

Shriners Hospital for Children, Portland, OR

INFORMED CONSENT TO TAKE PART IN A RESEARCH PROJECT OR STUDY

Participant _____

Principal Investigator(s)

William Rooney, PhD (503) 494-1840

Co-Investigators

Erika Finanger, MD (503) 494-2598

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Title of Project or Study

Magnetic Resonance Imaging and Biomarkers for Muscular Dystrophy

Introduction

When we say “you” in this consent form, we mean you or your child; “we” means the doctors and other staff.

You are being asked to take part in a research study. Research studies include only people who want to take part. Before you decide if you want to take part, it is important that you read and understand this consent form. Please take your time to make your decision. Discuss it with your friends and family. We encourage you to include your child in the discussion and decision if she or he is able to understand. Please ask questions about anything that you do not understand before deciding whether or not to participate.

The person in charge of this study is Erika Finanger, M.D. and William Rooney, Ph.D. There may be other people on the research team helping during the study.

Some parts of this study are optional, and are not part of the original study. You may participate in the main study without participating in the optional parts. The optional portion is the collection of saliva and urine. There is a separate consent form for the optional portion of this study, where the risks and procedures are discussed in detail. By consenting in this form, you are not agreeing to be a part of the optional study.

Why am I being asked to take part in this study?

You are being asked to take part in a study because you have Duchenne Muscular Dystrophy (DMD). DMD is a genetic muscle condition seen only in boys. DMD causes weakness of large hip and shoulder muscles which later spreads to the small muscles of the body. This weakness is responsible for a decreased ability to walk and to perform other daily tasks. This study requires annual visits to OHSU, and may include 3 month and 6 month visits in between annual visits. The length of this study is 5 to 10 years, depending on your enrollment date.

We hope to learn the following:

- To learn more about the functional and strength changes that occur in muscles of the lower leg and/or arms of boys with Duchenne Muscular Dystrophy (DMD).
- To develop an improved Magnetic Resonance Imaging (MRI) and Magnetic Resonance Spectroscopy (MRS) protocol to monitor the progression of disease in children with DMD.
- To compare the muscles of boys with DMD with muscles of children of the same age who do not have DMD and determine whether this new technique can be used to monitor disease progression. The amount of muscle damage that we measure will be related to your performance in daily activities such as walking and use of the arms.

How many people will take part in the study?

There will be approximately 200 DMD and 100 control subjects involved in this study at three separate sites (here, at Shriners Hospital for Children and OHSU in Portland, the Children's Hospital of Philadelphia, and the University of Florida at Gainesville). At Shriners Hospitals for Children – Portland/Oregon Health & Science University we expect that about 100 subjects will participate.

What will happen on this study?

Before I begin the study...

You will have the following tests or procedures to find out if you can be in the study.

- You will complete a phone screen to see if you are eligible to participate in this study.

During the study...

If you can be in the study, and you choose to take part, then you will need the following tests and procedures.

- A MRI/MRS session on your arm
- A MRI/MRS session on your leg
- Functional testing (walk around the lab, climb a few steps, and perform functional arm movements)
- Online questionnaires about your medical history and the medicines you take
- A puberty assessment

This study requires annual visits to OHSU, and may include 3 month and 6 month visits in between annual visits. The length of this study is 5 to 10 years, depending on your enrollment date.

What will happen in this study that is “research”?

There are no experimental procedures used in this study. The procedures mentioned above are standard methods used to assess muscle strength, function, anatomy of the muscles (MRI) and biochemistry of muscles (MRS).

The ways we will collect data about you for this study are outlined below.

PROCEDURES:

If you agree to participate, Magnetic Resonance Imaging (MRI), and Magnetic Resonance Spectroscopy (MRS) measurements will be performed on your leg and/or arm muscles. The MRI technique allows us to get pictures of your leg and/or arm muscles and MRS gives us biochemical information of your leg muscles. With this information we can tell damaged muscle from your healthy muscle. It will also give us more information about the fat inside of your muscles. To see how strong your leg and/or arm muscles are, we may ask you to walk around the lab, climb a few steps, and perform functional arm movements. We will also look at your medical records to get information about what medicines you take. We will also take a small blood sample for genetic testing of the dystrophin gene if it has not already been done.

