Technical White Paper:

# Biocompatibility of Sputtered Nitinol Thin Films

Nickel-titanium shape memory alloys (Nitinol) exhibit great mechanical and chemical properties which make them attractive candidate materials for various types of biomedical applications (e.g. staples for compression osteosynthesis, hip endoprosthesis and acetabular cups with integrated self-expanding NiTi elements)[1]. These alloys demonstrate good deformability that is associated with their superelastic behavior, a mechanically imposed strain in order of a few percent can be reversibly recovered after unloading. Besides these tremendous mechanical properties, NiTi is well suited for applications in the medical field since the material is known for its excellent biocompatibility[1], and a high number of FDA approved permanent implants made from Nitinol exist.

Acquandas NiTi thin film technology is a novel fabrication route for Nitinol devices which allows the fabrication of complex geometrical structures with micrometer precision from materials with high cyclic mechanical stability[2]. During the deposition process, the material goes through the gas phase, a fact that has an impact on microstructural features of the deposited Nitinol material: In contrast to standard Nitinol sputtered material lacks oxide and carbide inclusions, and exhibits therefore excellent mechanical fatigue and corrosion properties.

For determining the biological safety of Nitinol the corrosion of binary NiTi itself has been the subject of many studies[3,4,5,6]. For use as implant material a smooth surfaces with a homogeneous, defect-free corrosion-resistant titanium oxide is desirable and leads to low corrosion rates and low Ni release as well as high breakdown potentials[7,8]. Corrosion measurements in Hank's solution show a low corrosion rate of sputtered Nitinol thin films, see Fig. 1. At voltages of about 2V current increases steadily, but scanning electron microscopy reveals no signs of pitting corrosion. The increase in current can therefore be explained by gas formation rather than electrical breakdown[9].

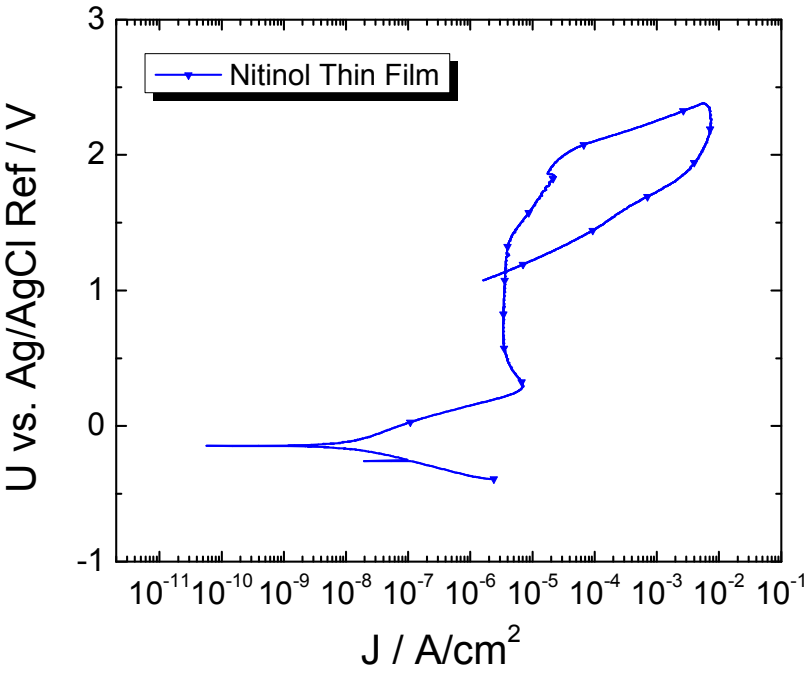


Fig 1. Corrosion measurement on circular, 1.08 cm diameter NiTi thin film samples, tested in Hanks solution according to ASTM standard[10]

In this regard, sputtered NiTi has already demonstrated great potential as a biomaterial for heart valve leaflets[11,12].

For materials for *in vivo* applications, biocompatibility and cell growth must be guaranteed. For analyzing biocompability of sputtered Nitinol, including cell viability and cytokine release human mesenchymal stem cells (hMSC) can be used as a cellular model.

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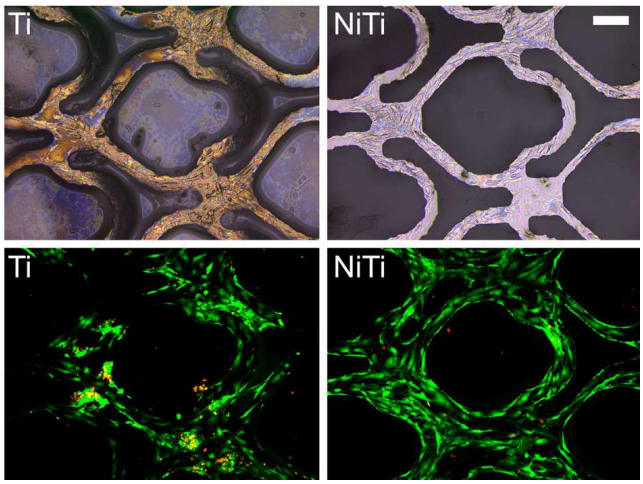


Fig.2. Lightmicrographs of titanium (Ti) and Nitinol thin films produced by magnetron sputtering (upper row) and fluorescence micrographs hMSC at the surface of those (Ti) and (Nitinol) thin films. HMSC were incubated on the different samples for 7 days and stained with calcein A M (green=living cells) and propidiumiodine (red=dead cells; scale bar=300 µm)[13].

