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INSTITUTIONAL REVIEW BOARD SUMMARY

Customized Orthosis for Children with Clubfoot Following Ponseti Casting

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STUDY TITLE: Customized Orthosis for Children with Clubfoot Following Ponseti Casting

A. PURPOSE OF THE STUDY

The purpose of this study will be to design a novel customized Ankle Foot Orthosis (AFO) using 3D topographic scanner and CAD/CAM based technology then:

1. Determine differences of the patient compliance by recording the time in the brace and comparing between customized AFO and traditional straight-last shoes
2. Compare changes of foot and ankle alignments between customized AFO and traditional Mitchell shoes
3. Evaluate changes of functional outcomes between the two groups in a follow-up

B. HYPOTHESIS / SPECIFIC AIMS

We hypothesize that following Ponseti casting, the implementation of customized ankle foot orthotics (AFO) with Ponseti bracing will improve patient compliance and functional outcomes as well as lead to fewer relapses in comparison to the standard bracing with Mitchell shoes.

C. BACKGROUND, SIGNIFICANCE, AND RATIONALE

Congenital Talipes Equinovarus (CTEV) is a complex three dimensional congenital deformity of the tarsal bones of the feet[1]. It is generally characterized by midfoot cavus, forefoot adductus, hindfoot varus and ankle equinus positioning of the foot[2]. CTEV is one of the most frequent pediatric foot deformities, occurring in 1-2 in 1000 live births[3,4,5]. Many different methods have been used over the last 2 centuries to manipulate and correct clubfoot ranging from extensive surgical procedures to simple bracing and casting. It has since been shown that the extensive surgical repair of CTEV leads to complications such as stiffness, adhesions, and arthritis [6]. Conservative techniques primarily achieve correction of clubfoot by slowly stretching tight structures, allowing time for soft tissue remodeling and for the position of the bones in the foot to be corrected. The very first conservative method was introduced by Hippocrates in 400 BC and many more methods have been introduced since [6]. In the 1930s Dr. Kite introduced his own conservative method of CTEV correction after being dissatisfied with the poor outcomes of surgical techniques [7]. His method consisted of serial manipulations with casting followed by night splinting wherein the feet were held in dorsiflexion and slight abduction. However, the success rate of his procedure was unable to be replicated in future studies and success rates were low. Then, in 1963 Ignacio Ponseti, a professor at the University of Iowa developed a similar treatment, coined the Ponseti method, which also used serial manipulations and casting in addition to a small tenotomy of the Achilles [8]. In his initial study Ponseti recorded a success rate of 89% [9]. His method was slow to catch on and only in the last decade has the Ponseti technique come to be widely accepted and used in clinic [10]. When used correctly Ponseti's technique has been shown to achieve correction of CTEV in up to 92-100% of cases [11]. Casting usually takes 21-42 days to fully correct with only 5-6 casts [6,12]. This is then usually followed by a percutaneous achilles tenotomy to improve the equinus deformity. After Ponseti casting, it is standard procedure to use a foot abduction brace to maintain the corrected clubfoot. While there are many different protocol for bracing schedules the most commonly used is a full time bracing (23 hrs/day) for the first 2-6 months following Ponseti casting [13]. After this, bracing for 2-5 years is recommended at night time only. There are many different types of foot abduction braces (FAB), but the most common technique is the attachment of the feet to the Ponseti bar using standard straight last-type of shoe as was initially recommended by Ponseti [14]. It is recommended that CTEV is treated starting with Ponseti casting within the first few weeks

of life. Beginning the management of clubfoot in early infants is technically less challenging due to childrens' rapid growth as well as easy tissue manipulation [15].