You must have the gene abnormality (mutation) associated with DMD in order to participate in this study. All boys with DMD who are between 3 and 18 years of age are eligible for this project, with the exception of those with any metal in their bodies that makes it unsafe to have an MRI/MRS. In addition, we cannot include patients who have had an injury to their legs and/or arms that make their muscles weaker.

The nature of the study, risks, inconveniences, discomfort, and other additional information is outlined below. You are urged to discuss any questions you have concerning the study with the staff members.

For subjects entering study on corticosteroids:

	Baseline	Annual Visits	*6month follow-up
Consent Discussion, Screening tests and medical history	X	X	X
Arm MRI	X	X	X
Leg MRI	X	X	X
Functional Testing	X	X	X
Total time	4-6 hours	4-6 hours	4-6 hours

For some subjects not entering on corticosteroids:

	Baseline	3month visit	6month visit	Annual Visits	*6month follow-up
Consent Discussion, Screening tests and medical history	X	X	X	X	X
Arm MRI	X	X	X	X	X
Leg MRI	X	X	X	X	X
Functional Testing	X	X	X	X	X
Total time	4-6 hours	4-6 hours	4-6 hours	4-6 hours	4-6 hours

Your child will be given a \$20 Toys R Us gift card for your participation in this study.

You may be asked to give us health information about your relatives. Any information you give us will be kept confidential as described in this consent. We will not contact your relatives without their permission. We may discuss with you the possibility of including your relatives in the study in the future.

The ways we will collect data about you for this study are outlined below.

Magnetic Resonance Imaging (MRI)

This part of the study will be done at the Advanced Imaging Research Center (AIRC) at OHSU.

MRI is a procedure that allows doctors to look inside the body by using a scanner that sends out a strong magnetic field and radio waves. You will lie on a platform inside the magnet. A series of images will be taken from your thigh and lower leg and/or arms. There may be two separate scanning periods for your arm and leg. Each scanning period will take approximately 90-120 minutes, during which you are required to lie still. During the entire procedure, one of the investigators will be present with you and will advise you of the progress of the study, making sure that you are comfortable. Although the measurement is painless, it will be somewhat noisy inside the magnet due to a hammering sound made when a large electrical current is pulsed through the magnet. Disposable earplugs will be provided to reduce the noise.

Magnetic Resonance Spectroscopy (MRS)

This procedure will give us biochemical information about your muscles and will help us discriminate between damaged muscle, healthy muscle and fat inside of your muscles. These measurements will be performed at the same time as the MRI procedure.

Muscle and Functional Performance tests

This part of the study will be done at Rehabilitation Services at OHSU.

Range of motion (ROM) measurements may be taken for the joints in your legs and/or arms. Your thigh and knee muscles, calf muscles and your ankle dorsiflexors (muscles on the front of your leg that allow you to pull up your toes) and/or selected arm muscles will then be tested using one of the strength testing methods. We may ask you to push or pull your foot or kick out your leg as hard as you can in order to determine your muscle strength and/or pull or push your arm to determine your muscle strength in your arms. Your knee and ankle or shoulder

and elbow will not move during the testing itself. We may also test your muscle strength manually by demonstrating a movement and then asking you to perform the movement with your arms or legs. If you are able to complete the ROM against gravity we may apply graded resistance with our hand or a hand held device called a dynamometry to see if you can hold that position. In addition to testing your muscles, you may be required to perform simple tasks such as getting up from the floor, climbing steps, and walking at different speeds and distances for up to 6 minutes. You may also be asked to perform simple tasks with your arms to determine your arm function. If at anytime you become tired you will be allowed to rest.

You may be asked to participate in motion analysis which would look at your walking pattern. If you are asked to do this you will have several small reflective balls which are self-adhesive placed on bony landmarks on your arms, legs, trunk, and head that will allow for several high speed cameras to capture your walking pattern. You will then be asked to walk at different speeds with the markers on your body. If at anytime you become tired you will be allowed to rest.

