

Advancement of Biomedical Treatment for Duchenne Muscular Dystrophy Using Robotic Technology

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ABSTRACT

Duchene Muscular Dystrophy (DMD) is an accelerated and one of the most prevalent types of muscle dystrophy. It is caused by lack of the protein, dystrophin, in the muscles. Due to symptoms such as fatigue and muscle weakness, most DMD patients lose the ability to walk at age twelve. However, studies show that repeated exercise for DMD patients lead to improved contractile function of the muscles and reduced fatigue (Baltgalvis, et al., 2012). Modification of current orthopedic treatments, such as wheelchairs, can be made by the utilization of a machine-guided chair for patients. The conception of the DMD Treatment Wheelchair in this paper was made using low resistance training and Vector Therapy treatments, in which patients were subjected to continuous movement of their muscles with minor applied forces. Movements at the joints in various combinations of ranges of motion induce enhanced muscle contractions while being able to take on multiple loading cycles as compared to a DMD patient without the treatment. Therefore, the aim of this design is to help DMD patients ease the inconveniences of being limited to certain movements, to provide a certain level of therapy, and most importantly, to improve their quality of life.

Keywords: Muscular Dystrophy, Bone mechanics, muscle mechanics, DMD treatment

1. INTRODUCTION

Duchenne muscular dystrophy (DMD) is one of the nine types of muscular dystrophy afflicted on approximately 1 in 4000 male births worldwide (Moser, 1984). Resulting from inheritance of an X-linked recessive gene, DMD predominantly affects males who inherit the disease through their mothers. Females can be carriers, but usually show no symptoms of the disease (Genetic Home Reference, 2012). DMD is caused by a mutation in the DMD gene; individuals with this particular defective gene lack the ability to synthesize the protein known as dystrophin in their muscles (Genetic Home Reference, 2012). Dystrophin, which can be found in the skeletal and cardiac muscles, function together with a group of proteins to reinforce muscle fibers and prevent them from injury while muscles contract and relax (Ehmsen J, et. el., 2002). Without well functioning dystrophin, repetitive contraction and relaxation of muscles, due to movement, damages muscle cells over time. The impaired muscle fibers will be replaced by fibrous and or fatty tissue which eventually leads to the weakening of the muscle fibers (Ehmsen J, et. el., 2002). The rapid-progression of voluntary muscle deterioration that DMD brings about will inevitably take away the patients' abilities to move their limbs like healthy patients [Emery, Alan E. H.].

The onset of symptoms typically takes place between the ages of two and six (Muscular Dystrophy Campaign, 2012). As the condition worsens in a fast-moving manner, almost all patients with DMD have to be wheelchair-dependent by the age of twelve (Muscular Dystrophy Campaign, 2012). Symptoms of the disease include weariness, possible mental retardation that does not exacerbate in due course, respiratory problems, joint stiffness, difficulty in motor skills (such as jumping and running), and muscle weakness that leads to frequent falls (DMD Fund, 2012). Muscle weakness begins in the thighs, calf muscles, and pelvis. After occurring in the aforementioned affected regions, muscle weakness proceeds to the arms, neck, and other areas (DMD Fund, 2012). The progress of muscle declining from specific parts of the body in turn explains why the patients are confined to a wheelchair for the rest of their lives. The serious condition of the disease does not exclusively bring inconveniences such as difficulty in mobility into the daily lives of patients, but also affects their life expectancies. The life span of the patients who are plagued with DMD is estimated to be 25 years (DMD Fund, 2012).

In spite of the fact that much research was done on the disease, there is still no cure found for DMD to date (DMD Fund, 2012). The only way to prevent DMD is to have a prenatal diagnosis in future pregnancies for woman who may be at risk of being an x-linked recessive carrier (DMD Fund, 2012). Albeit stated that it is impossible to cease the progression of DMD, patients undergo physical therapy to ease the severity of symptoms of the disease and to maintain the flexibility of their joints (Muscular Dystrophy Campaign). Considering how undergoing physical therapy helps DMD patients, our design of the DMD Treatment Wheelchair has the central aim of improving the quality of life of DMD patients by alleviating the difficulties in mobility they have to face.

