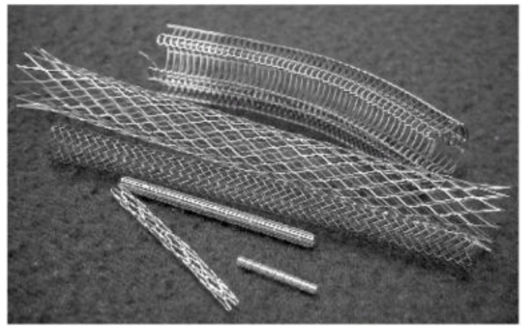

Unalloyed Pleasures: The Realities of the Materials of Tomorrow
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Recent discussions about the advantages of certain advanced materials serve to highlight difficulties facing designers and materials scientists when selecting high-performance alloys for medical use. In many situations, this advanced performance is achieved through the use of an alloying addition, that is, a separate element added to the parent, major metal. However, the character of this additive may be an anathema to the biocompatibility specialist because its presence can radically influence biological performance. This article addresses the importance of risk assessment in these situations.

Introduction
The March issue of "The Technological Edge"[1] describes the exciting characteristics of some shape-memory materials and the relevance of their characteristics to medical applications. That article was very timely in view of the current interest being shown in one of these materials, nitinol. Briefly, it will be recalled that within such alloys there is an irresistible urge to change their shape simply by undergoing a small temperature rise. The shape change is not arbitrary but predetermined so that an object can be prepared for use in one shape and that shape can be changed, remotely and on demand, by a subtle change in its environment.

The potential for these alloys in clinical practice is based on the fact that the temperature at which the shape change is induced can be arranged to lie between ambient and body temperature. A material or device can be shaped by the manufacturer or user at a temperature in excess of this transition point so that it assumes the size and/or shape that is ultimately required in the body. It is then cooled to ambient temperature when it can be deformed to assume a different shape, which is determined by the needs, for example, of a surgical technique. On implantation in the body, when the material is once again raised above the transition temperature, it will revert, or attempt to revert, to the original predetermined shape.

Thus, these materials are of interest, for example, for intravascular stents. They could also be appropriate in any other situation where a cylindrical device has to be inserted down a vessel or into tubular tissues, such as in the trachea or urinary tract; insertion has to be made easily and without traumatizing that tissue, the device then expands to gently fit the inner lumen of that vessel. The manufacturer, possibly by using an expandable mesh, arranges for the resting diameter to equate to that inner lumen, but compresses the structure below the transition temperature so that it occupies a much smaller volume and can be guided to the required site through an appropriate catheter, recovering its larger diameter when warmed by blood or infused saline.[2] Implantable vena-cava filters for the containment of emboli can be based on the same principle.

In orthopedics, there is interest in designing implantable hardware for altering skeletal shape, for example in the treatment of scoliosis or in fracture healing.[3] In orthodontics, the constant force directed onto a tooth by a wire that would rather be in a slightly different place, will slowly produce the required tooth movement.[4]

The problems of memory alloys

So far, so good. But what about the types of alloy that demonstrate this behavior? It will be of no surprise to learn that those few alloys that do this are not ideal for implantation in the body. As the previously mentioned article pointed out, only two such alloys have received commercial prominence, Cu/Zn/ Al and Ni/Ti. Others that possess shape memory, but are not readily available, are Ag/Zn, Au/Cd and Cu/ Al/Ni. Most of these do not have the right transition temperature, but even if they did they would not be acceptable biologically. It is the titanium-nickel alloy, referred to as nitinol, that is the most widely used and the one that can be contemplated for medical applications. Adjustment of the precise composition between Ti-55% Ni and Ti-58% Ni can produce a transition temperature anywhere between -50 and +SO 0C. The problem is, of course, that nickel is not the most highly desirable metal biologically.

The alloy is quite good from the point of view of corrosion, but nevertheless it does release nickel into the tissue, and the response of the tissue itself is somewhere between that associated with pure titanium, which is very good, and pure nickel, which is very bad. Fortunately, the passivity of the alloy is such that the behavior is closest to titanium, but with the putative hypersensitivity and carcinogenicity characteristics to consider, a degree of caution is required. The article pointed out that the polymeric analogue of the shape-memory alloy has yet to realize its potential because no mass markets have emerged. With the alloys themselves, although general applications are becoming widespread, the medical applications may be far more restricted. Because the prospects for biological safety are greater with the polymers, there may be a role reversal whereby shape-memory polymers are more attractive than shape-memory alloys.

The general lessons

This situation with shape-memory alloys provides a good example of how innovations in materials science can be translated into exciting developments in medical devices, but there is a price to pay. There will nearly always be trade-offs as designers and materials scientists attempt to balance functional performance with biological safety. As in this case, the questions often arise out of the toxicological considerations of the elements that have to be added to a parent metal for it to achieve those functional properties. The timeliness of the nitinol example is witnessed by the fact that this author has received numerous enquiries about its biocompatibility during the past year.

Several other examples of this type of dilemma may be cited. Silver-based alloys have widespread uses in devices and artefacts that contact skin or other tissues. The forming properties of these alloys, including, for example, brazing, are markedly influenced by the nature of the alloying additions, so much so that a few percent of the elements, such as zinc, gallium, or copper, may make a material that is normally unattractive, because of its inability to inexpensively shape, much more amenable to such processes.

In this case, even though the corrosion resistance of silver is good, the possibility of these minor elements being released into the tissue cannot be dismissed. Zinc will be no problem. The situation with traces of copper is more equivocal because it is known to have a few therapeutic effects, but it can have specific toxic effects, as its use in intrauterine devices shows. Gallium is more of an unknown. The widely used semiconductor material, gallium arsenide, has multiple toxicological deficiencies and it is still uncertain how much is due to the gallium and how much to the arsenic, and gallium nitrate is a powerful chemotherapy agent with strong biological activity. The biological safety of any alloy containing gallium has, therefore, to be questioned.

Another example is the use of beryllium-containing casting alloys in dentistry. The beryllium is an immensely powerful alloying addition, but also an extremely potent toxin. The role of the additions to titanium, which provide all the good mechanical properties in the alpha-beta alloys that are widely used for implantation, has often been discussed, especially in view of the fact that the two most common are aluminum and vanadium. Interestingly, all of the attempts to modify these materials to eliminate the possibility of harmful effects have centered around the replacement of the vanadium, whereas it is the aluminum that should be the cause for concern should it be released into the tissue.

It is an unfortunate fact of life that it is pure metals, chosen carefully, that can give the greater certainty of biological safety, whereas it is alloys that always give the better mechanical properties. The selection of alloys, therefore, has to be undertaken very carefully if the right balance is to be achieved. To go back to the initial point of the discussion, memories of shape are only useful if the medical device industry can utilize them.

References

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