Young Patient Education on Duchenne Muscular Dystrophy

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ROCHESTER INSTITUTE OF TECHNOLOGY

A Thesis submitted to the Faculty of The College of Health Sciences and Technology
In Candidacy for the Degree of
MASTER OF FINE ARTS
In Medical Illustration

Young Patient Education on Duchenne Muscular Dystrophy
by
Margaret Jane Atieno McFarland
02/10/2020
Abstract

Duchenne muscular dystrophy (DMD) is a genetic disorder that primarily causes the degeneration of major muscle groups. It’s caused by the absence of an essential sarcolemma protein called Dystrophin due to mutations in its gene that is in the X-chromosome. DMD affects 1 out of 4,000 boys worldwide with most being diagnosed between ages 3-5 and if left untreated, most patients would succumb to the disorder by their late teens or early twenties. While there currently isn’t a cure for DMD, there are different treatments available that are effective in prolonging patients’ lives.

Because DMD is such a deadly disorder, it is important for current and future patients to understand their disorder as soon as possible in order to prepare themselves for whatever the future may hold for them. Currently, there are many information resources about the disorder online. However, most of this information caters to adult audiences, like the parents of DMD patients, and there are very few that cater specifically to the young patients themselves. For this reason, I created an animated educational video about DMD for young patients, so they would be properly educated about the disorder.
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## List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ABD1</td>
<td>Actin Binding Domain 1</td>
</tr>
<tr>
<td>ABD2</td>
<td>Actin Binding Domain 2</td>
</tr>
<tr>
<td>AAV</td>
<td>Adeno-associated viral</td>
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<tr>
<td>BMD</td>
<td>Becker’s muscular dystrophy</td>
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<tr>
<td>CNS</td>
<td>Central nervous system</td>
</tr>
<tr>
<td>CK</td>
<td>Creatine kinase</td>
</tr>
<tr>
<td>DGC</td>
<td>Dystrophin-glycoprotein complexes</td>
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<tr>
<td>DMD</td>
<td>Duchenne muscular dystrophy</td>
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Part I: Introduction to Duchenne Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is the most common muscular dystrophy in children and causes progressive muscle degeneration, as well as respiratory failure and cardiomyopathy. About a third of DMD patients also develop behavioral problems and slow cognitive skills.1-3 These symptoms are caused by the absence of dystrophin, a protein located primarily in between the sarcolemma and muscle fibers of skeletal and cardiac muscles. Small amounts of dystrophin are also present in nerve cells in the brain.1-3

Dystrophin and its relations to DMD

Dystrophin is a 427 k-DA long, rod protein tethered between F-actin proteins in superficial myofilaments and protein complexes known as Dystrophin-glycoprotein complexes (DGC) in the sarcolemma. The protein consists of four functioning domains: the N-terminal actin binding domain (ABD1) that binds to the F-actin; the central rod portion that’s made up of 24 repeated units, with units 11-17 acting as the second actin binding domain (ABD2); a cysteine rich domain that attaches to two domains of the DGC; and the C- terminus that binds to the last domain of the DGC.4 The flexible structure of the protein stabilizes the muscles’ cytoskeleton and extracellular matrix during contractions and prevents excessive membrane tear.2,4,5 Dystrophin’s role in the central nervous system (CNS) is still being explored but is believed to be essential for proper neural and brain function, including cell signaling.3,4

For patients diagnosed with DMD, dystrophin is completely absent from the body. This will cause the myofibrils and sarcolemma to experience small ruptures during muscle contraction and cause increased infiltration of extracellular calcium ions and inflammatory cells.2 Unlike normal, minor muscle tears, this results in excessive muscle inflammation, which further damages the myocytes and leads to the damaged muscle tissue being gradually replaced with fibrous scar and fat tissue.1,2,6 The continuous inflammation and accumulation of connective tissue causes muscles to lose mass and atrophy until they no longer function. This outcome primarily affects the major proximal muscles in the limbs, especially in the legs and hips, and it gradually effects the muscles in the torso, back, neck, and distal appendages. The disease simultaneously effects the cardiac and respiratory muscles, causing the functional capacity of both the heart and lungs to diminish over time.1,2,6

The physical signs of the protein’s absence usually appear between ages 3-5, when the child starts showing difficulties performing basic activities including walking, running, and jumping.1,2 The muscles continue to weaken over a span of years and by ages 10-12, the patient becomes wheelchair bound. DMD patients also develop severe scoliosis, joint contractures, and lumbar lordosis.1,2 By their late teens and
early twenties, if left untreated, the patient will no longer have enough muscle strength to sit upright and are bed bound until they succumb to the disease. At least 75% of the deaths are caused by related respiratory problems while the rest are due to heart failure in the left ventricle.  

