A Healthy Future: Platinum in Medical Applications

Platinum group metals enhance the quality of life of the global population

doi:10.1595/147106711X566816 http://www.platinummetalsreview.com/

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The world's growing population demands increasing access to advanced healthcare treatments. Platinum is used to make essential components for a range of medical devices, including pacemakers, implantable defibrillators, catheters, stents and neuromodulation devices. The properties of platinum which make it suitable for medical device applications include its biocompatibility, inertness within the body, durability, electrical conductivity and radiopacity. Components can be manufactured in a variety of forms, from rod, wire and ribbon to sheet and foil, plus high-precision micromachined parts. As well as biomedical device components, platinum also finds use in anticancer drugs such as cisplatin and carboplatin.

Introduction

According to the United Nations Environment Programme (UNEP), the global population will reach over 9 billion by 2050 with nearly 90% of the world's people located in developing countries (Figure 1) (1). Since the early 1970s, platinum has been used in a variety of medical devices for people around the world suffering from such ailments as heart disease, stroke, neurological disorders, chronic pain and other life threatening conditions. In 2010, some 175,000 oz of platinum are estimated to have been used in biomedical devices, of which around 80 per cent was for established technologies such as guidewires and cardiac rhythm devices. The remaining 20 per cent was used in newer technologies, such as neuromodulation devices and stents. In addition, over 25,000 oz of platinum are used annually in anticancer drugs (2).

With an ageing and increasing world population, there will be an increasing demand for healthcare products and services that use components made from platinum, other platinum group metals (pgms) and their alloys. Increasing access to healthcare and advanced medical treatments in developing countries means that platinum contributes to improving the quality of life of people around the world.

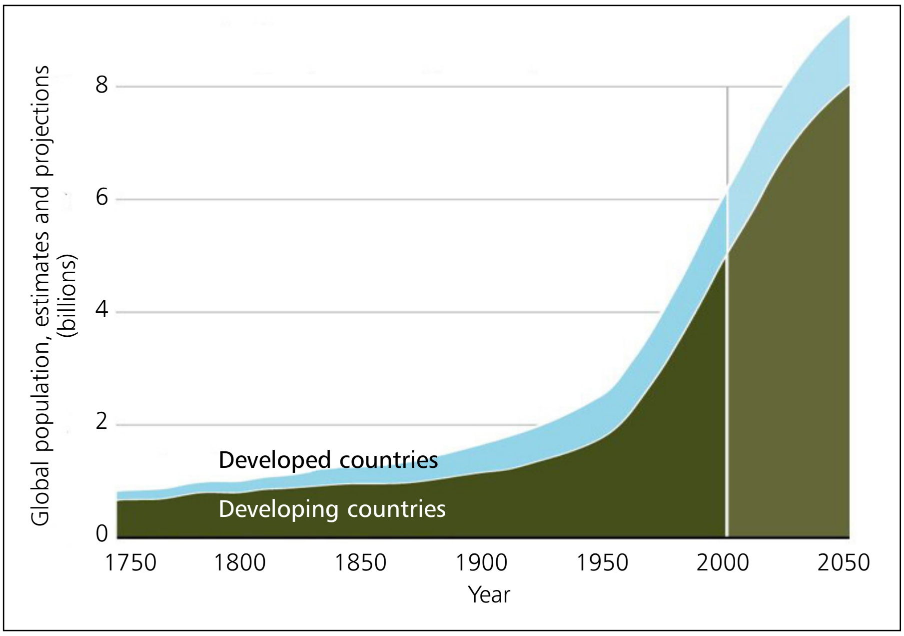

Fig. 1. Trends in population, developed and developing countries, between 1750–2050 (estimates and projections) (1) (Image: Hugo Ahlenius, Nordpil)

The Advantages of Platinum for Biomedical Uses

The chemical, physical and mechanical properties of platinum and its alloys make them uniquely suitable for a variety of medical applications. Agnew *et al.* (3) and Brummer *et al.* (4) carried out studies which confirmed the low corrosivity, high biocompatibility and good mechanical resistance of platinum and platinum alloys that are used for medical applications.

Platinum's biocompatibility makes it ideal for temporary and permanent implantation in the body, a quality which is exploited in a variety of treatments. As a metal, it can be fabricated into very tiny, complex shapes and it has some important properties not shared by base metals. It is inert, so it does not corrode inside the body unlike metals such as nickel and copper, which can sometimes cause allergic reactions. Modern, minimally-invasive medical techniques often use electricity to diagnose and treat patients' illnesses, and platinum's conductivity makes it an ideal electrode material. It is also radiopaque, so it is clearly visible in X-ray images, enabling doctors to monitor the position of the device during treatment. Some examples of areas where pgms are used in medical devices, together with some of the manufacturers currently active in the medical device market, are shown in Table I.

