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Medical Certification Strategies in Response to Technologically Advanced Prosthetic Devices

Eduard M. Ricaurte, M.D., M.S., FAsMA[1]
Nevine Mahmoud, M.D., M.S., M.S.[2]

[1]Venesco LLC, Chantilly, VA 20151
[2] Adena Regional Medical Center, Chillicothe, OH 45601

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16. Abstract

INTRODUCTION: Current medical technology provides an effective solution for applicants with either physical or mental conditions to obtain a Federal Administration Administration's medical certificate if the requirements of operational functionality in their flight duties are met. It is expected that aerospace medical professionals become familiar with currently available and projected advanced medical technologies and develop "new" methods of assessing their potential impact on the aeromedical safety and performance of both aviation and space crews and passengers. The purpose of this manuscript is to discuss few advanced technologies to illustrate some of the challenges associated with the use of new technologies and devices in a high stress environment. In addition, it will propose recommendations pertaining to the evaluation of advanced neuroprosthetics and aeromedical certification of amputee pilots. **DISCUSSION:** The implications of currently available advanced medical technologies on aerospace safety still remain unknown. The final decision to issue a medical certificate to any user of an advanced medical device will need to be made on a case-by-case basis. **RECOMMENDATIONS:** To mitigate the risks posed by the predicted increase in the number of devices and advanced technologies in the aerospace environment, it is highly recommended that AMCD start assigning specific pathological codes to pilots using advanced neuro-prosthetics, including microprocessor prosthetic legs and robotic limbs, as well as cochlear implants, and that the manufacturer, model, and software/hardware revision of the device(s) be documented and tracked along with the body region involved. Additional research will be needed to acquire technical data for developing the rules and regulations regarding the compatibility between the cockpit's environment, including avionics and control systems, with commercially available advanced medical prosthesis to meet the requirements of the MIL-STD-464 standard. Finally, it is important to determine the current population of pilots using advanced medical technology or affected by medical conditions that may potentially require the use of advanced medical technology in the future. Individualized evaluations, focused on performance in both standard and unusual operational settings, including a rapid egress from the cockpit to evaluate advanced prosthesis impact on aviation safety is recommended.

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"The goal for many amputees is no longer to reach a 'natural' level of ability but to exceed it, using whatever cutting-edge technology is available. As this new generation sees it, our tools are evolving faster than the human body, so why obey the limits of mere nature?"

Daniel H. Wilson

Contents

MEDICAL CERTIFICATION STRATEGIES IN RESPONSE TO TECHNOLOGICALLY ADVANCED PROSTHETIC DEVICES

INTRODUCTION

Advanced medical technology, including devices and diagnostics, have allowed people to enjoy longer and healthier lives with improved quality of life. Progress in medical technology is also responsible for increasing the life expectancy in the U.S. by five years, over the last three decades. At the same time, the incidence of heart-related fatalities, stroke, and breast cancer have all decreased by more than 50%. In addition, data analysis from the period 1980 through 2010 showed that advanced medical technology contributed to the reduction in the duration of hospital stays by 58%. This industry is responsible for about 2 million high-quality U.S. jobs and about $150 billion in annual sales. It has been projected that increased incentives for medical technology investments will generate $1.4 trillion over 25 years in U.S. economic gains (2).

An industry overview report on the global neuroprosthetics market analysis and industry forecast from 2013-2020 predicted that the market is expected to reach $14 billion by 2020, registering a Compounded Annual Growth Rate (CAGR) of 15.8% from 2014 to 2020. Traumatic injury, high prevalence of chronic diseases, and growing healthcare awareness has boosted the market growth for neuroprosthetic devices and implants (6). The report also included the application of neuroprosthetic devices and implants in the treatment of diseases such as Parkinson's disease, Alzheimer's disease, visual impairment and blindness, severe depression, epilepsy, cardiovascular disorders, auditory disorders, and kidney disorders. Although the report included conventional drug therapy and devices, external wearable devices, neurostimulators (brain-machine interfaces), and embedded systems, external stimulation technologies such as transmagnetic stimulation (TMS) were excluded. From a market perspective, visual neuroprosthetics and retinal implants are the fastest growing market segment, followed by motor neuroprosthetic applications for the treatment of chronic neurological conditions such as Parkinson's disease, Overactive Bladder Syndrome, and epilepsy (111). Motor prosthetics holds the largest share in the neuroprosthetics devices market due to the increasing incidence of chronic neurological conditions. Currently, the high cost of these products implies that consumers must have a high income to be able to afford it and therefore the biggest markets are located in developed countries. However, it is expected that patients living in countries with emerging economies, rising incomes, and better healthcare benefits will soon benefit from this technology (111).

Achieving a balance between reducing the overall cost of medical care and increasing patients' safety and survival rates is the main goal of today's advanced technologies (80). A couple of examples of emerging technologies under this category with promising future clinical applications are

1. **The "electronic aspirin**," (see Figure 1): This technology under clinical investigation at Autonomic Technologies, Inc. (ATI, Redwood City, CA), is designed for people who suffer from migraines, cluster headaches, and severe, chronic forms of headache related to the sphenopalatine ganglion (SPG), a facial nerve bundle (80). The Pulsante ™ SPG Microstimulator System is a patient-powered tool for blocking

SPG signals at the first sign or symptom of a headache. The system involves the permanent implant of a small nerve stimulating device in the upper gum on the side of the head normally affected by headache. The lead tip of the implant connects with the SPG bundle, and when a patient senses the onset of a headache, he or she places a handheld remote controller on the cheek nearest the implant. The generated signals then stimulate the SPG nerves and block the pain-causing neurotransmitters (13).

Inserted Neurostimulator | Remote Controller Placed on the Cheek | Handheld Remote Controller

Figure 1. Source: Reference (13)

2. **Needle-Free Diabetes Care**: Echo Therapeutics (Philadelphia, PA) is developing a prototype of a transdermal biosensor device that continuously monitor blood glucose levels through the skin without the use of needles (40). The technology involves a handheld electric-toothbrush-like device that removes a thin layer of skin cells to put the patient's blood chemistry within signal range of a patch-borne biosensor. Echo's flexible sensor utilizes a proprietary algorithm to continuously and non-invasively monitor glucose levels transdermally, which are then transmitted to any remote device or cloud service. The quarter size sensor wirelessly transmits accurate data every five minutes to a remote monitor, triggering auditory alarms when glucose levels are out of the patient's indicated range (40).

Current medical technology provides an effective solution for applicants with either physical or mental conditions to obtain a Federal Aviation Administration's medical certificate by fulfilling the requirements of operational functionality in their daily activities. This has a clear impact on the airman's professional environment as well as on aerospace medical professionals to operationally evaluate the risks a given applicant represents to aviation safety rather than focusing on a given medical diagnosis or condition. This "functional health" approach applies the practical evaluation of an "acceptable risk" provided that a patient's condition or limitation (imposed by a disease), has been compensated for to a "new-normal" performance by technologically advanced alternatives (63). For example, beginning in 2012 the United Kingdom became the second country in the world, after Canada, to issue class 1 medical certificates for insulin-dependent pilots " in cases where the existing risks are adequately compensated by the use of advanced technical options" such as continuous glucose monitoring (CGM) (63). The aeromedical process that made this policy change possible was based on: 1) a comprehensive protocol and specific guidelines developed by a panel of medical and aviation experts on the medical certification of insulin-dependent diabetes mellitus (IDDM) pilots, also known as type 1 diabetes; 2) a comprehensive review of current literature regarding hypoglycemia risks and experience from various transport modalities; 3) the patients' motivation to fly; and 4) the

patient's training in diabetes therapy in general, as well as in the use of CGM and insulin pumps (65). Another important factor was the fact that current CGM systems have proven to function properly under hypobaric conditions, and previous studies had indicated that CGM systems performed well up to 16,000 feet of altitude (1, 65).

It is expected that aerospace medical professionals become familiar with currently available and projected advanced medical technologies and develop "new" methods of assessing their potential impact on the aeromedical safety and performance of both aviation and space crews and passengers. From an aeromedical perspective, one of the challenges to evaluate and approve the use of currently available medical technology by crewmembers and passengers in the aviation and space sector is the relative lack of knowledge and experience with these advanced technologies (10). Unfortunately, there is almost no scientific information available today to characterize the performance and failure of many advanced medical technologies, particularly when the users of these technologies are exposed to unusually extreme and stressing environments. While emerging technologies such as genomics, gene therapy, microbiomics, stem cells, regenerative medicine, artificial replacement tissues and organs, neurotechnology, nanomedicine, body-worn medical sensors, body networks, personal biomedical devices, and medical robotics have a great potential to provide benefits to humans, they are still so new to the marketplace that their performance during extreme operating conditions is not fully known. This leaves many unanswered questions regarding the failure modes of these new technologies as well as to their performance characteristics during exposure to more stressing environments. Therefore, the use of these new technologies may induce additional and unexpected operational risks related to conditions germane to the aviation and space environments, such as decreased gravity, radiation, changes in barometric pressure, etc. (10). For example, as of today the manufacturers of currently available microprocessor (MP) controlled prosthetic knees (Genium®, X3®, C-Leg 4®, Compact®, Kenevo®, Rheo Knee®, etc.) have not published any report indicating their devices have been subjected to any tests under hypobaric or micro-gravity conditions. These devices use sensors that may not deliver reproducible signals under zero gravity conditions, resulting in potential control issues. Meanwhile, a number of military, commercial, and private pilots have been using MP controlled prosthetic knees while flying airplanes without any issues reported to the manufacturing company (65).

A detailed discussion of all currently available and future advanced prosthetic devices, particularly their impact on the aeromedical certification process, would not be practical due to the following reasons: 1) the size and complexity of the topic as well as the rapid rate of technological expansion and 2) the majority of these devices and technologies are in their early stages of development, and many of them may never make it to clinical trials and therefore will not become commercially available. Nevertheless, it is suggested that in addition to the performance testing documented in "normal" environments, new assistive technologies and devices with potential use in the aerospace environment, undergo specific "extreme" testing corresponding to the desired environment.

This manuscript will focus on a few advanced technologies to illustrate some of the challenges associated with the use of new technologies and devices in a high stress environment. It is important to clarify that neuroprosthetics, robotics, exoskeletons, and advanced prosthetics devices for individuals with an amputation are technical terms that describe different technologies for different patients' needs and medical conditions. Although these terms may be

commonly used within the sections, the reader should be aware that this paper will specifically provide a review of the most recent implementation and future use of brain-computer interfaces (BCIs), bidirectional interfaces, and neuroprosthetics, with emphasis in advanced prosthetic devices with current and foreseeable clinical applications and their aeromedical implications. In addition, it will propose recommendations pertaining to the evaluation of advanced neuroprosthetics and aeromedical certification of amputee pilots.

BRAIN-COMPUTER INTERFACE

A brain-computer interface (BCI) is "a system that measures and analyzes brain signals and converts them into real-time outputs that do not depend on the normal output pathways of peripheral nerves and muscles" (125). Generally speaking, systems that use recorded neuronal activity to perform specific tasks are referred to as brain-machine interfaces (BMIs), BCIs, or neuromotor prostheses (NMP). Although the terms BCI, BMI, and NMP, can be used interchangeably, neural interface system (NIS) is a generic term used to refer to any BCI, BMI, or NMP. All NISs record electrical impulses from neural activity, decode these impulses and transfer them as command signals-for the control of machines, computers, and various prosthetic devices (102). BCIs facilitate the control of motor functions (e.g. moving, reaching, grasping, or locomotion), by converting real-time brain signals into outputs, which are independent from the "normal" anatomical pathways of peripheral nerves and muscles. Thus, by using this type of communication between the brain and a robotic device, BCIs have been incorporated into and improved neuroprosthetic devices that use neurophysiological signals from undamaged components of the central or peripheral nervous system to allow patients to regain lost mobility (99). Bidirectional interfaces incorporate brain signal recording and relaying of coded information to and from the brain for the development of BCIs (102).

Different technologies used to record and measure activity of the brain are currently available. Some of the key characteristics of these systems include user performance that requires minimal effort to avoid cognitive fatigue and subsequent erroneous selection of targets; generation of intense brain signals, for fast and reliable interpretation; the ability of users to easily switch between thoughts to enable better control of their brain's activity pattern; and finally effective outputs (31, 103, 115). This recorded neuronal activity may be gathered by either **non-invasive** or **invasive techniques.** Each technique has its own benefits and limitations, with the common goal of integrating the external device with the patient's nervous system (39, 73, 102).

Non-Invasive Brain Activity Measurement: Non-invasive BCIs provide practical solutions for control and communication between the nervous system and prosthetic devices. However, some limitations associated with this method are costs, required training, and the quality of the neural signals. Another disadvantage of BCI methods is that data is obtained from neuronal activity generated by large cell populations, which implies a good temporal resolution but poor spatial resolution. This is likely caused by the poor electrical transmission of bones and soft tissues (115). Electroencephalography (EEG) is currently the most common non-invasive method for recording brain activity (99). The data is obtained from changes in magnetic fields, electrical current, and oxygen consumption. The main goal during motor neuronal activity recording is to obtain both high temporal and spatial resolutions (47). Due to the size of the equipment and the poor spatial resolution in terms of coordinated movement, these techniques are limited to few specific applications. Similarly, Electromyography (EMG) is another non-

invasive BCI in which individuals with an amputation and partially paralyzed are able to control limb prostheses and exoskeletons by voluntary activations of healthy remaining muscles (99, 130). As compared to EEG-based BCIs, these systems have shown to be a promising solution for individuals with an amputation who may have residual muscular activity by allowing them to interact with the external world (55, 99). Future research is focusing on lighter anthropomorphic transradial prostheses, which will have electromyography (EMG) signal processing embedded with tactile systems to provide feeling to the amputee (102). There are promising results from recent studies on artificial touch, indicating that building neuroprosthetics that mimic natural sensations of touch is the first step towards achieving the dexterity comparable to native hands (114). It is important to clarify that EMG and myoelectric control is useful for powered devices (i.e. current upper limb prosthetics) but not for passive prosthetic devices (i.e. current lower limb prosthetics). A myoelectric-controlled prosthesis is an externally powered artificial limb that is controlled with the electric signals generated by the remaining muscles located in the residual limb. Electrical signals are received by sensors embedded into the prosthetic socket when specific muscles are intentionally used. Sensors transmit the received information to a controller, which converts the data into commands for the electric motors to move hand, wrist, and elbow joints (95). At the present time, both myoelectric control and sensorimotor feedback are only available in upper limb prosthetics, therefore, the reported limitations of myoelectric control and the lack of sensorimotor feedback do not apply to lower limb prosthetics. These issues may become relevant in the future, once lower limb prosthetic devices that produce enough power to mimic concentric muscle action (e.g. for climbing stairs, etc.) are available (65).

