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論 文 内 容 要 旨

With improving living standard and medical level, the proportion of the world's population in the older ages increases continuously. Therefore, the maintenance of bone in our bodies has become crucial. Additionally, the number of serious road traffic injuries is likely to continue to rise in most regions of the world as motorization increases. Moreover, the number of people damaged in athletic sports also grows. The demand for biomaterials for replacement of functionally disordered hard tissue with artificial instruments such as bone plates, hip joints, spinal fixation devices, and dental roots increases rapidly. Titanium (Ti) and its alloys have attracted considerable attention as a result of their potential for use in several biomedical applications owing to their favorable mechanical properties, excellent corrosion resistance, and biocompatibility.

Presently, Ti biomaterials such as commercially pure titanium (CP Ti) and Ti–6Al–4V extra-low interstitial alloy (Ti64 ELI) are widely used in biomedical applications. However, some problems have been pointed out. For example, Ti64 ELI contains toxic vanadium (V) and CP Ti possesses only moderate mechanical properties. Moreover, the Young's moduli of Ti64 ELI (around 110 GPa) and CP Ti (around 105 GPa) are much higher than that of human bone (10–30 GPa). As a result, the mismatch in the Young's modulus between metallic implants and human bones leads to a stress shielding effect, which could possibly cause osteoporosis or poor osseointegration. Niimomi et al. reported that low Young's modulus is effective in inhibiting bone atrophy and leads to excellent bone remodeling. In addition, bone atrophy becomes more distinct with increasing Young's modulus of the implants. Thus, the materials low Young's modulus are preferred for biomedical applications. Recently, many new Ti alloys containing nontoxic elements and having a low Young's modulus (40–60 GPa) and good biocompatibility have been intensively investigated. Ti–12Mo–6Zr–2Fe, Ti–15Mo–5Zr–3Al, Ti–13Nb–13Zr, Ti–24Nb–4Zr–8Sn, and Ti–29Nb–13Ta–4.6Zr (TNTZ) were developed successfully.

Scoliosis is a three-dimensional deformity of the spine, characterized by a curve in the coronal plane of 10° or more. Spinal fixation is the most widely performed surgery for scoliosis to restore a more normal curve and appearance to the spinal column. The implant rods for spinal fixation undergo bending when manually handled by surgeons within the small space inside the patient's body for in-situ spine contouring. Therefore, the handling ability of these rods is very important for operation. The springback of implant rods should be small so that the implant offers better handling ability during operations. Generally, the amount of springback is considered to depend on both the strength and the Young's modulus of the implant rod. And the implant rod with low Young's modulus shows large springback, while implant rod with high Young's modulus shows small springback. Therefore, surgeons require materials having high Young's moduli to suppress springback and offer good handling ability during operations. However, patients require materials with low Young's moduli to prevent stress-shielding effect. In short, metallic rods used in spinal fixation devices are required to have not only a low Young's modulus to avoid the stress shielding effect but also a high Young's modulus to suppress springback. None of the current alloys meet the requirements of both surgeons and patients when used in spinal fixation applications.

To solve the problems in spinal fixation applications, a new concept was proposed for the development of novel biomedical titanium alloys with a changeable Young's modulus to satisfy the requirements of both patients and surgeons. Generally, the Young's modulus of a Ti alloy is not sensitive to deformation. However, the Young's modulus of Ti alloy is sensitive to the secondary phase or precipitates within the β matrix. Moreover, non-equilibrium phases, such as α′, α″, and ω, can appear in certain metastable β-type titanium alloys during deformation at room temperature. Utilize these deformation-induced phases is an effective way to obtain the changeable Young's modulus. If Young's modulus of the deformation-induced phase is higher than that of the original matrix, the Young's modulus of deformed part increases, but that of non-deformed part remains low.

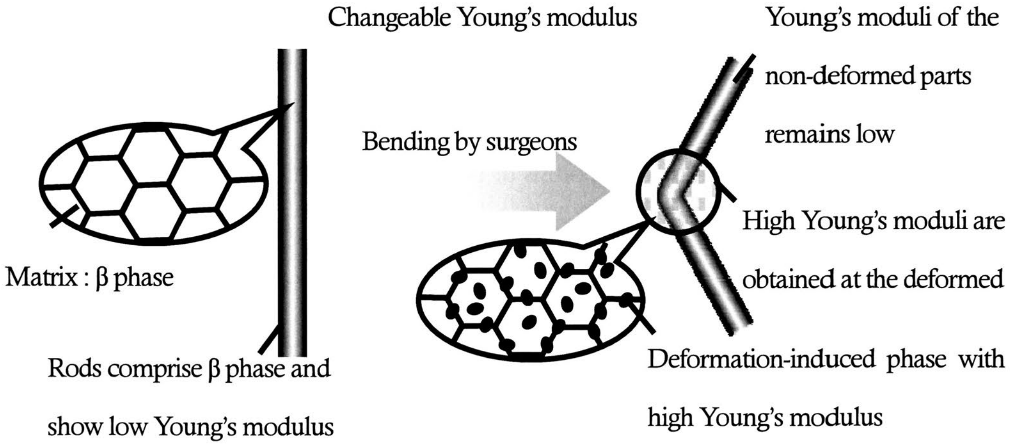

Fig. 1 Concept of changeable Young's modulus of implant rods by bending during operation.