As for DMD’s effects on the CNS, clinicians have recently found correlations between dystrophin’s absence and abnormal brain and spinal cord formation. It is hypothesized that dystrophin’s absence is connected to some patients developing behavioral problems and impaired cognitive abilities. Currently, however, this side of DMD hasn’t been explored enough, partly due to the low percentage of patients being diagnosed with any mental related problems and the severity of these problems can range from patients having minor language delay to extremely severe disorders similar to autism, thus making it difficult to properly conclude DMD’s effects on the CNS.

The cause of DMD

The absence of dystrophin in DMD patients is the result of mutations in the gene dystrophin, located on the short arm of the X chromosome. It is the largest gene in the human genome, being made up of 79 exons, and is documented to have many different mutation hotspots that would lead to DMD or the less severe phenotype known as Becker’s Muscular Dystrophy (BMD), which results in the production of smaller partially functioning dystrophin. The most common type of DMD mutation is a frameshift mutation that creates a premature stop codon and shifts the transcription reading frame, resulting in skipping essential exons from the mRNA that is required to make a functional protein. This leads to the production of very unstable proteins that are quickly degraded, thus eliminating any presence of the protein in the body.

Due to it being located on the X chromosome, males with the mutated gene are the ones who fully develop DMD. In contrast, women with the gene typically don’t develop DMD because the mutation is recessive, though it has been reported that some women exhibit muscle weakness in later stages in life but not to the same extent as their male counterparts. In addition, these women have a 50% chance of passing the mutation to their male offspring, while the female offspring have the same percent chance of inheriting and passing the mutation to future generations. This is why females with the mutation are known as “carriers” of DMD. It’s only in extremely rare cases that a woman would develop DMD-like symptoms and they’re instead known as “manifesting carriers.”

Diagnosing DMD

Currently, approximately 1 out of every 4000 males around the world are diagnosed with DMD and it is considered the most common form of muscular dystrophy that affect young boys. Because of the severe symptoms, clinicians highly recommend families with the inherited mutated gene, as well as
individuals who appear to be developing DMD-like symptoms at a young age, get diagnosed as soon as possible. Most patients are diagnosed between ages 3-5 through a series of tests. The tests not only confirm the diagnosis but also the determine the severity of the disorder.

Physical examinations are used first to identify signs of DMD. The examiners test the patient’s muscle strength and ability to perform simple activities, including running, jumping, and climbing stairs. One activity that is often assessed in these exams is a climbing technique called “Gower’s sign,” which tests the patient’s ability to climb themselves up from the ground using their leg and arm muscles. If the patient has difficulties performing these tasks, like waddling instead of walking or running, these are usual signs of muscle weakness but would also require further tests to determine if the cause is DMD. Examiners also look for physical deformities, such as abnormal curvatures in the back like scoliosis and kyphosis, as well as enlarged calves, which is caused by accumulated scar tissue.

Another type of test used is a blood screening which measures the concentration of creatine kinase (CK), an enzyme that is expressed after excess muscle inflammation and damage. Typically, in a normal body, the expression of this enzyme is very low in the blood stream; however, if the enzyme’s concentration is high, it would indicate that there is excessive muscle damage in the body. While this screening can give a strong indication if a patient has DMD, the other tests are sometimes still required to confirm since there can be other reasons for this results that may not relate to DMD.

The other tests needed to confirm the diagnosis are DNA screenings, to detect the mutated gene, and muscle biopsy, to examine muscle tissue for the presence of dystrophin. DNA screenings are used to verify the results of previous tests, especially the CK blood test, and to help establish the specific mutation that causes DMD. This test can also be used for prenatal diagnosis of DMD for expecting mothers, and for familial genetic counseling and screening. A muscle biopsy test can also confirm DMD but this method is only used if the DNA test is negative, which happens in less than 5% of cases.

Part II: Treatments and life management for patients and families

Despite the progress made in DMD research and clinical care, there is currently no cure. Physical damage caused by DMD can’t be reversed and attempts to rebuild muscle through conventional methods like exercise can exacerbate the muscle damage if practiced incorrectly. While surgeries and supplements can help maintain a patient’s wellbeing, these treatments are mainly for temporarily treating the heart, lungs, and bones, and have very little impact in stopping the disorder’s progression. However, since the late 1960’s, different forms of experimental clinical treatments have demonstrated their ability to help manage or slow DMD’s progression.
Corticosteroid therapy is the most established and commonly used treatment for DMD and it involves the use of steroid drugs such as prednisone and deflazacort.\textsuperscript{1,2,8,14} Clinical studies show that corticosteroids help patients retain muscle strength and extend their ability to walk by 3-5 years. The steroids also prolong cardiac and pulmonary capacity, thus extending the patients’ life expectancy. However, the main drawbacks of this treatment are the many side effects, including hypertension, vertebral fracture, cataracts, weight gain, stunted growth, and behavioral changes.\textsuperscript{8,14,15}

