Medical Devices: How reliable is the FDA's stamp of approval?

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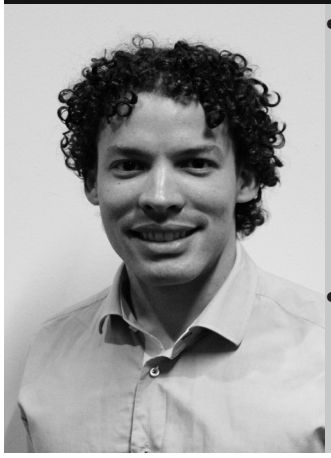

- The United States accounts for half the global market for medical devices allowing the U.S. Food and Drug Administration's (FDA) approval to influence medical devices developed and brought to the market globally.
- The FDA's 510(k) approval system allows for devices that are deemed similar to already approved products to bypass pre-approval trials.
- Recent attention has been drawn to this approval process as more and more devices approved through the 510(k) system show many unexpected failures, far outweighing the benefits these new devices were promised to have.

Bioengineered Intervention – A growing field

Mrs. AW, a 67 year old patient is slowly losing her battle with age related macular degeneration. She has also fought with arthritis in her hip for the past few years, placing her in constant pain. In a recent consultation with her ophthalmologist, she is told about a new device which can be implanted into her eye to aid her vision. During a separate consultation with an orthopaedic surgeon, she is advised to undergo a hip replacement. The surgeon suggests using metallic components which would allow her hip to function without pain.

There are over 500,000 medical devices on the market ranging from simple devices like bedpans, to more complex devices, such as pacemakers[1]. The global market for medical devices is worth approximately US$200 billion, with about half of this spending coming from the United States alone[2]. This allows them to have significant influence over medical device development and in turn those devices available globally. This article will look at the two devices recommended to Mrs.AW which exemplify both the strengths, limitations and safety concerns surrounding bioengineering. It will also look at how medical device approval by the United States Food and Drug Administration (FDA), which governs the safety of medical devices, can affect patients.

The Ophthalmologist's Recommendation – A feat of bioengineering

Age related macular degeneration (AMD) leads to irreversible blindness and affects over 8 million people in the United States[3]. AMD is of major concern due to projected increases in the advanced stages of the disease as the population ages[4-6]. Individuals with end stage AMD experience losses in their central visual field which have been shown to profoundly reduce a patient's ability to carry out physical tasks[5].

The Implantable Miniature Telescope (Fig. 1) has been designed for patients with advanced forms of AMD. Before the device's approval in 2010, the only devices to aid such patients were magnifying glasses or external telescopes, which often resulted in low patient satisfaction due to their bulkiness and limitations on the patient's field of vision and normal eye scanning. The Miniature Telescope however is designed to be implanted into the posterior chamber of the eye, facilitating movement of the device with normal eye movements[7]. Prior to approval, the FDA required this device to undergo clinical trials. Six months into clinical trials, the device was found to be well tolerated with reports of about 90% of patients having significant gains in visual acuity[7]. The device increased the ability to carry out tasks of daily living and showed the potential to profoundly increase quality of life in patients with AMD[8].

The Implantable Miniature Telescope is an inspiring example of what the partnership between engineering and medicine is able to achieve, providing a means to overcome the human body's inability to respond to various pathological challenges. Other examples of this dynamic collaboration include drug-eluting stents which have successfully revolutionised the treatment of coronary artery disease[9] and cochlear implants, capable of returning the ability to interpret speech in the deaf[10]. Closer examination of such developments however has demonstrated that interventions which might seem sound on paper or even in initial implementation, don't always go as planned.

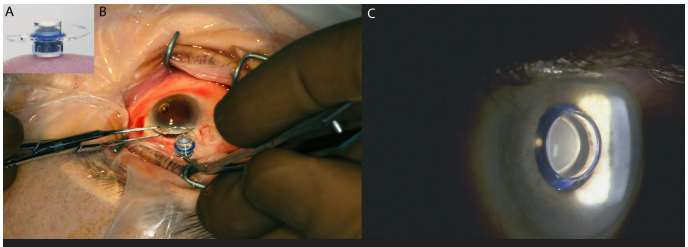

Fig. 1. The Implantable Miniature Telescope shown on the tip of a finger (A), being placed operatively into the posterior chamber of the eye (B) and in place within the eye of a patient (C). Fig. 1A,1C adapted from 9. Fig. 1B compliments James Gilman, Ophthalmic Photographer, Moran Eye Centre, The University of Utah

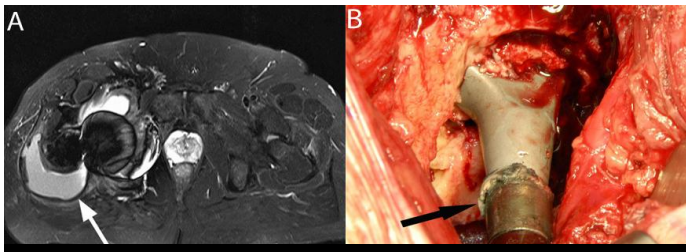

Fig. 2. Magnetic resonance image showing the presence of a large joint effusion (arrow), an adverse effect occurring with the placement of a metal-on-metal hip prosthesis (A). Intra-operative photo at joint revision showing metallic debris (arrow) around the base of a metal-on-metal hip prosthesis. Fig.2A,2B Adapted from 18

The Orthopedic Surgeon's Recommendation – A device with too hasty an approval?

Total hip replacements are one of the most commonly carried out surgical procedures in patients over the age of 60. This surgery has the ability to reduce a patients pain and dependence while increasing their ability to mobilise independently[11].

Interest in metal-on-metal devices for hip arthroplasty has peaked recently due to the advantages these components provide, such as their increased stability and decreased component wear[12,13]. The use of metal-on-metal hips has come under increased scrutiny in the past few years however due to concerns regarding the efficacy and safety of these devices. Though some designs have shown greater success than others, overall revision rates, where surgery is required to replace a prosthesis, have been reported to be consistently higher in metal-on-metal devices than those using non-metal-on-metal devices. Some reports have even shown revision rates to be as high as double that of those seen in other devices using non-metal-on-metal implants[14-16].

Not only do metal-on-metal prosthesis designs carry the same modes of failure that challenge the use of all load bearing artificial joints, they present their own unique challenges[12,17-20]. Additional modes of failure include: femoral neck fracture, local tissue reactions and early mechanical failure[17,18] (Fig. 2). It remains to be proven whether the advantages of using metal-on-metal bearings outweigh the risks associated with their use[13].

Why is it though that only now the risk to benefit ratio of using metal-on-metal implants is being considered? Did problems arise in pre-approval trials? The answer is that no trials were required for the approval of these devices by the FDA. So how does the FDA attempt to maintain the safety of such devices without actually evaluating how they performed in clinical trials? To understand this, we must take a look at their approval process.

Medical Device Approval – The role of the FDA

Firstly, it cannot be assumed that a device which has been "FDA-approved" has ever been used in or on a human or has any clinical research associated with it[21]. New devices also generally have much less evidence to support their use than new drugs[22].

Currently, the FDA places medical devices into one of three classes: Class I, II and III. Class I devices are associated with the lowest risks and include simple devices like bandages. These do not require clinical trials. Class III devices pose the highest risks to patients and include implantable heart valves and implantable cerebral stimulators[23]. All Class III devices require pre-market approval involving clinical trials. Approval is similar to that carried out on new drugs and may involve animal studies, randomised trials or basic research. Class II devices however, may or may not require pre-market approval depending on whether the device can be shown to be similar to an already approved device known as a "predicate". Manufacturers of such devices submit a 510(k) application and if found that significant equivalence exists, approval can be obtained without the use of trials[1,2]. In these instances, the FDA generally does not require safety data for the device and it is assumed to be as safe and effective as its predicate[22]. Interestingly before 1976 and the FDA's Medical Device Amendments, devices were not assessed for safety and efficacy at all. Devices approved before 1976 however, can be used as predicates[24].

The metal-on-metal hip devices discussed were approved by the 510(k) process and hence did not require clinical trials in order to receive FDA approval. In an analysis of high-risk recalls, those associated with life-threatening risks or posing serious hazards, it was shown that 71% of these recalls occurred in devices approved through the 510(k) process. The large proportion of high-risk recalls in this group of supposedly low to moderate risk devices is alarming[25]. Furthermore, even recalls which are not potentially fatal often require surgical removal resulting in unnecessary costs, not to mention the risks to the patient associated with further surgery[26].

Much attention has been drawn to this category of FDA-approval because of adverse effects arising in such devices. Such concerns have led the FDA to call for the In-

stitute of Medicine to review the 510(k) approval system. The Institute of Medicine has since advised that this form of approval be abolished. They state that 510(k) approval fosters the production of new devices at a higher cost which may offer only marginal improvements on existing devices. These benefits may also be outweighed by the potential for new risks associated with alterations in design of such devices. It has been suggested that a model-based approach be implemented for testing where randomised trials are not feasible. This would allow for insight into durability and efficacy and even provide information on short and long term effects on health that may not be provided in clinical trials[27].

Abolish the 510(k) program? – Choosing between the cost of production and the cost to patient's health

From an economic standpoint, a medical device requiring pre-market approval could cost upwards of US$12 million for a 24-month trial. If preclinical animal testing and larger trials are required, costs can rocket upwards of US$100 million[2].

The requirement of clinical trials for all Class II devices by abolishing the 510(k) approval system would drive the costs of producing these devices up which could stifle the production of many new and promising devices. A recent article in the New England Journal of Medicine however argues that it is the 510(k) system itself that suppresses innovation. Though it does allow for faster device approval, the 510(k) system encourages the production of "copy-cat" devices which are similar to existing predicates and have only incremental benefits if any over current devices[27]. Abolishing the 510(k) approval system is unlikely to affect the production of completely novel devices such as the Implantable Miniature Telescope discussed earlier. Such innovative devices will not have a predicate and could not be approved by the 510(k) process anyway.

A Brighter Future?

In the United States changes in the FDA's approval of medical devices are a likely scenario in the near future. This would result in a larger proportion of devices requiring clinical testing before approval, consequently increasing the costs required to bring devices to market. Unfortunately, this comes at a time when global recessions are pushing governments to cut medical costs. Even with overheads for production becoming more costly, producers of medical devices are being pressured to create more affordable devices if their uptake into the health care system is to occur. Will investors and inventors be more meticulous in the devices they produce? Will this lead to lower numbers of devices, but ones of higher medical impact? Or, will investment in medical devices slowly fade as production costs rise?

Place yourself in Mrs. AW's shoes for a moment. Are you happy to undergo your scheduled hip replacement, knowing the high failure rate of metal-on-metal devices? Would you be at ease receiving any device approved through the 510(k) for that matter? Should we as patients remain content with an approval system rooted in predicates or press for one of innovation and safety? We can only hope that the FDA considers the recommendations by the Institute of Medicine and puts forward a revised plan to cover the identified safety concerns and furthermore, act to encourage progress in the medical field.

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