2. CURRENT TREATMENTS

As of now there is no known cure for DMD (A.D.A.M. Medical Encyclopedia, 2012), but there are treatments that help ease the symptoms. There are medications like corticosteroids that can help increase the muscle strength (Mendell, et al, 1989). However, if taken for a long period of time, it can have negative effects on the bones (Mendell, et al, 1989). There are various therapies that can improve the patients' conditions.

2.1 SURGICAL TREATMENTS AND GENE THERAPY

There are various surgical procedures that can relieve problems associated with muscular dystrophy. Usually in muscular dystrophy, the patients' limbs tend to draw inward and become fixed in position. So a tendon surgery can loosen the joints and help the patients. Similarly, since DMD patients have trouble breathing – usually due to a sideways curvature of the spine – surgery is used to correct the alignment of the spine (Mayo Clinic, 2011).

2.2 LOW RESISTANCE TRAINING

Low resistance training for DMD patients is noninvasive and takes into consideration the major mechanical requirements of surgery, including loosening at the joints and misalignment of the spine. This kind of training is

highly beneficial (Ansved, 2001). Moreover, mobility aids, such as braces, are used to provide support for the weakened muscles and keep them stretched and active (A.D.A.M. Medical Encyclopedia, 2012). Since muscle contractions are critical in delaying exacerbations of DMD in patients, the use of mobility aids are useful for putting off sclerotic twisting of the spine and other bones in the body. The loss of muscle mass in the limbs should require the body's bones to carry more loading, leading to abnormal bone remodeling. Mobility aids, specifically braces, would help transfer some of the weight of the body, gravity, and any external forces, to the braces. This transfer of load from the bones to the mobility aids should lessen irregular bone growth by temporarily taking on the loads that normally would have been done by the muscles.

2.3 VECTOR THERAPY

There has also been ongoing research on Vector Therapy. Vector Therapy is a physical therapy solely based on assisting the patients to improve and maintain their muscular strength. This is done by inducing mobility at all angles at any region of their body, more specifically at the joints. Christopher J. Gatti from The University of Michigan has been studying the support of a vector machine, using healthy and pathological shoulder strengths as normative objective function. He discovered that the patients were able to gain optimal amount of strength through a daily use of physical therapy using vector mechanical devices. One of the devices is called a Least Support Vector Machine and shows that daily physical activities definitely deter the progression of muscle deterioration in DMD patients (Gatti, et al., 2008). By using an assortment of combinations of abduction and internal and external rotation of the shoulder, the Vector Therapy procedure confirmed the supportive roles of therapy machines. (Gatti, et al., 2008).

3. DMD TREATMENT WHEELCHAIR DESIGN

Due to the physical limitations for patients with Duchenne Muscular Dystrophy, constant exercise and treatment are required to ensure that a substantial amount of bone density is not lost. Infusing robotic technology with current wheelchair treatment designs, along with low resistance training and Vector Therapy treatment, DMD can be regularly treated to increase life span of a patient. Figure 1 shows the technical modifications on a wheelchair, which include individual movable arm and leg rests for exercise, a control panel for management and safety of the overall design, and a track and wheel system for better mobility. We believe that the wheelchair, which will subject patients to continuous exercise, will increase muscle movement, leading to more contractions and less fatigue.

3.1 AUTOMATIC AND MANUAL CONTROL OF DMD TREATMENT ON WHEELCHAIR

In order to treat the muscles and bones in the limbs of patients with DMD, these areas require recurring motion in various ranges and angles. Cast-like clamps are placed over the legs and arm rests, which are all separate from each other, and utilize bearings for joint movement. Movement at these joints is controlled by pre-programmed sequences that are coded according to the loading and joint-travel capabilities of different patients. Casts are placed over limbs and the torso portion of the body in order to allow the weakened muscles to stretch. This enables the limbs to move more efficiently during the treatment procedure since a portion of the loading will be transferred to the casts and allow the bones to grow normally, rather than displaying sclerotic behavior.

Furthermore, the cells in bones, specifically osteoclasts, respond to different forces so a diminutive force will be applied in the areas of movement. This will only be done after patients have already undergone treatment without any additional force applied. This will help patients' bodies adapt to external loading when applied. The additional force will be gradually added to make sure patient bones and muscles will not fracture or tear. The casts will enable DMD patients to move their limbs more effectively by lowering the moment arm created by internal and external forces.