For more than forty years platinum alloys have been employed extensively in treatments for coronary artery disease such as balloon angioplasty and stenting where inertness and visibility under X-ray are crucial. In the field of cardiac rhythm disorders, platinum's durability, inertness and electrical conductivity make it the ideal electrode material for devices such as pacemakers, implantable defibrillators and electrophysiology catheters. More recently, its unique properties have been exploited in neuromodulation devices (including "brain pacemakers", used to treat some movement disorders, and cochlear implants, to restore hearing), and in coils and catheters for the treatment of brain aneurysms.

Platinum in Biomedical Applications

Devices for Cardiac Rhythm Management

Abnormalities of the heart's rhythm are common, often debilitating, and sometimes fatal. For example, bradycardia is a condition in which the heart's "natural pacemaker" is set too slow, resulting in fatigue, dizziness and fainting. Other patients may be at risk of sudden cardiac death, a condition in which the heart's lower chambers (the ventricles) "fibrillate", or pulse in a rapid and uncoordinated manner. This prevents the heart from pumping blood and leads rapidly to death unless the victim receives cardioversion (a strong electric shock to the heart, which restores normal rhythm).

These and other cardiac rhythm disorders can now be managed very successfully using implanted

Table I

Markets for Medical Devices and the Major Device Companies

Medical device markets	Examples of application areas	Major medical device companies
Surgical instrumentation	Arthroscopic; ophthalmology; endo-laparoscopic; electro-surgical	Boston Scientific; Johnson & Johnson; Stryker; Tyco
Electro-medical implants	Pacemakers; defibrillators; hearing assist devices; heart pumps	Boston Scientific; Biotronik; Medtronic; St. Jude Medical
Interventional	Stents; angioplasty; catheter ablation; distal protection	Boston Scientific; Abbott Vascular; Johnson & Johnson; Medtronic
Orthopaedics	Spinal fixation; hip implants; knee implants	Biomet; Johnson & Johnson; Stryker; Zimmer

devices such as artificial pacemakers (5, 6) and implantable cardioverter defibrillators (ICDs) (7–9). These consist of a "pulse generator", a small box containing a battery and an electronic control system which is implanted in the chest wall, and one or more leads which run through a large vein into the heart itself. The electrodes on these leads deliver electrical impulses to the heart muscle – in the case of a pacemaker, these ensure that the heart beats regularly and at an appropriate pace, while in the case of an ICD, a much stronger electrical shock is delivered as soon as the device detects a dangerously irregular heartbeat. Each lead typically has two or more electrodes made of platinum-iridium alloy, while platinum components are also used to connect the pulse generator to the lead (Figure 2).

Catheters and Stents

Catheters are flexible tubes which are introduced into the body to help diagnose or treat illnesses such as heart disease (10–13). The doctor can perform delicate procedures without requiring the patient to undergo invasive surgical treatment, improving recovery time and minimising the risk of complications. Many catheters incorporate platinum components: marker bands and guidewires, which help the surgeon guide the catheter to the treatment site, or electrodes, which are used to diagnose and treat some cardiac rhythm disorders (arrhythmias).

One of the most common coronary complaints in the developed world is atherosclerosis, the "furring up" of the artery walls with fatty deposits, which can lead to angina and heart attack (14). Blockages in the coronary arteries are often treated using a procedure called "percutaneous transluminal coronary angioplasty" (PTCA, also known as balloon angioplasty) (15, 16). This treatment uses a catheter with a tiny balloon attached to its end, which is guided to the treatment site then inflated, crushing the fatty deposits and clearing the artery. Afterwards, a small tubular device called a stent (Figure 3) is usually inserted in order to keep the newly-cleared artery open.

The advent of the implantable metal stent to prop open the artery after angioplasty reduced the occurrence of restenosis (re-narrowing of the artery) by more than 25 per cent. In 2003 the US FDA approved the first drug-eluting stent for use within the USA (17). This type of stent is aimed at further lowering the rate of restenosis following angioplasty procedures.

Platinum's role in PTCA is to help ensure that the balloon is correctly located. First, the surgeon uses a guidewire to direct the balloon to the treatment site. This guidewire is made of base metal for most of its length, but has a coiled platinum-tungsten wire at its tip, which makes it easier to steer and ensures that it is visible under X-ray. Platinum is also used in marker bands, tiny metal rings which are placed either side of the balloon in order to keep track of its position in the body.