The other treatment currently being studied through clinical trials is gene therapy and its goal is to restore the body’s ability to produce dystrophin. One way to accomplish this is by repairing the protein’s reading frame through exon skipping by using drugs such as eteplirsen to manipulate the pre-mRNA splicing to skip common mutation hot spots and reinstate parts of the gene’s reading frame.\textsuperscript{16,17} Another gene therapy involves implanting dystrophin cDNA directly into muscles via adeno-associated viral (AAV) vectors.\textsuperscript{4,5,7} Both approaches are intended to produce small, but functioning dystrophin protein, which researchers hope will restore muscle function. However, despite the promising preliminary results, gene therapy has its own set of challenges, including the large size of the dystrophin gene, the immunological response to the AAV vectors as well as their restrictive size capacity, and the insufficient amount of miniature dystrophin the treatment produces.\textsuperscript{4,8,18}

Despite the shortcomings, these different treatments have made a noticeable impact on patients’ health over the past few decades by delaying the effects of DMD, thus extending the patients’ life expectancy. In fact, according to recent reports, most modern patients are now living past their late 20’s and early 30’s, as compared to patients before the 1980s, who usually only lived until their late teens and early 20’s. According to one report, researchers found that patients born between 1980 and 1990 had a nearly 50% survival past the age of 25 while patients born between 1960 and 1970 had a survival rate of nearly 14%.\textsuperscript{12,13} These statistics show how the evolving treatments and the improved standard of care have helped patients live longer, and can be seen as a steppingstone towards creating a cure for the disease.

In addition to the above treatments, health professionals like occupational and physical therapists help patients adjust to their limitations in and outside of their household and provide psychological treatments for the patients and their families. They also provide adaptive equipment to improve patients’ lives, such as scooters, wheelchairs, lifts, specialized automobiles for independent driving, and non-invasive, nocturnal ventilation systems for patients with weak lungs.\textsuperscript{10-12,19}
Part III: DMD awareness and patient education

Health professionals recognize the importance of educating their patients about their disease. Not only does education improve the relationships between the patient and their doctors, the information also helps patients and their caregivers to physically and mentally prepare for future changes the patient may experience, as well as for future treatments. And because most information is now easily accessible through the internet, mostly through medical websites and non-profit organizations like the Muscle Dystrophy Association (MDA), it is easy for anyone to become better educated on the disorder.

However, most of these resources seem to cater to adult audiences because they use complex terminology accessible to those with a high school education or higher, but not to young children. While these resources may be useful for parents of DMD patients, they are too complex for young, recently diagnosed patients to understand on their own. Though doctors and parents can explain the disorder to these patients, it is important and logical to have a comprehensive and engaging source of information that appropriately caters just to the young patients. This is the main motivation for my thesis project.

Part IV: The Thesis Project: Educational Video for Young DMD Patients

The project and its purpose

For my project, I created a simple and comprehensible source of information about DMD for young, recently diagnosed patients, so they can be properly educated about their disorder. It can be used by doctors and other professionals involved in the care of DMD patients to teach the patients and their families, though it can be used by anyone who is interested to learn about DMD. I hope this project can also help promote the usefulness of using media in patient education for very young patients who have complex ailments.

The medium

The project is a video consisting of different forms of animation and imagery accompanied by informative narration and comprehensible terminology. The video is posted online so it can be streamed or downloaded on any digital device.

Target audience

The primary audience for the project is young male patients, mainly between ages 3-6 because that is the age range of most patients diagnosed with the disorder. It can also be used for older patients who may be cognitively impaired or were diagnosed later in life. I also hope that the video can be useful
to the parents, teachers, legal guardians, and care takers of the patients, as well as anyone curious about the disease who may not understand the medical terminology often used in many of the public DMD archives.

Content

The video consists of verbal, written, and visual information about DMD, though there is a heavy emphasis on the visual information. One reason for emphasizing the visuals in this project is that visuals have proven to be useful tools in conveying information that may otherwise be difficult to comprehend solely through conventional written or verbal methods. For example, in a 2009 study on the effectiveness of visual multimedia programs in teaching science to 10-11 year old elementary school students, students who used visual aids performed significantly better on comprehension tests, answering approximately 80% of questions correctly, while students who didn’t receive the visual aid answered approximately 60% correctly. In a similar study from 2012 on the impact of cartoon illustrations in patient education programs for colonoscopy preparation, the individuals who used instructions with visual aids performed better bowel preparation than those who relied solely on written and verbal instructions. Though there were some exceptions and minor limiting factors, the researchers conclude that the inclusion of visual aids was extremely useful for conveying information to the recipients, so long as the visuals were comprehensible. Researchers also support the notion that visual aids are universally useful for people of different demographics, regardless of age and background knowledge, though they also state that the ones who benefit most from visual aids are those with low literacy skills.

