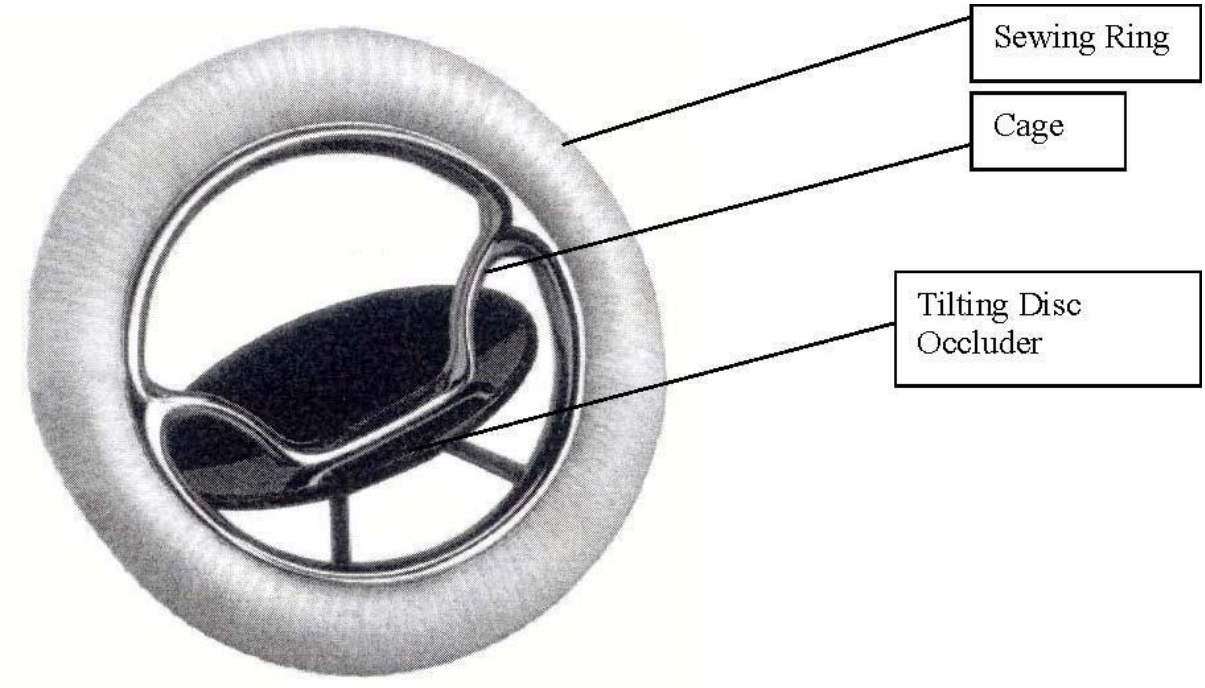
Case Study 1: Mechanical heart valve

Damaged or diseased heart valves are typically replaced by mechanical or bioprosthetic types of valves. Mechanical valves are by far the most common type used. A typical mechanical valve has a sewing ring to attach the valve to the heart, a cage or other support to house the occluder, and some form of occluder (to allow one way flow).

The picture below shows a Bjork-Shiley 60 Convexo-Concave Mitral valve. The strut is constructed from a metal alloy composed of cobalt, nickel, chromium and tungsten (Co-Ni-Cr-W). The occluder is a disc of pyrolytic carbon and the sewing ring is poly(tetrafluoroethylene) (PTFE: Teflon). These valves went onto the market in the late 1970's and were withdrawn from the market in 1986 due to strut fracture.

"Unfortunately, in an attempt to improve on the original valve, modifications were made to the valve to increase the opening angle of the disk and to reshape the disk to allow better flow. These models were called the 60-degree and 70-degree Convexo-concave models. Some of these Convexo-Concave models later developed cracks in the C-shaped, metal outflow struts holding the disk in place. Eventually, the struts would fail and the disk would escape from the valve. The patient would then become gravely ill and could die from leakage of blood back through the valve. The manufacturer of the valve was originally Shiley Laboratories. Shiley was purchased by Pfizer, a large pharmaceutical company, however, and now Pfizer has unwittingly taken on a potentially enormous liability risk. A law suit has already been settled calling for the expenditure of funds by Pfizer to develop methods to detect and prevent Bjork-Shiley CC strut fractures."
From *http://www.csmc.edu/pdf/Heart_Valves.pdf#search=%22heart%20valve%20market%22*



The following includes an excerpt from a NY Times article in 1985 and a letter from the US Food and Drug Administration (FDA) in 1992.