Stents are usually made of base metals (typically stainless steel or cobalt-chromium). However, in 2009, the American device manufacturer Boston Scientific introduced a cardiac stent made of a platinum chromium alloy (18–20). This stent has been approved in Europe, and the company is currently

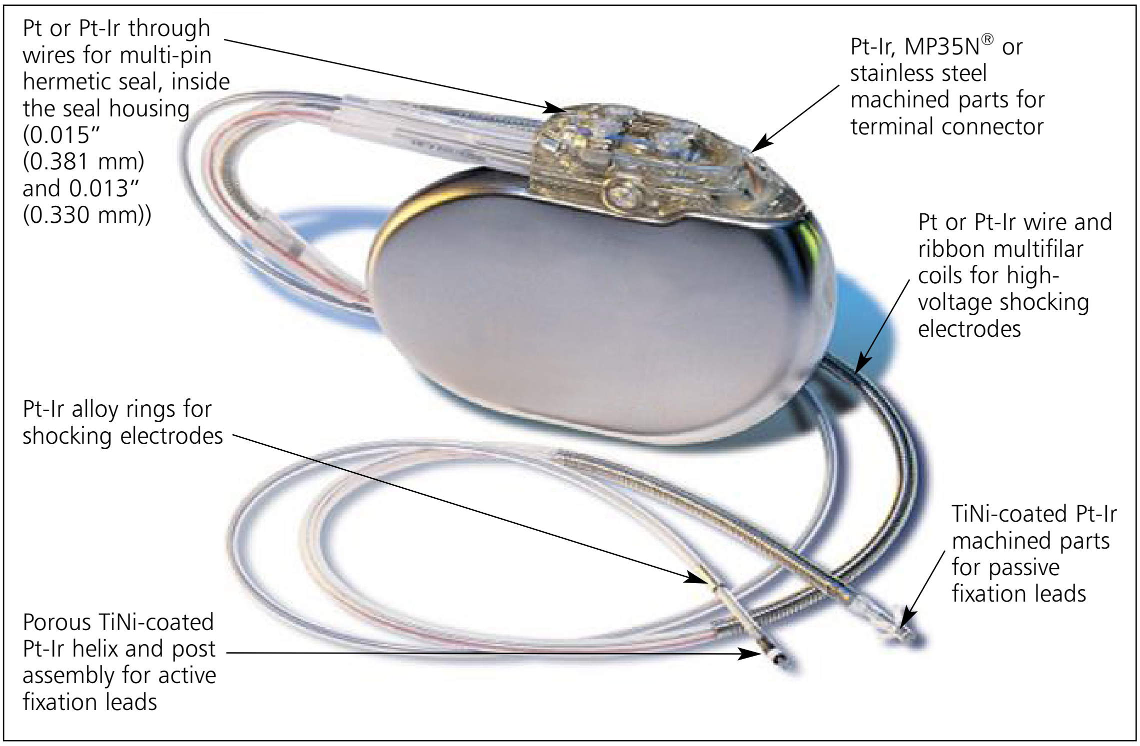

Fig. 2. An implantable cardioverter defibrillator, showing the components that are made from platinum or platinum group metal alloys

seeking approval from the US Food & Drugs Administration (FDA).

Catheters containing platinum components are also used to detect and treat some types of cardiac arrhythmia (21, 22). Devices called electrophysiology catheters (23), which contain platinum electrodes, are used to map the electrical pathways of the heart so that the appropriate treatment – such as a pacemaker – can be prescribed.

Other catheters with platinum electrodes are used for a minimally-invasive heart treatment known as radio-frequency (RF) ablation (24–26). Arrhythmias are often caused by abnormalities in the conduction of electricity within the heart, and it is often possible

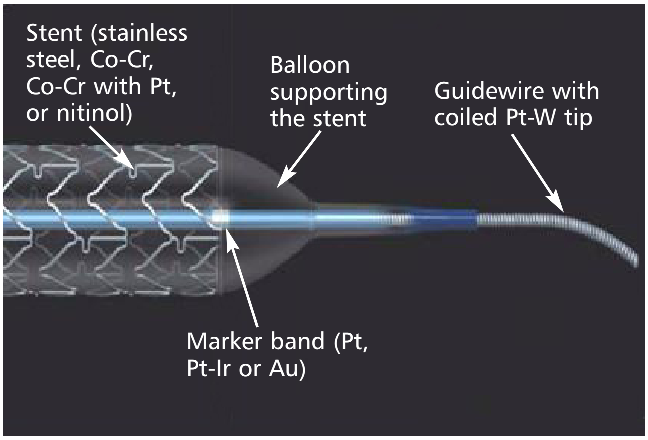

Fig. 3. A balloon-mounted stent used in percutaneous transluminal coronary angioplasty (PTCA, or balloon angioplasty) procedures (Copyright © Abbott Vascular Devices)

