

## Chapter 17

### **Biomedical Engineering Ethics**

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#### **Introduction**

Biomedical engineering remains one of the most dynamic disciplines in the world, standing at the intersection of engineering innovation and health care delivery. The growth of biomedical engineering can be seen in its increasing scope and pervasive application; from cellular and tissue engineering to biomaterial design for heart and neural implants. While exciting, this rapid growth of biomedical engineering raises several critical ethical questions that must be understood and resolved.

Biomedical engineering is unique as an engineering specialty, in that it is a synthesis of engineering principles and medical practice. The unique professional identity of biomedical engineering necessitates a set of ethical frameworks that are sensitive to both medical and engineering standards. Thus, whereas engineering ethics is narrowly focused on 'safety' and medical ethics on 'patient care' (Burgess et al., 2013), biomedical engineering ethics occupies the intersection of safety and patient care, beginning at scientific experimentation and design, and extending through medical practice and administration. Understanding the history of engineering ethics and biomedical ethics is thus essential to understanding the evolution and future of modern biomedical engineering ethics.

The goal of this chapter is to stimulate awareness of the need for ethical thinking in biomedical engineering, to trace the origins and essential fundamentals of engineering and biomedical ethics, and finally to highlight some considerations for Africa, where biomedical engineering is still in its infancy and regulatory policies remain limited.

#### **Engineering ethics**

While the origins of medical ethics can be traced to the centuries old Hippocratic Oath, the origins of engineering ethics are more recent and can be traced to the 2nd of September 1914 when the American Society for Civil Engineers (ASCE) defined six principles of engineering ethics focused primarily on an engineer's business obligations to his or her clients and employers. While progressive, it is noteworthy that these early engineering ethical canons made no mention of the engineer's responsibility to his or her community or the public at large. However, in response to the evolving social landscape and expectations in the 1960s and 70s as well as the United Nations sustainable development campaign, these canons were retooled to reflect a more socially

responsible engineering ethos focused heavily on the engineer's role in the world and public safety, as reflected below (ASCE, 2011):

1. *Engineers shall hold paramount the safety, health and welfare of the public and shall strive to comply with the principles of sustainable development in the performance of their professional duties.*
2. *Engineers shall perform services only in areas of their competence.*
3. *Engineers shall issue public statements only in an objective and truthful manner.*
4. *Engineers shall act in professional matters for each employer or client as faithful agents or trustees, and shall avoid conflicts of interest.*
5. *Engineers shall build their professional reputation on the merit of their services and shall not compete unfairly with others.*
6. *Engineers shall act in such a manner as to uphold and enhance the honour, integrity, and dignity of the engineering profession and shall act with zero-tolerance for bribery, fraud, and corruption.*
7. *Engineers shall continue their professional development throughout their careers, and shall provide opportunities for the professional development of those engineers under their supervision.*
8. *Engineers shall, in all matters related to their profession, treat all persons fairly and encourage equitable participation without regard to gender or gender identity, race, national origin, ethnicity, religion, age, sexual orientation, disability, political affiliation, or family, marital, or economic status.*

While this most recent iteration of the engineering code of ethics as articulated by the ASCE is an improvement over earlier versions, it still represents an unacceptably low ethical threshold for biomedical engineering (Monzon & Monzon-Wyngaard, 2009). For whereas traditional engineering focuses on the design, applications and manipulation of inert materials and inanimate objects, biomedical engineering has a broader scope that includes biological materials and human subjects – necessitating a higher ethical standard. Even more progressive than the ASCE's 2011 canon is the National Society of Professional Engineers (NSPE) code of ethics which advocates expansive socially responsible engineering ethics. Still, the more progressive engineering ethics code of the NSPE fails to meet the stringent ethical standards of medical practice that are expected of the biomedical engineer.

## **Medical ethics**

The content and structure of modern biomedical ethics has been shaped largely by contemporary forces such as legal and social events. Thus, despite the fact that the central ethos of the Hippocratic Oath 'first do no harm' had been articulated centuries earlier in medicine, biomedical research remained largely unregulated until the 1970s. This unregulated medical research and practice resulted in wonderful medical advancements, but also led to grotesque human experimentation that would most certainly be

considered criminal today. Scientists freely experimented with potential new treatments on their patients, sometimes with fatal or groundbreaking consequences.

In 1789 a country physician and surgeon from Gloucestershire England named Edward Jenner followed the anecdotal observation of a local milkmaid that “she could not get the small pox because she had already had the cowpox”, and injected his young son with pig pox producing an immune reaction against small pox (Burns, 2003). Following up on this observation, in 1796 Jenner inoculated James Phipps, an eight-year-old boy and the son of Edward Jenner's gardener, with pus obtained from cowpox blisters from the hand of a milkmaid who had caught cowpox from a cow (Williams, 1959). This dramatic act resulted in inoculation against small pox and introduced the golden age of vaccination that we still enjoy today. These invaluable studies by Edward Jenner saved millions of lives and pushed science forward. However by contemporary ethical standards, studies such as these are unacceptable as they violate several fundamental ethical principles as will be discussed below.

Unregulated biomedical experimentation such as Edward Jenner's cowpox inoculation was widespread until 1914, when the US Food and Drug Administration (FDA), founded in 1906, began instituting policies to limit the sale of some narcotics. Still, in the face of limited empirical evidence and hostile resistance from business interests, the efficacy and scope of the FDA in setting ethical standards for medical practice remained severely limited for decades, with detrimental consequences.

The Tuskegee syphilis experiment of the 1930s remains a classic case study of unregulated medical experimentation. On July 26, 1972 the Associated Press broke the story that for over 40 years, the US Public Health Services had maintained a study of untreated black males infected with syphilis, and the study was still ongoing (Howell, 2017). The world reacted with outrage and horror, wondering how this could have happened and for so long. However, in 1932 when the study was initiated, conversations on medical ethics had hardly begun. The demand for a syphilis test had grown, driven by laws requiring syphilis testing for marriage certificates, registering newborns, military recruitment, industrial physical examinations, and admissions to hospitals (Roy, 1995). To better understand the disease etiology and develop more accurate tests, human subjects were needed for both clinical observation and antibody development. The Tuskegee study was initiated with the specific objective of better understanding the natural life cycle of syphilis and to develop diagnostic tools and treatments to manage the disease (Roy, 1995; Howell, 2017).

Starting in 1932, 600 black men were unwittingly recruited and misinformed about procedures to be performed as part of the syphilis study. Over the next 40 years, clinical data and biological samples were collected from these research subjects both to understand the natural course of syphilis and to develop new diagnostic tools for the detection of the disease. It is noteworthy that while unethical and immoral, the Tuskegee

study was not illegal at that time, as the National Venereal Disease Control Act of 1938 had expanded the scope of the state to conduct human research (Roy, 1995). In response to a class action law suit in 1974, 70 surviving members of the Tuskegee syphilis human experiment received settlements; for most of the original study cohort however, this was too little too late (Howell, 2017).

Studies like Tuskegee were widespread during this era, not just in the United States but around the world. As the Tuskegee syphilis study unfolded in Alabama, Nazi scientists also experimented with war prisoners in Germany and occupied territories across Europe during World War II (Park & Grayson, 2008). After the war, these human medical experimentations were ruled as crimes against humanity and perpetrators (mostly research physicians) were convicted in the Nuremberg trials. In the collective determination to protect future human subjects from criminal human experimentation, a 10-point document entitled the Nuremberg Code, was articulated by the tribunal to guide future experiments with human subjects (Shuster, 1997; Park and Grayson, 2008). Whereas the Hippocratic Oath passively encouraged physicians to work in the interest of the patient, this new Nuremberg Code asserted that the consent of the patient is paramount, introducing a key pillar of modern biomedical ethics – informed consent. The Nuremberg Code thus provided the first explicit articulation of criteria that must be fulfilled before human experimentation can proceed (Shuster, 1997):

1. *The voluntary consent of the human subject is absolutely essential.*
2. *The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.*
3. *The experiment should be so designed and based on the results of animal experimentation and knowledge of the natural history of the disease or other problem under study that the anticipated results will justify the performance of the experiment.*
4. *The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.*
5. *No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.*
6. *The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.*
7. *Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability, or death.*
8. *The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.*
9. *During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.*

A human subject, in modern research language, is a living individual from whom a researcher conducting a study obtains data, samples or other personal information through intervention or interaction with the human. Interventions could refer to physical contact for data collection and alteration of the subject or their environment for possible reaction. Interaction could mean formal or informal discussion between researcher and participant (Howell & Obado-Joel, 2016).