Blood Sample

We may also ask you to donate a blood sample to perform genetic testing of the dystrophin gene. For this purpose a single blood sample will be taken from your arm by a member of the research team at Oregon Health and Sciences University (OHSU). A small, sterile needle will be inserted into a vein in your arm and less than 1 teaspoon of blood will be taken. A small bandage will be placed over the puncture site to reduce the risk of bleeding. This sample will only be asked to be taken if genotyping of the dystrophin gene has not already been done.

Previously Collected Skin Samples

We are no longer collecting skin samples for this study.

You may have had a skin sample collected in previous years of the study. As originally described in the consent form, the skin sample was collected and is stored in a tissue bank for future research and is only labeled with a code that will not identify you.

In the future, the collected skin sample may continue to be given to researchers for other research studies. These studies may include genetic research. The samples will be labeled as described in the Confidentiality section of this form.

The Optional Study

There is an optional portion to this study that has a separate consent form that we may ask you to participate in. You are not consenting to be a part of the optional study by signing this consent form. The optional study includes collecting saliva, blood, and urine samples. The optional study blood sample is different from the blood sample described above under Blood Sample.

Medical information

We will also get information about the medicine you take, your medical history, and the stage of puberty you are in. Your parent will be asked to login to the ImagingDMD secure website (<http://imagingdmd.org>) with a username and password to complete an online medical history, medication log, and questions to determine your stage of puberty. Depending on your parent's availability, we may collect this medical information over the phone or during your visit to OHSU. Your parent will be asked to update any changes to this information at every visit. This will take about 10 minutes or less to complete.

If your parent is not comfortable performing the puberty assessment, Dr. Barry Russman, Dr. Finanger, or an OHSU registered nurse will briefly look at your pubic area to assess what stage of puberty you have reached. This will be done in the presence of one of your parents or guardian.

The medical history will ask questions about your physical strength, use of assistive devices, recent surgeries or injuries, and other information. This medical information is collected for research correlations as well as your safety and eligibility in the study.

Consent for future contact

We would also like to know whether you would like to be contacted and asked about possible participation in future research studies related to muscular dystrophy. If you check the box below you may be sent an informational letter about your possible participation in other research studies involving muscular dystrophy from other agencies including but not limited to Parent Project Muscular Dystrophy. Please indicate your preference by checking yes or no below:

Yes: _____ No: _____

Your initials: _____

If genotyping of the dystrophin gene has not already been done, and a blood draw and genetic testing is performed as outlined in the Procedures section under the title Blood Sample, we will give you the results. This is not a full genetic report, but only analysis of the dystrophin gene. Dr. Erika Finanger will share the results with you. The results will not be put into your medical record.

Because genetic information is complex and sensitive, the results should be discussed with a genetic counselor or your primary care provider who can answer your questions or discuss your concerns. You would be responsible for all costs associated with having the test repeated and visiting a doctor or genetic counselor to discuss the results.

The MRI/MRS scan is being done to answer research questions, not to examine your leg or arm for medical reasons. This MRI scan is not a substitute for a clinical scan (the type a doctor would order). The research scan may not show problems that may be picked up by a clinical MRI scan. If we find an abnormality that requires urgent follow-up, we will contact you and your doctor (with your permission) to help answer questions and get the right follow-up care for you. It is possible that you could be unnecessarily worried if a problem were suspected, but not actually found.

You may request copies of your MRI/MRS scan to be burned to a disc. A radiologist report will not be provided to you. The disc will be marked for research use only, and specified that it is not to be used for clinical use. The results of the research MRI/MRS scan will not be made available to you because the research is in an early phase and the reliability of the results is unknown.

How long does the study last?

If you choose to participate in this study, you will be asked to attend at least one session each year consisting of MRI/MRS, strength, functional testing and quality of life measures at regular intervals (6 or 12 months) over a period of 5-10 years. Depending on your performance of daily activities, we expect that you will participate in about eight to twelve sessions. At the

beginning of the study, you will need to participate in two MRI/MRS sessions distributed over 1-2 days.