The other reason for heavily incorporating visual imagery in this project is to appeal to the target audience, very young children. Not only do children in the given age range have lower literacy skills compared to adults, and may rely on images to help them understand the information presented with it, it has been demonstrated numerous times that children are attracted to the visual imagery in their learning or entertainment material, like books or videos. The images stimulate their senses and imagination, and children simply find the images appealing. One problem is that there isn’t enough conclusive evidence that very young children can properly comprehend all visual information. Some studies indicate that the inclusion of images had little impact on children’s ability to understand the presented information and claim that children before the age of six simply have a harder time comprehending or remembering certain information compared to older children. However, I believe that including the visual imagery can still have an impact on young viewers if applied correctly, and there is hope that children will comprehend what the visual information represents.
Art style and composition

The educational video includes both three-dimensional (3D) and two-dimensional (2D) animation. Because the target audience is very young children, the art style is simple and cartoon-like because I believe this style is the most appealing to this demographic. And because I want the viewers to be able to follow along with whatever is being presented, the visuals are not overly detailed.

There isn’t an overall color scheme and most of the colors are moderately saturated so the video is engaging and not straining on the eyes, though some elements that are deemed important have noticeably higher saturation to highlight and contrast. In addition, some elements that relate to each other in some way have the same color; this feature is more of a subtle visual effect rather than an important aspect for viewers to pick up on.

Level of success

I will measure the success of this project by evaluating how well the viewers of the video understand the information presented. Because the final product is published online, it is attached to a questionnaire that would ask the viewers how well they understood the video. For young viewers, there is a disclaimer that instructs the parent or legal guardian to help the young viewer answer the questions or answer them on their behalf.

Part V: Development of the Thesis Project

Narrative script

Because the primary audience is young children, it was decided that the script wouldn’t contain complex, scientific words. The only exception is ‘dystrophin,’ which is followed by a simplified definition that could be understood by a young viewer. My thesis advisor and I believe that for the viewers to properly understand DMD, it is essential that they understand what dystrophin is and why it’s so important to the body. While the protein’s role is straightforward, we also believed that the young viewers may have a hard time comprehending it. In order to explain how dystrophin works in a way the young viewers would understand, I decided to include simple arts and crafts items in the video to help visually demonstrate how the protein stabilizes the body. I chose crafting glue to represent dystrophin and popsicle sticks to represent muscles, and in the video, a fully built popsicle stick house would represent a stable, normal body while a pile of sticks would represent an unstable, DMD-afflicted body. Though there would be narration in those scenes, I hope that the young viewers will recognize those crafting tools and understand how dystrophin holds the body together.
To further illustrate how DMD affects the body, the video shows how DMD affects body movements by comparing the movements between a character afflicted with DMD to a healthy individual. This section of the video is equally as important as the section explaining about dystrophin, as it applies the previous information regarding dystrophin and expands on how its absence affects the body in different ways. I’m hoping the viewers will be able to understand and make this connection mainly based on the visual information in this portion of the video.

The rest of the video consist of other short, informative segments about DMD, including the primary muscles that are affected, who gets affected and how many, etc. Though these segments don’t contain as much animation as the previously mentioned segments, it was important to include them to help properly educate the viewer about the disease. It was also important to clearly state to the young viewers that it isn’t their fault that they have the disorder, for young children are very impressionable and I don’t want to make the patients believe they are responsible for getting the disorder in the first place.

After incorporating these features into the final script and storyboard, the basic outline of the video came out like this:

The video begins with a brief explanation of DMD and shows the muscles that are first affected by it. This leads to the introduction of dystrophin and then to the presentation with the glue and popsicle sticks to demonstrate how the protein works in the body. Next, the video further demonstrates DMD’s effects on the body by comparing the movements between a character with the disorder and a healthy character. Afterwards, the video explains that DMD is inherited and it affects a small percentage of boys worldwide, emphasizing how the disorder is not the patient’s fault. At the end of the video, viewers will be assured that despite having DMD, they will be alright because they are in the capable hands of their doctors and their families.

My reason for creating this ending is because I felt it was necessary to reassure the impressionable viewers that despite having a lethal disease, it wasn’t the end of the world and there was hope that they would have a good life despite it. Essentially, I believed the video needed to end with a positive tone rather than a bleak one for the young viewers’ sake.

**Storyboard, audio, and animatic**

The script included the dialogue and the stage directions for the storyboard. Once the script was finalized, roughly sketched storyboard frames were constructed on paper and then reconstructed through Photoshop and Illustrator and were later used to make the animatic. A narrator was hired based on their ability to sound both attentive and informative at the same time, essentially sounding like a kind teacher.
that the young viewers could feel comfortable listening to. After the narration was produced, it was used to pace the animatic and the final animations. As the final animations were produced, they would replace the storyboard frames in the animatic. Subtle background music from the stock music website Bensound.com and sound effects were incorporated into the final animation.

