgeon's desires.

Figures 5a and 5b show the mold of Figure 4a being positioned upon a tibial surface (Fig. 5a), with the protrusion positioned within a corresponding anchor point, and (in Fig. 5b) with the tip of a biomaterial delivery cannula (56) positioned upon it, and with flowable biomaterial (58) being shown in the course of delivery.

Figure 6 shows a variety of alternative embodiments that include one or more preformed component. Fig. 6a shows a simple wedge shaped embodiment (60), in which the posterior portion (62) is significantly increased in size as compared to the anterior (64). Fig. 6b shows an implant (66) molded to provide portions (here, layers) having differing wear characteristics, including a preformed top having improved wear as compared to the separately formed bottom portion (70). Fig. 6c, by comparison, shows a plurality of components (72) adapted to be positioned and assembled in situ at the time of surgery. These include an upper portion (74) having improved wear characteristics as compared to the others, a bottom portion (78) being suitably formed to the patient's geometry and desired angular correction, and one (or more) central portions (76) adapted to be positioned between the top and bottom portions to achieve desired properties such as overall thickness, angles, and/or physical chemical properties (such as moduli).

The embodiment of Figure 6d shows a single piece (80) as might be cut from preformed material at the time of surgery, while Figure 7 shows a variety of alternative means for anchoring a preformed component such as that shown in Fig. 6d. These include the use of a grout (82) or other suitable interface material as shown in Fig. 7a; the use of a separate external retaining device (84) as shown in Fig. 7b; the use of externally provided pins, screws, sutures, etc. as exemplified by elements (86) which generally traverse the body itself as in Fig. 7c; and the use of one or more anchor portions (88) positioned along one or more suitable surfaces as shown in Fig. 7d.

Figure 8 shows a further variety for anchoring or stabilizing a preformed portion by the use of ancillary portions and/or surface texture, including a roughened surface (90) as in Fig. 8a; or tabs (e.g., provided by fabric or suture like materials) as shown as elements 92 and 94 of Figs. 8b and 8c, respectively. In practice, the

preformed components can benefit from any suitable combination of the various features and embodiments described or shown herein.

Figure 9 shows a variety of embodiments in a substantially closed (balloon like) mold is adapted to be inserted into the joint site and filled with a corresponding curable biomaterial, the mold itself providing a preformed articulating wear surface, including Fig. 9a which shows an inflatable balloon portion (96) that includes an integral preformed wear surface and portion (98), as well as a lumen (100) adapted to fill the inflatable portion with flowable biomaterial. Fig. 9b shows a corresponding balloon (102) though without a preformed portion, and including its biomaterial lumen (104). Although not shown, the balloon of this or any embodiment can include various interior and/or exterior surface coatings, and can have regions and/or layers having different desired physical-chemical properties (such as porosity). Fig. 9c shows a bi-compartmental closed balloon-like mold (106), wherein each compartment is adapted to conform to a respective medial or lateral tibial surface.

Figure 10 shows a mold adapted for use as an acetabular mold (110) in connection with the replacement of the articulating surface in a hip, when filled with biomaterial, the mold forming a concave portion adapted to retain a corresponding femoral head. The mold is shown providing a thin generally cup-shaped mold adapted to be filled in any suitable form (e.g., using a removable conduit (not shown) attached to the space between inner and outer sealed layers (116 and 114, respectively) forming the mold.

Figure 11 shows a patella-femoral joint form suitable for use in combination with the method and system of this invention. As shown in the views of 11a through 11c, the form includes a silicone or other suitable pad material (122) having aluminum or other suitable stay portions (124) and terminal handle or grasping portions (126). In use, with the knee at a generally 45 degree angle, the piece is formed to the femoral bone surface, with its form maintained by bending the aluminum stays. With anchor points cut into the femoral bone, if desired, the form is held tight against the bone with the upper handle held away from bone to permit the delivery of curable biopolymer between the form and the bone. As polymer is placed onto the bone (and into any anchor points) the form is maintained for a time sufficient to suitably form the polymer, whereafter it can be removed.

As described in Applicant's co-pending US provisional application 60/228,444, the present application describes a method and system for the creation or modification of the wear surface using an implanted material fixed to the support structure of the original wear surface, to generally conform to the shape of the original surface in a mammal. A method or system where the end of the bony surface is a rotating, sliding or rolling surface, such as in the knee, finger, hip, toe, spine, wrist, elbow, shoulder, ankle, or TMJ joint. The implant will function:

a) as a spacer,

b) as an impact absorber

c) as a surface with improved coefficient of friction (as compared to the diseased surface), and/or

d) to increase the weight bearing area and improve congruency of the joint surface (as compared to the diseased condition).

The method and system of this invention can be applied to areas of aseptic necrosis, such as the nevecular bone in the wrist. The material to be implanted consists of a plurality of materials, such as polymers, including polyurethane, polyethyelenes, polyureas, polyacrylates, polyurethane acrylates, hydrogels, epoxies and/or hybrids of any of the above.

In an alternative embodiment, the surface can be provided by any of a series of metals, including titanium, stainless steel, cobalt chrome millithium alloys and tantalum. Other surface materials can include various ceramics and biologic polymers.

The implantable material for the resurfacing can be formed ex vivo and/or in vivo as an injectable material that sets up to the molded shape. The methods for changing state from liquid to solid state include cooling or heating, the passage of time, which allows for a change of state, or a chemical reaction between different reactants. The reaction can be exothermic or endothermic. The set-up can be light activated or chemically catalyzed or it could be heat activated. Examples of such systems include flowable polymers of two or more components, light activated polymers, and polymers cured either by catalysts or by heat, including body heat. Molds can be used in the form of balloons, dams or retainers. They can be used in combination with the local anatomy to produce the desired shape and geometry.