Invasive Brain Activity Measurement: Invasive BMIs eliminate signal conduction issues caused by soft tissues and bones and therefore achieve a high signal-to-noise ratio. Using intracranially implanted electrodes, invasive BMIs are able to obtain recordings from populations of a few single brain cells rather than large cell populations. This produces brain signals of superior quality; however, because a surgical procedure is required, these methods involve additional risks to the patient. These risks include, but are not limited to, postoperative infection and/or rejection (71, 102). Recent multi-neuron population recordings, which supported the "population-centric " concept of distributed processing in neural systems, determined that because most neurons located in the new cortex code information in a crude manner, the distribution of sensory or motor processing is likely to be broadly distributed across neuronal populations (29). In addition to providing a better understanding on how information is distributed across several brain regions, this technique showed that mathematical analysis of neural population codes allows extraction of 'motor signals' from neuronal population recordings in the motor cortices, which can then be used in real-time to directly control movement of a robot arm, providing a means of interaction with objects through basic functional activities such as reaching (29).

Implantable brain electrodes and electrocorticography (ECoG) procedures were invented during the 1950s in order to identify the origin of epileptic seizures. In this method, electrodes are directly placed onto the brain's cortical tissue and have shown the possibility of controlling both a robotic arm and hand to perform basic activities such as reaching objects and interacting with them (99).

Another invasive technique used to record neuronal activity is the Multielectrode arrays (MEAs). As mentioned before, one major limitation of this approach is that surgery is required

for the transcutaneous wire implantation. MEAs also require biocompatibility of the neural implants' surface molecules with surrounding brain tissue, which is necessary for effective integration and data transmission (102). Novel materials, coatings, electrochemical/mechanical stability, and optimized shapes and geometries have contributed to recent improvements in biocompatibility (46, 100, 102, 104, 129). Unfortunately, silicon, a common fabrication in MEAs, contains particles that are carcinogenic to a variety of cells and organs. These particles may also elicit an immune response resulting in encapsulation of the device (46, 102). Thus, biocompatible materials are used whenever possible to increase the lifespan of devices and to minimize damage to healthy brain tissue (102).

EEG telemetry is another technique that is being investigated for use. A great advantage of using wireless EEG telemetry is that it allows subjects to move freely in real-world environments while acquiring data. Unlike MEAs, breakage of wires is not an issue in wireless neurointerfaces, so stable recording is expected. Another advantage is that the user interface or front end of these systems can be integrated in wearable devices such as headbands, sunglasses, baseball caps, etc. The potential applications of these systems include 1) monitoring epilepsy in children, where misdiagnoses are not uncommon; 2) delivering vibrotactile feedback sensations; and 3) operating the telephone keypads displayed on personal computer monitors operated by steady-state visually evoked potentials (SSVEP) (102).

In some emerging technologies, micro-optical arrays are being used to transmit neural signals by utilizing the conversion of low-energy light to power when it is transmitted through fiber optic cables (102).

INFORMATION TRANSFER VIA NEUROPROSTHESES

Additional advancements are being made through the use of neural prosthesis in which the neural systems interface directly to the prosthetic devices. Neuromuscular electrical stimulation (NMES), in which the electrical stimulation of an intact lower motor neuron is used to activate paralyzed or paretic muscles has been used for 50 years. The bi-directional communication between these external devices and the human nervous system allows the device to elicit an action or to perceive stimulus, restoring motor, sensory, and cognitive function (75, 91). Neuroprostheses use electric signals to stimulate neural structures, muscles, or receptors in order to restore motor or sensory neural dysfunction. Information can be transferred in one of two ways: 1) inward via remaining senses or electrical stimulation, and 2) outward information transfer, which involves recording biological information of muscles following neural activation and using this acquired information to elicit a response (91). In other words, neuroprosthetics can be considered output neural interfaces, which convert the brain's intentions to external actions (e.g., robotic arm), or as input neural interfaces, which take information from the environment and convert it into perceptions (e.g., cochlear implant, bionic eye, and tactile feedback) (75).

Neural prostheses use EEG and EMG interfaces in order to bypass dysfunctional pathways in the nervous system by applying electronics to replace lost function. Some of the most frequently used neuroprosthetic applications include 1) Cochlear implant, 2) Cardiac Pacemaker, 3) Deep Brain Stimulation, 4) Bladder Stimulation, and 5) Myoelectric Control for Neuroprosthetics.

1. **Cochlear implant**: A cochlear implant is a widely used method that enables deaf children to recover auditory limitations and speech commands. In order to use this implant system, the auditory nerve system has to be healthy and intact;
2. **Cardiac Pacemaker**: It is probably one of the most frequently used neuroprosthetic devices. A cardiac pacemaker is used either as a single chamber (the heart's right atrium or right ventricle is stimulated) or as a dual chamber (to correct disorders in atrioventricular transmission);
3. **Deep Brain Stimulation**: Deep brain stimulation is used for the treatment of severe movement disorders, such as Parkinson's disease. The brain stimulator is implanted between the pectoral muscle and the skin;
4. **Bladder Stimulation**: Bladder control is used for proper control of urinary flow, particularly in paraplegic patients; and
5. **Myoelectric Control for Neuroprosthetics**: Designed as an effective rehabilitation function for individuals with upper-extremities amputations, EMG provides the possibility to monitor their finger movements. A prosthetic hand controlled by EMG has the ability to control more joints than other conventional prosthetic hands. For example, functional upper-extremities prostheses can control no more than two joints. Control of prosthetic hands requires the individuals with an amputation to generate EMG patterns different from the patterns before amputation, therefore extensive training is required before the patient can adapt to the prosthesis (91).

Visual Prosthetics

As the average life span of the U.S. population increases, so does the incidence of age-related disease processes such as cataracts and macular degeneration. Pilots are at an increased risk of developing these ophthalmologic disorders due to their chronic exposure to UV-radiation. Currently, the FAA permits Food and Drug Administration (FDA)-approved multifocal and accommodating intraocular lens implants for all classes of medical certification but requires recent FAA documentation evaluating the eye and demonstrating stable visual acuity and refractive error, absence of residual side effects, and absence of visual deficits that may negatively affect aviation safety (5).

The World Health Organization estimates that about 285 million people are visually impaired worldwide; 39 million are blind and 246 million have low vision. Eighty-two percent of people living with blindness are aged 50 and above. The most frequent causes of visual impairment worldwide are uncorrected refractive errors, myopia, hyperopia, or astigmatism (43%); unoperated cataract (33%); and glaucoma (2%). Although 80% of all visual impairment can be prevented or cured, there is no cure for the remaining 20% (127). Some retinal conditions such as age-related macular degeneration, retinitis pigmentosa (RP), and Leber's congenital amaurosis are in the group of visual conditions with no cure. These retinal diseases cause a degeneration of photoreceptors which results in a reduction of visual acuity and ultimately in complete blindness (38, 103). Retinal prostheses were developed with the purpose of restoring useful vision in blind patients by electrically stimulating the remaining "healthy" inner retinal network. "Visual prosthetics" is a common term used to describe electronic devices that are implanted at different anatomical locations along the visual processing pathway.

Visual prosthetic technology can be implanted in one of the following anatomical locations: 1) retina, 2) optic nerve, or 3) visual cortex. Retinal implants are used to replace photoreceptor

function, which poses challenges due to retinal fragility. Although implantation and stabilization are difficult, implementation is easier than other visual prostheses because far less complex information is needed for stimulation. Optic nerve implants pose challenges due to the poor control over their position and the size of the evoked phosphenes. Visual cortex implants use electrodes that require high electrical current while providing higher spatial resolution for visual processing (103). Although extensive research in this area has been conducted globally, many questions still remain unanswered: What is the preferred location for an implant? What are the optimal electrical stimulation parameters? How many stimulation electrodes should be used, and what would be their ideal size and geometry? How should the visual scene be encoded? Safety issues in terms of maximal allowable electrical charge continue to be a problem without a consensus on accepted standards. It has been reported that pulse amplitudes of three volts were noxious to the retina, producing visible opaque spots on the stimulated tissue areas (38).

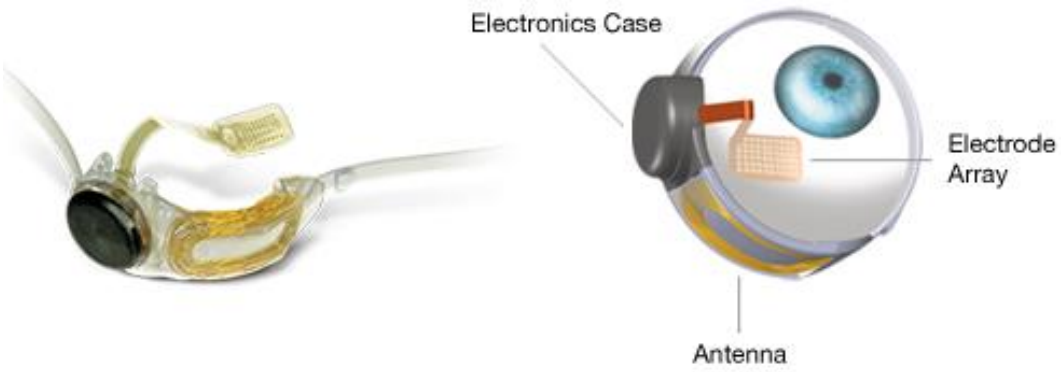
A Food and Drug Administration (FDA) approved bionic eye, the Argus® II device, also known as the retinal implant (manufactured by Second Sight Medical Products Inc., Sylmar, CA) (108), is an artificial retina for the treatment of blindness in patients with severe to profound retinitis pigmentosa (RP). It consists of a sheet of electrodes implanted in the patient's retina. A miniature video camera embedded in the patient's glasses capture the images in front of him/her and converts those acquired images into pixels, which are returned back to the array of electrodes, which in turn discharge small pulses of electricity. By bypassing damaged photoreceptors, these pulses stimulate the remaining cells of the retina to convey the visual information to the brain via the optic nerve, allowing the perception of patterns of light. As A result, the retinal implant allows the patients to interpret the visual patterns. Although the device does not restore full vision capacity, the patient is able to identify objects' shapes and boundaries. Consequently, according to the manufacturer the device is helping patients to move around more freely and to identify items such as a bus stop or the lines of a cross walk. Currently, the Argus® II Retinal Prosthesis System is available for patients with late stage RP in 17 cities in the U.S. and Canada. The FDA approved the Argus II in February 2013 and Health Canada approved it in December 2014 (19, 108).

In 2006, Second Sight Medical Products, Inc. (Sylmar, CA) announced that their Orion I ™ Visual Cortical Prosthesis, "the first wireless visual cortical stimulator" was successfully implanted and activated in a human subject (124). (See Figure 3)

According to the company's Chairman of the Board, "by bypassing the optic nerve and directly stimulating the visual cortex, the Orion I has the potential to restore useful vision to patients completely blinded due to virtually any reason, including glaucoma, cancer, diabetic retinopathy, or trauma" (124). However, the manufacturer clarifies that the effectiveness of this device to induce visual perception in blind patients with severe to profound RP has not been demonstrated.

The Implant

Epiretinal prosthesis surgically implanted in and on the eye includes an electronics case, an electrode array, and an antenna.



The External Equipment

Glasses, a video processing unit (VPU) and a cable that communicate with the implant are worn externally.

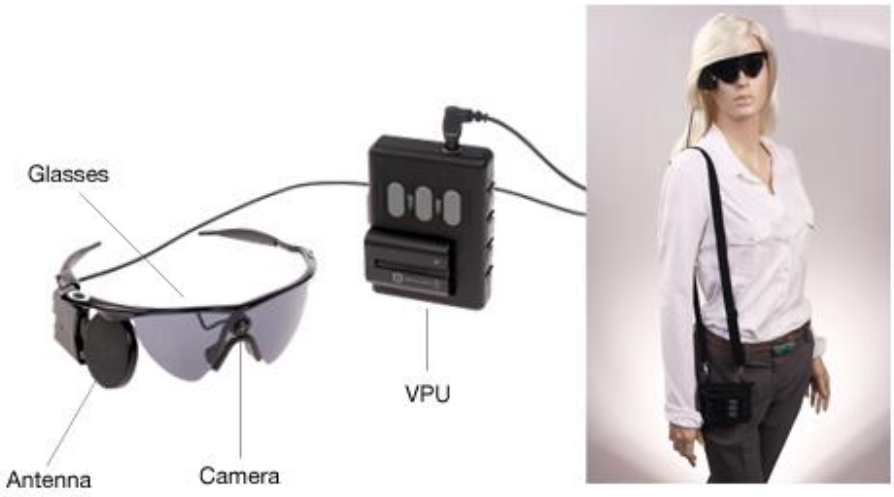


Figure 2: Pictures taken from www.secondsight.com and reprinted with permission of Second Sight Medical Products, Reference (108).