Figure 1 shows the concept of changeable Young's modulus of implant rods by bending during operation. Before deformation, the implant rods comprise β phase and show low Young's modulus, and after bending by surgeons, deformation-induced products with high Young's modulus appear. Thus, high Young's moduli are obtained at the deformed parts, while low Young's modulus remains at non-deformed parts.

The purpose of this research is to develop a novel biomedical titanium alloys that have good biocompatibility and changeable Young's modulus via deformation-induced ω phase transformation for spinal fixation applications.

The chapter 1 is a general introduction, which first introduces the increasing demand for biomaterials in the current world, and then recalls the development history of metallic biomaterials, the background of titanium and its alloys as biomaterials, after that introduces the background of spinal fixation, the existing problems and solutions to the problems in spinal fixation applications, followed by the purpose and structure of this thesis.

Chapter 2 is about the designs of Young's modulus changeable titanium alloys for spinal fixation applications, which includes select proper alloying element and content region. Metastable β-type Ti alloys have a low Young's modulus, as well as good mechanical properties and excellent corrosion resistance. Furthermore, non-equilibrium phases, such as α′, α″, and ω, which can change the Young's modulus, can appear in certain metastable β-type Ti alloys during deformation; hence, β-type Ti alloys are the materials of choice for this research. Non-toxic and allergy-free β stabilizers—Cr and Mo are selected for development of Young's modulus changeable Ti alloys for spinal fixation applications. Additionally, the deformation-induced martensites (α′ and α″) decrease the Young's modulus, while deformation-induced ω phase transformation increases the Young's modulus. It is necessary to eliminate the effect of the deformation-induced martensites (α′ and α″) on the Young's modulus. Therefore, a relatively high stability in the β phase has been chosen to suppress deformation-induced martensite transformation and promote deformation-induced ω phase transformation during deformation.

In chapter 3, the optimal chemical compositions of alloys for deformation-induced ω phase transformation and changeable Young's modulus is determined. The effect of deformation-induced ω phase transformation on mechanical properties, such as Young's modulus and tensile properties of Ti–Cr and Ti–Mo alloys are systematically investigated. The deformation-induced ω phase transformation and $\{332\}_\beta$ mechanical twinning occur in the Ti–(10–12)Cr and Ti–(13–18)Mo alloys during cold rolling. Changeable Young's modulus was obtained in Ti–(10–12)Cr and Ti–(15–18)Mo alloys. The increase in the Young's moduli of Ti–(10–12)Cr and Ti–(15–18)Mo alloys by cold rolling is attributed to the deformation-induced ω phase transformation. Ti–12Cr exhibits the lowest Young's modulus in solution treatment condition and the largest increment ratio of Young's modulus by cold rolling among the designed alloys. Moreover, Ti–12Cr is expected to exhibit high fatigue strength because of its high 0.2% proof stress. From the standpoint of mechanical properties including Young's modulus and tensile properties, Ti–12Cr alloy is the optimized alloy for spinal fixation application.

In chapter 4, the effect of deformation ratio on the deformation-induced ω phase transformation and Young's modulus is investigated. After cold rolling with a reduction ratio of 10%, the Young's modulus increase remarkably is attributed to the deformation-induced ω phase transformation. With an increase in the cold rolling reduction ratio from 10% to 70%, the increase in the Young's modulus of the Ti–12Cr alloy is negligible. It is confirmed that a small deformation is enough to introduce deformation-induced ω phase into Ti–12Cr alloy and increase its Young's modulus. In addition, the effect of grain size on the deformation-induced ω phase transformation and Young's modulus is also investigated. It has been found that the Young's modulus of Ti–12Cr alloy is not sensitive to the grain size and morphology of materials. Additionally, with an increase in the grain size, the increases in the Young's modulus are almost same. It indicates that the deformation-induced ω phase transformation is also not sensitive to the grain size.