Molds can be of materials that are retained and becomes part of the implant or could be removed after curing of the biomaterial component.

In an alternative embodiment, the material would be semi-solid and could be shaped and then set up in vivo. This would allow for the minimally invasive application, either through an arthroscopic portal or through a small mini arthrotomy. As a further embodiment, the material could be synthesized ex vivo and then machined to fit using imaging to pre-determine the desired geometry and size of the implant. As a further alternative, a range of implant sizes could be provided and sizing could be accomplished during the procedure. An ex vivo mold could be fit using molding materials and the implant could be molded on site just prior to implantation.

Fixation methods for the implant would include biologic glues to glue the implant to the underlying surface, trapping of the implant into a cavity on the surface that causes a mechanical lock, using various anchors to the underlying structure and fixing the implant to that surface or using mold retainers and/or screws, staples, sutures or pins. In alternative embodiment, anchors in the underlying structure may be used for fixing the implant to that surface and we may also use a tissue ingrowth system to secure anchoring.

In the preferred embodiment, the patient will have a diagnosis of osteoarthritis and have loss of cartilage on the articulating surface. A determination will be made of the amount of correction needed for the reestablishment of a normal angle of articulation. The ligaments will be balanced so that there is no loss of range of motion with the implant in place and the surface will be placed in such a position that the eventual resulting surface geometry reestablishes the same plane and orientation of the original articular surface.

Access to the site is obtained in a minimally invasive way. In a preferred embodiment, this is accomplished through arthroscopic means with arthroscopic portals. In an alternative embodiment, the access is accomplished by a mini arthrotomy with a small incision that allows access to the joint without sacrificing nerves, vessels, muscles or ligaments surrounding the joint. In the preferred embodiment fibrillated articulating cartilage that is degenerated is removed down to the subchondral surface. The surface is dried and prepared for appropriate anchoring.

This may include anchor points that give a mechanical lock or that alternatively simply supply horizontal and lateral stability. The surface may be prepared by drying and roughening in case a tissue adhesive is used. Pre-made anchors may be installed. These may be made of various metallic materials or of polymers and may consist of pegs that would extend up through the implant to anchor it to the underlying surface. This surrounding subchondral bone may be roughened to enhance tissue ingrowth or implant adhesion. The final geometry of the implant may be determined by a dam or mold that is placed on the joint at the time the material is implanted, when the implant is installed using an *in situ* cured technique (in the manner shown in Figures 1 and 4 of Applicant's provisional parent application).

For pre-made material formed at the surgical site within a mold, various forms of stabilization could be used, including anchor points or titanium screws. Alternatively, the pre-made material could be made off site to the specs developed from imaging of the patient's joint surface. In a third embodiment, multiple sizes could be made off site and the selection of the appropriate implant size could be chosen at the time of surgery. Two alternatives shown in Figure 2 of the parent provisional application include a single segment that can be installed through a portal or a series of segments that can be installed through a portal and locked together once inside the joint. They would be placed sequentially and then anchored to the bone by anchor points cut in the bone or by screws or tissue ingrowth. Finally, a robot, a jag or other cutting fixture could be used to prepare the bony surface for the pre-made implant to a fixed geometry of the anchor point.

Both the preformed component(s) and flowable biomaterial, if used, can be prepared from any suitable material. Typically, the materials include polymeric materials, having an optimal combination of such properties as biocompatibility, physical strength and durability, and compatibility with other components (and/or biomaterials) used in the assembly of a final composite. Examples of suitable materials for use in preparing the preformed component(s) may be the same or different from the *in situ* curing biomaterial, and include polyurethanes, polyethylenes, polypropylenes, Dacrons, polyureas, hydrogels, metals, ceramics, epoxies, polysiloxanes, polyacrylates, as well as biopolymers, such as collagen or collagen-based materials or the like and combinations thereof.

Examples of suitable materials for use in preparing the flowable biomaterial, if used, include polyurethanes, polyureas, hydrogels, epoxies, polysiloxanes, polyacrylates, and combinations thereof.

In a presently preferred embodiment, the preformed component(s) and the flowable biomaterial, if included, each comprise a biocompatible polyurethane. The same or different polyurethane formulations can be used to form both the preformed component(s), e.g., by an injection molding technique, as well as for the flowable biomaterial, if present.

Suitable polyurethanes for use as either the preformed component or biomaterial can be prepared by combining: (1) a quasi-prepolymer component comprising the reaction product of one or more polyols, and one or more diisocyanates, and optionally, one or more hydrophobic additives, and (2) a curative component comprising one or more polyols, one or more chain extenders, one or more catalysts, and optionally, other ingredients such as an antioxidant, and hydrophobic additive.

In the embodiment in which an *in situ* curing polymer is used, the present invention preferably provides a biomaterial in the form of a curable polyurethane composition comprising a plurality of parts capable of being mixed at the time of use in order to provide a flowable composition and initiate cure, the parts including: (1) a quasi-prepolymer component comprising the reaction product of one or more polyols, and one or more diisocyanates, optionally, one or more hydrophobic additives, and (2) a curative component comprising one or more polyols, one or more chain extenders, one or more catalysts, and optionally, other ingredients such as an antioxidant, hydrophobic additive and dye. Upon mixing, the composition is sufficiently flowable to permit it to be delivered to the body, and there be fully cured under physiological conditions. Preferably, the component parts are themselves flowable, or can be rendered flowable, in order to facilitate their mixing and use.