By IRVIN MOLOTSKY, SPECIAL TO THE NEW YORK TIMES
June 27, 1985

Inspectors for the Food and Drug Administration have found ''serious problems'' in the manufacture of artificial heart valves by Shiley Inc. that was linked last year to the deaths of at least 64 people. The Health Research Group, a consumer organization, obtained copies of F.D.A. findings under the Freedom of Information Act and asked the agency today to order the withdrawal of the heart valve from the market. A spokesman for the agency, David Duarte, said today that there was ''insufficient evidence of continuing violations'' to warrant removing the valves from the market. ''The F.D.A. continues to be concerned about the possibility of violative manufacturing practices in producing these valves and will take action if it is needed,'' Mr. Duarte said.

News 03/12/1992
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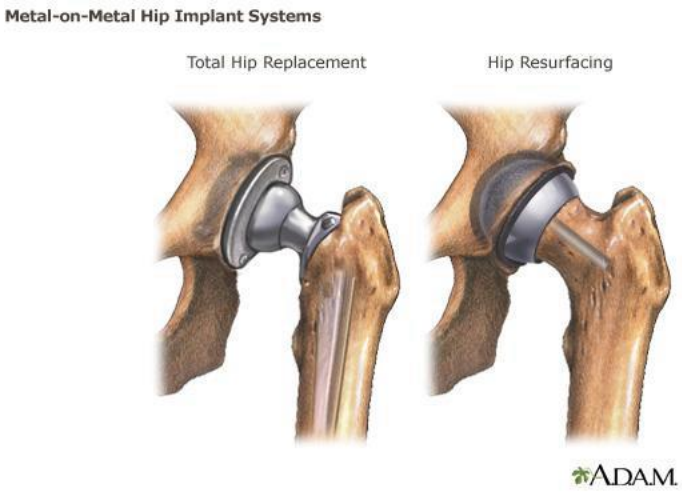
The Food and Drug Administration has asked Shiley Inc. of Irvine, Calif., the maker of Bjork-Shiley heart valves, to notify patients and physicians that risk of fracture for some sizes of these valves may be higher than previously thought.
The fracture rate for the large sizes of the 60-degree Shiley (C-C) valve is now thought to be as much as five times higher than previously estimated. Valve fracture is often fatal.
FDA believes that the risk of fracture of these large valves, over an eight-year period, when implanted to substitute for the heart's mitral valve, may be high enough for doctors and patients to consider replacing currently intact valves in some individuals.
"When a critical device such as a heart valve is found to have a problem that could result in death or serious injury, FDA has an obligation to see that doctors and patients are notified so that they can consider the new information in deciding on a course of action," said FDA Commissioner David A. Kessler, M.D.
About 23,000 people in the United States and Canada have 60-degree Shiley (C-C) valves. These valves were removed from the market in 1986. FDA has received about 350 reports of 60-degree valve fractures among the roughly 82,000 C-C valves implanted worldwide.
FDA requested Shiley to notify patients with these valves of the fracture problems, in a program begun in 1990 after the agency became aware of some risk of fracture. However, replacement of intact valves was not recommended at that time because the surgical risk was thought to far outweigh the risk of fracture. The risk of fracture depends on the age of the patient, valve size and valve position. The rate may be as high as 0.8 percent per year for people under 50.
http://www.fda.gov/bbs/topics/NEWS/NEW00269.html

Questions for discussion:

1. *Consider this device and the materials used and come up with some suggestions to explain why the metallic strut cage component might have failed.*
2. *What might be some of the ethical considerations of this case?*
3. *What might have been done differently to address any ethical issues?*

Case study 2: Metal-on-metal hip implants

Hip replacements to restore function to joints debilitated by arthritis have become increasingly common as the population becomes older and heavier and as the technology improves. These can be total hip replacements, in which case the acetabular cup (in the pelvis) and the femoral head are replaced, or hip resurfacing in which case the cup is replaced but the head is merely resurfaced with a metal cap. See the figure below (FDA).



