Surface Modification of Nitinol Alloy by Novel Biocompatible Zwitterionic PEG for Peripheral Arterial Stents

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Introduction: Stent placement is an accepted treatment for peripheral vascular occlusive disease.[1] However, long-term success of this procedure is still limited by development of chronic in-stent restenosis due to neointimal hyperplasia, which occurs in up to 40% of all patients who received stent placement in peripheral arteries.[2]

The basic requirements of peripheral arterial stents have biocompatibility, metallurgic properties, high radio-opacity, and physical properties. Among them, biocompatibility is one of the crucial factors for long-term applications. In order to develop better blood compatible materials, a vast number of researches have been directed toward chemical modification. In general, poly(ethylene glycol) (PEG) was reported to be more blood compatible due to its steric stabilization and chain motion effects. In addition, sulfobetaines ($-N^+-SO_3^-$) have recently received the increased attention to one of the biocompatible structures in the well-identified class of zwitterionic polymers. In this study, novel biocompatible zwitterionic PEG ($PEG-N^+-SO_3^-$) was synthesized from PEG and grafted on Nitinol alloy by nanosurface modification, and its characteristics were evaluated.

Methods: Zwitterionic PEG was synthesized from PEG (MW 2,000) through three reactive steps. The first step was to react the end groups of PEG with hexamethylene diisocyanate (HDI). The second step was to react one isocyanate group of OCN-PEG-NCO with N,N-dimethyl-ethanolamine (DMEA). Finally, OCN-PEG-DMEA ($PEG-N^+$) was reacted with propane sultone (PST) and tertiary amine through ring opening reaction to get finally zwitterionic PEG ($PEG-N^+-S^-$). The chemical structure of the obtained zwitterionic PEG was analyzed by FTIR, ^{1}H-NMR, and GPC. After the surface of Nitinol specimen (TiNi, Biosmart Co., Korea) was oxidized by hydrogen peroxide-butanol and O_2 plasma treatments, respectively, the zwitterionic PEG was grafted on Nitinol alloy in anhydrous toluene and stannous octoate by nanosurface modification. Oxidation and surface modification of Nitinol specimens were controlled by ATR-FTIR, contact angle, ESCA, and SEM.

Results / Discussion: The resulting zwitterionic PEG was confirmed by FTIR, ^{1}H-NMR, and GPC. Two oxidation conditions (hydrogen peroxide-butanol treatment or O_2 plasma treatment) were applied to Nitinol surface at the previous step for introducing the zwitterionic PEG. While the contact angle of Nitinol control was 67 degree, those of all surface-treated Nitinols were considerably low, indicating that the surface modification of Nitinol was achieved well and the surfaces were more hydrophilized (Table 1). In particular, $TiNi-PEG-N^+-S^-$ showed the least contact angle among other samples due to the coupling of hydrophilic zwitterionic PEG. From ESCA results (Table 2), Nitinol control displayed C1s and O1s, whereas Nitinol grafted with PEG-NCO and $PEG-N^+$ did C1s, O1s, and N1s. Furthermore, the sulfur atom of $TiNi-PEG-N^+-S^-$ appeared by the grafting of zwitterionic PEG having sulfonate group. In addition, blood compatibility of the zwitterionic PEG-grafted Nitinol will be demonstrated.

Conclusions: Newly synthesized biocompatible zwitterionic PEG was successfully grafted on Nitinol alloy by oxidation and surface treatment. Our result suggests the possibility of the usage for peripheral arterial stents which contact directly with blood.

Table 1. Contact angles of various Nitinol surfaces

Material	Contact angle (deg)		
	No treatment	H_2O_2+BuOH	O_2 Plasma
TiNi control	67	59	13
TiNi-PEG-NCO	43	36	40
$TiNi-PEG-N^+$	36	28	32
$TiNi-PEG-N^+-S^-$	35	20	23

Table 2. ESCA data of various Nitinol surfaces

Material	C	O	N	S
TiNi control	49.75	50.25	-	-
TiNi-PEG-NCO	61.56	35.74	2.70	-
$TiNi-PEG-N^+$	66.36	31.88	1.76	-
$TiNi-PEG-N^+-S^-$	63.49	34.15	1.56	0.80

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