The flowable biomaterial used in this invention preferably includes polyurethane prepolymer components that react either *ex vivo* or *in situ* to form solid polyurethane ("PU"). The formed PU, in turn, includes both hard and soft segments. The hard segments are typically comprised of stiffer oligourethane units formed from diisocyanate and chain extender, while the soft segments are typically comprised of

one or more flexible polyol units. These two types of segments will generally phase separate to form hard and soft segment domains, since they tend to be incompatible with one another. Those skilled in the relevant art, given the present teaching, will appreciate the manner in which the relative amounts of the hard and soft segments in the formed polyurethane, as well as the degree of phase segregation, can have a significant impact on the final physical and mechanical properties of the polymer. Those skilled in the art will, in turn, appreciate the manner in which such polymer compositions can be manipulated to produce cured and curing polymers with desired combination of properties within the scope of this invention.

The hard segments of the polymer can be formed by a reaction between the diisocyanate or multifunctional isocyanate and chain extender. Some examples of suitable isocyanates for preparation of the hard segment of this invention include aromatic diisocyanates and their polymeric form or mixtures of isomers or combinations thereof, such as toluene diisocyanates, naphthalene diisocyanates, phenylene diisocyanates, xylylene diisocyanates, and diphenylmethane diisocyanates, and other aromatic polyisocyanates known in the art. Other examples of suitable polyisocyanates for preparation of the hard segment of this invention include aliphatic and cycloaliphatic isocyanates and their polymers or mixtures or combinations thereof, such as cyclohexane diisocyanates, cyclohexyl-bis methylene diisocyanates, isophorone diisocyanates and hexamethylene diisocyanates and other aliphatic polyisocyanates. Combinations of aromatic and aliphatic or arylakyl diisocyanates can also be used.

The isocyanate component can be provided in any suitable form, examples of which include 2,4'-diphenylmethane diisocyanate, 4,4'-diphenylmethane diisocyanate, and mixtures or combinations of these isomers, optionally together with small quantities of 2,2'-diphenylmethane diisocyanate (typical of commercially available diphenylmethane diisocyanates). Other examples include aromatic polyisocyanates and their mixtures or combinations, such as are derived from phosgenation of the condensation product of aniline and formaldehyde. It is suitable to use an isocyanate that has low volatility, such as diphenylmethane diisocyanate, rather than more volatile materials such as toluene diisocyanate. An example of a particularly suitable isocyanate component is the 4,4'-diphenylmethane diisocyanate

("MDI"). Alternatively, it can be provided in liquid form as a combination of 2,2'-, 2,4'- and 4,4'- isomers of MDI. In a preferred embodiment, the isocyanate is MDI and even more preferably 4,4'-diphenylmethane diisocyanate.

Some examples of chain extenders for preparation of the hard segment of this invention include, but are not limited, to short chain diols or triols and their mixtures or combinations thereof, such as 1,4-butane diol, 2-methyl-1,3-propane diol, 1,3-propane-diol ethylene glycol, diethylene glycol, glycerol, cyclohexane dimethanol, triethanol amine, and methyldiethanol amine. Other examples of chain extenders for preparation of the hard segment of this invention include, but are not limited to, short chain diamines and their mixtures or combinations thereof, such as dianiline, toluene diamine, cyclohexyl diamine, and other short chain diamines known in the art.

The soft segment consists of urethane terminated polyol moieties, which are formed by a reaction between the polyisocyanate or diisocyanate or polymeric diisocyanate and polyol. Examples of suitable diisocyanates are denoted above. Some examples of polyols for preparation of the soft segment of this invention include but are not limited to polyalkylene oxide ethers derived form the condensation of alkylene oxides (e.g. ethylene oxide, propylene oxide, and blends thereof), as well as tetrahyrofuran based polytetramethylene ether glycols, polycaprolactone diols, polycarbonate diols and polyester diols and combinations thereof. In a preferred embodiment, the polyols are polytetrahydrofuran polyols ("PTHF"), also known as polytetramethylene oxide ("PTMO") or polytetramethylene ether glycols ("PTMEG"). Even more preferably, the use of two or more of PTMO diols with different molecular weights selected from the commercially available group consisting of 250, 650,1000, 1400, 1800, 2000 and 2900.

Two or more PTMO diols of different molecular weight can be used as a blend or separately, and in an independent fashion as between the different parts of the two part system. The solidification temperature(s) of PTMO diols is generally proportional to their molecular weights. The compatibility of the PTMO diols with such chain extenders as 1,4-butanediol is generally in the reverse proportion to molecular weight of the diol(s). Therefore the incorporation of the low molecular weight PTMO diols in the "curative" (part B) component, and higher molecular weight PTMO diols in the prepolymer (part A) component, can provide a two-part

system that can be used at relatively low temperature. In turn, good compatibility of the low molecular weight PTMO diols with such chain extenders as 1,4-butanediol permits the preparation of two part systems with higher (prepolymer to curative) volume ratio. Amine terminated polyethers and/or polycarbonate-based diols can also be used for building of the soft segment.

The PU can be chemically crosslinked, e.g., by the addition of multifunctional or branched OH-terminated crosslinking agents or chain extenders, or multifunctional isocyanates. Some examples of suitable crosslinking agents include, but are not limited to, trimethylol propane ("TMP"), glycerol, hydroxyl terminated polybutadienes, hydroxyl terminated polybutadienes (HOPB), trimer alcohols, Castor oil polyethyleneoxide (PEO), polypropyleneoxide (PPO) and PEO-PPO triols. In a preferred embodiment, HOPB is used as the crosslinking agent.