Auditory Prosthetics

The cochlear implant (CI) was designed to restore hearing capabilities by electrically stimulating the auditory nerve fibers (76, 123). It has been estimated that more than 300,000 patients worldwide have received a CI, allowing many of these individuals to sustain a conversation and interact with others via phone calls. Even very young babies with a CI are nowadays able to attend conventional schools. The CI has been effective not only in restoring

hearing to many deaf patients, but it has also led to the successful development of additional neural prostheses for the restoration of lost sensory or motor capabilities, for example, the visual prosthesis or a neural-controlled prosthetic limb (76, 119, 120). Simply stated, CIs elicit auditory stimuli by using electrical signals that stimulate the basilar membrane's sensory epithelium. The most successful cases have involved subjects who, during their critical developmental periods, were able to hear to some extent. By providing sensory input to the cortex, rather than the auditory nerve, it is possible to achieve a better hearing resolution. The CI may be placed into 1) the junction of the cochlear nerve/pons structures to treat a damaged auditory nerve; 2) the cochlear nucleus, in particular, the lateral foramen of Luschka; or 3) the inferior colliculus, the more distal sensory connection (68, 103, 104).

Although the CI is designed to electrically activate the auditory nerve, for some patients the only option to restore hearing capabilities is a central auditory brain implant (ABI) or auditory midbrain implant (AMI); particularly those whose auditory nerve has been damaged due to a head trauma or surgery to remove a tumor, or the congenital absence of a nerve or in case of patients whose cochlea will not allow implantation due to head trauma or ossification (76). The first ABI was positioned onto the surface of the cochlear nucleus by William Hitselberger and William House at the House Ear Institute in Los Angeles, California, in 1979. Initially designed and indicated for patients with neurofibromatosis type 2 (NF2), a genetic disease characterized by bilateral acoustic neuromas, the ABI became the only treatment available to those patients whose auditory nerves were completely damaged during the tumor removal procedure. In an effort to improve central auditory prostheses in patients with NF2, by stimulation within the inferior colliculus (IC), specifically its central nucleus (ICCN), some researchers have been trying to implant an electrode array into the midbrain. The advantage of this approach is that, unlike the brainstem, the midbrain is exposed during surgery allowing the surgeon to visually identify the trochlear nerve, which is responsible for rotational movement of the eyes. So, the damage to critical nerves involved with critical functions is minimized. The reasoning behind this procedure is that the sound information gets processed across multiple structures within the brainstem through several neural pathways (27, 76). The ICC integrates the ascending sound information and pathways. Auditory sensory pathways that go across the brainstem and thalamus to higher brain perceptual centers within the posterior, superior temporal gyrus contains the primary auditory cortex which receives auditory input. Therefore, it should be feasible to stimulate those pathways by implanting electrodes within the ICCN. The effectiveness of this procedure in restoring patients' speech perception has not been clinically evaluated yet. Nevertheless, modest improvements in terms of lip-reading capabilities, environmental awareness, and safety have been achieved. An upcoming clinical trial funded by the National Institutes of Health, testing modifications in the AMI array design, stimulation approach, and surgical procedure is expected to improve hearing performance in those patients (76).

Aeromedical Decision Considerations for Cochlear Implants

Currently, the FAA medically certifies pilots who use cochlear implants, provided that their hearing condition is stable; no side effects such as dizziness, disequilibrium or vertigo are present; and the applicant is released by his/her health provider for normal activities (4). The applicant will need to submit the following information to the FAA:

- A current summary of medical records from their treating physician that includes diagnosis, date of surgery, post-operative status, including side effects–if any, and prognosis
- Hospital records including a complete summary of admission /discharge notes, operative report, and reports from any diagnostic tests that may have been performed
- Post-recovery otolaryngology (ear, nose, and throat) evaluation, including audiogram with speech determination scores
- The technical data on the implant (manufacturer, model number, etc.)
- A letter stating the preferred FSDO location for the medical flight test (MFT)

Aeromedical Decision Considerations for Implanted Pacemaker

Cardiac pacemakers are widely used neuroprosthetics that use electrical impulses to regulate abnormal heart rhythms, also known as arrhythmias. Pacemakers monitor internal electrical signals from the heart to determine whether or not an electrical stimulus from the device is needed. A 2009 worldwide survey report on new users of pacemakers showed that implantation of this device reached a higher number, more than 700,000, as compared to a similar survey published in 2005. At the same time, modern technological advances have resulted in new sources of electronic radiation, which can pose a hazard to the proper function of a pacemaker (17, 87). Depending upon the treatment duration, these devices can be temporary or permanent. For practical purposes, only implantable pacemakers will be discussed below.

Permanent pacemakers are used for chronic or recurrent conditions requiring a long-term treatment. The device is usually implanted subcutaneously, in the area below the clavicle, above the pectoral muscle (prepectoral implantation). The pacemaker's leads (insulated wires) are inserted intravenously via a major vein all way up to the specific heart muscle. The other leads' ends are attached to the pulse generator. Sometimes, the pulse generator might be implanted subcutaneously on the upper abdomen. In summary, there are two main components of a pacemaker: the actual pacemaker containing the electronic circuit, and the leads which conduct the electrical impulses from the pacemaker to specific regions of the heart. Once implanted, patients typically must follow-up with a cardiologist every 6 months to have their device checked. This process is non-invasive and involves assessing the underlying heart rhythm, the life of the battery, how often the device is pacing, and if it is functioning properly. Current device models are less susceptible to electromagnetic interference (EMI). Nevertheless, published reports indicate that clinically significant interference can occur when pacemakers are exposed to certain external electrical forces, such as welding equipment or strong motor-generator systems. However, one study found that the EMI generated from hybrid electric vehicles was too low to cause dysfunction of implantable pacemakers, and therefore deemed safe to be used for patients exposed to such environments (109). In general, the risk of serious adverse events induced by environmental and industrial EMI sources in pacemakers' users is low, particularly when the exposure time is short and the distance is maximized (17, 56, 94).

The FAA currently approves medical certification of pilots who require cardiac pacemakers as long as they are not coupled with an automatic implanted cardioverter defibrillator, which acts to jumpstart a heart when it has stopped. A two-month recovery and stabilization period must pass after the pacemaker is implanted to apply for a special issuance. The following information must be submitted:

1. Copies of hospital/medical records pertaining to the requirement for the pacemaker manufacturer of the generator and leads, model and serial number, admission/discharge summaries, operative report, and all ECG tracings.
2. Evaluation of pacemaker function including description and documentation of underlying rate and rhythm with the pacer turned "off" or at its lowest setting (pacemaker dependency), programmed pacemaker parameters, surveillance record, exclusion of myopotential inhibition and pacemaker induced hypotension (pacemaker syndrome), and Powerpack data including beginning of life (BOL) and elective replacement indicator/end of life (ERI/EOL). In addition, clear samples of all electronic pacemaker surveillance records post-implantation or over the past 6 months, or whichever is longer. This record must include a sample strip with pacemaker in free running mode and unless contraindicated, a sample strip with the pacemaker in magnetic mode.
3. A current cardiovascular evaluation and statement from a physician regarding general physical and cardiac examination to include symptoms or treatment: the airman's interim and current cardiac condition, functional capacity, medical history, and medications.
4. A current report of fasting blood sugar values and a current blood lipid profile including total cholesterol, HDL, LDL, and triglycerides.
5. A current 24-consecutive hours Holter monitor evaluation, including representative tracings.
6. A current M-mode, 2-dimensional echocardiogram with Doppler report, including film video or any other images related to the study.
7. A current Maximal Graded Exercise Treadmill Stress Test equivalent to completion of Stage III (9 minutes) or the 12-lead Bruce protocol. Dependency of pacemaker is defined as an unpaced resting heart rate of less than 40 beats per minute. Dependency is disqualifying for first and second-class medical certificates, but third class applicants will be considered on a case-by-case basis.
8. It is the responsibility of each applicant to provide the medical information required to determine his/her eligibility for airman medical certification. A medical release form may help in obtaining the necessary information (36).

As many pilots are using pacemakers that combine pacemaker/internal cardiac defibrillators, it is important to know that the FAA does not currently allow the use of automatic implanted cardioverter defibrillators (AICDs) for any class of medical certificate (11).

EVOLUTION OF LIMB PROSTHETIC DEVICES: A BRIEF HISTORY

In a comprehensive review of the evolution of prosthetics, Norton (93) describes the beginnings of this field around 1500 B.C. through the current computerized leg (C-leg). The Egyptians appeared to be the pioneers of rudimentary prosthetic limbs with functional capabilities, made out of fiber (93). According to Norton’s review, in 1858, a bronze and iron artificial leg with a wooden core dating to about 300 B.C. was discovered in Capua, Italy and apparently was used by a below-knee amputee patient. He also cited Pliny the Elder (23-79 A.D.), a Roman scholar who reported that a Roman general in the Second Punic war (218-210 B.C.) had his right arm amputated. This general was able to return to the battle’s field using an iron hand designed to hold his shield. Iron hands were later introduced in 1508 in Germany. The hands could be manipulated and moved by relaxing a series of releases and springs while being suspended with leather and straps on a right-arm amputee (93).

Modern amputation procedures (1529) and prosthetic designs (1536) for individuals with upper- and lower- extremity amputations were introduced by Ambroise Paré, a French Army barber/surgeon. His work helped to better understand how the prostheses should function. One of the most important contributors to prosthetics at that time was Lorrain, a colleague of Paré's, and a French locksmith who used leather, paper, and glue to replace heavy iron in making a prosthesis (93).

The first non-locking below-knee prosthesis was developed in 1696, which is considered to be the beginning of current joint and corset devices. In 1800, a prosthesis made out of a wooden shank and socket, a steel knee joint, and an articulated foot controlled by catgut tendons from the knee to the ankle was built in London. The leg was known as the "Selpho Leg," because it was brought to the U.S. in 1839 by William Selpho.

In 1868, for the first time, Gustav Hermann suggested the use of aluminum instead of steel to make artificial limbs lighter and more functional. However, it was not until 1912 that the first aluminum prosthesis was made by Marcel Desoutter, a famous English aviator who lost his leg in an airplane accident. He worked with his brother Charles, an engineer on the design of this device (93).

During the U.S. Civil war, the number of individuals with an amputation increased dramatically. James Hanger, the first above-knee amputee of the civil war after a severe wound caused by a cannonball, made the "Hanger leg," an artificial leg hinged at the knee and made from whittled barrel staves. After his successful design, he was commissioned to make artificial limbs for wounded veterans.

A remarkable contribution to the evolution of limb prostheses was the design of the non-MP controlled "swing and stance" hydraulic knee, also known as the Mauch SNS model. Developed by Hans Adolph Mauch, a German aviation engineer who came to the US in 1946 after WWII ended, the SNS knee allowed for reciprocal gait on all types of terrains but was suitable only for individuals with an amputation who were physically fit. It has been reported that the Mauch SNS hydraulic knee designed in the late 1950s was the hardware basis for the development of current MPKs (122).

Following World War II, the U.S government made a deal with military contracting companies to improve prosthetic function, paving the way for the development of modern prostheses. This agreement was critical to the development and production of current prostheses which are "patient-customized" to fit each patient's unique anatomy and developed with functional capabilities using much lighter materials such as plastic, aluminum, and composite materials (93).

One of the most significant advances in the care of people with modern transfemoral amputations in the U.S. occurred in 1999 with the arrival of microprocessor-controlled knees (MPKs) such as the Otto Bock C-Leg ®. It is important to clarify that "Intelligent Prosthesis" is NOT a synonym for C-Leg. The "Intelligent Prosthesis" was a prosthetic knee with MP swing control only, developed originally by Kobe Steel, Tokyo, Japan, but licensed and commercialized by Chas A Blatchford & Sons Ltd, Basingstoke, UK, in the early 1990s (42, 51). Another Japanese company, Nabtesco (90), claims to be the first company to have developed the world's first MP controlled prosthetic knee with automatic swing control.

Nevertheless, the C-Leg was the first knee with MP stance and swing control, introduced in Germany in 1997 and in the US in 1999 (65). It was also the predicate device for the respective Medicare billing code L5856 (microprocessor control feature, swing and stance phase, includes electronic sensor(s), any type) that became effective on January 1, 2005 (77). The second MPK of that kind was the Rheo Knee® by Össur hf, Reykjavik, Iceland, that was introduced to the European market in 2004 (65). Currently, 90% of the MPKs used or fitted in the US have MP stance and swing control (65).

MPKs use electronic sensors, detect rate and range of joint and shank angles and moments, and provide instant friction or resistance adjustments to changes in gait pattern. They are also programmed to each individual user during walking to " …increase stability and confidence, reduce cognitive burden, improve quality of life and expand activity levels" (7). More importantly, frequency of falls decreases by 64-80% with the use of MPKs (58, 66). C-Legs help users with: stumble recovery, sitting, ramps and stairs, uneven terrain, and decrease mental fatigue because the patient does not need to concentrate on the terrain and mechanics of walking with the prosthesis (20, 26, 53, 54, 59, 64, 107). Although for lower limb prostheses, the goals are a safe, efficient, and comfortable ambulation with minimal expenditure of energy, the evidence for reduction in energy expenditure with MPKs is somewhat inconclusive (58). It is believed that the reduced fatigue perceived by patients at the end of a day might be mainly due to the reduction in cognitive demand or the combination of reduced metabolic and cognitive energy consumption. However, reduction in energy expenditure with an MPK may actually be due to the absence of the need to actively stabilize the knee during stance and improved swing control with better adaptation of resistances to changing and faster walking speeds (30, 58, 65, 106, 110, 126). Nevertheless, people with lower-limb prostheses use a higher oxygen consumption, which varies with different models of prostheses, as well as the level of the amputation. The more proximal the amputation level, the more the expenditure of energy (65, 106, 118, 119). Previous studies evaluating functional testing of different prosthetic knee joints in critical situations likely to cause an individual with an amputation to stumble or fall, such as stopping and sidestepping abruptly, stepping onto an obstacle, and tripping, found that the MP-controlled C-Leg knee joint significantly reduced the risk of falling and injury in those individuals as compared with non-MP controlled knee joints (23).

In a comprehensive literature review conducted by Kannenberg et al., analyzing the benefits of using MPK in a group of limited community ambulators[*] with a transfemoral amputation (TFA) in terms of safety, performance-based function and mobility and perceived function and satisfaction, it was reported that these subjects may significantly reduce the number of falls and their risk of falling, improve their balance, and better perform activities of community ambulation, categorized as part of the MFCL-3 mobility grade.[†] In addition, they suggested that the use of MP hydraulic stance only or MP stance and swing control

[*] Limited Community Ambulator or MFCL-2 as defined by Medicare in the Medicare Functional Classification Levels (MFCLs): "Has the ability or potential for ambulation with the ability to traverse low-level environmental barriers such as curbs, stairs, or uneven surfaces (8)."

[†] MFCL-3 mobility grade or Unlimited Community Ambulator: "Has the ability or potential for ambulation with variable cadence – A typical community ambulator has the ability to traverse most environmental barriers and may have vocational, therapeutic, or exercise activity that demands prosthetic utilization beyond simple locomotion (8)."

prosthetic knees may improve safety, function, and mobility of limited community ambulators with unilateral TFA (67).

The technical stability features of non-microprocessor controlled prosthetic knees (NMPKs) mainly aim at preventing knee collapse during level walking which is an important part but by far not the only concern of overall prosthetic safety that also comprises stability during walking on uneven terrains, slopes, stairs, sufficient toe clearance, and stumble recovery. Non-microprocessor controlled prosthetic knee mechanisms are characterized by an inverse relationship between stance stability and functions supported, i.e. the better a prosthetic knee prevents collapse during weight-bearing the less physiological gait it allows for on non-level surfaces. In addition to improving function and mobility on all kinds of terrains, MPKs reduce stumbles and falls, reduce indicators for risk of falling, improve balance, and improve confidence (22, 23, 53, 54, 64, 65, 67).

Bellmann et al. (18) investigated the immediate biomechanical effects patients experienced after transition to a new MP-controlled prosthetic knee joint. For this study, the group used a motion analysis laboratory and 11 subjects with unilateral transfemoral TF amputation to measure static prosthetic alignment, time-distance parameters, kinematic and kinetic parameters, and center of pressure. Their results suggest that a change to an even more advanced microprocessor-controlled artificial knee joint (from C-Leg® to Genium®) provides added advantages during various ambulatory activities, which may potentially lead to an increase in the diversity and range of activity, as well as more natural gait biomechanics and load distribution in patients with above- knee amputations (18). Blinding of prosthetic components, especially of knees, is extremely difficult (52, 65), therefore one of the limitations of this study resided in the fact that the subjects were aware of which knee components they were using during the experiment.

Meanwhile, a powered ankle-foot component is commercially available: The emPOWER® Ankle (emPOWER/BIOM®, BionX Inc.). According to the manufacturer, it is "the only prosthesis that controls ankle power, resistance and flexion in real-time for stability across variable terrain" (21). In addition, The emPOWER Ankle "helps center the user's balance for safety across variable terrain – such as rain, snow and dirt." The emPOWER® is the next generation design of the BiOM Ankle (21). Similar to research with passive, non-powered MP controlled hydraulic ankle-foot systems, studies have shown improvements in biomechanical parameters of gait. However, the clinical significance of these improvements remains controversial (65).

Huang and colleagues (60) investigated the use of surface electromyography (EMG) combined with pattern recognition (PR) to identify user locomotion modes. This is important because identifying locomotion modes is the initial step in developing effective powered prosthetic devices. They collected data from able-bodied subjects to identify the locomotion modes with precision. EMG signals were recorded from muscles above the knee, in both non-amputated subjects and individuals with long trans-femoral (TF) amputation, while walking on different terrains. The results showed reliable classification for the seven tested locomotion modes, suggesting that the concept of phase-dependent PR design is viable for the design of neural-controlled prosthetic legs. Control by EMG signals is standard for myoelectric hand/arm prostheses, and there is one commercially available pattern recognition system for upper limb prostheses (Complete Control®, Coapt LLP). In the past years, functionality of upper limb

prosthetic components has been improved remarkably; however, the lack of intuitive and simultaneous control has limited improvements in patients´ overall function. Pattern recognition is the first step towards more intuitive and simultaneous control of several devices and/or functions in upper limb prosthetics. It is believed that this has the potential to contribute to better user acceptance and lower rejection. Unfortunately, for lower limb prosthetics, pattern recognition is still experimental and not commercially available (65).

ADVANCED LIMB PROSTHETIC DEVICES: CURRENT STATUS

Worldwide, millions of people suffer from sensorimotor deficits due to limb loss, neurologic injuries, or other chronic diseases (72). Limb Loss is the loss of all or part of an arm or leg due to trauma, infection, diabetes, heart disease, cancer, or other diseases. Moreover, as our population ages, we are encountering more vascular diseases with potential for de-vascularization (28).

More than 2 million people live in the U.S with limb loss; 185 thousand have an amputation each year, with more than 500 people losing a limb each day. By 2050, approximately 3.6 million Americans will be living with a limb loss (9).

A comprehensive study on the epidemiological and time trends in the incidence of limb amputations and limb deficiency in the U.S. showed that peripheral artery disease (PAD) and diabetic neuropathy made up to 70-80% of all amputation etiologies (37). This is one of the most referenced studies in the prosthetics literature related to amputation etiology. Dysvascular amputations accounted for 82% of limb loss discharges and over the years of the study (1988-1996), the rate of dysvascular amputations had an estimated increase rate of 27%. In 1996, the rate of dysvascular amputations was almost eight times greater than the rate of the second leading cause of limb loss: trauma-related amputations (37). From a demographic perspective, it is important to distinguish between the causes of amputations at younger ages (primarily trauma-related) as compared to older ages (primarily dysvascular). People with diabetes and other peripheral artery disease are considered at risk for limb loss. Regarding the age at amputation, 82% of patients are included in the 45-84 age group; also, 65% of amputations occurred in lower limb as compared to 35% in upper limb with a gender distribution of 69% in males compared to 31% in females. In addition, lifetime healthcare cost has been estimated to be more than $500,000, compared to $361,200 for people without a limb loss; hospital charges for patients who underwent an amputation, not including costs for prosthetic devices (artificial limbs) or rehabilitation costs, totaled $8.7 billion (28). Risk of amputation increases with age, regardless of etiology, sex, and race, although among African-Americans with dysvascular amputations, the rate of increase is especially high. As related to gender distribution, men are at higher risk than women for limb loss, especially with regard to trauma-related amputations (37).

As previously mentioned, trauma is the second leading cause of amputation. Traumatic amputation is most common in young adults (20-29 year old). The main causes of traumatic limb loss in young adults include 1) injuries involving machinery (40%), 2) power tools and appliances (28%), 3) firearms (9%), and 4) motor vehicle crashes (8%). Although the incidence of trauma-related major amputation continues to decrease over time, U.S. engagement in the wars of Afghanistan and Iraq has resulted in more than 1,700 veterans who sustained traumatic amputations (33). It has been estimated that U.S. troops injured in Iraq have required limb amputations at a rate twice as high as the rate in previous wars. At the same time, only 1 in 10

troops injured in Iraq has died, which represents the lowest rate of any war in U.S. history. However, those who survive have much more serious wounds, particularly in upper and lower extremities (85).

In an attempt to explain the reduction in traumatic amputation, some of the cited factors included 1) new regulations, 2) safer farm and industrial machinery, 3) safety improvements in the work environment, and 4) advances in medical technologies and procedures for salvaging mangled extremities (92).

It has been suggested that, compared to the general population, pilots are more susceptible to suffer some form of sport-related trauma during their professional career because of their willingness to engage in outdoor activities and extreme and risky adventures both on and off duty; therefore, after severe trauma, they may suffer amputations (61). Unfortunately, there is no publicly available information on the prevalence of amputee pilots in the civilian aviation sector.

Components of Advanced Lower Limb Prosthesis (95)

Regardless of the functions provided by the most advanced prosthetic devices, the two key factors in the usefulness of an artificial leg remain: the fit of the socket and the alignment of the various parts to each other and the body. Nevertheless, significant skill on the part of the prosthetist and patient's cooperation—in addition to extensive training for both—is required to overcome the challenges of fitting and alignment (89).

The above-knee prosthesis has four major parts: the socket, the knee system, the shank/pylon, and the foot-ankle system (95) (See figure 3 below).

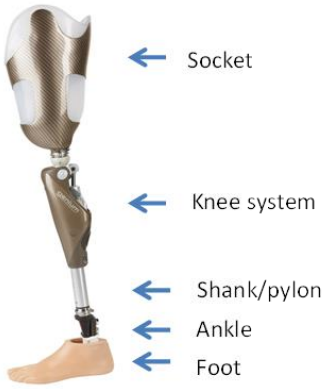


Figure 3. Components of Advanced Lower Limb Prosthesis
©Photo courtesy of Otto Bock HealthCare

Other components required to achieve the needs of each individual amputee are

- Liners: The liner is a protective cover made of a flexible, cushioning material. It is worn over the residual limb to reduce the movement and scratching between the skin and the socket. These can be made of different materials such as silicone, polyurethane, and copolymer, depending on individual needs. Liners act as a second skin.

- Sleeves: Sealing sleeves are needed for vacuum and suction suspension. They create a seal around the socket's top edge.
- Socket: This is one of the most important prosthetic components, as it enables the prosthesis to connect and fit to the residual limb and all the remaining parts are attached to it. It is also a common reason for prosthesis rejection when the socket is uncomfortable. Although other parts of the prosthesis are also weight-bearing, the socket is the component the amputee applies force to in order to control the entire prosthesis, therefore is usually made of a rigid material.
- Suspension system: The suspension system attaches the socket to the body. The more secure the connection between the socket and the limb, the higher the level of proprioception, and therefore it provides a better awareness, performance, and confidence to the patient. In the past, belts, straps, or a cuff were used. Currently, three types of suspension are offered: 1) Shuttle lock with pin, 2) Suction, and 3) Vacuum. In the shuttle lock, a padded liner with a pin at the end is used. The pin is inserted into a shuttle lock built into the bottom of the socket. It is indicated in older individuals with an amputation and patients with reduced mobility. A suction system consists of a soft liner, a one-way valve and a sealing sleeve. Excess air is expelled through the valve by inserting the liner-covered limb into the socket and applying body weight as the subject stands. In the vacuum suspension, a pump and exhaust valve remove the air between the socket and the liner. Although vacuum systems are indicated for the most active individuals with an amputation, they are also available for older, less mobile ones. Clinical data is still limited but promising (65).

The most important prosthetic component in individuals with an above-knee amputation is the prosthetic knee; it is also the key for a successful rehabilitation and reintegration in daily life (22, 66). For the purpose of this manuscript, Blumentritt's knee classification scheme of stance control mechanisms was used (22). The English version was translated, used, and provided by Kannenberg (22). It is based on the ability to allow knee flexion during weight-bearing mimicking the eccentric muscle function of the quadriceps in lowering the body during one-legged weight-bearing: no knee flexion (locked, friction brake, and 4-bar knees); limited knee flexion (polycentric knees with at least 5 axes); and unlimited knee flexion (hydraulics). Stance phase is the gait phase that lasts from heel strike to toe off, which accounts for 60% of a single gait cycle. During the stance phase, the foot is on the ground acting as a shock absorber, mobile adapter, rigid lever, and pedestal, and the body passes over its top. The stance phase can be divided in the following subphases: initial contact, weight acceptance, mid-stance, late stance, and terminal stance. As related to stance stability, traditional mechanical prosthetic knee mechanisms are characterized by an inverse relationship between their inherent technical stability on the one side, and voluntary control and technical support of function on the other. In other words, the more stable a mechanical prosthetic knee, the less voluntary control and function it supports, and vice versa (22, 66). A locked knee prevents knee collapse during stance under all circumstances but at the cost of walking with a stiff prosthetic leg at all times. Other types of mechanical prosthetic knees-friction brake, polycentric, and hydraulic control knees offer increasing function and voluntary control, but at the cost of reducing the level of inherent technical stability and thus requiring a higher level of motor control of the patient to safely operate the prosthesis (66).

As previously mentioned, Blumentritt (22) proposed a classification of prosthetic stance control mechanisms that is based on the ability of the knee to flex in the weight bearing condition, explaining the functional capacities of the prosthetic knee and the terrains the amputee is able to negotiate with it (See Table 1).

Knee flexion during weight bearing	**No**	**Limited**	**Unlimited (yielding)**
Knee mechanism(s)	• locked knee • friction brake knee • 4-bar linkage knee	• polycentric knees with 5 or more axes of rotation • knees with bouncing adapter	• fluid control knees (mechanical or microprocessor-controlled)
Terrains supported (+) or not supported (-) for negotiation with physiological reciprocal gait	+ walking on level ground - no support of stance flexion for - shock absorption - walking on uneven ground - alternate slope and stair descent	+ walking on level ground, + stance flexion for shock absorption + walking on slightly uneven terrain + alternate descent of shallow slopes (≤5°) - no support of alternate descent of steeper slopes (>5°) and stairs	+ walking on level ground, + stance flexion for shock absorption + walking on uneven terrain + alternate descent of slopes and stairs + sitting down while loading the prosthesis (only C-Leg, C-Leg Compact, Rheo Knee, Power Knee, Genium Bionic Prosthetic Leg)

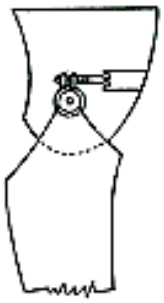
Table 1: Classification of prosthetic knee stance control mechanisms based on their ability to provide knee flexion during weight-bearing (22, 66).

Types of Stance Control Mechanisms

1. **Single-Axis Constant Friction Knee** (figure 4a). These types of knees are no longer available in North America or Europe and are mentioned in this section only as historical evidence of the evolution of knee's control mechanisms. A locked single axis knee does not need any kind of swing control as it is only unlocked manually for sitting down. The single-axis constant friction knee has a bolt connecting the socket (thigh) to the shank. The location of the bolt behind the path of the weight of the body to the floor prevents buckling when the patient is standing straight. Mechanical friction may be in the form of a simple adjustable brake, preventing the shank from swinging forward too quickly when the patient swings the artificial leg through to the next step (89). There are two major limitations to this type of prosthesis: first, stability is achieved only when the net ground reaction force passes anterior to the knee's center; without it, the knee will abruptly buckle or collapse, so to avoid stumbling, the patient must exercise great care during walking, especially on uneven surfaces (66, 89).

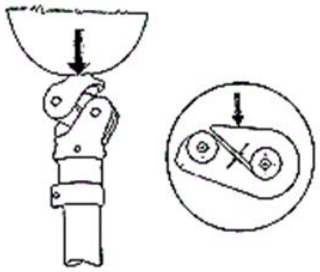
Because flexion at weight bearing is not allowed by constant friction knees, alternate descent of ramps/hills or stairs, sitting down, and walking on uneven terrain are not supported. To sit down, the prosthesis must be lifted by the patient to unload the knee and disengage the friction brake.

2. **Weight activated friction brake knees** (Figure 4b). Among knee systems, this is considered the second level of complexity. It includes two bolts, one of which pivots around the other when the patient is standing causing the weight of the body to engage a brake and prevent buckling of the knee. These types of prosthesis supports only level walking with reciprocal gait, as knee flexion is not supported when bearing weight as would be required for slope and stair descent. Therefore, these are indicated for slow-walking and very limited ambulators (66, 89).
3. **Polycentric Knees** (Figure 4c). Compared with the single-axis knee, the polycentric knee offers improved control over the above-knee prosthesis when standing and during the stance phase of walking, due to a moving center of rotation provided by mechanical linkages between the socket and shank. The linkages can project the instantaneous center of rotation posterior to the ground reaction force (weight-bearing line) and elevate it proximal, thus providing improved stability of the knee. This type of knee is indicated for patients requiring stability at heel strike**,** and either mechanical friction or fluid (pneumatic or hydraulic) resistance may provide the swing phase control (89). Another benefit of polycentric knees is the functional shortening of the calf during swing, thus resulting in increased toe clearance. Most of these knees have four points of rotation, each connected by a linkage bar, and are also referred to as 4-bar knee prosthesis (49, 66, 84). Multiaxial knees with ≥ 5 axes of rotation behave like 4-bar polycentric knees and offer the same clinical advantages such as easy swing initiation and increased toe clearance. In addition, they allow for limited knee flexion during weight-bearing for shock absorption and negotiation of shallow slopes and uneven terrain. They are indicated for mobility grade K2 (limited community) and K3 (unlimited community) ambulators who tolerate stance knee flexion (66).
4. **Hydraulic Knees** (Figure 4d). Systems vary in complexity; in the simplest prosthesis, the piston attaches to a pivot in the thigh section behind the knee bolt, and the cylinder attaches to a pivot within the shank. The resistance needed for a given walking speed is automatically provided by the oil forced through a small hole in the assembly (89). Individuals with an amputation using a hydraulic stance control knee, with good reflexes and strength can, with practice and training, learn to walk down slopes and ramps with reciprocal gait; some can even descend stairs, step over step, as the stance resistance gradually lowers them from one riser to the next. The sophisticated switching mechanisms of mechanical hydraulic prosthetic knees require both good coordination and strength. To ensure safe operation, these systems are only indicated for people with an amputation in very good physical condition (22, 66, 84).



Single-Axis
Constant Friction Knee

Figure 4a.

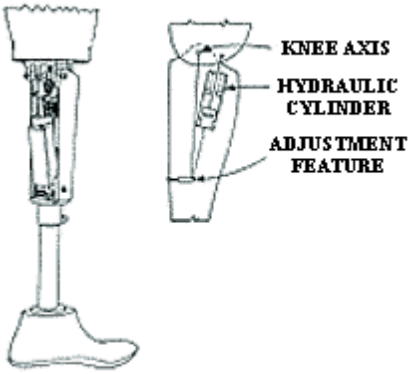


Schematic Drawing of a
Weight-Actuated Knee Brace

Figure 4b.

View of a polycentric knee.
The cosmetic cover has
been removed.

Figure 4c.



Views of a Hydraulic Knee Unit

Figure 4d.

Figure 4. Types of Swing Control Mechanisms.
©Drawings courtesy of Muilenburg Prosthetics and Orthotics, Houston, Texas (88, 89).

The swing phase of gait cycle is when the foot is no longer in contact with the ground. It begins when the foot leaves the floor and ends with heel strike of the same foot. It accounts for 40% of the gait cycle, and is the non-weight bearing phase of gait.

Swing phase control may be managed by constant friction or fluid (pneumatic or hydraulic) swing control.

1. **Constant Friction Swing Controls** are adjusted to support only one fixed cadence. When the patient attempts to walk faster, the added momentum causes the shin to swing into more flexion, forcing him or her to wait for the leg to swing through. Therefore, prostheses with constant friction swing control are suitable only for those individuals who are not capable of varying their cadence such as mobility grade K1 (household) and low to medium K2 (limited community) ambulators (22, 66).

2. **Pneumatic swing control**, pneumatic control cylinders are filled with air. Recent design enhancements have narrowed the distinction between pneumatic and hydraulic controls. Pneumatic dampers' primary functional advantage is that they aren't affected by changes in ambient temperature; therefore, the knee resistance will be the same after several hours of subzero winter activities as it is in a warm room. Pneumatic swing phase controls are suitable for individuals with an amputation who can vary their cadence but still use a limited range of walking speeds such as medium to high mobility grade K2 (limited community) and low K3 (unlimited community) ambulators (22, 66).
3. **Hydraulic swing control** is the most common variable-cadence control used clinically. These usually contain silicone oil, which creates a very high diminishing force to control the shin by restricting the flow of the hydraulic liquid. The more advanced hydraulic controls are designed in a way that the fluid becomes turbulent at higher cadences, greatly increasing the diminishing force applied to the shin. When properly aligned and adjusted, hydraulic swing phase controls allow the patient to walk at any speed, from very slow to a race-walking pace, and the knee resistance is automatically compensated. Hydraulic swing phase controls are indicated for individuals with an amputation who are able to walk with the full range of walking speeds, i.e., mobility grade K3 (unlimited community) and K4 (very active "athlete" ambulators (22, 66).

In summary, fluid swing control, whether pneumatic or hydraulic, has been shown to offer the smoothest, most nearly normal swing phase movement possible (22, 66).

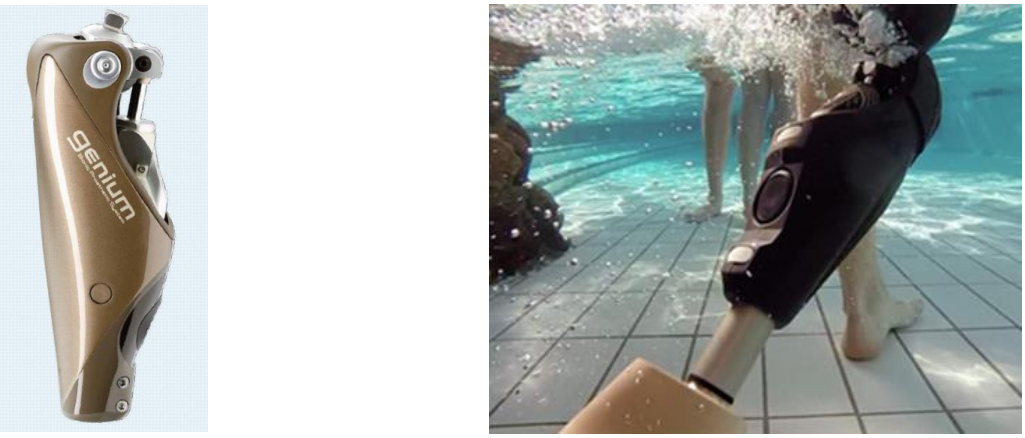


Figure 5. Left: The Genium MP Knee. Right: The Waterproof X3
©Photo courtesy of Otto Bock HealthCare. REF (95)

As a result of a collaborative effort between the Department of Defense (DOD) and Otto Bock®, a technologically advanced microprocessor prosthetic leg was designed: the Genium/X3 (65, 95). (See Figure 5). It consists of a set of 6 sensors that provide input for gait control software: knee angle, velocity and moment, axial load, shank inclination and velocity, and linear accelerations.

The benefits of Genium/X3 technology include 1) the ability for slight knee flexion (4 degrees) at heel strike which facilitates the use of knee stance flexion for shock absorption and reciprocal gait on uneven terrain, slopes, and stairs. All other knee mechanisms must be fully extended at heel strike; 2) it provides intuitive standing (i.e. the knee recognizes when the patient

stands still and locks itself to allow for full loading. Other knees have to be stabilized by active use of the residual limb; 3) it provides the amputee the ability to safely walk backward (65); and 4) it is salt-waterproof (X3 only).

Based on the above description, it appears that the hydraulic MP stance and swing control prosthesis would be the most advantageous in terms of providing the airman with the required functionality/dexterity to operate an aircraft, particularly during emergency situations when a rapid egress of the cockpit is required. However, we were unable to locate any previous studies assessing the effect of changes in the atmospheric pressure or other aviation/space environment changes on the operation and functionality of these advanced medical devices. As per current FAA regulations, pilots with prosthetic devices can be medically certified on individual basis in order to assess their ability to safely fly an airplane. There have been reported cases in which amputee pilots have been granted flying privileges after an extensive rehabilitation period and sufficient performance during the medical flight evaluation test.

FUTURE DEVELOPMENTS IN UPPER LIMB PROSTHESIS DEVICES

The use of electronics has become very common in artificial limbs. Myoelectric limbs, which control the power of the prosthetic devices by converting muscle movements to electrical signals, have become much more common. Myoelectric control makes sense for powered prosthetic components that mimic voluntary concentric muscle contractions, such as the ones used in upper-limb prosthesis for grasping, rotating the wrist, or flexing the elbow. Passive devices (e.g., lower-limb prosthesis) that mimic eccentric muscle contractions for dissipating energy, such as walking down stairs, do not currently use myoelectric control (65).

One of the current limitations of advanced upper limb prostheses devices is the cognitive burden produced by the lack of proprioceptive or tactile feedback, which forces the users to rely on visual feedback (65). To avoid the need for visual attention on the prosthesis, vibrotactile feedback must be provided. Future research is focused on electromyographic (EMG) signal processing embedded with tactile systems to provide feeling to the individuals with an amputation (103). Although this technology is in experimental stage in lower limb prosthetics, current passive MPK technology mimicking eccentric muscle functions (i.e., producing resistance against muscle elongation) for dissipating energy comes pretty close to physiological gait patterns that do not require concentric muscle action or active power generation by devices, respectively. Active control would be needed only when lower limb devices can produce enough power for mimicking concentric muscle action (i.e., muscle contraction) as for climbing stairs (65).

In a 2016 study published in Science Translational Medicine (STM) by the University of Chicago and Case Western Reserve University, neuroscientists reported that for the first time, a paralyzed human patient was able to “feel” through a robotic arm that he controlled with his brain (114). In this study, researchers implanted an electrode array in the brain, in cortical areas responsible for both hand movements and touch, providing the individual the ability to move the robotic arm and to experience the sense of touch. By testing normal subjects' ability to distinguish the magnitude of the sensations elicited when their nerves were stimulated via the implanted neural interfaces and the combination of advanced touch sensors data in robotic fingertips, using machine learning algorithms along with a better understanding on how the brain

discriminate touch, it is now possible to build neuroprosthetics that mimic natural but complex sensations of touch (114). Although it's difficult to predict how long it will take until this technology becomes commercially available (65), it is expected that this technology will need to be exposed to extreme aviation and space environments such as sudden decompression, hypobaric conditions, and microgravity environments to evaluate the functional stability of the device from an aerospace safety standpoint.

Because of the early stage of this advanced medical technology, a search of the literature did not suggest any implications of the future use of robotic limbs in the aviation and space environments. In other words, this technology has not being tested or exposed to extreme aerospace conditions; therefore, there is no reliable information available on how these devices functioned.

Brain-Computer Interfaces to Control Artificial Limbs

Foreseeable clinical applications have been envisioned by interfaces that can interpret and use brain activity to control mechanical and computer components in various fields, particularly in rehabilitative medicine. As previously mentioned, systems that use recorded neuronal activity to perform specific and complex tasks are referred to as BMIs, brain-computer interfaces (BCIs), or neuromotor prostheses (NMP). Neural interface system (NIS) is a term that may be used to refer to any BCI, BMI, or NMP (103). The recorded neuronal activity may be gathered by either non-invasive or invasive techniques. One of the most common invasive techniques used to record neuronal activity are multielectrode arrays (MEAs) (103).

Neural prosthetic implants or neuroprosthetics are based on the following principles: 1) operation through closed-loop BCI or BMI systems, with channels for the relaying of tactile information; 2) consistent neural interfaces; 3) the ability to adapt to changes in neuronal populations; and 4) tolerance to unfriendly physical brain and real-life environmental factors (104). As previously mentioned, inflammation initiated by non-biocompatible materials may eventually lead to scar tissue formation followed by glial response and neuronal death (103).

Current research in neuroengineering is growing rapidly; however, potential implications of future wearable, robotic arms on aviation safety are still unknown. Improvement in the function and control of artificial arms is a formidable challenge to individuals with a proximal amputation (131). Although myoelectric control is the most common method in use, it has its own limitations. For example, a proximal amputee can control only one joint or device function at a time. Moreover, this control method is not intuitive, and therefore it demands conscious effort (131) including visual attention, which could result in pilot's distraction during critical operational tasks.

As of today, no studies have been published on the topic of the use of myoelectric prosthetics in pilots, either commercial or private. In addition, myoelectric prosthetics devices have not been tested either in extreme aviation environments such as sudden decompression, hypobaric conditions, or in a microgravity environment. Therefore, little is known regarding the behavior of such devices under extreme aviation and space conditions. Nevertheless, exposure of these devices to hypobaric environments, which could be accomplished by simulating an unpressurized aircraft flight or a rapid decompression event in a pressurized aircraft to evaluate the functional stability of the device, is expected.

Targeted Muscle Reinnervation (TMR) for Myoelectric Control of Artificial Arms

Targeted Muscle Reinnervation (TMR) is an innovative neural-machine interface developed to improve myoelectric prosthesis control, particularly for upper-limb prostheses (69, 131). Myoelectric prostheses control motorized arm joints by using electromyogram (EMG) signals (i.e., the electrical signals generated during muscle contraction) from residual limb muscles. The TMR surgical technique developed by Kuiken et al. (69) at the Rehabilitation Institute of Chicago, improves artificial arms function by transferring the residual amputated arm nerves from the residual limb to the pectoralis major, which is surgically denervated before the nerve transfer is performed. In other words, with TMR, remaining arm nerves are transferred to residual chest or upper-arm muscles (69). After reinnervation and nerve growth, the target muscles act as biological amplifiers for motor commands and may generate electromyogram (EMG) signals on the skin's surface that represent a diversified spectrum of distinct intended movements that can be measured and utilized to control the corresponding components and functions of prosthetic arms. A recent study showed that TMR patients with the virtual prosthetic arm were capable of performing ten different motions of the hand, wrist, and elbow repeatedly, confirming the ability of TMR (combined with a pattern-recognition algorithm) to control advanced experimental upper-limb prostheses. The study acknowledges that further improvements, including a reduction in the size and weight of these advanced prostheses and an increase in their robustness, are needed (69). The biggest benefit of TMR is that it allows for simultaneous control of several prosthetic devices (e.g. elbow, wrist, hand) at the same time (65).

As previously mentioned, thus far robotic limbs and other advanced prosthetic devices have not been tested in either extreme aviation environments or microgravity. Although potential causes of malfunctioning in such environments may be primarily related to rapid/explosive decompression and exposure to microgravity, it would be necessary to conduct further tests using an altitude chamber and microgravity environments to properly address those issues. A particular area of concern includes devices held in place by a vacuum apparatus, which serve to eliminate dead space between the residual limb and prosthesis, as well as to provide a more secure attachment. If exposed to hypobaric environments such as flying an unpressurized aircraft in high altitude, these devices could potentially lose their vacuum and become dislodged or even fall off during critical phases of flight.

Current Limitations of TMR

Although the feasibility of this new neural machine interface has been demonstrated, still some limitations exist, for example, the application of a large number of electrodes, especially in lower limbs. Currently, there are no clinical applications of TMR on lower limb devices. Eventually, it will be applicable in the future when lower limb devices can produce enough power to mimic concentric muscle functions as for walking uphill and climbing stairs. In passive devices, such as current MP controlled lower limb prosthetic devices, this kind of control will likely not produce significant additional benefits (65). The biggest limitations of TMR can be summarized as follows: 1) age of the patient, as reinnervation works better in younger patients; 2) need for intense physical training; and 3) myosignal detection areas may migrate over time due to growth of the nerves in the muscle. Additional challenging factors with surface EMG readings, such as females' breast tissue or signals from deeper muscle regions, still need to be addressed. These particular drawbacks were overcome by applying implantable myoelectric sensors systems (IMES), which allow bypassing the skin interface and reducing subcutaneous fat

misreading, thereby improving signal content discrimination. As a result, more consistency and robust classification of algorithms were achieved (131). Unfortunately, IMES is still in experimental phase and therefore not commercially available. Other limitations include exploring acceptable locations and dealing with the challenges of recording EMG signals in a dynamic environment. Previous research suggests that after the amputation, the motor cortex dedicated to the lost limb and subsequent motor control pathways are permanently attenuated, which means the patient will require significant training to be able to evoke complex motor commands (131).

As of today, it is unknown if upper-limb amputee pilots are using technology involving TMR for real-time myoelectric control of multifunction artificial arms. Although the TMR prosthetics provides simultaneous multi-joint operation which could potentially decrease the time needed to complete a given task within an aircraft, current models are still relatively bulky and would require further testing in dynamic and extreme environments. Nevertheless, the aeromedical certification process approach should be similar to the one discussed later in this manuscript for advanced prosthetic devices applied to lower-limb amputee applicants.

SUMMARY OF NEUROPROSTHETICS

Neuroprosthetics' technology has opened the door to a new era of collaborative clinical research that is proving to be effective not only in providing an intuitive control over advanced prosthetic limbs but can also help on beneficial movement and communication devices in patients with paralysis (24). Similarly, BMIs are considered extremely useful platforms to better understand complex neural mechanisms and the implementation of rehabilitation therapies. Additional work is ongoing to determine how to fully restore sensory information. Future research is needed to improve patients' acceptance, integration, and use of neuroprostheses by repairing the sensorimotor loop (99). Although most of this technology is still in experimental stages and clinically unavailable, promising and encouraging results are suggesting a bright future for this type of technology.

Neuroprosthetics is a collaborative and multidisciplinary field integrated by neurologists, neurosurgeons, neuroscientists, engineers, computer scientists, mathematicians, and other researchers. Their main focus is to help patients with neurologic disease, injury, or limb loss to restore the communication, mobility, and independence by the use of advanced technology. BrainGate, a neurotechnology company, has shown that by implanting an array of micro-electrodes into the brain, "the neural signals associated with the intent to move a limb can be decoded by a computer in real-time and used to operate external devices" (24). The company cautions that this is still an investigational device or a research tool, limited by federal law to investigational use only. Nevertheless, BrainGate, an investigational system, has "allowed people with spinal cord injury, brainstem stroke, and ALS to control a computer cursor simply by thinking about the movement of their own paralyzed hand and arm." Previous clinical research has shown that this technology can provide intuitive control over advanced prosthetic limbs and give people with paralysis more control over the powerful assistive movement and communication devices developed to augment their capabilities (24). For example, quadriplegic patients using MEA were able to use electronic devices to "open emails; turn lights on or off; operate a television even during a conversation; perform basic actions with a robotic arm; and open and close a prosthetic hand" (25, 39, 102, 115).

Restoration of full-body mobility is nearer to becoming a commercially available reality through the use of next-generation cortical neuroprosthetic devices, specifically, enabled by the implantation of MEAs in multiple cortical areas. Wearable, whole-body, robotic exoskeletons may become the first clinically useful, safe, and reliable neuroprosthetic devices, thanks to anticipated advances. Some additional work is needed to address the biocompatibility of implanted systems, but a possible solution seems to be the use of novel arrangements, materials, and shapes. Invasive MEAs have shown a promising future for measuring neural activity, as they have a far higher resolution than anything else currently available. Next-generation invasive NIS devices will need to be fully and easily implantable, and made as small as possible. This will then likely lead to the eventual development of non-invasive NIS's, which will be further miniaturized to increase mobility and capability of automated implantation, eliminating the need for a skilled technician (102).

Along with the technological advances, some concerns related to the legal implications of neural implants have been raised. For example, some futurists are envisioning the use of advanced technology to enhance human brain functions in a way that would allow the development of brain implants with the "speed, power, and memory to replicate the functionality of the entire human brain" (128). Ray Kurzweil, a prominent futurist, has predicted that in 50 years from now, humans will be able to transfer both their memories and thought processes to computers, in a way that their thinking can be separated from their organic brains. Because many of the same methods will be used by brain enhancement technology and artificial intelligence (AI), Kurzweil predicted that "by the end of this century, humans and robots using strong artificial intelligence (AI) will be functionally indistinguishable" (128). As a result of the fast-growing advances of BCI and neuroprosthetics, potential criminal threats are expected. For example, hackers of pacemakers and other medical devices may be willing to attack advanced prosthetics, including wireless devices, prosthetic limb controls, or deep brain stimulators, which could result in the immediate death or serious injury of the user or those interacting with them (128). Because providers of brain implants and neuroprosthetics may have access to unique private information stored in the human brain, protecting such sensitive information in terms of data security, storage, disposal, and privacy policies will pose a significant challenge. As result, it is expected that as neural devices become more common, lawyers will need to learn more about technology, help legislators and regulators to develop and implement policies, and determine if new laws and methods to deal with users of neural devices will be needed (128).

There are some social justice and ethical issues in neuroprosthetics that have begun to be addressed. Along those lines, some guidelines have been established to implement fair selection criteria in providing patients access to neuroprosthetics research and balance the best interests of patients with technological innovation. It has been reported that the likely benefit of research and current and future therapeutic applications of neuroprosthetics can be ethically justified because it outweighs the risk involved. The potential neurogenerative benefits justify the ethical obligation to conduct this kind of research, however, there is no doubt that additional novel ethical and philosophical questions regarding individuals and their brains will continue to emerge from advances in neuroscience in the future (48).

AEROMEDICAL CERTIFICATION IN AMPUTEE PILOTS – THE PAST

It has been reported that the first bilateral lower extremity amputation case involving a pilot and published in the literature was the WWII RAF Captain Douglas Bader. In 1931,

while attempting some aerobatics maneuvers, Bader crashed and lost both legs. His right leg was amputated above the knee while his left was amputated below the knee (32). He eventually recovered, went back for flight training, passed his check flights, and requested to be reactivated as a pilot. At the time, no regulations applicable to military amputee pilots were available; therefore, he was retired against his will for medical reasons. After the Second World War began in 1939, Bader returned to the RAF and was accepted as a pilot. He successfully participated in two battles: France and Britain in 1940, shooting down more than twenty enemy aircrafts (121).

In 1971, Reid and Baker (101) published a case-review of six army aviators with below-knee amputation who had been returned to flight status. They established some guidelines to be used when considering lower-extremity aviator with an amputation for retention on flight status.

The guidelines focused on 1) service needs; 2) type of lower-extremity amputation and proper prosthetic fit; 3) age, motivation, career potential, and number of hours flown at time of amputation; and 4) time in service at the time of injury (101). Although the study offered practical recommendations regarding the parameters to be considered for amputee military aviators, the methodology involved only information obtained from questionnaires without addressing the specific type of prosthesis used. Also, at the time of the study, no aviator with an above-knee amputation had been returned to flight duties.

In the civilian sector, one of the first pilots with an amputation to be medically certified by the FAA was Jerry D. Leavy in 1957. Mr. Leavy was a double arm amputee at the age of 12 who inspired other individuals with an amputation in the aviation industry. Mr. Leavy suffered amputations after several weeks of battling gas gangrene, following complications of multiple compound fractures of both extremities after falling from a tree (74). In the late 1950s and 1960s Mr. Leavy was internationally recognized for his demonstrations using prosthetic devices to help people with an amputation learn to properly use them. In 1967, he was certified as a pilot instructor and flew his company's twin engine airplane throughout several South American countries on a 37-day trip to demonstrate the "newly" designed prosthetic devices. In 1977, he published his inspirational book, *It can be done: An upper extremity amputee training handbook* (74).

Another bilateral amputee case in the U.S. involved a 47-year-old male pilot, with 20,000 hours of flight time, who suffered traumatic amputation of both hands as a result of a high-speed car accident in 1993. He suffered a complete traumatic amputation at the wrist of the left upper extremity and a near total amputation of the right upper distal forearm with major neurovascular injury. He also had a head injury with temporary cognitive deficit in memory, reasoning, and judgment (83). Three weeks after the accident, he was transferred to a rehabilitation facility where he received physical therapy and speech therapy and a week later he was fitted with an Otto Bock® myoelectrically-controlled upper (right and left) extremity prosthesis (95). In 1995, he underwent a special medical flight test, which was successfully completed. FAA's previous aeromedical experience was limited to individuals with unilateral hand amputation with a single prosthetic replacement. In this particular case, in addition to the aeromedical concerns related to the pilot's cognitive deficits which were evaluated with favorable results; the FAA was also focused on 1) the pilot's ability to

manually operate an aircraft with his myoelectrically-controlled bilateral prostheses, and 2) the prosthesis functionality after the exposure to hypobaric environments and rapid decompression. All of these concerns were resolved favorably during the tests performed at the FAA's altitude chamber in Oklahoma City. Finally, other factors considered by the FAA to issue a third-class medical certificate with a Statement of Demonstrated Ability (SODA) included 1) flying experience; 2) his motivation to continue flying; 3) his successful completion of the neuropsychological, medical flight, and altitude chamber tests, respectively; and 4) his compliance with all other applicable medical certification standards (83). Although these factors were considered more than two decades ago, they are in line with recently recommended aeromedical assessment of applicants with musculoskeletal limitations, including individuals with an amputation. Unfortunately, as of today, no studies have been published indicating the estimated number of pilots with an amputation using advanced prosthetic devices. In addition, there is no data available regarding pilots using prosthetic limbs who have had an aircraft accident.

A comprehensive review of three aviators from the Israeli Air Force who had trans-femoral amputation, received an artificial limb (not an advanced prosthesis), and returned to active flying duty was published in 2005 (50). After following up the aviators for 5, 17, and 25 years, the authors did not find any functional disability in the cockpit related to the residual limb or the prosthetic device. These aviators were fitted with a side rotator hinge in the prosthesis (rotation adapter), which provided more flexibility of the prosthesis and reduced the time of getting in and out of the cockpit, particularly when the entrance or evacuation needed to be done quickly without affecting the device's integrity. The importance of this study is that, as of today, it is one of the few published cases of pilots returning to flying duties following an above-the-knee amputation. Nevertheless, the authors recommended that because of the lack of evidence supporting the return to high-performance aircrafts of above-knee amputee pilots in terms of the effect of significant G forces on the residual limb's blood flow and fluid shifting they should be limited to flight environments such as transport, observation, and helicopter flights (50).

Another study, Dreyfuss et al. (7), after reviewing 70 amputee Israeli Air Force Pilots, concluded that 59 (84%) of these pilots were able to return to flying, although only 30 of them (59%) returned to fly fighters and the rest were returned to another type of aircraft. They also concluded that, in order to determine the long-term success of military aviators returning to flying, a two-year evaluation period was sufficient.

In the U.S., few cases of military amputee pilots who were able to get back to the cockpit have been published. U.S. Air Force Lt. Col. Andrew Lourake's successful history is one of those few cases. In fact, he is the first pilot in the history of the U.S. Department of Defense with an above the knee amputation to be able to return to flying duties; he also holds an FAA medical certificate to fly (112). He was injured in a motorcycle accident in 1998. Three years after the crash, he had a left above-knee transfemoral amputation following a severe infection. He was determined to fly again and six years later he was able to do so using an advanced prosthetic device. After enduring 18 surgeries, long periods of side-effects from his medications, and more than 500 hours of physical therapy, he became the first U.S. military aviator to be fitted with a MP-controlled knee C-Leg®. Following a series of medical and mobility tests, and several hours of flight simulator testing he was medically cleared in 2004 (70). Those tests were conducted in

a week and included the following: On Day 1, medical and psychological evaluations were conducted; including strength tests to determine how much weight his prosthesis could press (a minimum of 130 pounds to be able to safely operate a C-130 rudder pedal was the set standard); Day 2: Cardio activity and stress test; Day 3: Egress testing in a Lear jet, including a total of six emergency evacuations, three from left seat and three from right seat, from being fully strapped in, to complete egress with both feet fully on the ground outside the aircraft. The evacuation goal criteria for satisfactory completion was set at 1 minute, he did it in an average of 18 seconds. (Note: There is no set egress standard test or time limit either on Air Force personnel nor for civilian pilots); Day 4: Taxiing an airplane and using the brakes, right and left rudders in different scenarios; and Day 5: Strength and coordination testing, similar to the one conducted on day 4, except that this time the test was conducted using equipment designed for measuring and graphing different pressures, forces, and coordination of basic to complex rudder, brake and control inputs (79).

Colonel Lourake flew his first operational mission in a C-20 aircraft (Gulfstream III) as a Co-Pilot (78) and after four more practice flights and an evaluation flight, he returned to full flight status with no restrictions as the first above-knee amputee in the Department of Defense, to the 99th Airlift Squadron. This is the Presidential airlift support squadron that transports high-level dignitaries including the First Lady, the Vice President, Secretary of Defense, and others around the globe (79, 116). Lt. Colonel (Ret) Lourake retired from active duty and is currently enjoying his family, flying his own Comanche airplane in Florida, and working as the Current Veteran Outreach Director, for Operation Second Chance (www.operationsecondchance.org). Their mission statement is: "We are patriotic citizens committed to serving our wounded, injured and ill Veterans. We support Veterans and their families by building relationships and identifying and supporting immediate needs and interests. We are dedicated to promoting public awareness of the many sacrifices made by our Armed Forces." Until recently, he served as Director of Veteran Outreach for the Veteran Airlift Command (VAC), a nonprofit organization that provides free air transportation to post 9/11 soldiers wounded in combat and their families for medical and humanitarian purposes through a national network of volunteer aircraft owners and pilots (117). He also serves as an inspirational encouragement to wounded soldiers, civilians and amputee pilots worldwide to pursue their dreams to return to flight activities and to fully recover from their traumatic experience (112).

Figure 9. Lt. Col. Andrew Lourake sits in an Air Force C-20 showing his C-Leg®. (U.S. Air Force photo by BOBBY JONES). Source: REF (70).

Another military aviator, Capt. Ryan McGuire, now a 4th Airlift Squadron pilot, lost his right leg in a boating accident in 2009 when he was a young Air Force lieutenant (62). The accident occurred during McGuire's training as a pilot. Six weeks after the accident, his leg was amputated below the knee. After detailed medical evaluations, rehabilitation and family and peer support, he was able to prove to the board that he was functionally capable of continuing with his pilot training and received his waiver to continue flying. In 2011, McGuire completed his pilot training and finished C-17 Globemaster III qualification training. Since then, he has been flying medical evacuation missions (62).

Another example is Capt. Christy Wise, who became the first female Air Force pilot amputee and returned to flight after losing her right leg on a boating accident on April 11, 2015. After spending fifteen months in rehabilitation, including learning to walk and run again, she was able to make her first flight as an HC-130J pilot with the 71st Rescue Squadron at Moody Air Force Base, GA, on July 22, 2016 (98).

Figure 10. Left: Air Force Capt. Christy Wise checking the wing of an HC-130J Combat King II.

Right: Air Force Capt. Christy Wise, left piloting an HC-130J with the 71st Rescue Squadron at Moody Air Force Base, GA.

Photo Credit: Ryan Callaghan/U.S. Air Force, July 22, 2016. Source: Defense Video Imagery Distribution System (DVIDS).

Other remarkable examples of U.S. military amputee pilots who were able to return to fly duties are summarized below:

Navy Lt. Juan Alvarez, MH-53J Pave Low pilot who, in 1996, lost his left leg after a helicopter crash in the Ecuadorian jungle. He sustained a below-the-knee amputation and after being retrained in survival and water survival to prove that he was able to run around, swim, and escape from a helo under water he was authorized to fly again. More than a year later, he was transferred to the Air Force Special Operations Command, AFSOC (57). He currently uses an advanced prosthetic limb.

Marine Lt. Andrew Kinard lost both legs as a result of stepping on an improvised explosive device in Iraq in 2006 during a routine foot patrol. After 75 surgeries and several months of rehabilitation, he decided to pursue his dream of being a certified sport pilot and successfully completed his training in 2013. Kinard was the first recipient of the AOPA – Able Flight Scholarship, which sponsored his six weeks of intense flight and ground school training (3, 45). He is currently a sport pilot and, although he uses MPKs to move around, he uses hand-controlled pedals while flying his airplane.

Another case of an above-knee amputee is the C-130 pilot Major Alan Brown, who lost his leg in a hunting accident in 1999. It took him 7 years to prove to the National Guard that he was able to fly again with his MPK prosthetic device, and since then he has been deployed several times to missions in Afghanistan (97).

Another below-knee amputee pilot is the U.S. military veteran, Ryan Kelly, a current and successful medevac helicopter pilot in Texas (14).

In summary, as of today, there are at least 12 amputee pilots in the US using advanced prosthetic devices: 9 airmen are either active in the US military service or retired, 2 are commercial pilots flying B777 and DC-10, and one is a GA pilot flying a Cessna 172 (79).

AEROMEDICAL ASSESSMENT AND PROCEDURES IN APPLICANTS WITH A LOSS OF LIMB/FUNCTION – THE PRESENT

From an aeromedical certification standpoint, as long as an applicant is able to demonstrate functionally capable performance in his or her flight duties, there is no reason to deny their application. However, due to the advancement in limb prosthesis technology in particular, the increasing use of micro-processors, electronic sensors, blue-tooth technology, and lithium batteries in modern prosthetic devices, some valid aviation safety concerns about the potential interference with cockpit avionics and electronic equipment have been raised. In addition, in case of an emergency evacuation, the pilot using the prosthetic device should be able to evacuate the airplane in a safe and timely manner. Medical flight tests can assist in the determination of whether or not flight safety is affected when compared to pilots who do not require the use of a prosthetic device.
The aeromedical assessment of an applicant's musculoskeletal fitness, including individuals with an amputation, can be made using the following principles (61):

1. **Mobility**: Adequate joint mobility is required, allowing the pilot, or other crewmember, to reach all areas of the cockpit and perform an adequate lookout;
2. **Strength**: The ability to demonstrate adequate and sustained limb strength without undue fatigability is required, allowing sustained force to be applied to controls in routine and emergency situations, such as asymmetric engine failure or rapid operation of emergency escape systems;
3. **Dexterity**: Movements must be skilled and quick, and of adequate range of motion and strength;
4. **Tendency for sudden change in function**: The presence of conditions that might cause sudden and significant effects on physical performance, such as a tendency to shoulder dislocation or locking of the knee, must be assessed. If they are ongoing, untreated and likely to occur in the flight environment, and if the consequence of the occurrence would, or could, be serious, then the applicant is not fit to perform the task; and
5. **Pain**: The presence of conditions such as back and neck pain, which might cause gradually increasing and painful distraction from the primary tasks, need assessment. Pain might also be referred to the limbs and provoked by flight duties where there may be no opportunity to gain relief by simple measures such as a change in position or stretching.

As of today, few cases have been published involving civilian pilots returning to flight after losing a limb, particularly an above-knee amputation, in both commercial and general aviation.

The FAA began issuing medical certificates to amputee pilots in the late 1920's. Since then, important factors to be considered regarding aeromedical certification included 1) the pilot's attitude toward the loss of a limb, 2) the nature of the loss (static or progressive), 3) successful completion of a medical flight test to demonstrate operational performance capability, 4) the prosthetic device's functional capability, and 5) the potential requirement to make minor modifications to the controls of the aircraft (86).

After conducting a comprehensive scientific literature review on the FAA Aeromedical Certification Division procedures applicable to pilots with advanced neuro-prosthetic devices, Mahmoud and Ricaurte (82) summarized some of the relevant potential aviation safety concerns of current robotic prosthesis as follows: 1) the risk of avionics interference from the wireless and blue-tooth technology controls integrated to some prosthetics; 2) the risk of malfunction or failure of the electric actuators, hydraulics fluids, and microprocessors in case of a sudden decompression; and 3) safety hazards of its rechargeable lithium batteries. It has been also reported that for those prosthetic sockets that use vacuum suspension in which the prosthesis is held in place by creating a partial vacuum between the residual limb and the socket, functional stability could be affected during exposure to hypobaric environment (e.g., flying an unpressurized aircraft or a rapid decompression in a pressurized aircraft). As a result, the trapped air between the limb residual limb and the prosthesis could expand; losing the partial vacuum and the prosthesis could become very unstable. This is particularly true for mechanical pumps that require walking to power the pumps and produce the vacuum. However, for electronic pumps, as they are designed to work independently of physical activity, they may be able to compensate for the loss of air pressure. Nevertheless, this condition has never been tested or studied (65, 105).

The Office of Aerospace Medicine (OAM) Guidelines for evaluating airman qualifications, Chapter 10, Musculoskeletal, states: "In the case of any disease or injury resulting in significant restriction of range of motion or motor deficit, consideration for certification may require a Medical Flight Test (MFT) to determine eligibility for a Statement of Demonstrated Ability (SODA). This procedure should be coordinated through the appropriate Regional Flight Surgeon, or AAM- 300 and the appropriate Flight Standards District Office (FSDO). A medical certificate should not be issued to individuals whose condition is progressive with significant adverse changes or with variable symptoms such as fluctuating pain or episodic motor weakness (44)."

Special Medical Flight Test (SMFT) is a process "which may lead to the issuance of medical certificates under Title 14 of the Code of Federa1 Regulations (14 CFR) part 67, § 67.401; frequently required for applicants who do not meet certain medical standards. Such testing is conducted solely by aviation safety inspectors (ASI) and may be conducted only after issuance of a letter of authorization (LOA). The LOA for an airman who has requested a special medical test must be issued by the Federal Air Surgeon; the Manager, Aerospace Medical Certification Division (AAM-300); or by a Regional Flight Surgeon. Operating limitations on pilot certificates issued to pilots with physical deficiencies may be added or removed as a result of the special medical flight test findings" (44).

Volume 5 Airman Certification, Chapter 8, Section H. Operating limitations Numeral 4) states, "If a pilot is returning to flying after receiving a disabling injury, such as a loss of limb or an injury to a lower extremity, it may be necessary for the pilot to re-demonstrate proficiency for each privilege authorized. Any rating not demonstrated that the inspector determines to be necessary must bear the limitation, "NOT VALID," until such time when competency in that category and class is demonstrated (44)." This affords the applicant an opportunity to demonstrate his/her ability to control the aircraft despite the handicap. The FAA inspector prepares a written report and indicates whether there is a safety problem. A medical certificate and statement of demonstrated ability (SODA) may be provided to the airman from the Aeromedical Certification Division/Regional Flight Surgeon's office "if the MFT is successful

and the airman is otherwise qualified" (35, 44). In addition, "if an applicant fails the certification portion of a combined test (special medical test in conjunction with the usual practical test for a pilot certificate) but passes the medical portion, any retest may be conducted by an ASI or a designated pilot examiner (DPE), except where the medical portion is dependent upon the demonstration of piloting skills in which case the decision to retest must be made in consultation with the Office of Aerospace Medicine" (44).

In summary, in the case of amputee pilots, the role of an ASI would be to observe and evaluate 1) the pilot's ability to reach and effectively operate all controls as well as any compensatory body movement or maneuver; 2) the pilot's ability to perform emergency procedures; 3) whether or not the pilot using a prosthetic limb is able to properly reach and operate the controls; and 4) whether the pilot's prosthetic limb warrants any restriction to a specific make and model of aircraft in which the medical flight test was conducted, or to aircraft modified with special equipment or control arrangements.

MEDICAL ELEGIBILITY AND ROLE OF THE AVIATION MEDICAL EXAMINERS (AMEs) IN AIRMEN WITH LIMB LOSS

General guidelines are summarized as follows: 1) the AME must address the underlying etiology of the limb loss for all amputee applicants. This involves a thorough medical history to determine whether it is congenital or acquired. Certain medical conditions such as diabetes or malignancy require further investigation; 2) the AME should address the psychological adaptation of the aviator to the prosthetic device; and 3) as per Title 14 of the Code of Federal Regulations (CFR) Guide for Aviation Medical Examiners Decision Considerations - Aerospace Medical Dispositions, Item 42 (Upper and Lower Extremities), the AME must defer all amputee applicants to the FAA Aerospace Medical Certification Division (AMCD) or to the Regional Flight Surgeon (RFS).

Required documentation to determine medical eligibility includes 1) all pertinent medical records (hospitalizations, surgeries, and rehabilitative services); 2) a current status report describing functional status such as degree of strength, range of motion, pain, medications (including adverse effects), and any other reports regarding associated medical conditions; 3) in case of advanced medical prosthesis, the AME must indicate the type of the prosthetic device and the appropriate fitness; and 4) as previously explained, according to the special medical flight test (SMFT) guidelines, the airman must demonstrate competency with the safe operation of an aircraft in routine and emergency circumstances with this handicap; although this does not include emergency egress, in practice this competency would be assessed by an ASI in a SMFT.

Finally, the guide for AMEs establishes that "when prostheses are used or additional control devices are installed in an aircraft to assist the amputee, those found qualified by special certification procedures will have their certificates limited to require that the device(s) (and, if necessary, even the specific aircraft) must always be used when exercising the privileges of the airman certificate" (35).

Once a SODA certificate is issued, it does not need to be modified or renewed unless the purpose for which it was issued has changed. Therefore, if an airman requires a new type of prosthesis, this might require a new SMFT and subsequently a new SODA (43).

If the applicant seeking medical certification already has a SODA based on an amputation, the AME may issue the medical certificate, provided there are no changes concerning the amputation or the device.

Again, from an aviation safety perspective it is expected that amputee pilots must maintain smooth neuro-musculoskeletal coordination of their prostheses' movements through a designated range of motion, have adequate dexterity and mobility, and demonstrate competency to operate an aircraft safely in routine and emergency situations. The prosthesis must also easily fit in the cockpit and must function properly at high altitude and must remain in place during the flight. However, in Chapter 8: Conduct A Special Medical Test—Title 14 CFR Part 67, Section 1 Issuance of a Medical Certificate and/or a Statement of Demonstrated Ability, or Letter of Evidence, specific situations such as "emergency egress" are not considered. Nevertheless, the inspector who conducts the test is responsible to ensure that on the basis of the MFT, necessary restrictions are placed on the airman certificate for safety purposes. Finally, the AME should be alerted of phantom limb syndrome, local residual limb pain, and how the prosthetic device fits the airman physically and emotionally. A pilot's motivation to return to flight can serve as a surrogate for aeromedical compliance that would help with the re-certification process and ultimately evaluate potential risk factors that could affect aviation safety.

Even after a rigorous aeromedical certification process, prosthetic failures may still occur. For example, an unusual incident was reported in 2014 when a 46-year-old commercial pilot lost control of his aircraft during landing, under dark and windy conditions, after his lower left prosthetic arm fell off. The incident report noted that his prosthetic limb became detached from the controls during "flare maneuver," the last stage of landing before touchdown. Fortunately, the pilot was able to use his right hand to regain control with power still applied (and possibly a gust affecting the aircraft), and managed to make a "heavy" but safe landing. No injuries were reported. An internal investigation resulted in the airline implementation of additional and rigorous series of prosthesis "malfunction" safety checks, to avoid this type of incident in the future (15, 16).

AEROMEDICAL CERTIFICATION APPROACH IN ADVANCED MEDICAL TECHNOLOGIES – BACK TO THE FUTURE

In general, the implications of currently available advanced medical technologies, including advanced prosthetic devices on aerospace safety, still remain unknown.

In terms of aeromedical certification procedures, the final decision to issue a medical certificate to an applicant who wears an advanced medical device will need to be made on a case-by-case basis.

CFR Title 14: Aeronautics and Space, Part §91.21 lists certain medical equipment and portable devices currently allowed to be used in aircraft including hearing aids, heart pacemakers, electric shavers, and any other portable electronic device that the operator of the aircraft has determined will not cause interference with the navigation or communication system of the aircraft on which it is to be used. FAA Advisory Circular AC No: 91-21,1B identifies "Medical-Portable Electronic Devices" (M-PED) such as automated external defibrillators and portable oxygen concentrators but does not mention advanced computerized prosthetic devices such as microprocessor knees or robotic arms (70). In fact, most advanced neuroprosthetic

devices have not been fully tested in the flight environment. Full testing to determine the functional stability and fitness of these devices for use in extreme flight conditions needs to occur to assess the potential of sustaining or even causing damage when used in these environments. It is also not known if the microchip and EMG technologies will maintain adequate operation when the pilot tries to perform routine or emergency flight duties or emergency evacuation (96).

Another area of concern requiring further research on advanced prosthetic devices is electromagnetic interference (EMI) which negatively affects the functionality of electronic devices and the device itself, which could adversely impact the operation of today's aircraft and aerospace vehicles. In fact, few studies reviewing the most common sources of electromagnetic interference (EMI) with cochlear implants in particular, as well as a detailed description of the mechanisms of electromagnetic interaction with CI, have been published. Some examples of frequent sources of EMI in everyday activities are mobile phones, electronic article surveillance systems (EAS), and metal detectors, which may affect the CI speech processor's operation and cause sound distortions (113). In addition, electrostatic discharge created by removing clothes over the head or by playing on plastic slides may cause serious damage to CI components or even a program corruption in the CI speech processor. The latter may pose a risk in case of an airplane evacuation slide. The most investigated EM interaction with CI is the magnetic resonance imaging (MRI) because of its serious effects both on the patient and on the implant. Therefore, MRI is contraindicated for patients with a CI except when the implant is designed for MRI compatibility and safety. Other medical treatments described as sources of EMI with CI are therapeutic ionizing radiation, electrosurgery, diathermy, neurostimulation, and electroconvulsive therapy. Finally, the authors concluded that more research will be needed to better understand EMI with CI (113).

One of the few studies conducted on the topic of electromagnetic compatibility between an aircraft's cockpit instruments and the use of an advanced implanted medical prosthetic by a crewmember was published by Araujo Caldeira et al. (12). They tested all navigation equipment and security instruments of an Embraer 120 aircraft on the ground, with the engines running, with a bilateral CI user sitting in the copilot's seat. During the test, no effect of the CI on any navigation equipment was found. At the same time, the CI user did not report any discomfort, hearing problem, headache or any other neurological symptom during or after the test. They concluded that the CI did not cause any interference in the tested aircraft and navigation equipment that could threaten flight safety. Also, no interference in the normal functioning of the CI due to the cockpit instruments of the aircraft was found.

Otto Bock®, one of the industry leaders in advanced prosthetics technology, introduced the C-Leg in the U.S. in 1999, two years after it was introduced in Europe and Canada. Since then, more than 60,000 units have been sold worldwide, most of them in the U.S. (95). Although Otto Bock's® MPKs have been tested in extreme temperatures and humidity levels using a climate chamber, the devices have not been tested in extreme aviation environments such as sudden decompression, hypobaric conditions, or in a microgravity environment. In a small number of cases, there is evidence of interference with the MPK's program functions caused by high level magnetic fields; however, so far no interference has been reported related to the MPK's Bluetooth capabilities. In addition, no safety issues have been reported related to the lithium battery component of the device (41, 65).

Current prosthetic technology has already provided a benefit by allowing several amputee pilots to continue or return to flight activities. Meanwhile, ongoing advanced technological improvements in upper- and lower-limb prostheses, i.e., more advanced MP prosthetic legs and robotic limbs, will continue to evolve and present unique challenges to aeromedical certification.

In summary, additional research is needed to identify the operational results of using advanced medical devices during human exposure to extreme environments such as aviation and space flights. A better understanding of the performance and risks of advanced medical technologies will be required among aerospace medicine providers involved in the aeromedical certification process of pilots, space crew, and the medical screening of space flight participants. Similarly, additional knowledge will be required for those tasked with the investigation of future aviation and aerospace vehicle accidents such as crash investigators, engineers, forensic pathologists, and coroners involved in the post-mortem analysis of vehicle damage, injury causation, and fatalities resulting from those accidents (10).

RECOMMENDATIONS

It is expected that more advanced neuroprosthetics, microprocessor prosthetic legs, and robotic limbs will be commercially available for the use of both military and civilian aviators in the near future. This will present new challenges to FAA's waiver-granting procedures.

The AMCD's current approach to waiver procedures in the case of individuals with an amputation is the same for both traditional limb prostheses and technologically advanced neuroprostheses, and is evaluated on a case by case basis (81). The FAA continues to work to better understand the impact of advanced prosthetics devices on flight safety. In order to track and mitigate the risks posed by the predicted increase in the number of devices and advanced technologies in the aviation and aerospace environment in the near future, it is highly recommended that AMCD start assigning specific pathological codes to pilots using advanced neuro-prosthetics, including microprocessor prosthetic legs and robotic limbs, as well as cochlear implants, and that the manufacturer, model, and software/hardware revision of the device(s) be documented and tracked along with the body region involved. This will allow for future problems associated with their use to be identified and repaired if they are found to pose a significant risk to the safe operation of vehicles in the aerospace environment.

As previously mentioned, there are potential safety concerns of advanced prosthesis devices related to the risk of interference with avionics, safety hazards of the rechargeable lithium batteries, wireless, and Bluetooth technology's controls integrated to some prosthetics. Additional safety concerns are related to the fact that other components such as electric motors, hydraulics fluids, and microprocessors have not been tested in extreme aviation environments particularly during sudden decompression. Prosthetic devices implanted into the inner ear, such as CIs integrate a pair of magnets (to ensure the precise alignment between the external transmitter and the internal receiver coil) that can be affected by electromagnetic fields. In addition, advanced prosthetic devices need to be tested to ensure continued performance and safety when used in challenging aviation and space environments. They need to be tested during exposure to hypobaric environments, which could be accomplished by simulating an unpressurized aircraft flight or a rapid decompression event in a pressurized aircraft to evaluate

the functional stability of the device (82). Additional research will need to be conducted in order to acquire technical data for developing the rules and regulations regarding the compatibility between the cockpit's environment, including avionics and control systems, with other commercially available advanced medical prosthesis to meet the requirements of the MIL-STD-464 standard (U.S. Department of Defense Interface Standard: Electromagnetic Environmental Effects, Requirements For Systems, 18-Mar-1997). This standard "establishes electromagnetic environmental effects (E3) interface requirements and verification criteria for airborne, sea, space, and ground systems, including associated ordnance" (34).

A different aviation safety perspective to be considered was described by an Orthotist and Prosthetist researcher, Scott Sabolich, the clinical director of a state-of-the-art prosthetic clinic in Oklahoma City: "After 27 years of experience in the field of advanced prosthetics, I am excited to see the recent advent of microprocessors, actuators, and artificial intelligence that is occurring daily in today's external prosthetic devices. It truly is giving people their lives back after limb loss. I do believe that at this point most communication used to program the prosthesis components is through Bluetooth® therefore a wireless adapter is required to connect with the components; along with other ways that are non-threatening to the airplane controls from the cockpit. The internal communication in a prosthesis doesn´t work through Bluetooth, it occurs through wires. Because Bluetooth is only used to program the components, most prosthetics would be about as dangerous as a pilot having a Bluetooth® enabled cell phone. In other words, it is highly unlikely that an MPK pairs with other electronics and communicates with them. However, this topic does bring up a good point that at some time will need to be studied. I am deeply concerned now that external prosthetics have on board batteries, microprocessors, and cavernous unused areas that can hide explosive materials. Although this is an issue of potential criminal attempt to use an advanced prosthetics device for terrorist attack purposes, it is unrelated to the device's functionality. Nevertheless, each prosthesis should be X-rayed for potential hidden bomb materials rather than just metal detected on the person. Unfortunately, that will require a private room for doffing and donning the prosthesis which I understand is a logistics issue, as well as a human rights issue. However, I do see it as our next major viable threat and should be studied immediately (105)."

Finally, from Dr. Andreas Kannenberg, Executive Medical Director Otto Bock HealthCare, LP, an interesting statement on prosthetics: "In my professional career, it has been my experience that medical technology has not advanced as fast as predicted by engineers and futurists in the past. However, the progress we have made in medical technology is amazing. With state-of-the-art microprocessor controlled prosthetic technology, many people with major amputation of a leg or arm are capable of performing competitive sports or flying airplanes. In the future, we will be able to compensate function in even more serious injuries, medical conditions, disabilities, and handicaps. That means that people with even more severe physical and neurological limitations and restrictions will have a chance to live nearly normal lives and do nearly normal activities, including flying airplanes. This, achievement however, will require considerably increased dependability and durability of the devices implanted in or fitted on the human body, because any malfunction may result in even more serious safety hazards as patients using these devices will suffer from more severe limitations and restrictions than aviators today, which would more dramatically affect their capability to safely fly and land an aircraft under all circumstances. This outlook will impose huge challenges to the aeromedical assessment of individuals by aviation medical examiners and of medical devices by the FAA. I am convinced

that testing standards will have to be developed and established to clear ever more advanced medical technology for future use by aviators (65)."

As a conclusion, more research needs to be conducted to determine the current population of pilots using advanced medical technology or affected by medical conditions that may potentially require the use of advanced medical technology in the future, including but not limited to cochlear implants, visual prosthetics, cardiac pacemakers, advanced limb prosthetics, robotic arms, exoskeletons, TMR for myoelectric controlled artificial arms (robotic arms), deep brain stimulation, bladder stimulation, and other state-of-the-art medical technology to realistically evaluate the potential impact of this technology on aviation safety. The authors recommend individualized evaluations, focused on performance in both standard and unusual operational settings, including a rapid egress from the cockpit to evaluate advanced prosthesis impact on aviation safety.

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