The DMD treatment chair is equipped with a control panel that is both automated and manual. The panel is mounted on a stand next to the seated patient and can be moved to be in front of them. The pre-programmed treatments can be selected after inputting the patient's physical information (i.e. age, weight). For instance,

exercise of the legs or arms separately or together can be selected and progress of the treatment will be tracked and displayed on the panel. An emergency “stop” button will be clearly placed in front so that the arm and leg rests return to their original position and the clamps open for maximum safety.

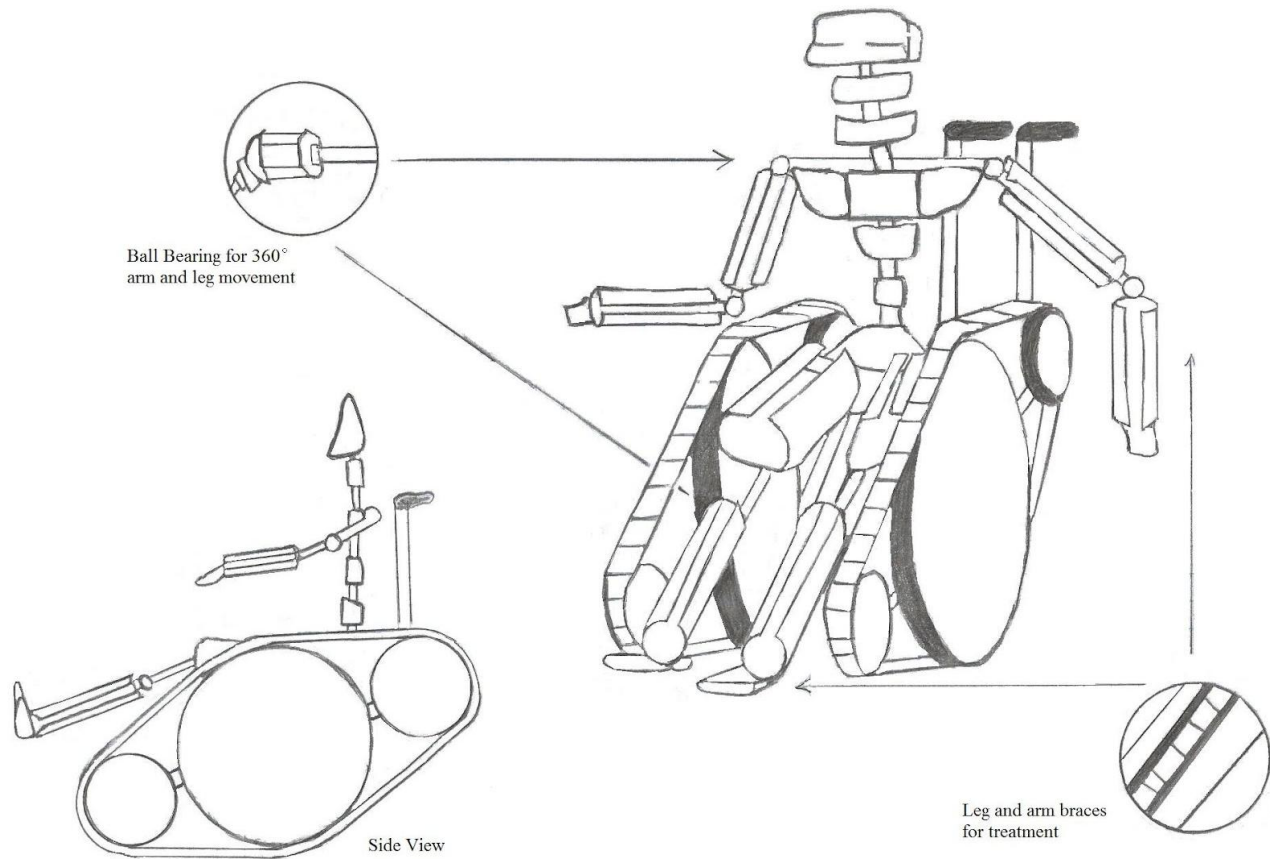


Figure 1: Design of DMD Treatment Wheelchair showing track and wheel system for mobility and arm/leg braces for bone and muscle treatment