**The 3D animation**

All the 3D elements were constructed, rigged, and animated in Autodesk Maya, while the UV maps were rebuilt in 3D-Coat, and the bump maps were constructed in Autodesk Mudbox. Most of the custom skin shaders were painted in Photoshop and Illustrator, while the others were premade and available in Maya. Once the key frames for the animations were completed and tested, the animations were rendered through the Autodesk Arnold rendering engine and the frames were compiled into an Adobe After Effects file. Most of the 3D objects used were made entirely from scratch, with the only exception being the dystrophin protein model portions, which were obtained from a credible research website. The following sections will go into greater detail of the construction and animation process of the most important 3D models in the project.

**The boy models**

The boy models were some of the most important 3D assets created for the project. One of their main purposes was to demonstrate the physical differences between a boy afflicted by DMD and a healthy boy when performing simple physical activities, including running, jumping and climbing stairs, while the other purpose was to show the primary muscles affected by the disorder. Though the overall style of the video was to be cartoon-like, it was decided that these boy models would have relatively realistic body proportions, with the exception of a slightly large head with cartoon-like facial features. The reason for this design was because I believed that the viewers would be able to identify with the model and recognize the motions better on a realistic model than one with exaggerated proportions, and I believed that attempting to do so would have been difficult. Once the concept illustrations were completed (Figure 01-A, the images were uploaded into Maya and were used as the template to create the boy models.

**Construction**

During the construction, I built the head separately from the rest of the body because I believed it was easier to construct them as separate parts and add details to one part without affecting the other and prevent any sculpting or morphing problems. Both the heads and the bodies were built up from simple shapes with simple building tools. Though it would have been easier to buy a premade model for this
project, I chose to build my own model to test my 3D sculpting skills and so I would retain my rights over the assets for any future use.

Once the prototype model head and body were completed, they were attached to a simple, custom skeleton rig to test its range of motion by animating it to walk. The legs’ movements worked as intended but it was noticed that the upper torso would cave in and morph when the arms would move, even after manipulating the skin weights in that area. I attributed this issue to how I had constructed my model’s body, specifically by having arms rest at an approximate 90° angle relative to the body (Figure 01-B.)

Figure 01: A- Concept illustration of the boy model; B- the boy model, mid-construction; C- the prototype for the boy model with prototype shaders for the body and face; D- one of the final models with placeholder skin shaders for the body and face.
I also found that the general, linear skinning method used to attach the model to the skeleton rig also caused unnatural morphing of the limb joints when bent. To fix these problems, I altered the body by repositioning the arms so they would rest at a lower angle, and I used the dual quaternion skinning method which preserved the mass of the limbs when bending (Figure 01-C). These changes greatly improved the appearance of the model during the motion tests. Additional minor alterations were added to the body, such as slight enlargement of the hands and feet to improve the model’s proportions and to have it fit more in line with the cartoony aesthetic. I additionally created an alternative version of the body with detached hands in order to prevent any further unwanted morphing in the arms but I found that this change was not entirely necessary after the other changes made, but was still useful for motions that required a lot of hand or wrist movements. In the end, both the attached hands and detached hands versions of the body were used in the final video for different actions.

Sculpting the head had its own share of issues, but the process allowed for more experimentation with different sculpting tools. Because I wanted to include eye movement in the animation, detached eyeballs were created and were eventually fitted with two different eye skins, blue and brown, which are used to further help distinguish the models from one another during the animation process and for aesthetic purposes. The prototype head had somewhat realistic proportions, but it didn’t fit the cartoony appearance I had envisioned, and it looked very stiff and unexpressive. To fix this, I altered the face by enlarging the eye sockets and rounding the face to make it look more youthful and cartoon-like. I also created detached eyebrows and eyelashes to make the face more expressive. A high polygon version of the head was created in hopes to create alternative versions of the head with different hairstyles and facial features that could’ve been used to distinguish the characters from one another. However, this idea was scrapped because I decided that this wasn’t necessary for this project and I didn’t want to confuse the viewers by having too many different characters or adding details that may distract from the purpose of the models. So, though the high polygon head was built, the low polygon version was used throughout most of the video (Figure 02). In the end, three different models of the boy character were built; one shirtless model and two fully clothed models, with one having his hands attached to his arms while the other’s hands were detached.
For these models, I used the basic AI Surface shaders but replaced the color with custom painted skins. After altering the shape of the prototype head, I also changed the painted skin colors to match better with the body, but I soon realized I needed to do more for this shader. Initially, I only painted the face with one color because I had assumed that the facial features would still be visible after rendering like they were when it wasn’t rendered (Figure 02-B). But after rendering the face, I saw that the facial features were nearly invisible, especially at certain angle. This was because the skin I had painted made the face look flat (Figure 02-B; Figure 03-A; Figure 03-B.) To fix this, I painted highlights and shadows where the creases and protrusions were on the face, like under the nose and lips. I found that doing made
the facial features more noticeable than before. I even added small features like hinted blush and freckles to make the face look more organic (Figure 03.) Though those addition weren’t necessary, I believed adding them made the face of the character look more appealing.