This chemical crosslinking augments the physical or "virtual" crosslinking of the polymer by hard segment domains that are in the glassy state at the temperature of the application. The optimal level of chemical cross-linking improves the compression set of the material, reduces the amount of the extractable components, and improves the biodurability of the PU. This can be particularly useful in relatively soft polyurethanes, such as those suitable for the repair of damaged cartilage. Reinforcement by virtual cross-links alone may not generate sufficient strength for *in vivo* performance in certain applications. Additional cross-linking from the soft segment, potentially generated by the use of higher functional polyols can be used to provide stiffer and less elastomeric materials. In this manner a balancing of hard and soft segments, and their relative contributions to overall properties can be achieved.

Additionally, a polymer system of the present invention preferably contains at least one or more, biocompatible catalysts that can assist in controlling the curing process, including the following periods: (1) the induction period, and (2) the curing period of the biomaterial. Together these two periods, including their absolute and relative lengths, and the rate of acceleration or cure within each period, determines the cure kinetics or profile for the composition. Some examples of suitable catalysts for preparation of the formed PU of this invention include, but are not limited to, tin and tertiary amine compounds or combinations thereof such as dibutyl tin dilaurate, and tin or mixed tin catalysts including those available under the tradenames "Cotin 222",

"Formrez UL-22" (Witco), "dabco" (a triethylene diamine from Sigma-Aldrich), stannous octanoate, trimethyl amine, and triethyl amine. In a preferred embodiment, the catalyst is Formrez UL-22 (Witco). In an alternative preferred embodiment, the catalyst is a combination Cotin 222 (CasChem) and dabco (Sigma-Aldrich).

The *in vivo* and *ex vivo* cured polyurethanes of this invention can be formed by the reaction of two parts. Part I of which (alternatively referred to as Part A) includes a di- or multifunctional isocyanate or quasi-prepolymer which is the reaction product of one or more OH-terminated components, and one or more isocyanates. Part II of the polyurethane (alternatively referred to as Part B herein) is a curative component that includes of one or more chain extenders and one or more polyols, and one or more catalysts, and other additives such as antioxidants and dyes. For a suitable formed PU, the stoichiometry between Parts I (quasi-prepolymer) and II (curative component), expressed in terms of NCO:OH molar ratio of the isocyanate terminated pre-polymer (Part I) and the curative component (Part II) is preferably within the range of about 0.8 to 1.0 to 1.2 to 1.0, and more preferably from about 0.9 to 1 to about 1.1 to 1.0.

Optionally, a reactive polymer additive can be included and is selected from the group consisting of hydroxyl- or amine-terminated compounds selected from the group consisting of poybutadiene, polyisoprene, polyisobutylene, silicones, polyethylene-propylenediene, copolymers of butadiene with acryolnitrile, copolymers of butadiene with styrene, copolymers of isoprene with acrylonitrile, copolymers of isoprene with styrene, and mixtures of the above.

Suitable compositions for use in the present invention are those polymeric materials that provide an optimal combination of properties relating to their manufacture, application, and *in vivo* use. In the uncured state, such properties include component miscibility or compatibility, processability, and the ability to be adequately sterilized or aseptically processed and stored. In the course of applying such compositions, suitable materials exhibit an optimal combination of such properties as flowability, moldability, and *in vivo* curability. In the cured state, suitable compositions exhibit an optimal combination of such properties as strength (e.g., tensile and compressive), modulus, biocompatibility and biostability.

When cured, the compositions demonstrate an optimal combination of properties, particularly in terms of their conformational stability and retention of physical shape, dissolution stability, biocompatibility, and physical performance, as well mechanical properties such as load-bearing strength, tensile strength, shear strength, shear fatigue resistance, impact absorption, wear resistance, and surface abrasion resistance. Such performance can be evaluated using procedures commonly accepted for the evaluation of natural tissue and joints, as well as the evaluation of materials and polymers in general. In particular, a preferred composition, in its cured form, exhibits mechanical properties that approximate or exceed those of the natural tissue it is intended to provide or replace.

To achieve these desirable uncured and delivery properties, a "polymer system", as used herein refers to the component or components used to prepare a polymeric composition of the present invention. In a preferred embodiment, a polymer system comprises the components necessary to form two parts: Part I being an NCO terminated pre-polymer (optionally referred to as an "isocyanate quasi-polymer"). The quasi-polymer of Part I typically includes a polyol component, optionally in combination with a hydrophobic additive component, and an excess of an isocyanate component. Part II of the two component system can include one long-chain polyols, chain extenders and/or cross-linkers, together with other ingredients (e.g., catalysts, stabilizers, plasticizers, antioxidants, dyes and the like). Such adjuvants or ingredients can be added to or combined with any other component thereof either prior to or at the time of mixing, delivery, and/or curing.

In a particularly preferred embodiment, a polymer system of this invention is provided as a plurality of component parts and employs one or more catalysts. The component parts, including catalyst, can be mixed to initiate cure, and then delivered, set and fully cured under conditions (e.g., time and exotherm) sufficient for its desired purpose. Upon the completion of cure, the resultant composition provides an optimal combination of properties for use in repairing or replacing injured or damaged tissue. In a particularly preferred embodiment, the formulation provides an optimal combination of such properties as compatibility and stability of the biomaterial parts, ex vivo or *in situ* cure capability and characteristics (e.g., extractable levels,

biocompatibility, thermal/ mechanical properties), mechanical properties (e.g., tensile, tear and fatigue properties), and biostability.

The volume ratio of the parts can also be used to improve and affect the uncured and curing properties Compositions having two or more parts, are preferred. Where two parts are used, the relative volumes can range, for instance, from 1:10 to 10:1 (quasi-prepolymer to curative components, based on volume). A presently preferred range is between 2:1 and 1:2. As those skilled in the art will appreciate, given the present description, the optimal volume ratio is largely determined by the compatibility and the stability of part A and B.

