



The Brittle Bone Disorders Consortium (BBDC) is a group of physicians, researchers, and educators dedicated to learning more about Osteogenesis Imperfecta (OI). We aim to develop new treatments and to improve the overall care of patients with OI by connecting patients with support groups, expert doctors, and clinical research opportunities.

Welcome Message

From Consortium PI, Brendan Lee, M.D.



Welcome to the Brittle Bone Disorders Consortium's (BBDC) 1st newsletter. It is my hope that this newsletter will keep you updated on the research that the consortium is planning for the coming years. The BBDC is a consortium within the Rare Disease Network established by the Office of Rare Diseases Research, NCATS. We are a group of [researchers](#) across the United States and Canada interested in learning more about Osteogenesis Imperfecta (OI). The BBDC currently has 9 participating clinical sites and 1 data management site. We are also proud that the Osteogenesis Imperfecta Foundation is a participating advocacy site with leadership in training and education. Our partnership with the Osteogenesis Imperfecta Foundation and all of the families with OI is a critical component of our mission. Through the support of the OI Foundation supported Linked Clinical Research Centers (LCRC) and your participation, we were able to gather important information about individuals living with OI and form the foundation on which the BBDC was built. While the LCRC no longer exists, with its mission now superseded by the BBDC, we are now

positioned to answer many important questions about the natural history of OI and improved approaches to treat OI. In future newsletters, we will update you on specific projects and inform you about how to best participate.

Now a little about me! I am a physician and scientist who has studied genetics of bone diseases for over 25 years. I have been proud to have cared for many of you or your family members as part of the Skeletal Dysplasia Clinic at Texas Children's Hospital and Baylor College of Medicine. Our current research is focused on identifying new genetic causes of OI, developing better tests to distinguish OI type and potential response to treatment, and common mechanisms that cause brittle bone as targets for new treatments. For example, we have plans to test a drug that may be useful in the treatment of severe forms of OI. Ultimately, we hope that our research will allow physicians to better care for individuals living with OI.

Our research is only meaningful if we are partners together. Please stay in contact with us, stay informed, and let us know what is important to you and your families. Your needs and ideas will drive our efforts. Our team looks forward to seeing you at one of our participating clinical sites.

Brendan Lee, M.D., Ph.D.
Chairman, Department of Molecular and Human Genetics



Summer 2016 Newsletter

BBDC PARTICIPATING CENTERS

Clinical Sites

Baylor College of Medicine

Principal Investigator: V. Reid Sutton, M.D.

Children's National Medical Center

Principal Investigator: Laura Tosi, M.D.

Hospital for Special Surgery

Principal Investigator: Cathleen Raggio M.D.

Kennedy Krieger Institute / Hugo W.

Moser Research Institute

Principal Investigator: Emily Germain-Lee, M.D.

Shriners Hospital for Children, Chicago / Marquette University

Principal Investigator: Peter Smith, M.D. Co-PI: Gerald Harris, PhD, PE

Shriners Hospital for Children, Montreal

Principal Investigator: Frank Rauch, M.D.

Oregon Health and Science University

Principal Investigator: Eric Orwoll, M.D.

University of California Los Angeles

Principal Investigator: Deborah Krakow, M.D.

University of Nebraska Medical Center with Children's Hospital & Medical Center

Principal Investigator: Eric Rush, M.D.

Patient Advocacy Partner

Osteogenesis Imperfecta Foundation:

Principal Investigator: Tracy Hart, C.E.O.

Cores

University of South Florida

Principal Investigator: Jeff Krischer Ph.D.

University of Washington

Principal Investigator: David Eyre Ph.D.



The Brittle Bone Disorders Consortium (U54 AR 068069) is part of the Rare Disease Clinical Research Network (RDCRN), an initiative of the Office of Rare Disease Research (ORDR), NCATS, and is funded through collaboration between NCATS, and the National Institute of Dental and Craniofacial Research (NIDCR), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) and National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS).

A message from the BBD Consortium's 1st Participant

by Andersson

The Longitudinal Study of OI opened for enrollment August 2015. Our 1st participant would like to share a few words.

Q&A

Q: Tell us a bit about yourself.

A: *My name is Andersson, I am 15 and in 9th grade at Xavier Academy. I enjoy math the most. But when I'm not at school I like to play video games and I write a lot. I'm working on a sequel to a book I wrote a few years ago.*

Q: What do you aspire to be in the future?

A: *I'd like to be an author or something to do with animals.*

Q: You were the 1st participant in the Linked Clinical Research Centers study and the 1st participant in The Brittle Bone Disorders Consortium Longitudinal Study. Why did you participate in the studies and how was the

experience?