to cauterise part of the heart muscle in order to restore normal heart rhythm. For example, ablation is increasingly used to treat a very common heart problem called atrial fibrillation, in which the upper chamber of the heart (the atrium) quivers rapidly and erratically. Using a catheter equipped with platinum-iridium electrodes, the surgeon "ablates" or makes small burns to the heart tissue, causing scarring, which in turn blocks the superfluous electrical impulses which trigger the fibrillation.

Neuromodulation Devices

Neuromodulation devices deliver electrical impulses to nerves and even directly to the brain, treating disorders as varied as deafness, incontinence (27, 28), chronic pain (29) and Parkinson's disease (30). Many of these devices are based on an extension of heart pacemaker technology, and they are sometimes referred to as "brain pacemakers" (31). Like heart pacemakers, they have platinum-iridium electrodes and may also incorporate platinum components in the pulse generator.

There are a number of different types of neurostimulation, depending on the condition that is being treated. Spinal cord stimulation (the commonest neuromodulation therapy) is used to treat severe chronic pain, often in patients who have already had spinal surgery. Small platinum electrodes are placed in the epidural space (the outer part of the spinal canal) and connected to an implanted pulse generator. The patient can turn the stimulation off and on, and adjust its intensity.

In deep brain stimulation (DBS) (32–34), the electrodes are placed in the brain itself. As well as pain, DBS may be used to treat movement disorders such as Parkinson's disease, and it is being investigated as a potential treatment for a wide range of other illnesses, including epilepsy and depression. Epileptic patients can also be treated using a vagus nerve stimulation device (the vagus nerve is situated in the neck).

A cochlear implant (35–38) is used to restore hearing to people with moderate to profound hearing loss (many patients receive two implants, one in each ear). A typical device consists of a speech processor and coil, which are worn externally behind the ear, an implanted device just under the skin behind the ear, and a platinum electrode array which is positioned in the cochlea (the sense organ which converts sound into nerve impulses to the brain). The speech processor captures sound and converts it to digital information, which is transmitted *via* the coil to the implant. This in turn converts the digital signal into electrical impulses which are sent to the electrode array in the cochlea, where they stimulate the hearing nerve. These impulses are interpreted by the brain as sound. It is believed that around 200,000 people worldwide have received one or more cochlear implants.

At present, neuromodulation is expensive and is only available in a small number of specialist centres; even in developed countries only a small proportion of potentially eligible patients receive this treatment. However, neuromodulation can be used to help patients with common and sometimes difficult to treat conditions (such as chronic pain, epilepsy and migraine). Its use might therefore be expected to increase significantly in coming years as new indications for these therapies are established.

Other Implants

Platinum's biocompatibility makes it ideal for temporary and permanent implantation in the body, a quality which is exploited in a variety of treatments in addition to the heart implants already discussed. Irradiated iridium wire sheathed in platinum can be implanted into the body to deliver doses of radiation for cancer therapy (39–41). This treatment takes advantage of platinum's radiopacity to shield healthy tissues from the radiation, while the exposed iridium tip of the wire irradiates the tumour. Although this procedure is gradually being replaced by other forms of radio- and chemotherapy, it remains a useful weapon in the battle against cancer.

A more recent development is the use of coils made of platinum wire to treat aneurysms, balloonings in blood vessels caused by weaknesses in the vessel walls (42). If the blood pressure rises, the vessel may rupture, causing a haemorrhage. Although this can occur anywhere in the body, platinum is mainly used to treat aneurysms in the brain, where surgery is difficult and fraught with risk. Platinum is used because it is inert, easy to shape, and radiopaque.