In chapter 5, the springback and cytocompatibility of the optimized alloy are evaluated. Springback is evaluated by tensile loading-unloading tensile test to confirm the effect of changeable Young's modulus on the springback. Cyto-compatibility is evaluated by cell experiment. The ratio of springback of Ti–12Cr is smaller than that of TNTZ and closes to that of Ti64 ELI. The ratio reaches a stable value when the applied strain is greater than 2%. All alloys show healthy morphologies of cells with a flattened spindle shape. Ti–12Cr shows the highest cell density, which is considerably higher than that of SUS 316L and Ti64 ELI, and similar to that of TNTZ. These results of s indicate that Ti–12Cr alloy has greater potential for spinal fixation applications than TNTZ.

Finally, the concluding remarks are given and future research work is proposed in the chapter 6.

論文審査結果の要旨

人体機能再建のための、骨プレート、股関節、脊椎固定器具あるいは歯根などのような人工器具を用いた硬組織の置換術が急速に普及している。チタン（Ti）およびチタン合金は、優れた機械的性質、耐食性および生体適合性を有することから、医療応用への関心が寄せられている。現在、工業用純チタン（CP Ti）やTi-6Al-4V ELI 合金（Ti64 ELI）のようなチタン系生体材料は、広く医療応用されているが、いくつかの問題点も指摘されている。たとえば、Ti 64 ELI は毒性元素であるバナジウム（V）を含んでおり、CP Ti は機械的性質が十分とはいえない。さらに、Ti64 ELI および CP Ti のヤング率はそれぞれ 110 GPa および 105 GPa であり、骨のヤング率（10~30 GPa）と比べて著しく高い。その結果、金属製インプラントと骨とに加わる荷重のミスマッチが生じ、骨に対する応力遮蔽効果が生じる。一方、脊柱側弯症は脊柱の三次元的な奇形であり、治療法として脊椎固定術が施行されている。脊柱を矯正するために用いられる脊椎固定用インプラントロッドは、手術中に患者の体内という狭い空間で医師の手作業で曲げて使用されるため、操作性が極めて重要となる。したがって、脊椎固定用インプラントロッドには、低ヤング率だけでなく、スプリングバックを抑制するための高ヤング率も要求される。本研究では、変形誘起 ω 相変態を利用した、脊椎固定器具用ヤング率可変型 β 型チタン合金を開発することを目的としている。

第一章では、緒言として、世界的に増加する生体材料の需要、金属系生体材料の開発の歴史、生体用チタン合金開発の背景などについて述べている。さらに、生体用チタン合金の脊椎固定器具への応用に際しての問題点およびその解決策を示し、本学位論文の目的を述べている。

第二章では、脊椎固定器具用ヤング率可変型 β 型チタン合金の設計するための、適切な合金元素の選定やその添加量について述べている。本研究では、ヤング率可変型 β 型チタン合金の開発のための合金元素として、クロム（Cr）とモリブデン（Mo）を選択している。

第三章では、変形誘起 ω 相変態が生じ、ヤング率が上昇するために最適な合金の化学組成について検討した結果が示されている。Ti-Cr 合金および Ti-Mo 合金について、ヤング率や引張特性などの機械的性質に対する、変形誘起 ω 相変態の影響について系統的に調査し、Ti-(10-12)Cr および Ti-(15-18)Mo の範囲でヤング率が上昇し、比較的良好な機械的性質を示すことが明らかにされている。冷間圧延によるこれらの合金のヤング率上昇は、変形誘起 ω 相変態に起因し、ヤング率上昇率と引張特性の良好性の観点から、本研究では Ti-12Cr 合金が脊椎固定器具として最適であると判断している。

第四章では、開発合金の変形誘起 ω 相変態およびヤング率上昇に及ぼす変形量（ここでは冷間圧延の圧下率）の影響について検討した結果が示されている。Ti-12Cr 合金のヤング率は、圧下率 10%まで上昇し、その後はほぼ一定値を示している。したがって、変形誘起 ω 相の導入により、ヤング率を上昇させるためには、小さな変形で十分であることが明らかにされている。さらに、開発合金の変形誘起 ω 相変態およびヤング率上昇に及ぼす結晶粒直径の影響についても検討しており、変形誘起 ω 相変態やヤング率上昇は、結晶粒直径の影響を受けにくいことが明らかにされている。

第五章では、開発合金のスプリングバックと細胞適合性を評価した結果が示されている。スプリングバックは引張負荷・徐荷試験により評価し、変形によるヤング率上昇がスプリングバックに与える影響について検討している。一方、細胞適合性が細胞実験により評価され、実験結果から、Ti-12Cr 合金は TNTZ よりも脊柱固定器具への応用が期待される。

最後に、第六章では、本研究の結言と本研究の今後の展開について提案されている。

本研究では、相変態を利用して新機能を付与した生体用 β 型チタン合金が開発されており、研究目標を達成している。よって、本論文を博士(工学)の学位論文として合格と認める。