A: *My parents encouraged me to join the studies. They told me it would help doctors learn more about Osteogenesis Imperfecta, so they could help others. The experience has been easy and painless- it just took some time. But it is well planned.*

Q: What does research mean to you?

A: *The more you know, the better. **Knowledge is power.***

Q: Where do you want the research to go?

A: ***Of course I'd love a cure for OI!***

Q: What do you expect to see from the new consortium?

A: *Since there are more cities involved there will be many more people with OI in the study. And with more people, the doctors will have more information to study.*

Andersson's love of animals inspired the story of Missy, a homeless lion adopted by a family in Illinois.



Andersson is the author of "Missy"

Advocacy Partner

by Tracy Hart, CEO Osteogenesis Imperfecta Foundation

The OIF – A Valuable Brittle Bone Disorders Partner

As the Brittle Bone Disorders Consortium becomes more and more active the participation of the Osteogenesis Imperfecta Foundation becomes more important. As you already know, one impressive feature of the Rare Diseases Clinical Research network is the direct involvement of supporting patient advocacy groups in network operations, activities and strategies. Each consortium in the network includes relevant patient advocacy groups in the consortium membership and activities. The OI Foundation is the leading patient advocacy organization serving people with OI and medical professionals. As a strong BBDC partner the OI Foundation has taken the lead role of preparing and providing educational materials for

medical professionals that may or may not see a large number of people with OI. It's critical that medical professionals have the resources they need when treating a person with a rare disorder and the OI Foundation is providing that link between physician and the person with OI.

For more information about the Foundation please visit www.oif.org.



Drs. DiMeglio, Tosi, and Nagamani at the Interdisciplinary Symposium on Osteoporosis (ISO) 2016 Meeting sponsored by the National Osteoporosis Foundation

UPCOMING EVENTS



2016 OIF National Conference Orlando, FL | July 22-24, 2016

More than 600 members of the OI community will come together for three days of specialized sessions on managing OI, free medical consultations and fun social events for attendees of all ages! The entire conference will take place at the Walt Disney World Swan & Dolphin Resort.

The American Society of Bone and Mineral Research Annual Meeting and Exhibit Atlanta, GA | September 16-19, 2016

As part of the Ancillary Program, the OI Foundation is sponsoring the Rare Bone Disease Working Group meeting at the 2016 ASBMR Annual Meeting. The OIF will also have a booth in the exhibit hall. More information will be released as it becomes available.

FUN FACTS

3 billion

The average human heart beats more than three billion times in average lifespan. —National Geographic

8%

Your blood makes up about 8% of your body weight. —National Geographic

300

A baby's skeleton consists of as many as 300 bones. Over time, many of those bones fuse together. —Pbs.org

Meet the Doctors

V.Reid Sutton, M.D.

My initial interest in osteogenesis imperfecta (OI) was spurred by my colleague and mentor, Dr. Brendan Lee. His vision was to advance care for children with OI and other skeletal dysplasias by establishing a multidisciplinary clinic at our institution. He asked me and our colleague Carlos Bacino to join with him as attending physicians for the clinic. Dr. Francis Glorieux had just published his results of pamidronate therapy for children with OI and we realized the need to ensure that our patients had available to them these emerging therapies.

It has truly been amazing to see the transformation in patient care and research in OI over the past 15 years. I now have teenage patients with OI type IV who have received treatment from birth and are now living their lives fully; I have one girl who takes contact karate lessons and a boy who plays contact football (certainly not at my recommendation but they are having fun and it is amazing to see!). Additionally, many children with OI types III & IV are able to walk independently at home or school through medical and surgical advances that are truly improving their quality of life.

About seven years ago, I was fortunate to be offered the opportunity to participate in further advancing care and treatments for OI, in collaboration with the OI Foundation (OIF) and Dr. Peter Byers. We developed a longitudinal study of OI (the Linked Clinical Research Centers multi-site study of OI) that ultimately enrolled over 550 people with all forms of OI. Through research on how things changed year-to-year for people with OI, we were able to improve our understanding of brittle bone disease and this has resulted in multiple publications of new discoveries and a fuller understanding of the challenges people with OI face. Based upon the success of the OIF-funded longitudinal study, we were awarded a prestigious grant from the National Institutes of Health to establish a Brittle Bone Diseases Rare Disease Clinical Research Consortium (BBD-RDCRC). This multi-site study will continue on the longitudinal study, specifically focusing on the following issues:

- Scoliosis
- Dental & craniofacial health

*Dr. Sutton at the Kleberg Genetics
Clinic at Texas Children's Hospital*



- Pregnancy
- Quality of life
- Vertebral compression fractures in type I OI
- Developing new biological markers for diagnosis and the monitoring of new treatments
- Research on new medications to treat OI

It is really incredible to reflect upon how far we have come in the past decade and I know that this is just the beginning of a transformation to new therapies for OI. It is incredible to have the opportunity to be part of this revolution and I am incredibly grateful for all that my patients and their parents have taught me about OI. We would not be where we are today without your participation as well as the commitment of the OIF and the collaboration of all my colleagues. Thank you for guiding me on this exciting journey.