This treatment was first introduced about 20 years ago. In the late 1980s, a doctor and inventor, Guido Guglielmi (43–45), developed a detachable platinum coil which could be used to treat brain aneurysms. Coils are delivered to the site of the aneurysm by microcatheter, then detached using an electrolytic detachment process; once in place, the coils help to coagulate the blood around the weak vessel wall,

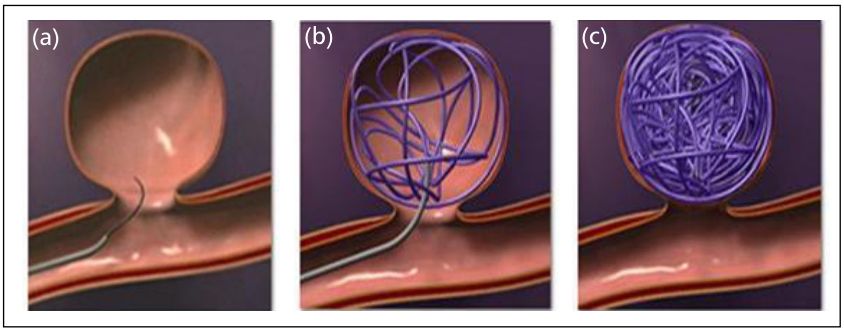

Fig. 4. Detachable platinum coils being used to treat an aneurysm: (a) a microcatheter is used to deliver the platinum coils to the aneurysm; (b) the coils are detached using an electrolytic process; (c) more coils are added to fill the aneurysm and allow blood to coagulate, forming a permanent seal

forming a permanent seal (Figure 4). The coils, numbering between one and around thirty depending on the size of the aneurysm, are left inside the patient indefinitely. The Guglielmi Detachable Coil (GDC® Coil) device was approved in Europe in 1992 and in the USA in 1995, and by 2009 this and subsequent generations of platinum coil technology were being used in an estimated 30–40% of US patients treated for brain aneurysms.

The Manufacture of Platinum Biomedical Components

There are many technologies used to produce pgm components for biomedical applications, ranging from rod, wire, ribbon and tube drawing, to sheet and foil manufacture and highly precise Swiss-Type screw machining (micromachining) (see Figure 5).

Rod and wire are manufactured in diameters ranging from 0.125" (3.175 mm) down to 0.001" (0.0254 mm). Dimensional consistency is assured by laser measurement. Rod is used as the starting material for a variety of machine components, with most of the pgm parts being used in pacemaker, defibrillator and other electrical stimulation products. Wire products are used primarily in three applications:

(a) platinum-tungsten and platinum-nickel fine wires are used on balloon catheters as guidewires for positioning the catheter in exactly the right location;
(b) other pgm wires are used as microcoils for neurovascular devices such as treatments for brain aneurysms;
(c) platinum-iridium wires are also used as feed-through wires or connector wires used to connect the pacemaker lead to the pulse generator.

Fig. 5. Micromachined parts made from precious metal alloys for biomedical device applications, with a pencil tip for scale

Ribbon is manufactured in the form of continuous strips of rolled wire in a variety of platinum alloys. Ribbon is often used in place of round wire to produce coils with minimum outside diameter, and is generally used for guidewire and microcoil applications. Ribbon is sometimes preferred over wire because wire can be harder to coil. It can also be used for markers instead of traditional cut tubing. Table II shows some typical specifications and applications for pgm rod, wire and ribbon.

Fine diameter platinum, platinum-iridium and platinum-tungsten tubing (0.125" (3.175 mm) internal diameter and below) cut to specific lengths is used for markers or electrodes on angioplasty, electrophysiology and neurological catheter devices, aneurism tip coils, feed-through wires used to connect the pacing lead to the pulse generator (also known as "the can") which houses the hybrid microelectronics and the battery, and pacemakers. Some applications of thin walled precious metal tubing are shown in Table III.

Table II

Specifications and Applications of Platinum and Platinum Alloy Rod, Wire and Ribbon Components

Applications	Types of component	Specifications
Stimulation devices	Rod for manufacture of machine components	Diameters from 0.001" (0.0254 mm) to 0.125" (3.175 mm); Cut lengths from 0.02" (0.508 mm)
Balloon catheters; stent delivery; stimulation leads	Guidewires; feed through wires; tip coils	

Table III

Specifications and Applications of Platinum, Palladium, Gold and Precious Metal Alloy Thin Walled Tube Components

Applications	Types of component	Specifications
Balloon catheters	Radiopaque marker bands	Inside diameter 0.0045" (0.1143 mm) to 0.250" (6.35 mm), (tolerance: ± 0.0005" (0.0127 mm)); Wall thickness 0.001" (0.0254 mm) to 0.005" (0.127 mm), (tolerance: ± 0.0005" (0.0127 mm)); Length 0.015" (0.381 mm) to 0.200" (5.08 mm), (tolerance: ± 0.003" (0.0762 mm))
Electrophysiology catheters; stimulation devices	Electrode rings	

Sheet and foil is mainly made from pure platinum, platinum-iridium alloys or rhodium. It can be shaped, formed and rolled to a variety of dimensions. Sheet or foil can be cut, formed and placed on a catheter for marking in a similar way to ribbon. Rhodium foil is used exclusively as a filter inside X-ray mammography equipment to enhance the viewing image. Table IV shows some examples of applications of pgm sheet and foil.