In a small group of subjects that enter into the study steroid naïve, if and when you decide to start steroids, we may request two additional sessions in between your annual visits which would be at 3 month and 6 month intervals.

If you are unable to complete the 10m walk/run at your annual visit, you may be asked to come back in 6 months for a follow-up visit, and then continue with your annual visit schedule.

The total visit length in hours will be 4-6 hours.

Can I stop being in the study?

Yes. You can drop out of the study at any time and no one will be upset. It will not affect your other care and treatment.

Your study doctor may decide to take you off this study under the following circumstances:

- If she or he believes that it is in your best interest
- If you are no longer eligible for the study
- If you are not able to follow directions for the study

What are the risks of the study?

This study involves no more than minimal risks, which means that we expect that you will have no more risk than those you have in your normal daily life or routine physical examination or tests.

The magnetic resonance imaging (MRI) machine is a powerful magnet. There are no known risks from the magnet itself. However, if you have metal in your body, the magnet may cause the metal to move. If you know of any metal in your body, tell the investigator because you may not be able to have an MRI. Review any dental treatments you have had with the investigator, since these may involve metal. The most common discomfort of an MRI is the length of time you must lie still or flat while the scan is being performed. Some people with claustrophobia (fear of closed spaces) may find the MRI machine too confining. Finally, the MRI scanner makes loud beeping or thumping noises, so you may be offered protective earplugs to wear during the scan.

If you have not had genotyping of the dystrophin gene, we will draw blood from your arm. You may feel some pain when your blood is drawn. There is a small chance the needle will cause bleeding, a bruise, an infection, or fainting.

Some of the questions we ask regarding your puberty stage, medical history, and disease progression may seem very personal or embarrassing. They may upset you. You may refuse to answer any of the questions that you do not wish to answer. If the questions make you very upset, we will help you to find a counselor.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Be aware that this federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. GINA also does not protect you against discrimination if you have already been diagnosed with the genetic disease being tested.

Although we have made efforts to protect your identity, there is a small risk of loss of confidentiality. If the results of these studies of your genetic makeup were to be accidentally released, it might be possible that the information we will gather about you as part of this study could become available to an insurer or an employer, or a relative, or someone else outside the study. Even though there are certain genetic discrimination and confidentiality protections in both Oregon law and federal law, there is still a small chance that you could be harmed if a release occurred.

Are there benefits to taking part in the study?

No promises are being made that you personally will benefit from this study.

What other options are available to me?

Your other choices may include:

- Getting standard treatment or care without being in a study
- Taking part in another study, if available
- Getting no treatment

Talk to your doctor about your choices before you decide if you will take part in this study.

How will information about me be kept private?

We will take steps to keep your personal information confidential, but we cannot guarantee total privacy.

We will create and collect health information about you as described in this form. Health information is private and is protected under federal law and Oregon law. By agreeing to be in this study, you are giving permission (also called authorization) for us to use and disclose your health information as described in this form.

The investigators, study staff, and others at Shriners Hospital for Children may use the information we collect and create about you in order to conduct and oversee this research study.

We may release this information to others outside of Shriners Hospital for Children who are involved in conducting or overseeing research, including:

- The funder of this study, National Institutes of Health, and the funder's representatives
- University of Florida

- The Office for Human Research Protections, a federal agency that oversees research involving humans
- The Department of Health and Human Services
- Oregon Health & Science University

We will not release information about you to others not listed above, unless required or permitted by law. We will not use your name or your identity for publication or publicity purposes, unless we have your special permission.

Under Oregon Law, suspected child or elder abuse must be reported to appropriate authorities.

Shriners Hospitals for Children complies with Oregon state requirements for reporting certain diseases and conditions to local health departments.

When we send specimens or information outside of Shriners Hospitals for Children, they may no longer be protected under federal or Oregon law. In this case, your specimens or information could be used and re-released without your permission.

Data from this study may be shared with other investigators for future research studies. All identifying information about you will be removed from the samples before they are released to any other investigators.