In choosing an optimal volume ratio for a given formulation, those skilled in the art, given the present description, will appreciate the manner in which the following considerations can be addressed. The viscosity of the reactive parts, at the temperature used for either injection-molding preformed components, or for *in situ* cure, should provide an acceptable degree of mixing and flow rate, without causing mechanical failure of any component of the delivery system including cartridge, static mixer, gun and other components.

Preferably, the biomaterial is sufficiently flowable to permit it to be delivered (e.g., injected) into the mold or tissue site. The composition of both reactive parts must be such that these parts are homogeneous and phase stable in the temperature range of the application. Generally, the maximum temperature of the reaction exotherm is proportional to the concentration of the reactive groups in the mixed polymer. A high concentration of the reactive groups might evolve too high reaction exothermal energy and therefore cause thermal damage to the surrounding tissues. The reactive parts will preferably remain substantially liquid in form during mixing.

A desired and stable volume ratio of the components can be achieved in any suitable manner, e.g., by the use of dual-compartment cartridges with constant volume ratio or by using the injectors with delivery rates independently variable for each component.

Compatibility of the composition can also be affected (and improved) in other ways as well, e.g., by pre-heating the components prior to polymer application. To enhance the homogeneity of the components, the components of a preferred composition of this invention are preferably preheated before mixing and delivery,

e.g., by heating to about 60 C to about 80 C for about 2 to about 6 hours prior to use. Preferably, the composition parts are cooled back to about 35 C to 37 C before use in injection.

Fully cured polymeric (e.g., polyurethane) biomaterials suitable for use in forming components of this invention provide an optimal combination of such properties as creep and abrasion resistance. Preferably, for instance, the biomaterial provides DIN abrasion values of less than about 100 mm^3, more preferably less than about 80 mm^3 and most preferably less than about 60 mm^3, as determined by ASTM Test Method D5963-96 ("Standard Test Method for Rubber Property Abrasion Resistance Rotary Drum Abrader").

CLAIMS

What is claimed is:

1. A system for the creation or modification of the wear surface of an orthopedic joint within a mammalian body, the system comprising one or more partially or fully preformed polymeric components, adapted to be inserted and positioned at a joint site to provide an implant having at least one major surface in apposition to supporting bone, and at least a second major surface in apposition to opposing bone.

2. A system according to claim 1 wherein one or more of the polymeric components are formed at the time of use, by the use of a curable polymer system adapted to be at least partially cured and partially formed by *ex vivo* molding in order to provide an implantable component adapted to be inserted and positioned *in vivo*, under conditions suitable to permit the implanted component to become finally formed upon reestablishing the natural joint space and in conformance with the opposing bone surfaces of the orthopedic joint site.

3. A system according to claim 1 wherein the polymeric components comprise a plurality of packaged, preformed components adapted to be assembled at the orthopedic joint site in a minimally invasive fashion to provide a final prosthesis having surfaces in conformance with the opposing bone surfaces of the orthopedic joint site.

4. A system according to claim 1 further comprising an *ex vivo* mold having a molding surface adapted to provide a roughened, patterned, and/or contoured surface to the partially preformed component, in a manner sufficient to provide improved retention and fit of the component at the joint site.

5. A system according to claim 4 wherein the mold further provides ancillary means adapted to be incorporated into the preformed component for securing the component once formed in the joint site.

6. A system according to claim 5 wherein the ancillary means comprise one or more protrusions adapted to be attached to either soft tissue and/or bone at the joint site to improve fixation.

7. A system according to claim 4 wherein the contoured surface comprises a contour having one or more protrusions, integral with the preformed component, and formed during the *ex vivo* molding process.

8. A system according to claim 6 wherein the protrusions are adapted to be integrated into the preformed component during the *ex vivo* molding process.

9. A system according to claim 7 wherein the protrusions are comprised of sutures and/or fibrous biomaterials integrally formed with the component itself.

10. A system according to claim 4 further comprising separate means, not associated with the mold itself, for securing the component to the joint site, selected from the group consisting of adhesives, sutures, pins, staples, screws, and combinations thereof.

11. A system according to claim 1 wherein the one or more preformed polymeric component(s) are adapted to be inserted into a joint in a minimally invasive fashion.

12. A system according to claim 2 in which the preformed component(s) and/or corresponding mold(s) are provided in a plurality or range of styles and sizes for selection and use in the surgical field.

13. A system according to claim 1 wherein the implant is adapted for use on the tibial surface of the knee, and provides portions adapted to conform to the shape of the femoral condyle and corresponding medial tibial plateau, lateral tibial plateau, or both.

14. A system according to claim 1 wherein the polymeric component is fabricated from a material selected from the group consisting of polyurethanes, polyureas, hydrogels, polysiloxanes, polyacrylates, and epoxies, and combinations thereof.

15. A system according to claim 14 wherein the polymeric component comprises a polyurethane.

16. A system according to claim 15 wherein the polyurethane is prepared from polyisocyanate(s), short and long chain polyols, and optionally including one or more ingredients selected from the group hydrophobic additive(s), tin and/or amine catalyst(s), and antioxidant(s).

17. A system according to claim 16 wherein the polyurethane comprises aromatic polyisocyanates, PTMO's, and short chain diols.

18. A system according to claim 16 wherein the hydrophobic additive comprises hydroxyl-terminated polybutadiene, and the tin and/or amine catalyst(s) are adapted to promote the isocyanate - hydroxyl reaction preferentially and are selected from the group consisting of UL22, Cotin 222, 1,4-diazabicyclo[2.2.2]octane (dabco), and dibutyltin dilaurate (DBTDL), and combinations thereof.