Micromachined parts are very complex and very small – some are only 0.006" (0.152 mm) in diameter and barely visible with the naked eye (Figure 5). Fabrication must be extremely precise to maintain the necessary quality and dimensional tolerances, which can be as low as ± 0.0002" (0.005 mm). Highly specialised equipment and techniques must be used, such as computer numerical controlled (CNC) Swiss Screw machines and electrical discharge machining (EDM) (Figure 6). The automated high-production Swiss Screw machines are used to fabricate the main components and EDM is used to achieve the fine details required for many platinum parts.

Specialty metal micromachined parts (0.8" (20 mm) diameter and smaller) are made from a variety of materials including pure platinum, platinum-iridium alloys and gold plus non-precious metals and

Table IV

Specifications and Applications of Platinum, Platinum Alloy and Rhodium Sheet and Foil Components

Applications	Types of component	Specifications
Stimulation devices	Electrodes; machine components; tip coils	Thickness from 0.0007" (0.018 mm); Width from 1.0" (25.4 mm) to 3.75" (95.3 mm)
X-Ray equipment	Imaging filters (rhodium foils)	

Fig. 6. The production floor at Johnson Matthey's Medical Products micromachining facility in San Diego, California, USA

alloys such as stainless steel, titanium, MP35N® cobalt-nickel-chromium-molybdenum alloy, Elgiloy® cobalt-chromium-nickel alloy, Kovar® iron-nickel-cobalt alloy, and materials such as Vespel®, Delrin® and Teflon® (see Table V for examples). These products serve device applications such as coronary stents, pacemaker and defibrillator pulse generator and lead components, heart valve splices, endoscopic catheters, blood gas analysers, kidney dialysis, and other medical device and related equipment.

Parts made from pgms are often complemented with a coating technology. Precious metal powders,

Table V

Applications and Materials for Precision Micromachined Components

Applications	Precious metals*	Other materials, metals and alloys
Stimulation	Platinum; platinum alloys; palladium; palladium alloys	Nitinol; stainless steel; MP35N®; Haynes® alloy 25 (L605); polymers
Manufacturing fixtures	Platinum; platinum alloys	Stainless steel 303/304/316; polymers
Orthopaedic	Platinum; platinum alloys	Titanium; titanium alloys; stainless steel; ceramics
Cardiac implants	Platinum; platinum alloys; karat golds	Elgiloy®; Nitinol
Hypotubes	Platinum; platinum alloys	Stainless steel; Nitinol
Precision pins, tips and rollers	Platinum; platinum alloys; silver	–
Bushings, shafts, shims and spacers	Platinum; platinum alloys	Aluminium
Precision fixtures and assembly tools	Platinum; platinum alloys; Biomed™ series palladium-rhenium alloys	Brass; copper; Kovar®

**Platinum alloys used include platinum-iridium, platinum-10% nickel and platinum-8% tungsten* titanium nitride or iridium oxide are applied to create a more porous surface structure. The creation of a porous coating reduces the electrical impedance from the lead to the battery and allows for a good electrical connection, while reducing the energy needed to run the battery. This helps the battery to last longer. Most pacing lead systems manufactured today have some form of porous surface. The end use applications for coated pgm parts are the same as described above for uncoated parts.

Anticancer Drugs

As well as its use in biomedical device components, perhaps platinum's most remarkable and unexpected quality is its ability, in certain chemical forms, to inhibit the division of living cells (46). The discovery of this property led to the development of platinum-based drugs (47), which are now used to treat a wide range of cancers.

Although cancer remains one of the most feared diseases, its treatment has advanced rapidly since the late 1960s. Many types of cancer can now be treated very effectively using surgery, radiation and drug-based (chemo-) therapies. Chemotherapy drugs work by killing cells. They are designed to target cancer cells as specifically as possible, but inevitably cause damage to healthy cells as well, causing the side effects for which chemotherapy is well known.

One of the most remarkable advances in the last few decades has been the improvement in the survival rate of patients with testicular cancer – it is estimated that 98% of men with testicular cancer will be alive 10 years after their diagnosis. The platinum anticancer drug cisplatin (47) has played a vital role in making testicular cancer one of the most survivable cancers. This drug, along with its successor drug, carboplatin (48), is also widely used in the treatment of other common tumours, including ovarian, breast and lung cancer.

