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Influence of different grained powders and pellets made of Niobium and Ti-42Nb on human cell viability

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ABSTRACT

Nowadays, biomaterials can be used to maintain or replace several functions of the human body if necessary. Titanium and its alloys, i.e. Ti6Al4V are the most common materials (70 to 80%) used for structural orthopedic implants due to their unique combination of good mechanical properties, corrosion resistance and biocompatibility. Addition of β-stabilizers, e.g. niobium, can improve the mechanical properties of such titanium alloys further, simultaneously offering excellent biocompatibility. In this in vitro study, human osteoblasts and fibroblasts were cultured on different niobium specimens (Nb Amperit, Nb Ampertec), Nb sheets and Ti-42Nb (sintered and 3D-printed by selective laser melting, SLM) and compared with forged Ti6Al4V specimens. Furthermore, human osteoblasts were incubated with particulates of the Nb and Ti-42Nb specimens in three concentrations over four and seven days to imitate influence of wear debris. Thereby, the specimens with the roughest surfaces, i.e. Ti-42Nb and Nb Ampertec, revealed excellent and similar results for both cell types concerning cell viability and collagen synthesis superior to forged Ti6Al4V. Examinations with particulate debris disclosed a dose-dependent influence of all powders with Nb Ampertec showing the highest decrease of cell viability and collagen synthesis. Furthermore, interleukin synthesis was only slightly increased for all powders. In summary, Nb Ampertec (sintered Nb) and Ti-42Nb materials seem to be promising alternatives for medical applications compared to common materials like forged or melted Ti6Al4V.

1. Introduction

Constraint or loss of functions in the human body can be the result of tumors, fractures, injuries as well as chronic diseases, infections or simply aging [1]. Nowadays, maintenance or replacement of those functions can be achieved through the application of biomaterials mainly consisting of metals, ceramics or polymers [2–4]. Titanium and its alloys are the most common used implant materials in orthopedic surgery with an amount of 70 to 80% [5–7]. Their application ranges from load bearing areas like in orthodontics and orthopedics to gastroenterology as well as cardiovascular and reconstructive aspects. They possess appreciable mechanical properties, good corrosion resistance and biocompatibility [8–12]. The most frequently used titanium-based material is the titanium aluminum vanadium alloy Ti6Al4V (also referred to Ti Grade 5) [13–16]. However, by now the elemental component vanadium is proved to be toxic and aluminum is suspected to cause e.g. Alzheimer disease [7,17–19].

Titanium alloys in general crystallize in a hexagonal close-packed α-phase (stable at 25 °C) which at 882 °C reversibly transforms into a β-phase with body-centered cubic crystal structure. Addition of alloying elements may stabilize this phase or cause crystallization, i.e. stabilization of $\alpha + \beta$ mixtures [20]. The β–type titanium alloys possess significantly smaller Young's moduli compared with α- or $\alpha + \beta$ alloys. Some of the even build deformation-induced martensite structure possessing a shape-memory effect [21]. The formation of the β–type structure may avoid a mechanical mismatch in elasticity of bone and implant, causing stress shielding associated with implant loosening. Specific β-stabilizers for titanium alloys further improve the material properties [22–26]. For example, non-toxic and non-allergenic niobium represents a relatively new and promising implantable biomaterial, which is proved for its biocompatibility in vitro and in vivo. It has a corrosion resistance superior to titanium resulting from a self-passivating inert (native) oxide surface layer [27–32]. Furthermore, some niobium alloys offer a shape memory effect (SME) and possess superelastic properties, analogous to selected nickel alloys [7,32,33]. Nickel titanium alloys (NiTi) gained in importance in the last decades [34] being accounted for by its SME up to 8% [35], biocompatibility and mechanical properties (elastic modulus, compressive strength) which are close to bone. Even though NiTi is corrosion and wear resistant [35–38] there are concerns including toxicity, allergenic reactions and carcinogenic potential of dissolved nickel ions [27,39,40].

Niobium and Ti-Nb alloys or niobium oxide (Nb_2O_5) materials represent excellent alternatives for medical applications [31,39,41,42], even

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though mechanical properties require for improvement [2]. Moreover, one of the problems of biomaterials used is the surface contamination with residues or particles within the production process and the formation of wear debris due to mechanical strain and friction of articulating implant components [43–45]. Particles and wear debris can accumulate in the periprosthetic tissue being size-dependent phagocytosed and activating or inhibiting the attendant cells. For example, osteoblasts, macrophages and osteoclasts are known to interact in various fashions [43, 45–47]. Those particles cause inflammatory reactions and moreover, lead to increased differentiation of bone resorbing osteoclasts and inhibition of bone forming osteoblasts. Finally, all these factors result in osteolysis and aseptic implant loosening [43,45,47].

The intention of the present study is to demonstrate the superior biocompatibility of Ti/Nb-based alloys compared with conventional metallic implant materials like Ti6Al4V. This includes biomedical issues, i.e. preservation of cell activities (osteoblasts, fibroblasts) and non-toxicity as well as (bio-) mechanical aspects, which are work in progress and will be published subsequently. The focus is not only on intrinsic material properties, but also on their morphologies, also considering 3D-printed bulk materials.