V. Reid Sutton, MD
Professor
Department of Molecular & Human Genetics



Clinical Research Studies

Current:

Natural History Study (BBD7701)

The purpose of this natural history study is to perform a long-term follow-up of a large group of people with osteogenesis imperfecta (OI). We will collect information including:

- medical history
- number of broken bones
- surgeries done
- medications taken
- ability to walk
- pain
- lung function and breathing
- hearing
- bone mineral density

The overall goal is to improve the health and quality of life of people with OI. We will ask you come in for yearly study visits for at least 5 years.

[More Information](#)

Contact Registry

The Rare Diseases Clinical Research Network (RDCRN) Brittle Bone Disorders Consortium (BBD) Contact Registry is a way for patients with brittle bone disorders and their family members to learn about BBD research studies they may be able to join. Contribute to knowledge about rare diseases by answering questions about yourself, your health, and your quality of life.

[More Information](#)

Biomarker Study

The purpose of this laboratory study is to develop a non-invasive test to determine OI subtype.

We will collect urine samples and look at various OI biomarkers in urine.

[More Information](#)

Upcoming:

Dental Craniofacial Features of OI (BBD7704)

The purpose of this study is to find out more about the facial and dental structures of individuals with OI. You must be enrolled in the Longitudinal study to be eligible for this study. We will perform a cone beam CT of your jaw and correlate the physical findings with your genetic findings.

Pregnancy Survey (BBD7705)

The purpose of this study is to learn more about the course of pregnancy and birthing outcomes in women with OI. All women with OI are eligible to take this online survey. We will use this data to create a more extensive clinical study to determine if bone density changes during and after pregnancy in women with OI.

PROMIS study tool (BBD7702)

The PROMIS tool is a self-reporting on-line survey allowing individuals with OI to report their quality of life. We plan to compare the self-reporting results with the clinical data collected in the Longitudinal study to validate the PROMIS tool.

Drug Therapy Trial (BBD7706)

This clinical trial will help us determine if a new drug is helpful in the treatment of OI. The first phase of this trial will focus on drug safety and tolerability. We will be recruiting and enrolling adults with severe OI.

You will come to a participating clinical center for an infusion(s) of Fresolimumab. You will be asked to provide blood samples to determine the safety profile of the drug over the course of 6-12 months. We will look at your bone density and quality of life to determine if these features change while you are on the study medication.

How to Participate:



Use the following links:

[Participating Clinical Centers](#)

[Get Involved](#)

[ClinicalTrials.gov](#)

[Osteogenesis Imperfecta Foundation](#)

Publications:

PMID: 26426884

PMCID: PMC4818203

[Genet Med.](#) 2015 Oct 1. doi:

10.1038/gim.2015.131.

Cesarean delivery is not associated with decreased at-birth fracture rates in osteogenesis imperfecta.

[Bellur S](#)¹, [Jain M](#)¹, [Cuthbertson D](#)², [Krakow D](#)^{3,4,5}, [Shapiro JR](#)⁶, [Steiner RD](#)^{7,8,9}, [Smith PA](#)¹⁰, [Bober MB](#)¹¹, [Hart T](#)¹², [Krischer J](#)², [Mullins M](#)¹, [Byers PH](#)^{13,14}, [Pepin M](#)^{13,14}, [Durigova M](#)¹⁵, [Glorieux FH](#)¹⁵, [Rauch F](#)¹⁵, [Sutton VR](#)^{1,16}, [Lee B](#)^{1,16}; [Members of the BBD Consortium](#), [Nagamani SC](#)^{1,16}.

Description

Osteogenesis imperfecta (OI) is a connective tissue disorder that predisposes to recurrent fractures and bone deformities. Severe forms of OI are characterized by *in utero* fractures and the mode of delivery that would be safest for the fetus in such situations is not known. In a study involving 540 patients with OI, researchers of the Brittle Bone Disorders Consortium found that cesarean delivery was not associated with a decrease in the at-birth fracture rates in OI. This study provided evidence-based answers to a question relevant for the clinical care of individuals living with OI.