Reports on the failures of the Ponseti method have shown that the non-compliance with the bracing regimen following Ponseti casting is the primary reason for relapse [16]. Relapse or reoccurrence is defined as the reappearance of any of the components of the deformity including midfoot cavus, forefoot adductus, hindfoot varus and ankle equinus positioning of the foot [9,11]. A study done by Dobbs et al. 2004 showed that individuals who were non-compliant with their bracing were 183 times more likely to relapse. Previous literature reported that relapse rates between 10-30% are common[17]. Of these relapses it is estimated that 78% of all relapses occur due to non-compliance with bracing, whereas only 7% of relapses occur with full compliance[17]. Thus, it is critical that bracing regimens be followed strictly and consistently. One of the ways that this can be addressed is through improving brace design for comfort and long-term wear. Some of the most problematic causes for non-compliance with bracing are skin lesions such as blistering, sleeping problems from discomfort, parental concerns about the restrictiveness of leg movement in the brace, and dislodgment of the foot from the brace due to kicking [14,17,18]. In recent years the focus for the improvement of outcomes of CTEV following Ponseti casting has focused on the production of a brace that leads to higher compliance rates and therefore better treatment outcomes by addressing these four main problems with FAB. A few studies have reported increased compliance with reduced rates of relapse when adapting the bracing methodology via improving the standard rigid bar to be more dynamic [14,19]. In addition, Chen et al. 2007 created custom AFOs that they fastened to an articulating bar and found success in decreasing skin blistering (3.6% of patients in compared with 22% with traditional FAB) and non-compliance rates (7.2% compared to 42% with traditional FAB) as reported by parents. The AFO made by Dr. Chen was made of one-eighth-inch plastic copolymer physically molded to the patient's foot. A custom Duraflex liner was then inserted into the plastic molded piece and attached to an articulation bar. However, one drawback of their custom orthoses is that the average cost for the custom bracing was nearly 4 times that of the traditional brace [17]. Our orthoses would be more beneficial because it allows for the use and improvement of the already widely used Mitchell shoes, a much more cost-effective option. In addition, our orthoses are different in that the feet are scanned in 3D and edited in CAD before the inserts will be 3D printed. In general, most studies have focused on the feet are implementation of dynamic bars that allow greater range of motion [14,19]. The standard for the Ponseti brace is maintenance of the completely corrected foot in 60-70 degrees of external rotation on the affected side and in 30-40 degrees of external rotation on the normal side. The bar should be bent 5-10 degrees with the convexity pointing away from the child to hold the feet in a valgus position. The feet should be placed on the bar so that the heels of the shoes are at shoulder width [11]. Knees are left free so the child can kick straight and stretch the Achilles tendon. It is also important to note that compliance rates are almost always overestimated when being reported through parental survey and thus we will be assessing compliance rates using heat sensors inserted into the back of the insert orthotics in order to get a more accurate reading of time spent in the bracing apparatus [20]. The use of these sensors is new to research on bracing compliance for clubfoot and would be one of the first extremely reliable measures of parental compliance. Our custom orthotics should correct for the slipping of the infant's foot out of the Mitchell shoes as well as decreasing the number of skin lesions from rubbing on the leather shoe, thus increasing compliance and overall functional outcomes.

D. DESIGN AND METHODS

Patients will be recruited by Dr. Van Valin during normal clinic hours by asking existing patients if they would be willing to participate in our small study attempting to improve aspects of the bracing process. . . Patients will be randomized as they are recruited via coin flip until we have 5 spots filled in one group then assign all others to ensure 5 patients with the FO + Mitchell shoes and 5 patients with just the Mitchell shoes. Customized orthotic group will receive a customized AFOs inserted into Mitchell shoes; "Mitchell" groups will receive standard Mitchell shoes only. Inclusion criteria are as follows: less than 12 months old (no age minimum), no neuromuscular disease involved, treated by Ponseti casting, idiopathic bilateral or unilateral clubfoot, no other congenital foot deformity, and no previous open surgeries to treat the deformity. Exclusion characteristics for this study include: patients with prior surgical treatment, not treated by Ponseti casting, an underlying syndrome, or neurological disorder.