Therefore, in the present in vitro study, human osteoblasts and fibroblasts were cultured on two different niobium specimens (Nb Amperit, Nb Ampertec), Nb sheets as well as Ti-42Nb specimens (sintered and manufactured by SLM), compared with forged Ti6Al4V and referenced to tissue culture polystyrene (TCPS) as growth control. Furthermore, human osteoblasts were incubated with four particulates of the above mentioned groups to imitate influence of wear debris.

2. Materials & methods

Niobium powders and niobium sheet used in this study are commercial products produced and distributed by H.C. Starck Tantalum and Niobium GmbH, Goslar, Germany. Product data sheets can be obtained on request from www.hcstarck.com. Spherical Ti-42Nb powder was obtained by EIGA (Electrode Induction Melting Gas Atomization, EIGA) of Ti-42Nb rods. Appropriate SEM images are displayed in Fig. 1. Chemical analysis, particle size and abbreviations of the different powders used in this study are provided in Table 1. Additionally, chemical analysis of niobium sheet is given.

2.1. Preparation of test specimens

All specimens prepared for cell-biological investigations were cylindrical pellets with dimensions of d × l = 10 mm × 2 mm compounded from the above mentioned powders. Nb Amperit was uniaxially pressed at 25 °C using a lab toggle press applying a load of 65 bars. Nb Ampertec was uniaxially pressed at 25 °C using a lab toggle press applying a load of 65 bars and subsequently sintered in vacuum at 1200 °C for 10 min. Ti-42Nb powders could not successfully be compacted by uniaxial pressing due to their spheroidal shape. Accordingly, powder consolidation was performed pressureless by sintering at 1000 °C for 10 min of a 3 mm powder bed in Al_2O_3 sinter rings on Nb sheets. As-obtained specimens were machined to 2 mm height. Ti-42Nb specimens were obtained by additive manufacturing, i.e. selective laser melting (SLM) of Ti-42Nb (sieve fraction < 63 μm) using a TruPrint 1000 equipment (TRUMPF GmbH + Co. KG, Ditzingen, Germany) operated at Laserzentrum Hannover, Hannover, Germany. The following laser/scan parameters were applied: laser power 50 W, scan speed 400 mm/s, hatch 120 μm, powder bed feed rate 50 μm/layer. Surface roughness of the test specimens (Rz, Ra) was analyzed by means of a tactile measurement method using a Hommel-Etamic T1000 and a sampler (TKU300, probe tip radius 5 μm,) (both: Jenoptik, Jena, Germany). Thereby, a probe tip with defined radius slides across the surface of the test specimen permeating into the surface subject to the probe tip radius. The measuring range was 320 μm and the length of tactile measurement was 8 mm. Three surface points per specimen ($n \geq 3$) were swept (Table 2).

To illustrate surface properties of the several metallic samples field emission scanning electron microscopic (FESEM) images were generated. The sample surface is gold-plated (~25 nm) using a sputter coater (Leica SCD004, Wetzlar, Germany) and figured with a Merlin VPcompact microscope (Carl Zeiss AG, Oberkochen, Germany) with a 50-fold magnification (Fig. 2).

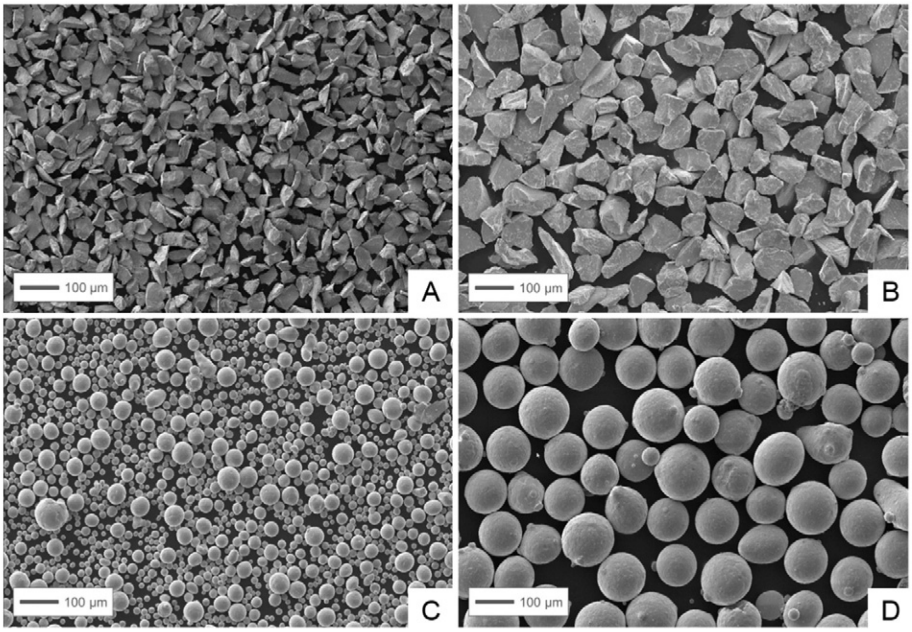

Fig. 1. SEM images of niobium powders recorded at 100× magnification. A: AMPERIT 160 NIOBIUM METAL 14–45 μm, B: AMPERTEC NIOBIUM EB MELTED 45–75 μm, C/D: AMPERTEC MAP Ti-42Nb powders - C: powder fraction <63 μm, D: powder fraction 103 μm - 350 μm.