19. A system according to claim 14, wherein the preformed polymeric component comprises one or more surfaces having attached thereto a biologically active agent selected from the group cytokines, growth factors, autologous growth factors, hydroxyapatite, collagen, and combinations thereof.

20. A system according to claim 14 wherein the surface of the preformed component is provided or modified with reactive groups to promote tissue adhesion.

21. A system according to claim 20 wherein the reactive groups are provided by the polymers used to fabricate the polymeric component, and are selected from amines, hydroxyl groups, or other reactive or hydrogen bonding functionalities.

22. A system for the creation or modification of the wear surface of an orthopedic joint within a mammalian body, the system comprising one or more preformed polymeric components adapted to be positioned within the joint site and one or more flowable biomaterial polymer compositions adapted to be arthroscopically injected into contact with a preformed component and cured *in situ* at the joint site in order to provide a composite implant.

23. A system according to claim 22 wherein the preformed polymeric components comprise an inflatable balloon having a preformed top weight-bearing wear portion and a preformed bottom portion adapted to conform to the shape of supporting bone.

24. A system according to claim 23 wherein the one or more portions of the balloon are fabricated from a natural or synthetic fabric adapted to permit tissue in-growth, and sufficiently permeable to permit air to escape while retaining the curable biomaterial.

25. A system according to claim 24 wherein the fabric is of sufficient permeability to permit physical interpenetration of the flowable polymer.

26. A system according to claim 23 wherein the bottom and/or top portions comprise materials selected from polyurethanes, polyethylenes, polypropylenes, metals, ceramics, biopolymers or the like and combinations thereof.

27. A system according to claim 23 wherein the top and bottom portions are provided with forms corresponding to the shape of a femoral condyle and tibial plateau, respectively.

28. A system according to claim 23 wherein the balloon further comprises a port adapted to fill the balloon with flowable biomaterial *in situ*, in a manner sufficient to force the top portion toward corresponding bone.

29. A system according to claim 23 wherein the bottom portion provides a raised protrusion sufficient to improve retention within the joint site and/or to provide a site for suturing, stapling, pinning, or screwing the portion within the joint site.

30. A system according to claim 22 wherein separate means are provided for securing the preformed component within the joint site.

31. A system according to claim 22, further comprising one or more biologically active agents adapted to be provided on one or more surfaces of the resultant composite implant.

32. A system according to claim 22 wherein the surface of the preformed component and/or resultant composite material are provided or modified with reactive groups to promote adhesion.

33. A system according to claim 32 wherein the reactive groups are either provided by the preformed component itself, or are separately added by suitable surface treatment of the component or resultant composite, and the reactive groups are selected from amines, hydroxyl groups, or other reactive or hydrogen bonding functionalities.

34. A system according to claim 22 in which one or more of the preformed components are provided in a plurality or range of styles and sizes.

35. A system according to claim 22 wherein the one or more flowable biomaterial(s) are adapted to be inserted into a joint using minimally invasive means.

36. A system for the creation or modification of the wear surface of an orthopedic joint within a mammalian body, the system comprising a plurality of packaged, preformed components adapted to be assembled at the orthopedic joint site in a minimally invasive fashion to provide a final prosthesis having surfaces in apposition to and conformance with the opposing bone surfaces of the orthopedic joint site.

37. A system according to claim 36 wherein one or more of the preformed components are provided with surfaces suitably roughened, patterned, or contoured to provide maximum adhesion and fit when placed, and optionally further fitted and secured, within the joint site.

38. A system according to claim 36, wherein one or more of the preformed components are formed at the time of use by the use of a curable bomaterial adapted to completely cure when preformed and then placed and optionally further fitted or secured inside the joint site.

39. A system according to claim 36 wherein one or more of the preformed components provide means for further securing the component once placed in the joint site.

40. A system according to claim 39 wherein the retention means to secure the component includes the use of tissue adhesives to improve fixation.

41. A system according to claim 39 wherein the retention means comprise one or more protrusions adapted to be sutured, pinned, stapled, screwed or combinations thereof or otherwise mechanically attached into the surrounding soft tissue and/or bone to improve fixation.

42. A system according to claim 41 wherein the protrusions are themselves integral with the preformed component.

43. A system according to claim 42 wherein the protrusions are integrated into a flowable biomaterial during the *ex vivo* molding process used to form the preformed component.

44. A system according to claim 43 wherein the protrusions are comprised of sutures or fibrous materials.

45. A system according to claim 39 wherein means to secure the component are external to it and secured once inside the joint site by the use of adhesives, sutures, pins, staples, screws or the like and combinations thereof to improve fixation to the surrounding soft tissue and/or bone to improve fixation.

46. A system according to claim 36 wherein the one or more preformed component(s) are adapted to be inserted into a joint in a minimally invasive fashion.

47. A system according to claim 36 in which the one or more preformed component(s) are provided in a plurality or range of styles and sizes.

48. A system according to claim 37 wherein the assembled components conform to the shape of the femoral condyle and tibial plateau, medial, lateral or both.

49. A system according to claim 37 wherein the preformed component(s) are fabricated from materials selected from the group consisting of polyurethanes, polyethylenes, polyureas, hydrogels, polysiloxanes, polyacrylates, epoxies, and combinations thereof.

50. A system according to claim 49 wherein the material comprises a polyurethane.

51. A system according to claim 50 wherein polyurethane is prepared from polyisocyanate(s), short and long chain polyols, and optionally including one or more ingredients selected from the group hydrophobic additive(s), tin and/or amine catalyst(s), and antioxidant(s).

52. A system according to claim 51 wherein the polyurethanes are prepared from aromatic polyisocyanates, PTMO's, short chain diols.