3.2 TRACK AND WHEEL SYSTEM FOR IMPROVED MOBILITY

To perfect the mobility, implementation of a track and wheel system enables the DMD treatment chair to be able to travel on uneven terrain as well as rising or falling elevation (Gajitz, 2011). The wheels inside the parallel tracks semi-retract into a larger fixed wheel in the middle of the tracks. This facilitates movement on staircases using acoustic proximity sensors. These sensors transmit sound waves through a transducer at different frequencies and measure the time it takes for the wave to reflect from an object onto a second transducer (Ragesh, 2012). Multiple proximity sensors on the front and back of the treatment chair detect a different length since they are placed at different angles. The bottom sensors detect the absence of ground, signaling a decline in terrain, or the presence of foreign objects, including declining stairs. The angle of incline or decline is detected by the higher proximity sensors and the information is used for advancement of the retractable wheels at specific angles. These angles, along with a gyroscope underneath the seat, align the chair for better balance. In addition, the bottom of the seat of the wheelchair itself is located at one half the radius of the large wheel. This lowers the center of gravity and allows for increased stability during movement. Emphasis on improved maneuverability allows patients to undergo regular treatment regardless of their location by adapting to various surfaces.

4. BIOMECHANICAL EFFECTS OF DMD TREATMENT WHEELCHAIR ON MUSCULOSKELETAL SYSTEM

The contraction of the skeletal muscle requires force, which is dependent on the muscle length and is the summation of contraction occurring in every single sarcomere in the muscle fibers (Kandura, 2007). The force generated by the muscle is dependent on the force acting on it. An isometric contraction causes the muscle to exert a force without shortening, unlike when the muscle applies force in the extended position also known as eccentric contraction. A contraction in which muscle shortens and applies force is concentric which help the rotation of body functions (Bill Sellers, 2012). The strength of the muscle greatly relates to the size of the muscle.

The increase in frequency of the stimulation by motor nerves, known as motor units, increases actin and myosin cross-links. The increase of this stimulation also increases a twitch sustained contraction, thereby a tetanic contraction is elicited (Kandura, 2007). More motor unit recruitments increase maximal contractions, and have greater motor unit activation. In healthy muscles, up to 100 percent of motor units are activated (Moritani, 1998).

In relation to DMD patients who have damaged or incomplete dystrophin protein in the muscle cell, the previous discussed skeletal muscle biomechanics and function differ greatly. The dystrophin protein serves as the connection and communication bridge between the cell membrane complex and the actin strands, as shown in Figure 2. Dystrophin provides the strength and stability for each muscle fiber, thus the entire muscle during contractions. Without the dystrophin protein, the muscle is more susceptible to damage (Van Putten, et al., 2012). The dysfunctional dystrophin leads to “segmental necrosis” of the muscle, causing the fibers of the muscle to progressively deteriorate (Cornu, 2001). Hence the deterioration of every muscle occurs in the body over time. This deterioration is the most common characteristic of DMD. Dystrophin is essential to muscle stability, the direct function of dystrophin is unknown but studies suggest that it alters intra-cell calcium processing and function (Blake, et al., 2002). This is essential since calcium ions increase in concentration signaling astropomyosin and troponin to enable actin and myosin contraction (Cooper, 2000).

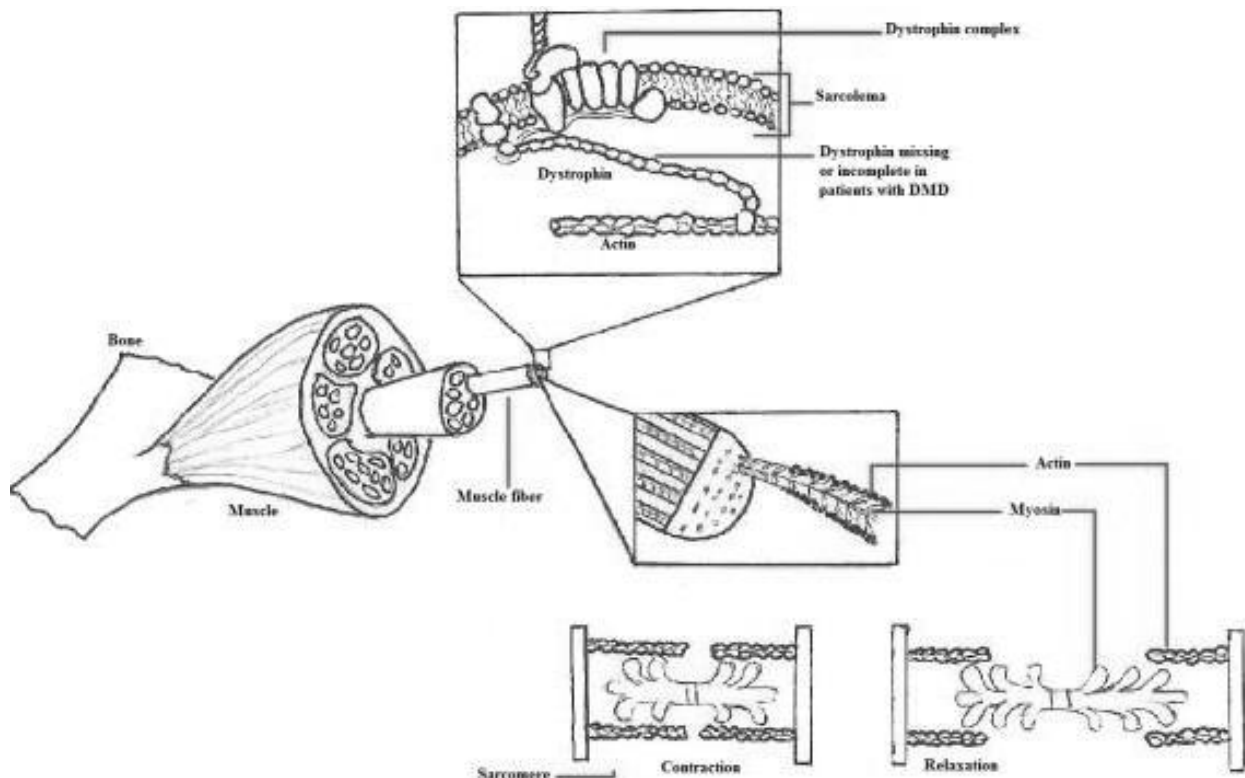


Figure 2: Sliding filament theory and dystrophin protein

Figure 3 displays graphs from an earlier experiment used to compare mechanical properties between normal muscles and muscles affected by DMD. The experiment compared the effects between male and female muscles.

However, it can be seen that there is significant difference in the strength and elasticity between normal muscles and DMD affected muscles in both males and females. The fracture point for DMD muscles occurs at much lower stresses than for normal muscles, which emphasizes on the decrease in fatigue resistance.

