Distribution of Elements Near the Free-Surface of Medical Products Examined by a TEM

Pavel L. Potapov, Dominique Schryvers and Dimitri E. Aslanidis

Abstract

Today, a Nitinol alloy is used in a wide variety of medical devices because of its unique mechanical properties, durability and biocompatibility. However, as Nitinol consists of about 50 at. % of toxic Ni, certain applications are still hindered by the concern of free Ni release in tissues. The latter is controlled by the structure of near-surface layers and might be strongly affected by various surface treatments. A proper application of advanced sample preparation techniques allows us to characterize the Nitinol near-surface structure by transmission electron microscopy (TEM) equipped with electron-energy-loss spectroscopy (EELS) and energy-dispersive X-ray analysis (EDX). The oxide layer of 8nm thickness appears to be primarily TiO₂ with addition of about 5 % of Ni. Elemental maps of the Ti, O and Ni distribution near the surface, and concentration profiles are presented. The developed routines allow one to characterize the surface structure of a wide range of medical products.

Introduction

Metallic materials implanted in human tissues are involved in complex electro-biochemical reactions with interchange of ions on the implant-tissue interface. Among others, Nitinol implants are recognized as having unique mechanical properties (super-elasticity, shape memory and excellent fatigue resistance) [1,2]. Peripheral stents made of Nitinol can stand more than 400M cycles in various bending, rotary and tension-compression fatigue modes. At the same time, Nitinol consists of about 50 at. % of Ni (balance Ti), which is known to provoke severe toxicological and allergic responses [2]. Despite of a potential Ni hazard, good biocompatibility is documented because a release of Ni is efficiently blocked by a thin titanium dense oxide layer formed naturally at the surface of Nitinol medical products [3]. The structure of this layer is crucial for controlling biocompatibility and therefore for mass application of Nitinol medical products. A proper application of advanced sample preparation techniques allows us to make an electron-transparent cross section of Nitinol implants near their free surface. The electron transparency is obtained by applying ion polishing with a gradually decreasing attack angle at the place of interest. The parameters of ion polishing are optimized in such a way that the resulted cross sections represent adequately the intrinsic structure of a sample while the ion-induced damage is minimal [4]. In particular, the natural oxide layer of 8nm thickness formed at the surface can be visualized (Fig. 1). Furthermore, the near-surface structure of implants can be characterized by all powerful means of TEM including the elemental analysis in the nanometer scale.

Energy Dispersive X-ray Analysis (EDX)

The easiest way to visualize the distribution of chemicals over the place of interest is energy dispersive X-ray analysis (EDX) coupled to STEM (Fig. 2). EDX mapping is easy in operation and processing and allows one to quantify the content of heavy elements with a good precision. At the same time, quantification of light elements like oxygen is much less reliable because their characteristic X-ray radiation tends to be absorbed predominantly in the material. EDX mapping shows reasonable results in samples up to 80nm thick while, at a higher thickness, the spatial resolution deteriorates due to the increased spread of the beam.
Electron Energy Loss Spectroscopy (EELS)

In contrast to EDX, electron energy loss spectroscopy (EELS) is well suited for analyzing light elements and also shows a higher spatial resolution. Resolution better than 1 nm can be routinely observed for elements having characteristic ionization edges at energies less than 1000 eV. The fastest way to obtain an EELS elemental map is the energy-filtered TEM (EFTEM), in which a TEM image is...

Fig. 2: (a) STEM coupled to EDX elemental maps. The oxide layer is hardly visible in the STEM dark-field image while it shows up in the oxygen map. The Ti map reveals clearly the metal-oxide interface, which is characterized by a slight Ti depletion; however, no clear features are observed in the Ni map. (b) The O, Ti and Ni concentration profiles across the free surface of an implant. The concentration of Ni slowly increases from the bulk (about 50 at.% Ni) towards the surface (about 60 at.% Ni) and abruptly drops down at the metal-oxide interface denoted by the red line.

Fig. 3: (a) EFTEM images taken consequently in the energy regions of inelastic electrons, O K, Ti L2,3 and Ni L2,3 edges. Comparing with the EDX maps in Fig. 2 the resolution is drastically enhanced revealing the chemical sharpness of the metal-oxide interface. (b) The concentration profiles integrated across the interface demonstrate the resolution of about 1 nm. A red line denotes the metal-oxide interface.
formed by inelastic electrons selected in the energy range (10-50eV in width) of a characteristic ionization edge. For extrapolation and subtraction of the background scattering, few extra images should be taken in the energy region preceding the ionization edge [5]. Fig. 3 shows the EFTEM maps of the near-surface area revealing a sharp separation of elements in the metal-oxide interface. The resolution is enhanced at least three times comparing with EDX mapping of the same place. The concentration profiles confirm an increase of Ni and depletion of Ti near the metal-oxide interface.

Quantification of EELS results is more complicated than in the case of EDX. The best results are achieved by taking few nanometer probes under controlled diffraction conditions and recording the spectra in the energy region covering all the ionization edges present in a sample. Such local probes reveal that the oxide layer consists of about 31 at. % Ti, 5 at. % of Ni and 64 at. % O, i.e. quite close to the stoichiometric TiO$_2$ oxide.

EELS, however, is very sensitive to the quality of a sample. The best results are obtained when preparing a sample thinner than 20nm, while an increase of the sample thickness leads to a dramatic deterioration of the signal-to-noise ratio and a loss of resolution.

**Concluding Remarks**

The combination of advanced thinning techniques with analytical TEM methods – EDX and EELS – allows one to visualize the distribution of chemicals near the free-surface of medical products and, thus, to predict the response of human tissues to external invasion. EELS seems to be best suited for such analytical examination due to the analytical resolution of 1nm or better. EELS poses, however, very high requirements to the quality of the sample preparation. EDX can be an easier alternative for the cases where heavy elements are of interest and the spatial resolution doesn’t need to be better than 3nm.

**References**


**The Authors**

Dr. Pavel L. Potapov (left in the photo) studied physics and materials science in the Moscow Institute of Steel and Alloys. He obtained his Ph.D. in the Bardin State R&D Center of Ferrous Metallurgy in 1993. Currently he is a research fellow in the Electron Microscopy for Materials Science (EMAT) Centre in Antwerp, involved in TEM characterization of a range of materials – metals, ceramics, coatings, organic films.

Prof. Dr. Dominique Schryvers (right in the photo) studied Physics at the University of Antwerp. He obtained his Ph.D. in 1985 at the University of Antwerp on HRTEM of order-disorder phenomena in Pt-based alloys and his Habilitation in 1991 at the Free University of Brussels on the martensitic transformation in Ni-Al. Currently he is Professor in Physics at the University of Antwerp. His research concerns the use and development of advanced TEM techniques including HRTEM and EELS for the characterization of various modern as well as historic materials.

Dr. Dimitri E. Aslanidis is the managing director of Medical technologies. He obtained his Diploma Engineering degree at Technical University Athens, and holds a Ph.D. in Materials Science and Engineering from Katholieke Universiteit Leuven.

Pavel L.Potapov, Dominique Schryvers EMAT, University of Antwerp, Groenenborgerlaan 171, 2020 Antwerp, Belgium Tel. +32 (0)3 265-3472, +32 (0)3 265-3247 Fax +32 (0)3 265-3257 Pavel.Potapov@ua.ac.be, schryver@ruca.ua.ac.be

Dimitri E. Aslanidis, Medical technologies n.v Daelemveld 1113, 3540 Herk-de-Stad, Belgium metallurgy@skynet.be