We may continue to use and disclose your information as described above indefinitely.

Some of the information collected and created in this study may be placed in your Shriners Hospitals for Children medical record. While the research is in progress, you may or may not have access to this information. After the study is complete, you will be able to access any study information that was added to your Shriners Hospitals for Children medical record. If you have questions about what study information you will be able to access, and when, ask the investigator.

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

What are the costs?

You will not be paid for taking part in this study.

There will be no cost to you for participating in this study.

In the case of injury or illness resulting from this study, medical treatment is available. To the extent the Shriners Hospitals for Children provides medical services at its facility, those will be at no cost. If you get that care somewhere else, your usual healthcare coverage would apply. Shriners Hospitals for Children is not able to offer financial compensation for a research-related injury or other problems. Although no funds have been set aside to pay you for injury or illness, you do not give up any of your legal rights by signing this form.

What are my rights if I take part in this study?

You do not have to join this or any research study. You do not have to allow the use and disclosure of your health information in the study, but if you do not, you cannot be in the study.

If you do join the study and later change your mind, you have the right to quit at any time. This includes the right to withdraw your authorization to use and disclose your health information.

If you no longer want your health information to be used and disclosed as described in this form, you must send a written request or email stating that you are revoking your authorization to:

Laura McMahon
Oregon Health & Science University
Advanced Imaging Research Center
3181 SW Sam Jackson Park Road
Mailstop Code L452
Portland, OR 97239-3098
mcmahola@ohsu.edu

Your request will be effective as of the date we receive it. However, health information collected before your request is received may continue to be used and disclosed to the extent that we have already acted based on your authorization.

We will tell you about any new information or changes in the study that may affect your health or willingness to stay in this study.

Samples taken during this study may be used for research and development purposes not related to your treatment or condition. You will not have any property rights or ownership interest in products or data which may result from your participation in this study.

If in the future you decide you no longer want to participate in this research, no one will be upset, and you will not be asked to come to any further visits. However, the MRI/MRS data and information acquired about you in the study will not be destroyed and we will continue to use it for research.

Whom can you call if you have questions or problems?

If you have any questions, please ask us. If you have any questions later, please call Erika Finanger [503-494-2598 (work) or 503-308-0702 (cell)], or Bill Rooney [503-494-1840 (work) or 503-944-9065 (cell)].

You can contact the Institutional Review Board ("IRB") at (503) 494-7887 or irb@ohsu.edu for answers to questions you might have about research and about your rights as a research participant.

It is important that you tell your study doctor if you feel that you have been injured because of taking part in this study. In the event of research-related injury, please call Erika Finanger

[503-494-2598 (work) or 503-308-0702 (cell)], or Bill Rooney [503-494-1840 (work) or 503-944-9065 (cell)].

Your signature below will show that you agree that your child will take part in this research study, that you have had a chance to ask questions and all of your questions have been answered, and that you have read the information above. You will be given a signed copy of this informed consent form which is yours to keep.

<p style="text-align: center;"> OREGON HEALTH & SCIENCE UNIVERSITY INSTITUTIONAL REVIEW BOARD PHONE NUMBER (503) 494-7887 CONSENT/AUTHORIZATION FORM APPROVAL DATE </p> <p style="text-align: center; border: 2px solid red; padding: 5px;"> APR 26, 2016 </p> <p style="text-align: center;"> Do not sign this form aft8r the expiration date of: APR 25 2017 </p>

Signature of Witness	Date	Signature of Parent or Legal Guardian	Date
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Relationship to Participant (Parent, Legal Guardian, etc.)

Signature of Witness	Date	Signature of Parent or Legal Guardian	Date
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Relationship to Participant (Parent, Legal Guardian, etc.)

Signature of Witness	Date	Signature of Participant	Date
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(Signature of both parents should be obtained where possible and signature of patient should be obtained if 13 years of age or over.)

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Using language that is understandable and appropriate, I have discussed this project and the items listed above with the participant and/or his authorized representative.

Signature of person who conducted the informed consent discussion	Date
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