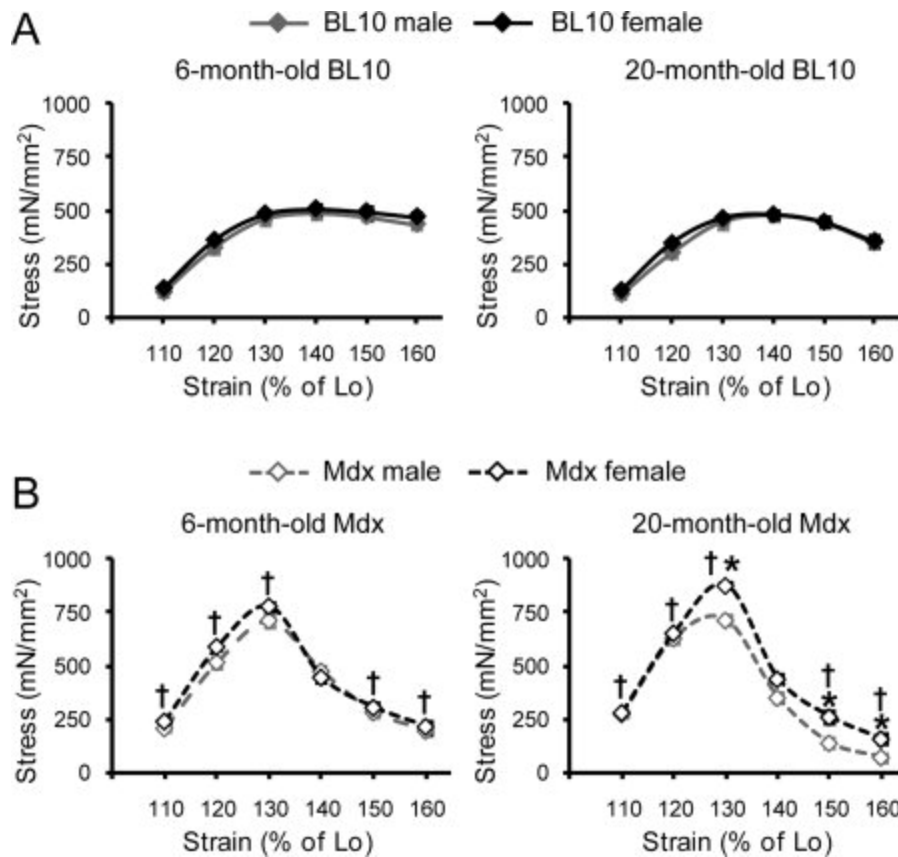


Figure 2: Gender differences in contractile and passive properties for (a) normal muscles (b) muscles affected by DMD (Hakim et al., 2012)

Bones undergo tensile and compressive stresses caused by loadings. They are composed of cells which react to its surroundings by detecting the amount of loading, or that lack of thereof, on the bone. If a bone doesn't undergo a lot of loading, which is generally any form of movement, osteoclasts start absorbing bone cells, causing the bone density to decrease. However, the loadings cannot be too high either. A very high loading could cause tensile and compressive fractures. In the case of DMD, lack of mobility in the femur bone starts bone density loss over prolonged periods. In order to make sure the bones of DMD patients are able to continuously withstand tensile and compressive loads, the DMD Treatment Wheelchair produces small loads on the limbs that are in casts. This is done to ensure proper absorption and remodeling of bones by bone cells. The low resistance treatment of the casts and the small amounts of load enable support for improved muscle contractions. The weak muscles of DMD patients are not as capable of having enough contractions for independent movement so the automated protocols facilitate the movement for them. Since the force generated by the muscle is dependent on the force acting on it, as stated before, the minor external force is necessary to produce a greater muscle force. This should in turn gradually increase the size, and therefore the strength, of the muscle.

The wheelchair will help prevent bone loss by allowing bones in the body to undergo loadings during movement. This will be similar to the use of physiotherapy during rehab. However, a patient could be independent of any human help and could perform exercises at any time of convenience. For example, the movable leg portion of the wheelchair would help the femur, which otherwise becomes weaker as the patient loses the ability to move it on his or her own. Movement of the muscle in different ranges of motion is critical for noninvasive muscle treatment.

The wide range of joint movement by incorporating Vector Therapy treatments onto the DMD Treatment Wheelchair should improve plantarflexor muscle function due to increased exercising of the muscles. In addition, low intensity exercise training in DMD patients have shown less exhaustion after repeated cycles as well as mitochondrial adaptations without the worsening of DMD (Baltgalvis, 2012). However, low intensity exercise training has been successful when the training was done voluntarily. Therefore, emphasis must be placed on the DMD Treatment Wheelchair encouraging voluntary muscle activity, which is done by gradually increasing the amount of load the muscle will undergo during movement. It is important for the therapeutic benefits of the DMD Treatment Wheelchair to be used at an early stage while the patients have an adequate amount of muscle mass.

5. CONCLUSION

The integration of contemporary DMD treatments and robotic technology allow medical progress to accelerate by improving and increasing the quality of a patient's life. The DMD Treatment Wheelchair employs gradual physical therapy of the human body in all important limbs in order to slow the weakening of the bones, muscles, and eventually heart and lungs. Since physical exercise is difficult for DMD patients on their own, the treatment chair would ensure that their body is able to move and respond to everyday forces. The guided operation by the chair significantly improves safety, comfort, efficiency, and patient health.

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