The infant's feet will be scanned following removal of the second to last cast (allowing for orthotic production time and no extra visits) -from the middle of the tibia to the entire foot suing Milwaukee Topographic system (located in the CHW Musculoskeletal Functional Assessment Center), which consists of handheld wand with two CCD cameras and one sensor to define trunk position in 3D space (Polhemus FastSCAN Scorpion, Colchester, VT). Only subjects receiving the custom orthotic insert will undergo scanning. The scanning procedure will take place after the final cast is removed and should take no longer than 5 minutes. The child will be placed into a supine position and the foot/feet will be passively manipulated to 60-70 degrees abduction and 10-15 degrees of dorsiflexion. The physician will hold the foot in place and a tech will scan the foot. Its geometry will be imported into the CAD software (Rodin4D, Paris, France) for designing the FO21. The scan will be uploaded to the epic system and a report will be generated. The report will then be sent to the Engineering team at the Orthotic Design Company, which is within the Milwaukee School of Engineering (MSOE), for manufacturing. The report will only contain raw topographic data and no identifying information. Patients will be assigned numbers to keep track of braces. The brace will be composed of biocompatible polyurethane (Elasto-75D). Following this the braces will be sent back and the patient will return to have the orthotic fitted by an orthoptist. This will likely take about a week and in the meantime all patients will wear the Mitchell shoes (Figure 1). A wireless temperature data logger (Orthotimer®) will be used to monitor brace wear for each patient (n = 10 sensors). The sensors featured a 3V battery and a data storage capacity allowing for the storage of temperature (precision of ± 0.1°C), date, and time every 15 minutes for 100 days. Batteries will not need to be changed since the minimum lifespan of the battery is 18 months. The sensors will be imbedded in the outside of the brace sandals, just above the heel, to avoid locations prone to skin irritation[22]. The sensor will be fused into the back of the Mitchell shoe and covered with a fabric flap that is sewn onto the shoe. The sensor and battery will not be removeable and will not therefore pose a choking risk. Sensors will be calibrated upon fitting of the brace. The use of FO may cause skin redness, blisters, or rubbing. If these issues will be discovered during the regularly scheduled clinic visits, physicians will immediately request the orthotist to trim the orthosis or place additional foam on it. It must be addressed at the same time as the regularly scheduled clinic visits. It should be noted that the patient and their insurance company will be responsible for the cost of the standard Mitchell shoes and Ponseti bar,but will not be responsible for the costs of the FO, batteries, or sensor. All follow up appointments will coincide with normal clinical care except for a few additional processes during these visits (Table 1). At the end of the 6th month patients will be required to return the Orthotimer sensors but will be able to keep the custom orthotics. They should not need to get new orthotics because in the first 6 months of bracing, children often use the same shoes. We may assess the orthotic and have the orthoptist adjust the fit.

Table 1. Table of tasks to be performed at each clinical visit from the beginning of intervention to the end of the study period. Gray colored boxes indicate the task will be performed.

Task	Last Brace Removed	2 Week Follow Up	12 Week Follow Up	24 Week Follow Up
Check Foot				
Measure Dimeglio Score				
Scan Foot (Milwaukee Topographic System)				
Initial Survey				
Follow up Survey				
Transfer Data from Sensor				
Assess Fit and Adjust Orthotics as Needed				

Analysis of clubfoot functional outcomes will be assessed using Dimeglio Scores before and after Ponseti Casting as well as after 2, 12, and 24 weeks of bracing. Dimeglio scores are often used to assess the severity of clubfoot deformities and will give us a baseline as well as a level of improvement after casting and bracing. Dimeglio scores have been shown to provide good prognostic significance [5]. Other clinical parameters that we will be recording are: unilateral or bilateral CTEV, any surgeries performed (ex. achilles tenotomy, anterior tibial transfer, soft tissue release), level of brace adherence as reported by sensor, number of relapses, number of Ponseti casts needed to achieve correction, passive end dorsiflexion and abduction angles, and instances of rocker bottom deformity. The sensor to detect the body temperature will be embedded inside of the AFO and data will be stored in the sensors for three months. At follow up, the data will then be transferred to and saved to the computer via Bluetooth. In addition to these parameters we will use a parental questionnaire recording the following: occurrences of skin lesions, age of treatment initiation, age at each follow up, sex of child, prior treatments, family history of CTEV, parental marital status, insurance type, highest educational level achieved by parents, yearly family income, brace adherence as reported by parents, and reported of instances of foot slipping out of brace as well as any reasons for decreased compliance. Investigators will review the survey during clinical visits and will be able to address parent's concerns at that time. We are collecting data on these socioeconomic factors in order to help identify groups that may need additional attention or interventions in order to help reduce disparities in outcomes. Images of the child's feet in the orthotic or bracing device may be taken.

E. TOTAL NUMBER OF HUMAN RESEARCH PARTICIPANTS PROPOSED FOR THIS STUDY AT THIS SITE AND GLOBALLY. WHAT ARE THESE NUMBERS BASED ON?

We will be aiming to have 10 individuals in our preliminary trial before we move on to trying this method with larger cohorts. These numbers will allow us to run a power analysis to determine the number of individuals needed for a follow up study to confirm or refute any results we have found.

F. DRUGS OR PROCEDURES (*may attach activity table if available - lab draws, EKG, chest x-rah, surgery, genetics, survey)*

The participants will be scanned from the tibia to the tip of the toes by the Milwaukee Topographic system which consists of a handhold wand and sensors as well as spinal metrics. There will be a parental survey as a part of the research design. Manipulation of the foot via a trained individual will occur in order to assess the functionality and degree of deformity of the infant foot as we cannot assess gait at this early stage.

G. RISK CATEGORY:

X **(1) 45 CFR 46.404 - Research not involving greater than minimal risk to the children.**

(2) 45 CFR 46.405 - Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual child subjects involved in the research.

(3) 45 CFR 46.406 - Research involving greater than minimal risk and no prospect of direct benefit to the individual child subjects involved in the research, but likely to yield generalizable knowledge about the subject's disorder or condition.

(4) 45 CFR 46.407 - Research that the IRB believes does not meet the conditions of 45 CFR 46.404, 46.405, or 46.406, but finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children.

H. RISKS AND THE PRECAUTIONS WHICH WILL BE TAKEN TO MINIMIZE RISK EXPOSURE

There is a risk of blisters from wearing the custom ankle foot orthotics but that risk should be minimal because we are using materials that hope to reduce the incidence of blisters and the custom fit should allow for less friction rubbing. Another risk is that personal health information could accidentally be shared with someone that they did not consent to sharing the information with. This will be prevented by standard practices when reviewing the medical record and erasing personal identifiers on any documents transported out of the clinic. The patient's reports will only contain raw topographic data and the patient will be assigned a number to keep track of the braces. The legend containing the linked numbers and patient data will be stored securely on the department computer under password protection. These reports will not include any images of the scans. These reports will not include any images of the scans.

I. PROVISION FOR THE PROTECTION OF PRIVACY OF SUBJECTS *(confidentiality, health and financial risks)* AND TO MAINTAIN THE CONFIDENTIALITY OF DATA

As of October 2017 the NIH has updated their policy on Certificates of Confidentiality and are automatically issuing these for eligible studies that are NIH funded. They no longer issue a paper certificate, nor only submit on request.

Does this study qualify for automatic issuance of a Certificate of Confidentiality by the NIH?
☒No ☐Yes

For help in determining this see the IRB guidance document or visit the NIH website for information at: https://humansubjects.nih.gov/coc/index

Updated NIH policy can be found here: https://grants.nih.gov/grants/guide/notice-files/NOT-OD-17-109.html

If you answered yes, and language regarding this is not included in the consent form(s) you will need to update the consent form to include this language (see NIH suggested consent language at https://humansubjects.nih.gov/coc/suggested-consent-language)

All research projects that collect electronic data must use appropriate security measures to ensure that data is protected from theft or loss in order to prevent breaches of confidentiality. You must indicate what encryption tools (or why they are not necessary) from the options below.

The IRB will not review this protocol unless you indicate the encryption tools being used to secure your research data. If you do not have encryption in place on your systems, please contact your Information Systems support to arrange for one of the encryptions options listed below.

The following encryption products employ cryptographic modules that the National Institute of Standards and Technology has certified as meeting FIPS 140-2 requirements. Children's Hospital and Health System endorsed the use of these products made to encrypt hard drives and removable media. All electronic research data must be encrypted using one or more of these products.

Please indicate which encryption tools you are using to secure your research data.

___Credent Mobile Guardian (RS, PD)
___GuardianEdge Hard Disk and GuardianEdge Removable Storage Encryption (HD, RS, PD)
___IronKey encrypted flash drives (RS)
___McAfee Endpoint Encryption (HD, RS)
_x_Microsoft Bitlocker (HD, RS when used with Windows 7 and FIPS compliant algorithms are enabled)
___PGP Whole Disk Encryption and PGP Portable (HD, RS)
___SafeNet Protect Disk and SafeNet Protect File (HD, RS)

___Seagate Secure Self-Encrypting Drives (HD when encryption option is enabled)
___Symantec Endpoint Encryption (HD, RS, PD)
___WinMagic SecureDoc encryption (HD) (for MCW owned computers)
_x_Other (*add description*)- Sandisk USB

Does not apply because:
___ Data is de-identified – no PHI collected (*please provide detailed information on data elements in your protocol application)*
___ Data is stored on paper only
_x_ Data is stored on CHW secured shared drives.
_~~x~~_ Data is stored on MCW secured shared drives.

Key
HD = Hard Drive
RS = Removable Storage (USB flash drive, CD, etc.)
PD = Portable Device (iPod; iPhone; PDA, etc.)

J. PROVISIONS FOR MONITORING DATA TO ENSURE THE SAFETY OF SUBJECTS; AND ADDITIONAL SAFEGUARDS TO PROTECT THE RIGHTS AND WELFARE OF SUBJECTS WHO ARE LIKELY TO BE VULNERABLE

All paper records will be locked in a file cabinet or inside a locked room. All electronic data will be stored on encrypted external drives or stored in a desktop in locked room.

K. ANTICIPATED BENEFITS ASSOCIATED WITH THE PROTOCOLTO HUMAN RESEARCH PARTICIPANTS AND SOCIETY

The current research and orthotic implementation may decrease the risk of clubfoot relapse and it may provide a greater level of comfort for the child throughout the bracing process. It may also allow for the use of traditional Mitchell shoes in infants with especially small and malformed feet. Specifically it may reduce the incidence of heal slippage and thus lead to a longer wear time and lower likelihood of relapse.

L. STOPPING POINTS THAT WOULD NOT ALLOW THE STUDY TO CONTINUE AS PROPOSED

Any parent who objects to their child wearing the brace will be removed from the study at their wish. If parents of the children wish to only participate in the traditional bracing protocol their wish will be respected and will not be included in either of the study cohorts.

M. IS THERE A DATA SAFETY MONITORING BOARD IN PLACE? WHO ARE IT'S MEMBERS? HOW OFTEN DO THEY MEET?

There is no safety monitoring board in place for this study.

N. DESCRIBE HOW THE CONSENT AND ASSENT PROCESS WILL TAKE PLACE. INCLUDE A LIST OF APPROPRIATELY TRAINED PERSONNEL WHO WILL BE INVOLVED.

Investigators will receive consent from all parents and answer all questions. We are requesting a waiver of assent for study because the children participants will be less than 12 months old and thus will be unable to assent.

O. PROCEDURES TO BE EMPLOYED IN ANALYZING DATA AND THE ANTICIPATED SIGNIFICANCE OF THE PROPOSED STUDY

A power analysis will be performed to determine the exact number of patients needed for future study. We will be aiming to have 10 individuals in a preliminary trial run and then move on to larger cohort studies. In children with bilateral clubfoot, each foot will used as an independent observation in the statistical analysis. Means will be compared using Student's t-test. Statistical significance will be considered at a two-tailed level of < 0.05.

P. FINANCIAL RELATIONSHIPS

There are no financial partnerships implicated in this study. This research is funded by the Department of Orthopaedic Surgery.

Q. ADVERTISEMENTS / FLIERS

No fliers or advertisements will be used.

R. BIBLIOGRAPHY

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