Cell adhesion can also be controlled geometrically by 2D micro patterns of extracellular matrix proteins. It is thus possible to control cell life and death by choosing a specific pattern geometry [14] and to influence cell shape, focal adhesion and actin stress fiber formation[15]. Such patterns can also be created using Nitinol thin film technology. The biological impact of Nitinol meshes with rhombic holes of different size, fabricated by Nitinol thin film technology, can be characterized by the adhesion of autologous progenitor cells (CD133+) and smooth muscle cells. Scanning electron microscopy (SEM) and fluorescence microscopy analysis of cells adhering to the meshes at two different time points (after 24 h and after seven days of incubation) demonstrate the biocompatibility of the material and a dependence of cell growth on hole and strut dimensions.

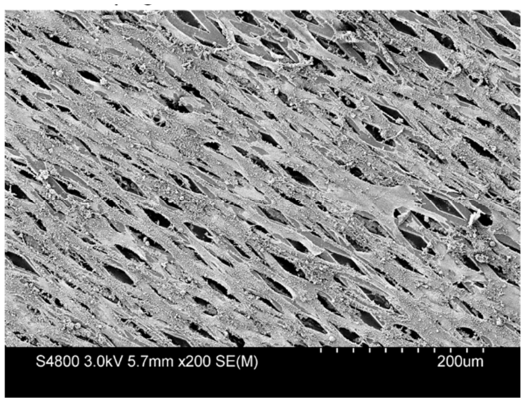


Table 1 Strut width and rhombic hole size of differently sized NiTi mesh scaffolds. S (Small), M (Medium) and L (Large) denote the different structure sizes o

| | S | M | L |
|---|---|---|---|
| **Strut width / µm** | 5,3 ± 0,2 | 7,5 ± 0,2 | 9,2 ± 0,2 |
| **Rhombic width / µm** | 15,1 ± 0,1 | 19,7 ± 0,2 | 24,7 ± 0,2 |
| **Rhombic length / µm** | 45,0 ± 0,2 | 64,2 ± 0,1 | 84,5 ± 0,2 |
| **Rhombic hole size / µm²** | 440 ± 8 | 820 ± 21 | 1309 ± 37 |

Fig.3. SEM image of CD133+ cells Nitinol mesh structure S.Fibers are clearly visible and mainly aligned along the longitudinal direction of the rhombic holes[16].

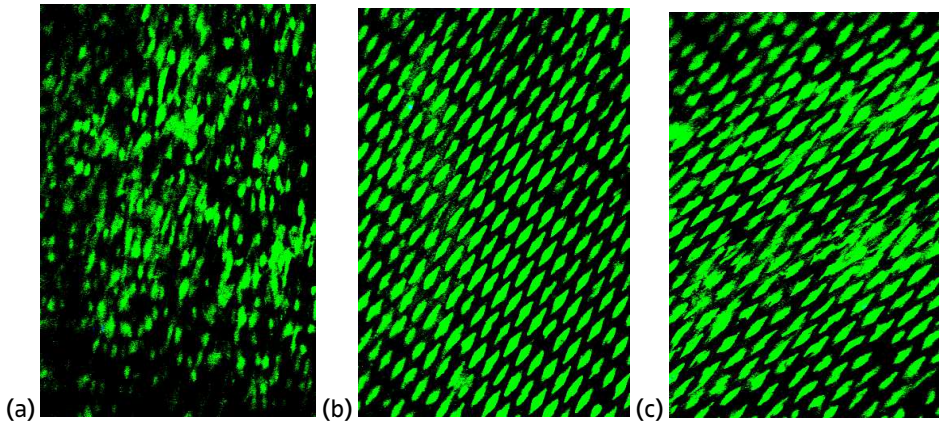


Fig.4. Smooth muscle cells (SMC) (green) stained with Calcein A M on Nitinol meshes after seven days of incubation. (a): Cells on structure S. B: Cells on structure M. C: Cells on structure L. The samples are Seeded one sided. Both sample sides were investigated. Cells are growing on both sides of the samples, covering the black NiTi grid partially.

NiTi thin film meshes are promising biomaterials for the fabrication of mechanically and geometrically well defined, free-standing tissue engineered implants. The effective mechanical properties of the scaffold can be adapted to implant requirements by varying the hole and strut size and the macroscopic dimensions of the Nitinol film. Nitinol thin film meshes are highly biocompatible and cell adhesion can be controlled by the size of the rhombic holes in the mesh.
The suitability of Nitinol scaffolds for biological applications in general is proved. The inflammatory response shows a lower TNF-$\alpha$ level for tissue enclosed meshes than for bare NiTi meshes, and furthermore, the superior biocompatibility of NiTi compared to stainless steel was confirmed.

**About ACQUANDAS GmbH:** ACQUANDAS GmbH is a technology company that supplies thin film components to the healthcare industry – in particular to medical device OEMs – and other industrial markets, such as the automotive and consumer electronics industries. ACQUANDAS is located in Kiel, Germany.
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