SUREPACE WALKER: A POWERED WALKER FOR CHILDREN WITH CEREBRAL PALSY

ETHICAL IMPLICATIONS OF HUMAN GERMLINE EDITING THROUGH CRISPR-CAS9

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On my honor as a University student, I have neither given nor received unauthorized aid on this assignment as defined by the Honor Guidelines for Thesis-Related Assignments.

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Introduction

The technical topic of this thesis prospectus involves the design of an intelligent powered walker for the purpose of aiding children with cerebral palsy. Cerebral palsy is a neurologic condition that significantly affects motor movement due to spasticity. Part of the standard care for children with cerebral palsy is the need for a walking aid, whether it be a mechanical walker or a cane. However, even with a walking aid, movement for the child tends to be extremely tiring and therefore their duration of movement tends to only be in short bursts, which prevents them from doing any sort of prolonged exercise and physical therapy. The intended purpose of the intelligent powered walker is to aid the patient by analyzing their gait and hip movement and provide them with small burst of movement through the walker to allow them to walk as normally as possible. In doing so, they will be able to reduce their own energy output for simple movements and be able to reap the benefits of daily exercise. The purpose of the technical topic is to enhance the design of this intelligent powered walker through CAD and conduct proper marketing and commercialization of the product.

The STS topic of this thesis surrounds the ethics of human germline editing through CRISPR-Cas9. CRISPR-Cas9 is a gene editing tool that has the ability to remove genomic data sequences depending on its attached RNA sequence. This tool provides limitless therapeutic options, especially in genetic disease that were previously thought to be virtually incurable. However, the introduction of this tool into mainstream medicine carries with it multiple ethical concerns, the most prominent of which is the issue of germline editing. Germline editing refers to the editing of either germ cells or embryos in an individual, which theoretically affects all cells not only in the individual, but any offspring that they may produce. The purpose of the STS topic is to explore the major concerns surrounding human germline editing and a potential solution to it when moving forward with gene editing as a whole.

Technical Topic

Cerebral palsy is a static neurologic condition resulting from brain injury that occurs before brain development is complete. The disease is characterized by motor impairment and can present with global physical and mental dysfunction. One of the defining features of cerebral palsy is spasticity, which refers to an abnormal increase in muscle tone and definition as well as stiffness of the muscle (Krigger, 2006; Reddihough & Collins, 2003). Cerebral palsy occurs in approximately 2 to 2.5 per 1,000 live births and the total number of children with cerebral palsy has remained stable; however, in resource-poor areas, the incidence of cerebral palsy is significantly higher (CDC, 2020; Gladstone, 2010). The treatment of cerebral palsy involves both mental and physical care for the child with whom the disease has been diagnosed. Also, due to a large majority of children with cerebral palsy also experiencing spasticity, physical therapy is highly recommended to help manage it and is considered a standard part of care for the disease (Aisen et al., 2011; Novak et al., 2020; O'Shea, 2008). However, since spasticity can cause movement to both be painful and tiring, physical therapy and daily exercise can be extremely difficult for children diagnosed with the condition (Graham, Paget, & Wimalasundera, 2019; National Institute of Neurological Disorders and Stroke n.d.). The purpose of this technical topic is to help address these movement difficulties by designing an intelligent powered walker using computer-aided design that will help aid in the daily activities of children afflicted with cerebral palsy.

The intelligent powered walker is a motorized posterior walker that assists children with cerebral palsy with their daily movement. To assist with the children's movement, the walker analyzes the gait and hip and waist movement of the user and applies small amounts of force in the direction of the child's movement to allow them to exert less energy while walking. This powered walker allows for the child to move as normally as possible compared to its traditional passive counterpart. Although not as efficient as a traditional or motorized wheelchair in terms of pure movement, the intent of the powered walker is not to allow the user to move completely freely with no effort. Rather, the intelligent powered walker is intended to help the child move normally to enable them to experience the benefits of daily movement and exercise without significantly tiring themselves out in a short period of time by allowing them to distribute their energy expenditure throughout the day, compared to using all of their energy to traverse only a short distance. Therefore, the powered walker will serve as an excellent therapy tool and will hopefully play a beneficial role in the daily lives of children with cerebral palsy in the near future. Currently, a similar robotic walker is also in development under a separate research group and hopes to achieve the same outcome as the intelligent powered walker (Alazem et al., 2020).

The current design of the intelligent powered walker is a complex assembly; the particular focus of this project involves the hardware. The powered walker's structure mainly resembles that of a passive, mechanical posterior walker. The posterior walker design was chosen over that of an anterior walker because of its popularity with caregivers and those actually afflicted with cerebral palsy (Poole, Simkiss, Rose, & Li, 2018). In addition to this basic mechanical framework, there are multiple hardware attachments that allow for the walker's motorization and intelligent movement. A computer box is attached near the hip level of the walker which contains the components of a Windows computer. The rear wheels contain a motor and gearbox which receives input from the computer to adjust the power appropriately. To analyze the gait and hip movement of the user, two motion sensing cameras are located at both the foot level and the hip level to allow the computer to process the user's movement through its internal algorithm and provide movement assistance accordingly.

The introduction of the intelligent powered walker has many potential implications on the medical industry and lifestyles of patients outside of those with cerebral palsy. One of the possible major applications of this technology is assisting the movement of the elderly. In many ways, the elderly can receive the same benefits from using the intelligent powered walker as those afflicted with cerebral palsy, i.e. daily movement and exercise. Although the current prototype design is suited for children, the basic mechanical framework is easily adjustable to accommodate the size of an adult. Additionally, this can also help other patients of physical therapy as well, such as those with newly received prosthetics and other patients with movement-debilitating diseases. The potential applications of the intelligent powered walker are limitless and could transform the medical aid industry.

STS Topic

One of the novel technologies introduced in modern medicine is the ability to edit an individual's genomic data. This process, colloquially known as gene editing, presents an almost infinite amount of possibilities in therapeutics, particularly in correcting faulty genetic data that contributes to a wide variety of hereditary diseases. The majority of gene editing is done through a bacterial DNA sequence known as CRISPR (clustered regularly interspaced short palindromic repeats) along with a complementary protein known as Cas9 (CRISPR-associated protein 9) (Gupta et al., 2019; Savić & Schwank, 2016); together, they form the complex enzyme known as CRISPR-Cas9. CRISPR-Cas9, as it was developed by Jennifer Doudna and Emmanuelle Charpentier and currently used today for genome editing, consists of two major components: the CRISPR-Cas9 complex itself, which cleaves a targeted sequence a specified target sequence for destruction, and a guide RNA, which provides the CRISPR-Cas9 component with its respective target sequence (Doudna & Charpentier, 2014). After the genomic data has been cleaved, other genomic tools can be used to replace the missing sequence and splice it to the original sequence. This discovery of using CRISPR-Cas9 as a genomic editing tool is one of the greatest biological discoveries of the 21st century and brings with it numerous potential applications not only in humans, but also in natural biology as well. However, the introduction of this technology also presents a myriad of ethical issues, the most prominent of them being the issue of human germline editing. The purpose of this STS topic is to explore the issue of human germline editing in the context of gene editing and offer insight and potential solutions to this major ethical concern.

Human germline editing is the process by which the genomic data of a germ cell or embryo is edited, thereby affecting all cells that are derived from it. Notably, this can include any offspring that are produced from the individual bearing these modified cells. Germline editing is contrasted with somatic editing, which only focuses on cells that are not a part of gamete formation (i.e. non-reproductive cells) (Ormond et al., 2017). The inherent nature of germline editing with respect to its effect on any potential offspring that the individual may produce already presents a major ethical issue. Genome editing is not a foolproof technique and presents a considerable amount of risk involved with its usage. Because of this, any sort of accidental deletion of genomic data that is caused by usage of CRISPR-Cas9 will also affect the offspring of the individual, thus resulting in their lineage potentially marred by this genetic defect. Not only is this a significant hindrance to the individual and their offspring physically, this also affects them mentally as well due to the lingering idea that any potential children in the future that they have may inherit this defect (Brokowski & Adli, 2019; Fogleman, Santana, Bishop, Miller, & Capco, 2016; Patrão Neves & Druml, 2017). The only way to correct this is through another expensive gene editing treatment (the cost in itself is another ethical issue worth discussing) which carries with it the same risks as the original procedure.

Another major issue with human germline editing is the potential for human enhancement. While the main use of gene editing is for therapeutic purposes, there is proven potential for CRISPR-Cas9 to be used for genetic enhancement. Genetic enhancement refers to any sort of modification to the genome that does not serve any sort of therapeutic purpose and is instead either used for aesthetics or modifying potential physical or mental prowess. The idea of using CRISPR for enhancement has brought up a fear of "designer babies," which are offspring that are genetically modified to be rid of any sort of subjective imperfection according to the individual responsible for its modification. One of the major ethical issues surrounding these designer babies is the lack of individuality of the babies themselves; their characteristics and traits were all chosen by whoever their designer was, namely their parents. This also has the potential to exacerbate social tensions between classes due to the potential price barrier that exists to access genome editing technology. Enhancement also becomes a concern when used to improve athletic and mental prowess. While this does also apply to the designer babies mentioned prior, this can also apply to those attempting to abuse genetic editing for militaristic purposes. Genetic Captain America-like "super soldiers" have the potential to impede on the global power balance, favoring first world countries that have the ability to fund this type of research and can be used to impose a much more menacing position on the global stage (DiEuliis & Giordano, 2018).

Despite gene editing having limitless potential as a therapeutic tool, human germline editing must be addressed in some way. One method of doing this is through anticipatory governance of the technology, something that has already been done by the Council of Europe

(Peng, 2016). Strict international regulations must be imposed on human germline editing, as its potential for wrongdoing and abuse are as limitless as its benefits. As mentioned before, the Council of Europe has unanimously banned human germline editing due to the risks and abuse associated with it. It is strongly encouraged that other countries impose some sort of regulation on the national level as well. Ultimately, a global ban on human germline editing via the United Nations would be the ideal outcome.

Research Question and Methods

The main research question with regards to the technical topic is how to optimize the design of the intelligent powered walker while allowing it to remain affordable for the general populace. Some of the key factors to consider are, but not limited to, the motor's power output, the durability of the base mechanical walker, the size of the walker itself, the camera quality, and the price of each part used. Design of the intelligent powered walker will include research into what is currently available to use in industry and its compatibility with the current prototype under given design specifications. After each design change, the walker will be given for patients with cerebral palsy to test and use. Feedback from both the patients and their respective caretaker will be considered with each design change and this process will be iterated until a satisfactory design is attained. Afterwards, market research and commercialization will need to be conducted in order to maximize product awareness and profits.

The research question for the STS topic is how to address the future possibility of human germline editing in modern society. Research methods for this will primarily consist of reading bioethics review articles and synthesizing multiple perspectives on the issue to form a general proposal. In addition to this, research will be conducted into how current governing bodies are either addressing it or approaching it. Another factor to consider is how each governing body's current laws on gene editing (if any exist at all) must be modified to take into account human germline editing.

Conclusion

For the technical topic, the intelligent powered walker presents a novel way of aiding children with cerebral palsy with their daily activities. The benefits of the powered walker for the growth and development of these children are significant and will introduce a new way of approaching physical therapy for the users. The intelligent powered walker also has room to expand into other demographics as well, such as the elderly and those requiring physical therapy due to other afflictions. Overall, the powered walker has a considerable amount of potential and must be optimized to reach it.

For the STS topic, gene editing, while limitless in its potential in its uses for therapy, must be approached with caution with regards to human germline editing. There are a myriad of ethical concerns that must be considered when approaching a technology as groundbreaking as this and action must be taken ahead of time to prevent misuse and abuse of it. Anticipatory governance of this technology is a must if society is to proceed forward using gene editing as a therapeutic tool, but multiple perspectives must be synthesized first before legislation is passed on it.

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