Summary

For over forty years, platinum and its alloys have been used in a wide range of medical treatments, including devices such as coronary and peripheral catheters, heart pacemakers and defibrillators. Newer technologies such as neuromodulation devices and stents also rely on the biocompatibility, durability, conductivity and radiopacity of platinum to make key components in a variety of forms. Platinum is used in pharmaceutical compounds that extend the lives of cancer patients. Medical device manufacturers and pharmaceutical companies continue to invest in new technologies to satisfy the need for advanced medical treatments in both the developed world and, increasingly, the developing world. Platinum, the other pgms and their alloys will inevitably play a vital part in these developments.

Acknowledgements

The assistance of Richard Seymour and Neil Edwards, Technology Forecasting and Information, Johnson Matthey Technology Centre, Sonning Common, UK, in the preparation of this manuscript is gratefully acknowledged.

References

1 UNEP/GRID-Arendal, 'Trends in population, developed and developing countries, 1750–2050 (estimates and projections)', UNEP/GRID-Arendal Maps and Graphics Library, 2009: http://maps.grida.no/go/graphic/trends-in-population-developed-and-developing-countries-1750-2050-estimates-and-projections (Accessed on 9th February 2011)

2 J. Butler, "Platinum 2010 Interim Review", Johnson Matthey, Royston, UK, 2010, pp. 21–22

3 W. F. Agnew, T. G. H. Yuen, D. B. McCreery and L. A. Bullara, *Exp. Neurol*., 1986, **92**, (1), 162

4 S. B. Brummer and M. J. Turner, *IEEE Trans. Biomed. Eng.,* 1977, **BME-24**, (5), 440

5 *Acta Med. Scand*., 1969, **186**, (S502), 10–13

6 C. Walton, S. Gergely and A. P. Economides, *Pacing Clin. Electrophysiol*., 1987, **10**, (1), 87

7 R. A. Winkle, S. M. Bach, Jr., R. H. Mead, V. A. Gaudiani, E. B. Stinson, E. S. Fain and P. Schmidt, *J. Am. Coll. Cardiol*., 1988, **11**, (2), 365

8 M. M. Morris, B. H. KenKnight, J. A. Warren and D. J. Lang, *Am. J. Cardiol*., 1999, **83**, (5), Suppl. 2, 48

9 D. S. Cannom, *Am. J. Cardiol*., 2000, **86**, (9), Suppl. 1, K58

10 A. M. Rudolph, *Am. J. Surgery*, 1964, **107**, (3), 463

11 J. E. Lock, J. F. Keane and K. E. Fellows, *J. Am. Coll. Cardiol*., 1986, **7**, (6), 1420

12 J. J. Rome and J. F. Keane, *Prog. Pediatric Cardiol*., 1992, **1**, (2), 1

13 J. D. Moore and T. P. Doyle, *Prog. Pediatric Cardiol*., 2003, **17**, (1), 61

14 C. A. McMahan, S. S. Gidding and H. C. McGill, Jr., *J. Clin. Lipidol*., 2008, **2**, (3), 118

15 A. S. Jacob, T. S. Goldbaum, A. D. Richard and J. Lindsay, Jr., *Catheterization Cardiovascular Diagnos*., 1986, **12**, (1), 64

16 N. H. Singh and P. A. Schneider, 'Balloon Angioplasty Catheters', in "Endovascular Surgery", 4th Edn., eds. W. S. More and S. S. Ahn, Elsevier Saunders, Philadelphia, PA, USA, 2011, Chapter 8, pp. 71–80

17 US FDA, Recently-Approved Devices, CYPHER^{TM} Sirolimus-eluting Coronary Stent – P020026, Approval date: 24th April, 2003: http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/Recently-ApprovedDevices/ucm082499.htm (Accessed on 10th February 2011)

18 'Platinum-Stainless Steel Alloy and Radiopaque Stents', C. H. Craig, H. R. Radisch, Jr., T. A. Trozera D. M. Knapp, T. S. Girton and J. S. Stinson, SciMed Life Systems, Inc, *World Appl*. 2002/078,764

19 B. J. O'Brien, J. S. Stinson, S. R. Larsen, M. J. Eppihimer and W. M. Carroll, *Biomaterials*, 2010, **31**, (14), 3755