Given that each hip bears one-half the body weight and that the two surfaces are continuously rubbing against each other, there will be wear. And if there is wear, there will be wear products (debris) and these may be toxic. The debris can invade the tissue surrounding the implant and it may get into the bloodstream cause problems elsewhere.

The materials from which the cup and head are made are obviously important. Material pairs available in the US are (FDA):

- Metal-on-Polyethylene: The ball is made of metal and the socket is made of plastic (polyethylene) or has a plastic lining.
- Ceramic-on-Polyethylene: The ball is made of ceramic and the socket is made of plastic (polyethylene) or has a plastic lining.
- Metal-on-Metal (MoM): The ball and socket are both made of metal.
- Ceramic-on-Ceramic: The ball is made of ceramic and the socket has a ceramic lining.

There is increasing evidence that some metal-on-metal devices have a higher failure rate than other devices and may lead to bad reactions.

One MoM device (DePuy) was withdrawn from the market in 2010.

In June 2012, the Australian Therapeutic Goods Administration (TGA) advised that a metal liner of an acetabular system was being recalled (TGA).

The UK Medicines and Healthcare Regulatory Authority (MHRA) recommended monitoring recipients of large-diameter (36 mm or more) metal-on-metal hips (MHRA).

Symptoms are thought to be a consequence of metal ions derived from wear of the cobalt-chromium alloy used in these devices. The ions seep into local tissue and cause damage. Elevated levels of cobalt and chromium ions have been found in blood and in urine (Cohen 2012). The advice from the FDA to surgeons (see below) recommends against using MoM devices in patients with impaired renal function. This is because the kidneys are an important excretion route for cobalt and chromium. If renal function is impaired, metal levels in blood will rise, possibly causing damage elsewhere.

At the same time, it is worth noting that most metal-on-metal hip implants do not fail and that cobalt-chrome alloys have been used in other implants, such as artificial knees and hardware for bone fracture repair, without incident (Cohen 2012). The UK MHRA advice (above) to monitor patients with large-diameter heads (only) implies that small-diameter heads are safe(r).
Why were implants with large diameter femoral heads manufactured in the first place? One argument is that the large diameter head allows the joint greater range of movement and reduces the likelihood of dislocation (Lancet) A slightly more cynical view is that introducing a new model of hip with a modified design may grab a larger share of the market (Cohen 2012).

Questions for discussion

1. *Your grandmother needs a hip replacement. Her surgeon recommends a metal-on-metal device. She asks you, as a biomedical engineering student, what she should do? You check the TGA, MHRA and FDA web sites and find that there are no adverse findings against this particular device. What is your advice?*

2. *Who do you think has most influence on the choice of the type of total hip replacement? (Patient, GP, surgeon ...)*

3. *Who should approve devices such as these for use and how strict should they be?*

4. *Who should monitor performance of devices that are implanted and who should keep records? Should it be mandatory?*

5. *Which is more important, fostering innovation or ensuring safety?*

Additional Reading for Metal on Metal Hip Replacements

Q and A

The following are selected excerpts from Metal-on-metal hip replacement Q & A on the Arthritis Research UK web site (Skinner).

What are the concerns about metal-on-metal hips?

When they work well, metal-on-metal hip resurfacing and total hip replacements give years of trouble-free use with very low levels of wear. However, some metal-on-metal implants can fail, increasing the amount of wear and producing small amounts of debris. This debris is particles (ions) of cobalt and chromium that make up the implant. This debris can trigger a response in your body, which can cause erosion of bone and loosening of the implants. The National Joint Registry states that 3% of implants loosen after 9 years. However, implants fail for other reasons too, so the overall failure rate is about 1% per year.

In most people the metal ions are absorbed into the bloodstream, then filtered by the kidneys and passed out in the urine. By measuring the concentration of these ions in the blood we can discover how the hip is wearing. These levels are very low and are measured in parts per billion (ppb). However, the concentration of metal ions in the fluid around the hip joint can be much higher. It's these high local concentrations of metal ions that cause damage to the tissues, either by local toxicity or by your body's response as it tries to get rid of them.

While all hip debris causes some reaction in the nearby tissues, often with no major problems, in some people it can cause extensive tissue damage and in some rare cases death of tissue cells, including those of the muscles, tendons, nerves and bones.

Are metal-on-metal implants still being used?

Yes. It's the only way to perform a resurfacing operation where the thigh bone is simply capped. There's some clinical evidence that in younger men (under 55 years) or men who are very active, some metal-on-metal hip resurfacing replacements give equal or slightly better results than total hip replacements. However, overall the use of metal-on-metal hips has reduced very sharply in the last two years.

What are the advantages of metal-on-metal hip implants?

It allows hip resurfacing and can allow much larger diameter femoral heads to be used in total hip replacement. Larger heads can also allow a greater range of movement of the hip and give greater stability, making dislocation less likely.

When they're designed and made well, working well, positioned well and lubricated well by joint fluid, metal-on-metal implants show some of the lowest wear rates of any materials used in hip replacement. This is what made them so popular. However, if any of these factors aren't right, then the wear can be extremely high and this leads to the problems caused by metal debris.

How do surgeons decide what type and material of hip replacement to use?

Most surgeons find two types of hip replacement that they're happy with. This is usually one for young and active patients and one for the much larger group of older patients (those more likely to need the operation). There are many good hip replacement options that have good follow up and excellent results published in medical literature.

FDA advice to surgeons before surgery (FDA)

General Considerations for Orthopaedic Surgeons BEFORE Metal-on-Metal Hip Implantation Surgery

1. Because the success of metal-on-metal (MoM) hip systems is highly dependent on proper implantation technique, you should use MoM hip only if you are:
   - trained in the technical aspects of each individual implant and its unique surgical instrumentation, and
   - familiar with the manufacturer's specific recommendations for implantation and surgical technique.
2. Do not implant MoM hip systems in:
   - Patients with known moderate to severe renal insufficiency
   - Patients with known metal sensitivity (e.g. cobalt, chromium, nickel)
   - Patients with suppressed immune systems
   - Patients currently receiving high doses of corticosteroids
   - Females of childbearing age
3. Be aware that previously implanted hardware at or near the hip joint may impact the generation of wear debris or the amount of metal exposure to the patient who receives a MoM implant.
4. When obtaining informed consent for MoM hip procedures, ensure that the patient understands:
   - The alternative treatment therapies along with their respective risks and benefits.
   - The potential risks associated with MoM systems which include but are not limited to:
     - Elevated metal ion levels in the joint and blood.
     - Development of local inflammatory reactions and lesions including soft tissue masses and tissue necrosis.
     - Development of potential systemic events related to elevated metal ion levels.
   - The potential for and risks of revision surgery.
5. There is currently no evidence to support the use of pre-operative skin patch testing to predict implant sensitivity prior to surgery.

References

Cohen, D. 2012, "How safe are metal-on-metal hip implants?", BMJ, vol. 344.

Food and Drug Administration. a, , *Metal-on-Metal Hip Implants > Hip Implant Systems* [Homepage of FDA], [Online]. Available: http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/MetalonMetalHipImplants/ucm241594.htm [2012, 9/10/2012]

Food and Drug Administration. b, 2012-last update*, Metal-on-Metal Hip Implants > Information for Orthopaedic Surgeons about Metal-on-Metal Hip Implant Surgery* . Available: http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/ImplantsandProsthetics/MetalonMetalHipImplants/ucm241667.htm [2012, 9/10/2012]

MHRA *, Metal-on-metal hip implants : MHRA* [Homepage of MHRA], [Online]. Available: http://www.mhra.gov.uk/Safetyinformation/Generalsafetyinformationandadvice/Product-

specificinformationandadvice/Product-specificinformationandadvice–M–T/Metal-on-metalhipimplants/index.htm [2012, 9/10/2012]
Skinner, J. , *Metal-on-metal hip replacement Q and A | Arthritis Research UK* [Homepage of Arthritis Research UK], [Online]. Available: http://www.arthritisresearchuk.org/arthritis-information/surgery/mom-hip-q-and-a.aspx [2012, 9/10/2012]

Therapeutic Goods Administration , *Metal liner components of R3 acetabular system (used in hip replacements)* [Homepage of Therapeutic Goods Administration], [Online]. Available: http://www.tga.gov.au/safety/alerts-device-r3-acetabular-metal-liner-120613.htm [2012, 9/10/2012]

Williams, D. 1987, "Advanced applications for materials implanted within the human body", *Materials science and technology,* vol. 3, no. 10, pp. 797-806.