Although the Nuremberg Code was developed in response to Nazi atrocities, and subsequently proved invaluable to modern medical ethics, it was largely ignored for a few decades after its articulation until it was revived and expanded as the Declaration of Helsinki by the World Medical Organization in 1964 (Shuster, 1997; Park & Grayson, 2008). The Helsinki declaration is an internationally accepted guide for the conduct of ethical medical research. Similar to the Nuremberg Code from which it evolved, the declaration of Helsinki includes respect for individuals, their right to self-determination and the right to make informed decisions. Thus when a research participant is incompetent, physically or mentally incapable of explicitly giving consent, or is underage, abundant allowance should be provided for surrogate consent to be obtained from an individual authorized to act in the subject's best interest.

Unlike the Nuremberg Code which was relatively abstract and philosophical, the Helsinki Declaration was more concrete and specifically addresses clinical research, providing detailed prescriptive steps for the medical community to regulate itself. Beyond its specific prescriptions for ethical medical research, the Helsinki declaration is 'active' and continues to undergo revisions as new ethical challenges emerge. The current edition of the Helsinki declaration from 2013 serves as the basis of most Institutional Ethics Review Boards, and contains both general principles like the Nuremberg Code as well as specific prescriptions such as the ethical use of placebo and the need for local institutional review boards (Shuster, 1997; WMA, 2013).

### *Informed consent*

At the heart of modern biomedical ethics is informed consent, a concept introduced in the Nuremberg Code and contained in the Declaration of Helsinki. Despite the growing interest and popularity of informed consent as a principle of biomedical ethics, the question – what is informed consent – remains particularly complex for both practical and theoretical reasons. Does simply obtaining a participants signature alone guarantee informed consent? What is the standard required for consent to be considered informed? This question is important for practical reasons because if we use overly loose criteria such as a signed consent form, informed consent becomes too easy to obtain and loses its moral significance. On the other hand if we use overly demanding criteria for informed consent such as complete understanding and full disclosure, informed consent becomes

almost impossible to obtain. To resolve this dilemma local institutional policies and rules, governed by institutional ethics review boards, set local standards of consent (Howell, 2017).

### *The challenge of vulnerable populations in biomedical research*

One major contribution of the Declaration of Helsinki was the discussion of how to treat vulnerable populations during biomedical research and clinical practice. Vulnerable populations can be broadly considered as subjects or participants not sufficiently informed or able to make self-protective decisions or actions and thus likely to be misused by coercion or ignorance in the course of biomedical research. Vulnerable populations include but are not limited to children, the elderly, the mentally disabled, prisoners, the infirm, the uneducated and the poor (Burns, 2003; Park & Grayson, 2008). Although pervasive, the ethical treatment of the vulnerable has not always been a priority.

It is worth noting that efforts to prevent the exploitation of vulnerable populations also present a major practical dilemma. For instance, restrictions on research on children have resulted in a dramatic under-representation of children in most clinical trials. A recent estimate suggests that as much as 80% of medicines prescribed by pediatricians have not been systematically studied in pediatric populations for dosage, efficacy and risk because of the limited clinical studies in pediatric populations – sometimes resulting in fatal consequences (Fost, 2005; Park & Grayson, 2008).

### *Privacy and confidentiality*

The researcher must respect and maintain the privacy of human subjects and the confidentiality of their information or data. The need for privacy and confidentiality is among greatest challenges of biomedical research. For many research participants, the loss of privacy can have significant consequences including loss of career, insurance, job, or family, as well as stigma. Beyond protecting the privacy of research subjects, maintaining privacy and confidentiality helps maintain research integrity. Consequently every possible measure must be taken to protect the confidentiality and privacy of every research subject. This means no sensitive information on research subjects must be revealed outside the confines of a research study and when such information is shared, this must be done using the 'need-to-know' principle, meaning each member of the research team should only know the identity of participants when absolutely necessary to support their role in carrying out the study (Howell & Obado-Joel, 2016). Beyond applying the 'need-to-know' principle, additional measures such as anonymizing participant data, data encryption, using passwords, and safe storage, must be strictly enforced. In addition, certain regions and institutions have more specific privacy rules that provide specific security provisions for safeguarding medical information. In these

cases, it is the duty of the ethical researcher to be both thoroughly familiar with such local privacy rules and to implement them as the loss of participant privacy and confidentiality can have fatal consequences.

## Research on animals

Significant successes and breakthroughs in health care delivery have been made possible by scientific research using animals, for example the treatment of diabetes and leukaemia, and heart transplants. Animals that have been used include mice, rats, guinea-pigs, hamsters, rabbits, cats, dogs, ferrets, equids, pigs, goats, sheep, cattle, primates, birds, reptiles, amphibians, and fish-rats, guinea pigs, sheep, frogs, dogs, cats, and primates (CBRA, 2018).

Risks and uncertainty in the results of administering untested and unproven treatments on human subjects has necessitated the use of animals in research studies. However, with the use of research animals, harm to the animals must be minimised while maximising the benefits to healthcare. With these principles in mind, research on animal subjects is governed by institutional ethics review boards, in a similar manner as for research on human subjects. The study protocol must ensure that the number of animals used is minimised and if possible, appropriate alternatives should be used (e.g. computer models, tissue and cell cultures). Animal models are used in medical research because of the biological resemblance of animals to humans. Because research animals have shorter a life span than humans, studies can be done across their life span and across generations; in addition their environment (diet, temperature, lighting) can be controlled more easily than with humans (Bateson et al., 2004). Animal models give valuable insight into human biological processes and provide effective experimental flexibility and control that are difficult to obtain in humans.

However, these advantages have not been without resistance as those against the use of animals in research have stated that using animals for humans are inappropriate, citing the differences between humans and animals. Reference is made to the case of the limb defects observed in children of women who took the drug thalidomide during pregnancy, the damaging effects of which were not predicted in animal studies. More recently, it has been pointed out that the use of animals in research contributes to the high failure rate of drug trials as drugs that work in animals might simply not work in humans, and in addition, several human diseases and mutations simply cannot be studied in animals due to interspecies differences (Akhtar, 2015).

Still, the use of animal models for research in place of human subjects has been immensely beneficial to both humans and animals (CBRA, 2018). Medicines and vaccines developed for humans are now used to treat animals, for example vaccines for rabies and distemper in dogs and cats, feline leukaemia, infectious hepatitis virus, tetanus, and

heartworm. Other benefits include the preservation of nearly extinct species of the California condor and the tamarins of Brazil, owing to new reproductive techniques.

In the face of immense benefits derived from animal research, the three R's are proposed for ethical animal research: replacement, reduction and refinement (Flecknell, 2002). According to these widely accepted standards, ethical animal research must constantly seek replacement alternatives for animals. For instance, the studies should where possible be performed in a different system such as induced pluripotent stem cells instead of animals. If animals must be used, a reduction approach must be considered, namely to use the lowest number of animals to answer the research question. Finally the ethical animal researcher must seek ways to refine the protocol to ensure the least amount of pain and harm to each animal during the study. The ethical researcher must find new ways to adopt the three R's during research with animals.

### **Ethical principles in the communication of research**

Following the successful conduct of research, the next important task of the scientist is to communicate their work effectively and accurately. This responsibility of communicating scientific information with integrity presents new ethical challenges for the researcher. Specifically, ethical scientific communication must avoid plagiarism, fabrication and falsification (Kaiser, 2014). Fabrication has been defined as recording or reporting data or results that have been made up. Falsification entails the manipulation of research materials, equipment, or processes, or altering or omitting data or results, resulting in inaccurate representation of the research in the research records. Plagiarism is the appropriation of the ideas, methods, results or words or others without giving due credit. Since integrity and truth are the currency of science, plagiarism, fabrication and falsification are regarded as egregious scientific communication misconduct and can have significant personal and professional consequences.

### **A case of biomedical engineering ethics failure**

The preceding sections introduced the concepts of engineering ethics and biomedical ethics. The long-term goal of this chapter is stimulate contemplation on how best to navigate complex ethical issues. The quintessential biomedical engineering ethics case below, on the failure of the Björk-Shiley heart valve, provides material for such contemplation. The description below is adapted from (Blot et al., 2005; Monzon & Monzon-Wyngaard, 2009).

Heart failure remains a leading cause of death in many countries around the world. Dysfunction in the valves leading into and out of the heart is a major contributor to heart failures. In 1976 the Björk-Shiley convexo-concave prosthetic heart valve (also known as BSCC) was developed and introduced to the global market to provide effective relief for patients with diseased native valves. After its adoption in 1978 the BSCC heart valve



became the most popular prosthetic valve for over decade. Shortly after introduction to the market however, fractures of the outlet struts of the BSCC valve, resulting in functional anomalies and often death, began to be reported. While the obvious biomedical engineering objective was to create a reliable implantable device that opened-closed in patients several thousand times a day for years, internal investigations later revealed the BSCC valves were known by the manufacturers to be substandard with poor welding and quality control. Furthermore, during clinical trials, the valve was reported to show material fatigue leading to weld fractures. The manufacturer altered its welding and quality control procedures, but the faulty BSCC valves were not withdrawn from the market, nor were patients informed of eventual failures. Complicating matters further, the FDA, responsible for biomedical regulation, delayed recommending removal of the valve from the market, which led to more disastrous outcomes. Pfizer, the parent company of the manufacturer, reached a settlement with affected patients in 1992, which included patient compensation and funds set aside for research to identify recipients of heart valves at risk of fracture. By December 2003, outlet strut fractures had been reported in 633 BSCC valves (0.7% of 86 000 valves implanted), often with fatal outcomes.

A more recent study reported that there are still over 7,000 patients worldwide wearing the BSCC heart valve, living with the knowledge of its questionable structural integrity and the possibility of its collapse at any time with fatal consequences (Batts, 2014).

## **The challenge of biomedical engineering ethics in Africa**

We have highlighted several fundamental principles and challenges of biomedical ethics. It is worth noting that while universal, each of these principles and challenges must be adapted to local realities and customs. In Africa, each of the principles and challenges discussed above may assume a richer and more complex role depending on local customs, religions and social structure. Still the principles remain the same. In this spirit, it is the duty of the ethical biomedical engineer to find new ways to adapt these universal principles to local realities. For instance, to truly obtain informed consent when working in a remote community with limited English language, might require translating informed consent forms to local dialects, so as to ensure that local research participants understand what they are participating in, no assumptions can be made. Furthermore, the need to adapt ethical principles such as privacy and confidentiality to local realities is even greater in certain countries, where medical information is stigmatised, and where the revelation of a research participant's personal information such as HIV status or sexual orientation might have severe personal, even fatal, consequences. In this context biomedical engineering ethics requires an understanding of the general ethical principles of participant privacy and confidentiality as well as an understanding of local laws and participant risks.

## Conclusion

Modern science is neither pure nor infallible, but a continuous struggle towards clarity; a struggle against imperfect methodology as well as psychological, technical and social limitations (Kaiser, 2014). In light of these limitations the task of the biomedical engineer, like that of any scientist, is to struggle honestly and ethically. An early commitment to ethical biomedical research and clinical practice can provide an excellent long-term guide to help navigate the rapidly evolving field of biomedical engineering. The consequences of poor biomedical engineering ethics can be devastating and long lasting, both for individuals and for communities. The public faith in science can easily be shattered if behaviour emerges suggesting scientific misconduct.

While this chapter has highlighted a few major topics in ethics, a sea of questions remains and new questions continue to emerge daily. A few of these questions worth contemplating include: Privacy: how do we maintain patient privacy in the era of big data? Patent rights: who owns the rights to advancements derived from patient specimens? Regulations: what happens when local regulations, laws and policies lag behind biomedical engineering innovations? Augmentation, eugenics and life extension: as advances in biomedical engineering continue to improve our capacity to implant new devices, edit undesirable genes and prolong life artificially, should there be a limit to these advances?

Modern biomedical engineering ethics is continuously evolving, driven by forces of local law, culture, evolving social consciousness, and morality. Ethical questions in biomedical research can be difficult as revealed by the Tuskegee syphilis study, where the study was both legal and unethical. This dilemma makes it imperative for the ethical biomedical engineer to uphold a standard higher than local laws but grounded in ethical principles. The pioneers of biomedical engineering in Africa, for whom this book is intended, will have the opportunity not just to contribute to the science of biomedical engineering, but also to shape its public image and ethical landscape. A commitment to the principles of ethics discussed here should provide a stable first step towards a culture of ethical biomedical engineering.

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