20 I. B. A. Menown, R. Noad, E. J. Garcia and I. Meredith, *Adv. Ther*., 2010, **27**, (3), 129

21 G. V. Irons, Jr., W. M. Ginn, Jr., and E. S. Orgain, *Am. J. Cardiol*., 1968, **21**, (6), 894

22 W. H. Barry, E. L. Alderman, P. O. Daily and D. C. Harrison, *Am. Heart J*., 1972, **84**, (2), 235

23 J. G. Panos, J. L. Cincunegui and E. K. Chong, *Heart Lung Circ*., 2007, **16**, Suppl. 2, S117

24 J. F. Swartz, C. M. Tracy and R. D. Fletcher, *Circulation*, 1993, **87**, (2), 487

25 H. Calkins, *Med. Clin. North Am*., 2001, **85**, (2), 473

26 'Ablation Catheter Assembly Having a Virtual Electrode Comprising Portholes', G. P. Vanney, J. D. Dando and J. L. Dudney, St. Jude Medical, Daig Division, Inc, *US Patent* 6,984,232; 2006

27 R. D. Mayer and F. M. Howard, *Neurotherapeutics*, 2008, **5**, (1), 107

28 P. M. Braun, C. Seif, C. van der Horst and K.-P. Jünemann, *EAU Update Series*, 2004, **2**, (4), 187

29 P. L. Gildenberg, *Pain Med*., 2006, **7**, Suppl. s1, S7

30 W. Hamel, U. Fietzek, A. Morsnowski, B. Schrader, J. Herzog, D. Weinert, G. Pfister, D. Müller, J. Volkmann, G. Deuschl and H. M. Mehdorn, *J. Neurol. Neurosurg. Psychiatry*, 2003, **74**, (8), 1036

31 M. L. Kringelbach and T. Z. Aziz, *Scientific American Mind*, December 2008/January 2009

32 D. Tarsy, *Epilepsy Behav*., 2001, **2**, (3), Suppl. 0, S45

33 J. Gimsa, B. Habel, U. Schreiber, U. van Rienen, U. Strauss and U. Gimsa, *J. Neurosci. Meth*., 2005, **142**, (2), 251

34 P. Limousin and I. Martinez-Torres, *Neurotherapeutics*, 2008, **5**, (2), 309

35 G. Clark, "Cochlear Implants", Springer-Verlag, New York, USA, 2003

36 J. T. Roland, Jr., *Oper. Tech. Otolaryngol. Head Neck Surg*., 2005, **16**, (2), 86

37 E. G. Eter and T. J. Balkany, *Oper. Tech. Otolaryngol. Head Neck Surg*., 2009, **20**, (3), 202

38 M. Cosetti and J. T. Roland, Jr., *Oper. Tech. Otolaryngol. Head Neck Surg*., 2010, **21**, (4), 223

39 J. G. Stella, S. Kramer, C. M. Mansfield and N. Suntharalingam, *Cancer*, 1973, **32**, (3), 665

40 N. J. Daly, B. De Lafontan and P. F. Combes, *Int. J. Radiation Oncol. Biol. Phys*., 1984, **10**, (4), 455

41 J. L. Habrand, A. Gerbaulet, M. H. Pejovic, G. Contesso, S. Durand, C. Haie, J. Genin, G. Schwaab, F. Flamant, M. Albano, D. Sarrazin, M. Spielmann and D. Chassagne, *Int. J. Radiat. Oncol. Biol. Phys*., 1991, **20**, (3), 405

42 R. T. Higashida, V. V. Halbach, C. F. Dowd, S. L. Barnwell and G. B. Hieshima, *Surg. Neurol*., 1991, **35**, (1), 64

43 G. Guglielmi, F. Viñuela, I. Sepetka and V. Macellari, *J. Neurosurg*., 1991, **75**, (1), 1

44 G. Guglielmi, F. Viñuela, J. Dion and G. Duckwiler, *J. Neurosurg*., 1991, **75**, (1), 8

45 G. Guglielmi, *Oper. Tech. Neurosurg*., 2000, **3**, (3), 191

46 B. Rosenberg, L. Van Camp and T. Krigas, *Nature*, 1965, **205**, (4972), 698

47 E. Wiltshaw, *Platinum Metals Rev*., 1979, **23**, (3), 90

48 C. F. J. Barnard, *Platinum Metals Rev*., 1989, **33**, (4), 162

Further Reading

"Biomaterials Science: An Introduction to Materials in Medicine", 2nd Edn., eds. B. Ratner, A. Hoffman, F. Schoen and J. Lemons, Elsevier Academic Press, San Diego, CA, USA, 2004

"Materials and Coatings for Medical Devices: Cardiovascular", ASM International, Materials Park, Ohio, USA, 2009

Granta: Materials for Medical Devices Database, Cardiovascular Materials and Orthopaedic Materials: http://www.grantadesign.com/products/data/MMD.htm (Accessed on 10th February 2011)

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