As for the body skins, though the addition of light and shadows weren’t necessary, they serve a purpose and required different work done on them. In order to distinguish the models from one another during the movement segments, I created skins with different shirt colors and designs that would correspond with the condition they represent in the video; the boy that is affected by DMD has a red shirt with the word “DMD” on it with a graphic of a broken planet, while the boy not affected by DMD was in the yellow shirt with the word “Dystrophin” and a graphic of a rocket ship. The colors of the shirts were chosen to reference other elements throughout the video, such as the yellow dystrophin model that appeared in an earlier in the video, and whenever the acronym “DMD” which always appears red on
screen. Though these details weren’t vital to understand the information presented and colors and graphic were mainly for aesthetic appeal, I still wanted to keep some consistency with the colors used throughout the video.

![Rendered images of the final boy models built with different skin to distinguish them from each other, with (C) having an altered body structure. A- model with the red shirt represents a boy afflicted with DMD; B- model with the yellow shirt represents a ‘normal’ boy not afflicted DMD. C- the shirtless model.](image)

Excluding the two different shaders for the eyes, I made a total of five custom skins for the different parts of the boy models; two different skins for the heads, and three different skins for the bodies, with two of them being for the fully clothed models and one for the shirtless model. And because I didn’t want to make additional shaders for the different versions of the fully clothed models, I slightly altered the UV map of the detached hand model by incorporating the UV maps of the hands into it, and had the models use the same shader.

**Rigging**

The custom rig skeletons from the motion tests were revised throughout the reconstruction process and were used in the final animations. The final version of the rig included parent, joint, and direction constraints on most of the joints and were controlled with NURB shape controllers, IK handles and pole vector constraints on the arm and leg joints, and orientation controls for the eyes (Figure 05-A; Figure 05-B; Figure 05-C.) The reason for designing the rig this way is because it was easier to control and animate the models through constraints. I used the IK handles and pole vector constraints mainly for
simple repeating movements, like in a walking cycle. For single irregular movements, like lifting an arm and turning it at an angle, the NURB constraints provided better, precise control. So, when animating, I would switch between using the NURB constraints to the IK handles and pole vector constraints for the different movements.

Figure 05: A- Frontal view of one of the boy models with its constraints visible; B- Same view but with the X-ray feature enabled, showing the constraints and the rigged skeleton; C- Side view of the model with the skeleton and constraints visible; D- a screenshot of the model in running motion on top of a custom landscape that resembles a racing track, with the constraints visible; E- fully rendered screenshot of (D).
I used motion references from an online resource library called EndlessReference.com as well as my own reference videos to create the key frames for the ‘normal’ movement animations. For the ‘DMD-afflicted’ movement animations, I duplicated the ‘normal’ movement model and altered the key frames and make additional adjustments based off reference videos of real DMD patients. The narrative audio for each scene was used to pace the length of the full animations. I also built simple landscapes for each action segment; a racing track for the running models, a jumping sand pit for the jumping models, and a set of stairs for the climbing models. Additional adjustments were made to the keyframes to make them look like they were interacting with the landscapes (Figure 05-D; Figure 05-E,) for some of the action segments, I would have both the ‘normal’ and ‘DMD’ models occupy the same space in order to better demonstrate the difference between their movements. After testing the movements again and making final adjustments, the animations were rendered into series of TIFF files and were converted into video segments in After Effects.

**Dystrophin, sarcolemma, and associated proteins models**

In the portion of the video that introduces dystrophin, the video briefly shows the sarcolemma with dystrophin and the other associated proteins. To create the sarcolemma, I used a FX dynamic tool in Maya to duplicate a simple phospholipid model on a flat, multiple polygon plane. The edges on the plane were shifted to give more dynamic to the placement of the phospholipids and the sigmoid curve tool was used to bend the plane in order to give a subtle, organic curve to the membrane. The phospholipids, as well as some of the associated proteins like parts of the DGC, were made up of rudimentary shapes. The other models, such as the F-actin, myosin bundles, and the rest of the DGC, were made of simple shape that were modified with basic sculpting tools. The only model in this set that was more complex than the other models was the dystrophin model, which was intended in order to distinguish itself from the other models in the segment.

The dystrophin model was made up of multiple Protein Databank (PDB) files obtained from the Research Collaboratory for Structural Bioinformatics Protein Databank (RCSB PDB) website. The files of dystrophin’s rod portions and actin binding site were modified into lower polygon models for easier rendering and animation. Because the dystrophin protein is reportedly very long in proportion to the other elements of the sarcolemma, I took artistic liberties to change its size and length to fit with the other structures but retained its distinctive shape to make it more noticeable. It was deemed unnecessary to replicate a perfect model of the protein, especially with the other overly simplified models, but making it distinct from the rest of the sarcolemma was necessary for the narrative of the video. Though this short
segment involved many model parts, I hope I simplified it enough for young viewers to understand without being overwhelmed by the visuals.

