Development of New Minimally-Invasive Medical Devices and Their Clinical Applications

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1. Research Purpose and Significance

There is a strong demand to improve the maneuverability, reliability, and safety of the “endovascular treatment” devices that utilizes guide wires, catheters, and stents, as well as to expand the application scope of these devices to the peripheral system. The purpose of this research is to develop medical devices and new medical core materials that use shape-memory alloys. The research development and practical application of these materials, which impart functionality never before had in previous medical devices, may be the highly significant research that has been long-awaited by the medical industry.

2. Goals To Be Accomplished By the TUBERO Deadline and Their Research Method

The research representatives and joint research personnel will complete the new core materials made up of new smart materials, such as Cu, Ti, Ti-Ni base alloys that are being studied, and at the same time, research and evaluate the process of using these alloys to manufacture the devices by cooperating with medical device manufacturers and clinicians. The specific goals are described below:

(1) Development of Ni-free Ti-Mo-Sn superelastic alloy and its application to micro-catheter

(2) Suggestion for balloon expandable-type Ti-Ni-Nb superelastic stent and assessment of its biological functionality

(3) Development of highly-maneuverable guide wire and its clinical assessment (Cu-Al-Mn and Ti-Mo-Sn alloys)

In this research, the researchers designed, dissolved, and manufactured alloys, assembled devices, and assessed their functionality, conducted anodic polarization measurement, cytotoxicity assessment, and considered performing biological safety assessment and maneuverability assessment that utilizes animals and developing new medical devices in order to achieve the aforementioned goals.

3. Status of Goal Accomplishment

(1) Development of Ni-free Ti-Mo-Sn superelastic alloy and its application to micro-catheter

Recently, there have been some concerns about allergy to Ni contained in the Ti-Ni shape-memory alloy. The research optimized performance and made tubes out of Ti-Mo-Sn shape-memory alloy with a Ti base that does not contain Ni and attempted to apply it to micro-catheters. Figure 1(a) shows the stress-strain curve of a wire made of Ti-Mo-Sn alloy. This alloy shows a low Young’s modulus of about 40GPa and a recoverable strain of over 3%. This alloy wire has acquired a manufacturing authorization for use as dental material for a new highly-elastic wire clasp (Controlled
medical device, Class II, Certification number: 218AFBZX0003800, Distribution name: Neo-Titanium Wire). Furthermore, by adding Sc that has a strong oxide formation tendency and selecting proper manufacturing method, the flexibility and degree of superelasticity could be improved as shown in Figure 1(b). Figure 2 shows that the alloy was successfully formed into a tube, which would allow development of a catheter core made of superelastic metal that is safe for the body. Also, the anodic polarization measurement and cytotoxicity assessment confirmed that this alloy is more corrosion-resistant and has greater cell compatibility than stainless and Ti-Ni alloy.

(2) Development of highly-maneuverable guide wire and its clinical assessment

The core material of functional graded guide wire with superelastic ends and highly rigid body was developed by controlling the material composition of the core material's lead end to the tail end using Cu-Al-Mn base alloy and Ti-Mo-Sn base alloy. Figure 3 shows the prototype for functionally graded guide wire and Figure 4 shows the characteristics of the core material. This research uses the gradient heating furnace shown in Figure 4(b) to grade the rigidity by controlling the structure of the material. As Figure 4 (b) shows, the guide wire possesses the characteristics of the functionally graded-type properties: a highly rigid body and superelastic lead ends. Figure 4(i)-(vi) represents the tension stress-strain curve of core wire parts, (i)-(vi). We found that the functionally graded guide wire has a highly rigid body, which allows it to have an excellent protrusion and torque transmission as well as a superior maneuverability because of its flexible ends.
(3) Suggestion for balloon expandable-type Ti-Ni-Nb superelastic stent and assessment of its biological functionality

Focus was given to Ti-Ni-Nb superelastic alloy as a core material for the balloon expandable-type Ti-Ni-Nb superelastic stent that has a high voluntary indwelling and a following capability of blood vessel wall in self-expandable stent. We obtained basic knowledge to develop its functionality. The shape-memory alloy exhibits superelastic and shape-memory effects through reversible metamorphosis from martensite structure to austenite structure. The concept of this research is to place a flexible martensite stent inside a body and transform it into superelastic austenite through heating. On the other hand, because heating within the body may run a risk of negatively affecting the body tissue, we have discovered a potential application of stent for peripheral blood vessels that does not require heating after balloon expansion. Figure 5 shows the repeated load-push curve of bent Ti-Ni-Nb sample that represents the stent flexion. (Reference inserted Figure for the testing method). The stainless (SUS316L) and Co-Cr base alloy are also shown in order to compare the core materials mainly used in the balloon expandable-type stent. The stainless and Co-Cr base alloy have higher degrees of elasticity and strength, but is more susceptible to plastic deformation and leaves a significant plastic strain after a large deformation. We found that Ti-Ni-Nb alloy on the other hand may have low strength, but has a large area of elastic deformation and is not susceptible to plastic deformation compared to other materials. This makes Ti-Ni-Nb alloy a potential candidate for the highly elastic, balloon expandable-type stent. This alloy is also known to have the same corrosion resistance and cell compatibility as the existing clinical material Ti-Ni alloy and this research will test the highly elastic, balloon expandable-type stent based on the aforementioned knowledge (Figure 6) and attempt to conduct an animal study using external iliac artery of a beagle.

4. Future Perspective

Currently, we are working on material development, device prototype, and evaluation of animal studies, but we will continue to demonstrate maneuverability and biological safety and aim for practical application. The Ti-Mo-Sn tube is a superior new stent core material because of its high corrosion-resistance and biological safety, and we will establish a technology to create thinner tubes. Also, we anticipate the development and specification of dissimilar metal welding-type guide wire with strong materials like cobalt on the body and Ti-Mo-Sn or Cu-Al-Mn superelastic alloy on the lead end. The Ti-
Ni-Nb alloy that can control the superelasticity through strain load is expected to be the third stent core material that can ensure high voluntary indwelling and following capability of blood vessel wall after indwelling. The application of this alloy to blood vessel of the brain and other peripheral system will be verified by animal studies.

5. External Publication List


【Exhibition, Forum】

(1) Advanced Technology Association at Tohoku University, Tokyo, 2/1/2005

(2) The 2nd Tohoku University Bioscience Symposium, Sendai, 5/16/2005

(3) Innovation Japan, Tokyo, 9/27-29/2005


(6) Meeting of Corporations and Academic Research Institutes, Fall 2006, Sendai, 11/2/2006

(7) Innovation Fair, Tokyo, 2/1/2007

(8) The 3rd Western Saitama Prefecture Industrial Technology Exhibition and Association, Saitama, 2/15/2007