53. A system according to claim 52 wherein the hydrophobic additive comprises hydroxyl-terminated polybutadiene, and the tin and/or amine catalyst(s) used promote the isocyanate - hydroxyl reaction preferentially and are selected from the group consisting of UL22, Cotin 222, 1,4-diazabicyclo[2.2.2]octane (dabco), and dibutyltin dilaurate (DBTDL) or the like and combinations thereof.

54. A system according to claim 36 wherein the preformed components provide one or more surfaces having attached thereto a biologically active agent selected from the group cytokines, hydroxyapatite, growth factors, autologous growth factors, collagen or the like and combinations thereof.

55. A system according to claim 36 wherein the surface of one or more preformed component(s) is provided or modified with reactive groups to promote tissue adhesion.

56. A system according to claim 55 wherein the reactive groups are covalently attached to the polymers used to fabricate the preformed component(s), and are selected from amines, hydroxyl groups, or other reactive or hydrogen bonding functionalities.

57. A system according to claim 36 wherein the preformed component(s) are selected from the group consisting of a) a single preformed component, b) a plurality of components adapted to be layered upon each other at the tissue site, c) a plurality of components adapted to be assembled at the tissue site in an interlocking fashion, such that the components cooperate to provide a respective portion of the first and second major surfaces.

58. A system according to claims 1 or 22 or 36 further comprising the use of one or more additional materials and/or steps adapted to a) prepare the bone surface itself, b) provide a desired interface between bone, component(s), and/or the physiologic environment, and/or c) treat one or more surfaces of the component(s) in order to provide them with different or improved properties as compared to the inherent properties of the material providing the surface.

59. A system according to claim 58 wherein the materials and/or steps are adapted to affect, improve or provide a surface property or function selected from adhesion, lubricity, smoothness, conformance, tissue in-growth, or biocompatibility.

60. A system according to claims 1 or 22 or 36 wherein the system is adapted to be used for repairing a variety of mammalian joints, including human joints selected from the group consisting of the tibial plateau of the knee, the acetabulum of the hip, the glenoid of the shoulder, the acromion process of the shoulder, the acromio-clavicular joint of the shoulder, the distal tibial surface of the ankle, the radial head of the elbow, the distal radius of the forearm, the proximal phalanx surface of the great toe, the proximal metacarpal surface of the thumb, and the trapezium of the wrist.

61. A system according to claim 60 wherein the system is adapted to be used for repairing the tibial plateau of the knee.

62. A system according to claim 60 wherein the system is adapted to be used for repairing the acetabulum of the hip.

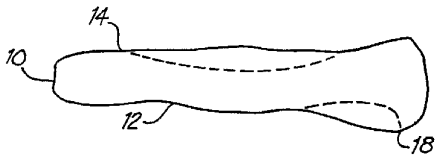

FIG. 1a

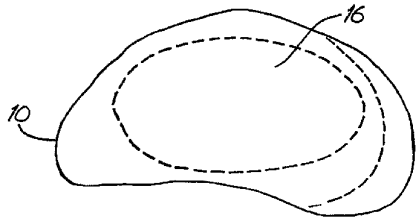

FIG. 1b

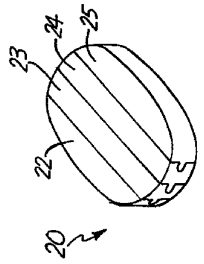

FIG. 2b

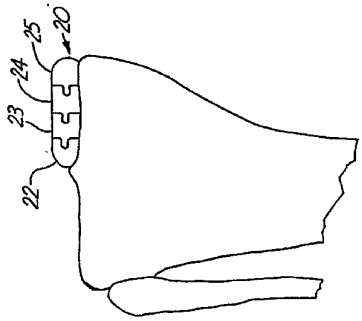

FIG. 2a

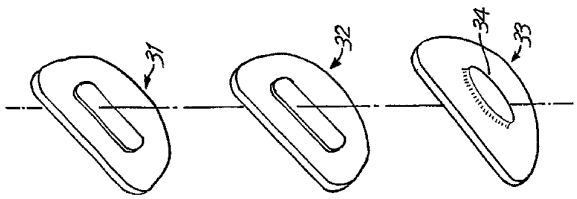

FIG. 3c

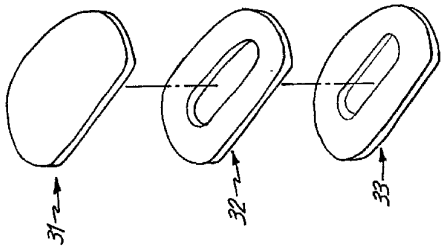

FIG. 3b

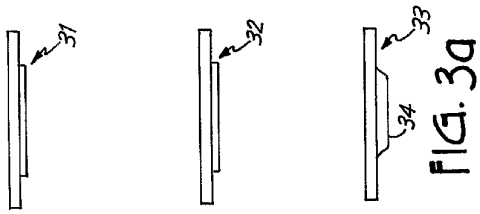

FIG. 3a

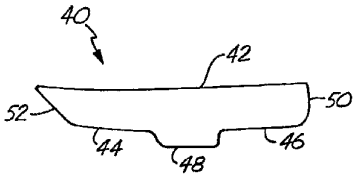

FIG. 4a

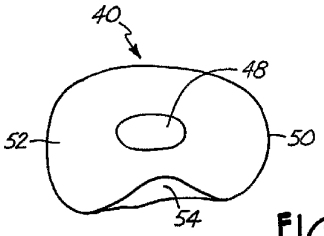

FIG. 4b

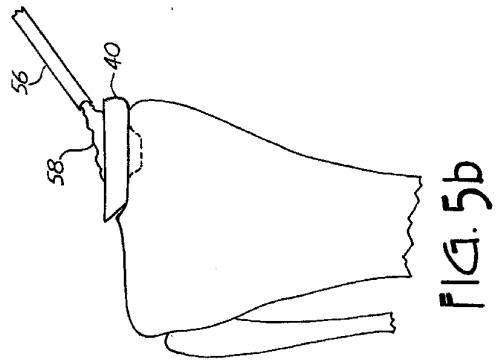

FIG. 5b

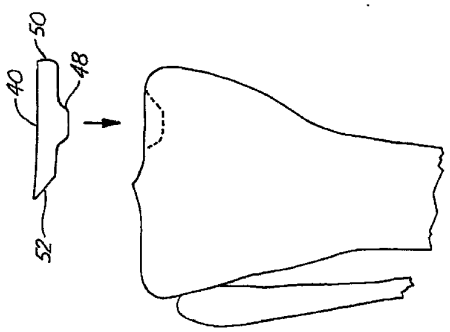

FIG. 5a

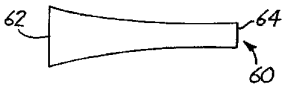

FIG. 6a

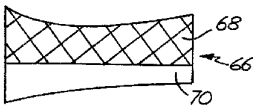

FIG. 6b

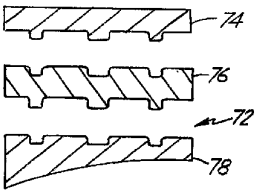

FIG. 6c

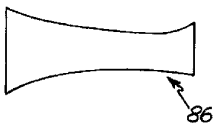

FIG. 6d

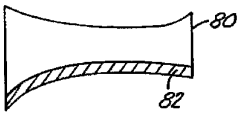

FIG. 7a

FIG. 7b

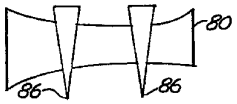

FIG. 7c

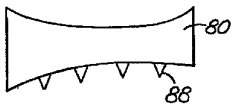

FIG. 7d

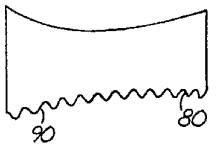

FIG. 8a

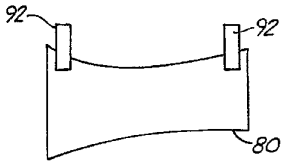

FIG. 8b

FIG. 8c

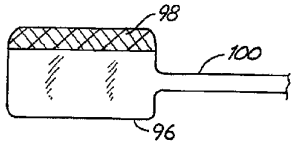

FIG. 9a

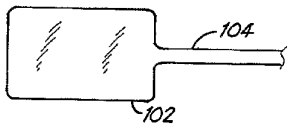

FIG. 9b

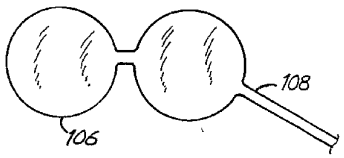

FIG. 9c

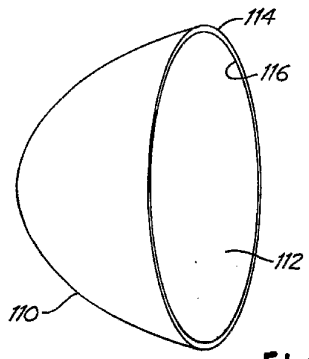

FIG. 10

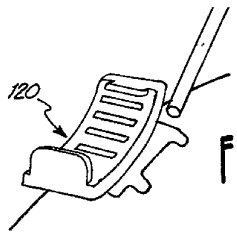

FIG. 11a

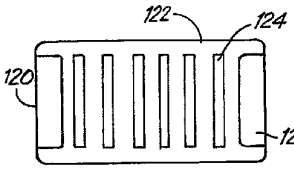

FIG. 11b

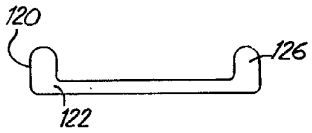

FIG. 11c

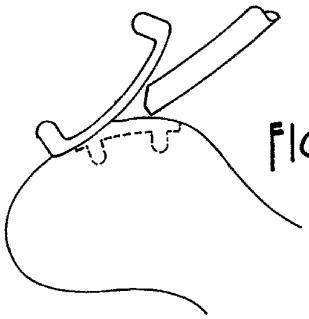

FIG. 11d

【手続補正書】
【提出日】平成15年5月1日(2003.5.1)
【手続補正１】
【補正対象書類名】明細書
【補正対象項目名】請求項１０
【補正方法】変更
【補正の内容】
【請求項１０】
型それ自体に関連せず、構成成分を関節部位に固定する別の手段をさらに含んでなり、前記手段は接着剤、縫合糸、ピン、ステープル、ねじ、およびそれらの組み合わせから選択される、請求項４に記載のシステム。

【国際調査報告】

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/41908

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61F2/30 A61L27/18

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 A61L A61F

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, PAJ, FSTA, INSPEC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 795 353 A (FELT JEFFREY C) 18 August 1998 (1998-08-18) cited in the application column 3, line 1 - line 36 column 4, line 12 - line 56 column 5, line 4 - line 66 column 7, line 46 - line 59 -/--	1-9,11, 12, 14-22, 32-44, 46,47, 49-60

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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"A" document defining the general state of the art which is not considered to be of particular relevance

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"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

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Date of the actual completion of the international search	Date of mailing of the international search report
25 April 2002	13/05/2002

Name and mailing address of the ISA	Authorized officer
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	Menidjel, R

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/41908

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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INTERNATIONAL SEARCH REPORT

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4C097 AA03 AA04 AA07 AA11 BB01 CC01 CC03 DD04 DD07 EE08
EE19