Figure 06-A: Frontal view of the sarcolemma with dystrophin and other associated protein models labeled. Only dystrophin was labeled in the video. Figure 06-B: Three-quarter view still frame of the sarcolemma from the final animation. The dystrophin model has an overly detailed design and saturated color, while the others are made up of simpler forms with desaturated colors.
Cel shading with colors

The shaders used for these models are different from the shaders used on the boy models and landscapes. Instead of using the standard base color for the skin, I created a custom toon shader, or “cel shader.” This shader used emission color feature in the Arnold Standard Surface shader, and it was attached to the network consisting of a ramp shader controller, a color corrector, and facing ratio controller (Figure 07-A.) The ramp shader gives the models their colors and consist of three values, a dark tone, medium tone, and light tone. The colors in the ramp shader were not blended into gradients and instead separated with sharp edges (Figure 07-B.) The facing ratio controller kept the orientation of the ramp shader’s colors relative to the position of the rendering camera, so the colors would stay in the same position regardless of the object’s angle or position to the camera. The design of this shader essentially made the models look flat and cartoony while retaining some of the model’s dimensions (Figure 07-C.) This style was chosen to fit with the visual style of the rest of video.

As mentioned before, colors and color manipulation were an important feature of this project, and this was evident in this segment. The dystrophin model’s shader consisted of bright, saturated yellow and orange tones, which would contrast with the other protein models’ muted tones. This contrast is further emphasized in the final product with After Effects, in which all of the models except dystrophin lose all color at the end of this animated segment. This contrast is intended to further bring attention to the dystrophin model, which is meant to be the focus of the segment. Though it is already distinguishable by its unique shape, the use of bright colors illustrates the model’s importance within the segment. The choice to make dystrophin yellow also relates to the other segments of the video, specifically the movement animations with the ‘normal’ yellow shirted boy model.
Popsicle stick house and glue bottle models

As mentioned previously, it was decided to animate simple arts and craft objects, popsicle sticks and glue, to demonstrate how dystrophin stabilizes the body. I chose to create these items as 3D models instead of 2D illustrations because there were certain techniques that I had intended to use that were best accomplished in 3D. These models were constructed from rudimentary shapes with sculpting tools, and their simple designs made it easier to animate them, though there were some complications, which will be explained below.
Rigging and animation

At a certain point in the video, I wanted the popsicle sticks to collapse into a pile to represent the muscles when dystrophin is absent. Initially, I was going to use the nDynamics simulation system to make the popsicle stick house collapse on itself by converting the individual stick objects into nCloth objects and using invisible colliders to knock them over. However, after testing the simulation and adjusting the falling settings, I found that the objects wouldn’t fall the way I wanted them to and my computer had difficulty calculating the data. Instead, I animated the popsicle sticks traditionally by keyframing their positions. Though the process was tedious, this gave me better control over how the objects would fall into place and it was less straining on my computer.

For the glue bottle, which represented dystrophin in this segment, I intended to animate the bottle being squeezed. I used the BlendShape controller, which was an easy task because of how simple the bottle was; I first created a duplicate of the bottle body and morphed into the desired ‘squeezed’ shape, I connected it to the original bottle body as a blend shape, and through the BlendShape controller, created keyframes of the original bottle morphing to make it look as though it was being squeezed.

Cel shading with painted layers

The shading for the popsicle sticks and the glue bottle are similar to the cel shaders used on the protein models, except the colors were replaced with custom painted skin images created in Photoshop and Illustrator. There were two versions: a lighter shade and a darker shade (Figure 09.) I found that despite replacing the colors with the custom skins, the models still retained the 2D appearance I was aiming for and they looked as though they were vector illustrations instead of 3D models. For the popsicle house, I created four pairs of skins for the sticks; three pairs for the sticks that made up the main house and one pair for the red roof and chimney lining (Figure 08.) While all the sticks could have had the same appearance, I wanted to make the model visual interesting, so I experimented with different designs and colors to create the final design.

For the glue bottle, only the bottle body had custom shader with the skins created in Illustrator to create clean raster images so the label would be legible when rendered. Like the dystrophin model and the yellow shirted boy model, the bottle was intentionally colored yellow because it’s related to dystrophin.
Figure 08: Three-quarter view of the 3D popsicle stick house model; A- un-rendered with the AI standard gray shader, B- rendered with custom cel shaders.

Figure 09: A-Three-quarter view of the rendered dystrophin glue bottle with normal toon shaders used on the bottle top and cap and a custom toon shader for the body; B- The lighter shade of the bottle body; C- the darker shade of the bottle body.
The 2D elements

Most of the two-dimensional illustrations and animation in the video were created in Adobe Illustrator, with only two being created in Photoshop for minor art details. Illustrator was preferred over Photoshop because it creates clean-edged vector images which do not change in quality when resized, while raster images from Photoshop quickly degrade in quality. It was during the production of these illustrations that I was able to focus on the cartoon-like aesthetic. Nearly all the illustrations had the same art style, consisting of thick lines and moderately saturated colors, with the exception of visuals that are deemed important, which would have noticeably saturated colors to contrast with the surrounding images (Figure 10.) The following sections will go into greater detail of how some of the 2D illustrations were utilized in the project.

![Image of 2D illustrations](image)

Figure 10: A compilation of some of the 2D illustrations used in the video, created in Illustrator. Despite the difference in subject matter for each illustration, the art style was kept mainly consistent with thick outlines and moderately saturated colors. One exception is the biceps muscle on the flexing arm which was created in Photoshop. Most of these illustrations were animated in After Effects.

Combined 2D and 3D illustrations

The video includes a segment that shows the muscles first affected by DMD and it was decided to combine 2D and 3D visuals in this segment. The 3D shirtless boy model was constructed for this section,
and its front and back were used as a template to build 2D muscles through Illustrator (Figure 11.) The main reason for creating the muscles as 2D illustrations instead of 3D models because I believed that constructing the muscles in 3D would have been time-consuming and was unnecessary for such a short segment. The other reason was I believed the muscles would look more aesthetically interesting in the medium, especially when juxtaposed with the 3D model. I’m hoping, however, that the contrast in art style and medium won’t be too distracting to viewers.

Figure 11: A- the rough concept illustration of a boy with the anterior exposed muscles; B- 3D render of the shirtless boy without exposed muscles; C- 3D rendered boy with the 2D anterior muscles added; D- 3D render of the shirtless boy’s back with the 2D posterior muscles added.
**Figure animation**

The 2D animation in the video was done by manipulating Illustrator files within After Effects. I first created the character sprite within Illustrator with each body part that I intend to animate created separately into multiple layers. If a character sprite was intended to have many specific movements or poses, such as the doctor character in Figure 12-A, I created multiple versions of each body part for the desired positions (Figure 12-A to 12-E). The parts were labeled and arranged to prevent disarrangement of the parts so the sprite wouldn’t look disheveled when animating (Figure 12-F.)

Once the character sprites were complete, the files were imported into After Effects, which automatically separates and arranges the individual body part layers as they were in Illustrator. Within After Effects, the character sprites were animated by manipulating the position and opacity of the body part layers with key frames, much like in Maya. For the body parts that would normally move on a pivot, like an arm or a leg, the anchor or pivot point of the layer was shifted to accomplish the pivoted movement. A total of eight Illustrator files were used for this type of 2D animation, with the doctor character sprite consisting of the most since, as the narrator, it is the most prominent visual throughout the video.
Final product

The final video was made up of twelve 3D animation segments and over twenty 2D illustrations, with eight of them being animated. After completion, the video was presented to my advisors for their feedback and approval. Once it was approved, the video was uploaded to my personal social media webpages, including YouTube, Google+, and Behance, allowing public access to the video. Thanks to its availability, anyone can access it, including health professionals like my content advisor, Dr. Ciafaloni. Though unnecessary for the project, I also created an online questionnaire via Google forms to assess the effectiveness of the video, asking the viewers how effective the video was in educating them about DMD as well as asking their feedback on the quality of video and the visuals. Though it is unlikely I will receive a lot of feedback, I hope I do receive some constructive criticism which will be of use in future projects in this field of medicine and patient education.

Part VI: Conclusion

This project proved to be an interesting process that required me to experiment with many more techniques than initially anticipated. While it was disappointing that some of my initial ideas had to be discarded, I’m still pleased with what I was still able to include. If I had a chance to do anything differently, I would have tried to redesign the rigging skeleton for the boy models to allow complicated movements, specifically Gower’s sign. I believe having the models perform this movement would have been extremely useful for patients and their caregivers, since the maneuver is used to diagnose DMD and the technique is taught to patients to help themselves get up without assistance. Regardless, I feel that the custom rig I constructed was fine because it was still able to do all of the other movements clearly for viewers.

Despite the minor complications I had during the production of the project, I’m very pleased with the results and I hope that is will be of use to my advisor as well as anyone seeking simple and comprehensible information about DMD. What I hope to see in the medical field is further development in patient education for young patients with complex diseases like DMD in order to help them better understand their disorders and be prepared for what the future may hold for them.
Links to the thesis project video:

https://www.youtube.com/watch?v=N-jowtwbzrU
https://youtu.be/N-jowtwbzrU
https://www.behance.net/gallery/74568741/Brief-Introduction-to-DMD-for-Young-Patients
References:


