JuggerStitch™ for Meniscal Repair
Post Market Clinical Follow-up Study

PROTOCOL NUMBER: CMG2017-14SM

Protocol date: March 7, 2024

NCT number: NCT04228367



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1 STUDY OVERVIEW

Complete Protocol Title	JuggerStitch™ for Meniscal Repair Post Market Clinical Follow-up Study
Protocol Number	CMG2017-14SM
Short Protocol Title	JuggerStitch
Sponsor	Zimmer GmbH
Manufacturer	Biomet Sports Medicine
Study Device(s)	JuggerStitch™ Meniscal Repair Device
Study Objectives/Endpoints	The objectives of the study are to calculate the overall clinical success rate and the performance and clinical benefits and confirm the safety of the JuggerStitch Meniscal Repair Device. • The clinical success will be evaluated by the absence of reoperation due to meniscal tear • The performance and clinical benefits will be evaluated by functional outcomes measured using standard scoring systems such as the Lysholm Knee Scoring Scale, Tegner Activity Scale, International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form and McMurray Test and Joint Line Tenderness Test • The safety of the system will be assessed by monitoring the frequency and incidence of adverse events The primary endpoint of this study is defined by the absence of reoperation due to meniscal tear. This will be measured against the success criteria of the

	absence of reoperation in 90.2% of the cases at one year.
Indications/Target Population	Subjects suffering a vertical longitudinal full thickness tear of the meniscus (red-red and red-white zones) indicated for treatment with JuggerStitch, who also meet the inclusion/exclusion criteria.
Inclusion/Exclusion Criteria	<u>Inclusion criteria</u> 1. Subject qualifies for meniscal repair based on the physical exam and medical history and meets the approved indications for use of the study product; OR in case of retrospective enrollment: subject treated with the Juggerstitch Meniscal Device Implant for meniscal repair 2. Older than 18 years and skeletally mature; 3. Willing and able to comply with the study procedures; 4. Subject is capable of understanding the doctor's explanations, following his instructions and is able to participate in the follow-up program; 5. Subject is able to read and understand the ICF and has voluntarily provided written informed consent. <u>Exclusion criteria</u> 1. Meniscal tears in the avascular zone of meniscus; 2. Meniscal tears not suitable for repair because of the degree of damage (marked irregularity and complex tearing) to the meniscus body including degenerative, radial, horizontal cleavage and flap tears; 3. Presence of active infection; 4. If female, subject is pregnant;

	5. Subject is vulnerable (prisoner, mentally incompetent or unable to understand what participation to the study entails, a known alcohol or drug abuser, anticipated to be non-compliant); 6. The subject is unwilling or unable to give consent or to comply with the follow-up program; Subject meets any contraindications of the appropriate Instruction for Use.
Study Design	Prospective/Retrospective, multicenter, non-randomized, non-controlled study
Clinical Phase	Post-market
Sample Size	104
Length of Study	5 years (4-year enrollment plus 1-year follow-up) Required post-operative clinical follow-up visits: • 6 weeks (optional for retrospective enrollment) • 6 months (optional for retrospective enrollment) • 1 year
Data Collection	Paper/Electronic
Statistical Reporting	Data collected will be summarized and reported to each participating investigator. Statistical analysis will be conducted by Zimmer Biomet or its designee. Survivorship will be evaluated using Kaplan-Meier.
Scores/Performance Assessments	• McMurray Test • Joint Line Tenderness Test • Lysholm Knee Scoring Scale • Tegner Activity Score • International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form

Standards	The PMCF is compliant with the below: • ISO 14155: 2020 - Clinical investigation of medical devices for human subjects - Good clinical practice. • The Declaration of Helsinki (DoH) - Ethical principles for medical research involving human subjects. • European Regulation (EU) 2017/745
Study Funding	Funding for this clinical study is made available by Zimmer Biomet to support clinical data collection, IRB/EC review fees and other expenses associated with the conduct and execution of this study protocol as outlined in the fully executed Clinical Trial Agreement.

This Clinical Investigation Plan was initially drafted in accordance with ISO14155:2011 “Clinical Investigation of medical devices for human subjects – Good clinical practice” but is now updated to comply with new ISO14155:2020 [1]

2 Introduction

The meniscus is involved in several important functions such as load bearing, load transmission, joint lubrication, and absorption of the shock in the knee joint [2]. It also contributes to proprioception and stabilization of the knee joint [3, 4]. Its importance has been recognized early in the medical history with the first meniscal repair surgery being done in 1883 [5, 6]. Today, surgical interventions involving the meniscus alone and/or involving ACL and PCL are constantly growing mainly due to population becoming more physically active for longer durations of time. In United States alone, surgical interventions involving the meniscus are performed in close to one million patients per year [7], making thus the knee injury management a matter of concern among health care providers “pushing” for a rapid optimization of the meniscal surgery procedure and for better clinical outcomes.

As summed up by Smillie in 1967, “If it is torn, take it all out. Even if you think it’s torn, take it out” [8, 9] in the earlier years meniscectomy was the golden standard when dealing when meniscal tears. However the tremendous improvement in surgical techniques and the adoption of arthroscopy led to numerous studies that suggest that preservation of meniscus is beneficial for subjects on the long run [10] and helps decrease the degenerative results that follow meniscal removal [11]. Despite the refinement of these techniques and advancement of the surgical instrumentation, not all types of meniscal tears (Figure 1) are conducive to repair. It is now widely accepted that the degenerative tears do not have a very good healing prognosis [12]. The indications for meniscal repair have been well defined and take into consideration the location (Figure 1a and Figure 2) and type of tear (Figure 1b-g), the quality of tissue, the level of chronicity [13], the stability of the knee, age of subject and level of activity. The “ideal” tear showing the best functional outcomes is an acute, vertical, longitudinal tear occurring in peripheral one-third of a meniscus (Figure 2) of young subjects with a stable knee [14].

Different approaches have been successfully conducted to address different types of tears. Historically, permanent sutures were used to repair longitudinal tears in the vascular (figure 2) region of the meniscus. Such suture techniques are generally categorized as inside-out, outside-in, and all-inside outside depending on how the suture is manipulated [15]. The “all inside” procedure has several benefits due to its smaller incision, reduced risk of neurovascular injury and less postoperative pain and complication rate [16]. These characteristics would theoretically suggest a faster recovery time that would match the subjects’ expectations after meniscal surgery [17]. However at present, according to Centinkaya et al. 2016 [18] no single meniscal repair procedure or instrument is superior in all situations needing thus further technical improvements that would allow for a simpler and more efficient suturing method.

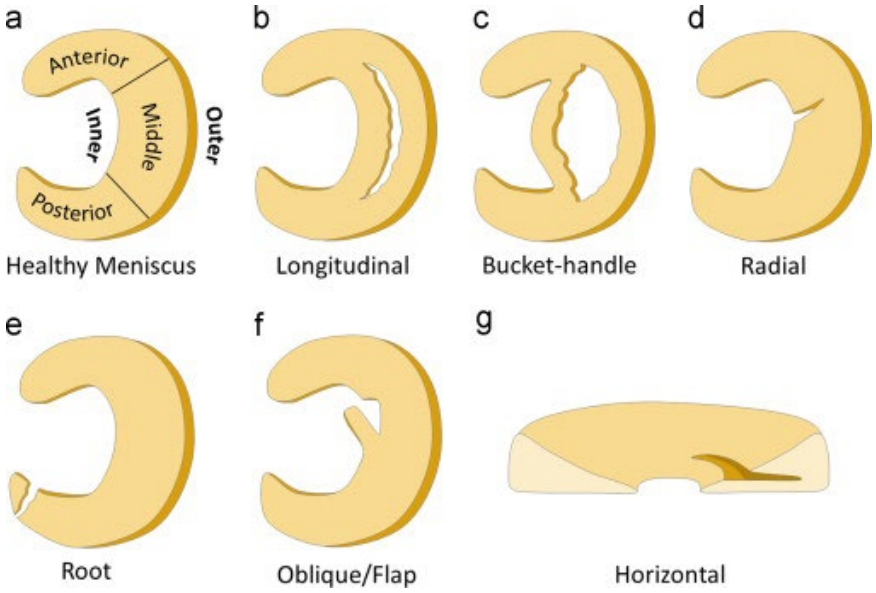


Figure 1 Meniscal tear types – (a) intact healthy meniscus labeled according to convention, (b) longitudinal, (c) "bucket-handle," (d) radial, (e) root, (f) oblique/flap, and (g) horizontal tear types. Edd et al., 2015 [19]

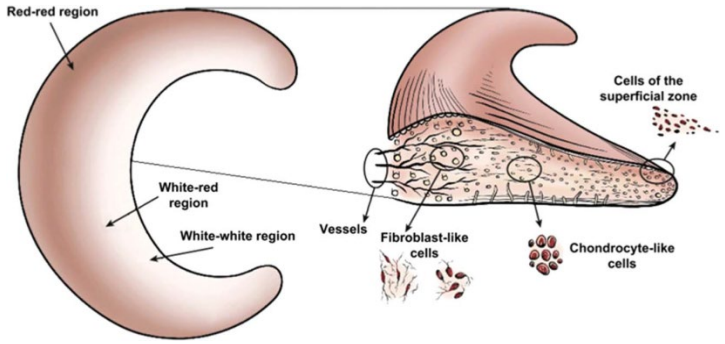


Figure 2 Anatomical variation in vascularization of the meniscus. ***Left:*** Red-Red region contains the biggest majority of blood vessels; this region has the highest potential for healing. Red-white zone shows an intermediate potential for healing since there is no blood supply from the inner surface of the lesion. *White-white zone* is the avascular region of the meniscus and has almost no potential for healing. ***Right:*** the direction of vessels in the meniscus. Fox et al., 2015 [20]

In order to address the current clinical changes in the field of meniscal repair, Zimmer Biomet has improved its previous meniscal repair systems, MaxFire and MaxFire MarXmen, and launched JuggerStitch: an all suture anchor (no metal) device. The purpose of the present study is to confirm the performance and clinical benefits and safety of the JuggerStitch Device

when used in a heterogeneous population undergoing meniscal repair with or without ACL or PCL reconstruction.

3 Implant Information

3.1 Description of the Device

The all-inside JuggerStitch device (Fig 3) is the result of technological development of the previous systems MaxFire and MaxFire MarXmen that can be used to repair vertical longitudinal meniscus tears. In comparison with its predecessors, JuggerStitch simplifies deployment during surgery and allows for knotless meniscal repair. It incorporates two soft anchors and a ZipLoop™ suture construct:

- **The ZipLoop construct** is created by passing a single piece of UHMWPE suture through the inner core of its braided polyester sleeve, creating a self-locking adjustable loop, eliminating thus the pre-tied knots near the articular surface of the knee.
- **The anchors** of the system consist of two size 2 coreless sleeves of polyester suture, one 1.4 centimeter long anchor and one 1.7 centimeter long anchor, on an adjustable size 2-0 single strand of ultra-high molecular weight polyethylene (UHMWPE) Max-Braid™ suture loop. The suture passes through the center of the sleeve and exists through both ends. During the meniscal repair procedure the two anchors are deployed separately at the desired location in the meniscus through a 1.6 mm diameter needle specific for JuggerStitch.

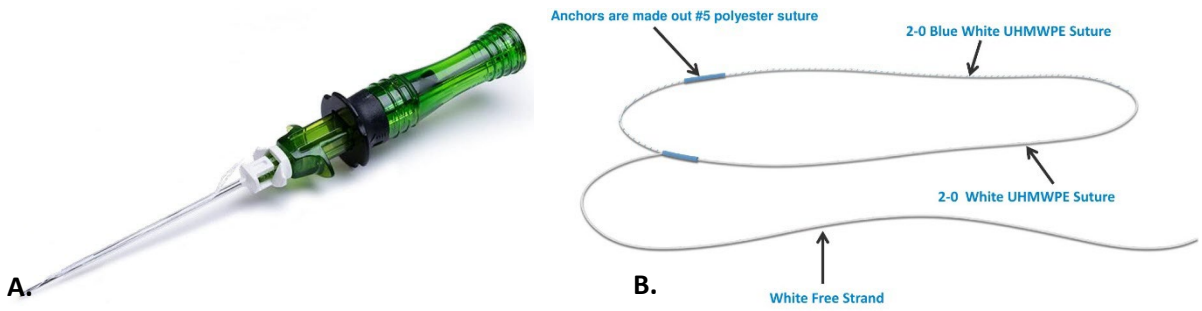


Figure 3 A) JuggerStitch Meniscal Repair Device (JMRD) insertion instrument with the JMRD loaded onto the distal tip. **B)** MaxBraid™ suture passing through sleeve of JMRD.

4 Study Population

The study population will include both males and females who require meniscal repair with or without ACL and PCL reconstruction and meet the inclusion/exclusion criteria as stated in this protocol and as outlined in the JuggerStitch Instructions for Use (IFU). In order to avoid selection bias, each Investigator will offer study participation to each consecutive potential subject for meniscal repair using the commercially available JuggerStitch device. If required, each subject may receive more than one JuggerStitch device per knee to repair the meniscus.

4.1 Inclusion Criteria

Subjects will be assessed to ensure they meet all of the inclusion criteria to be considered for study participation:

1. Subject qualifies for meniscal repair based on the physical exam and medical history and meets the approved indications for use of the study product; OR for retrospective enrollment: subject treated with the Juggerstitch Meniscal Device Implant for meniscal repair
2. Older than 18 years and skeletally mature;
3. Willing and able to comply with the study procedures;
4. Subject is capable of understanding the doctor's explanations, following his or her instructions and is able to participate in the follow-up program;
5. Subject is able to read and understand the informed consent and has voluntarily provided written informed consent.

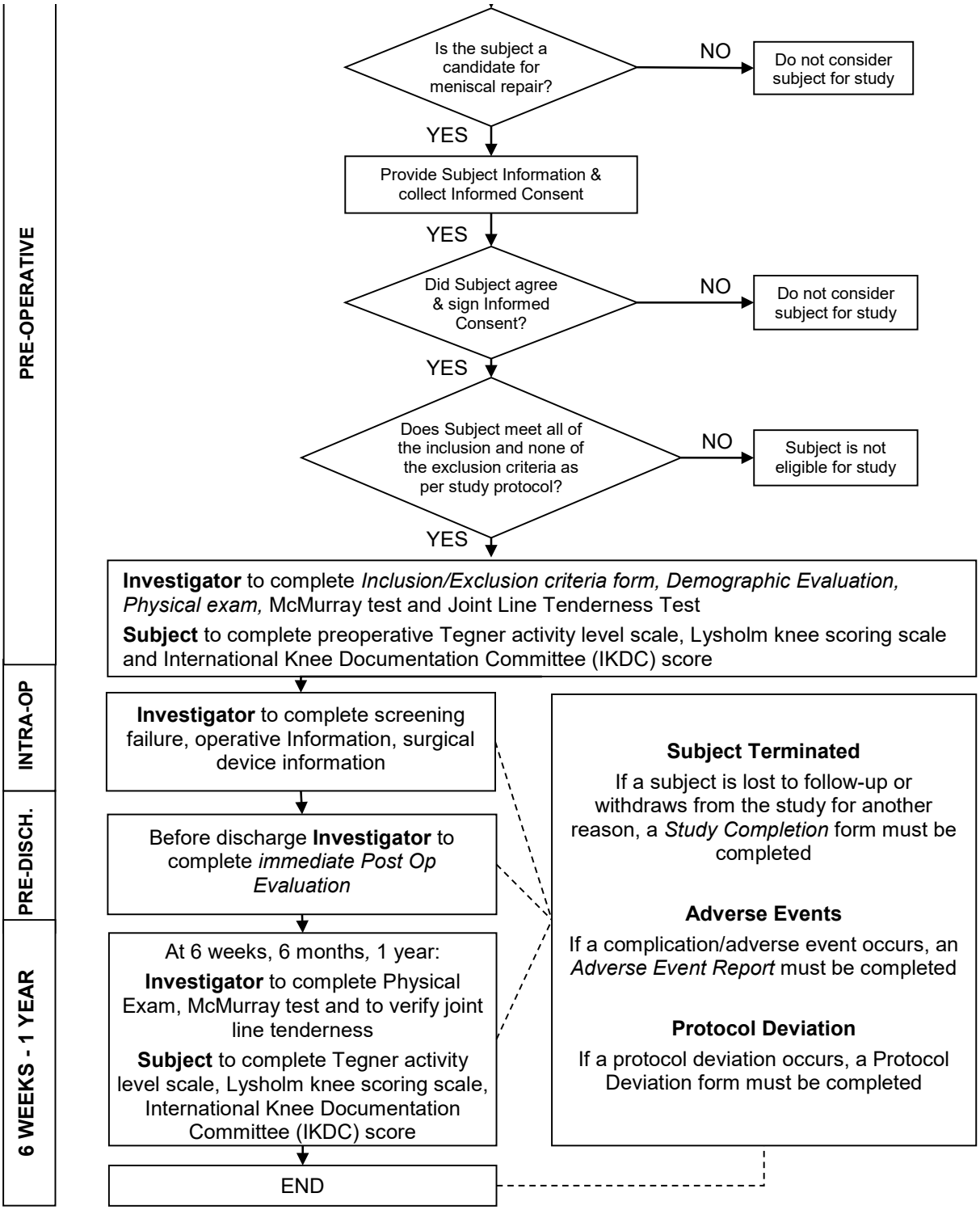
4.2 Exclusion Criteria

Subjects will be assessed to ensure they do not meet any of the exclusion criteria to be considered for study participation:

1. Meniscal tears in the avascular (white-white) zone of meniscus;
2. Meniscal tears not suitable for repair because of the degree of damage (marked irregularity and complex tearing) to the meniscus body including degenerative, radial, horizontal cleavage and flap tears;
3. Presence of active infection;
4. If female, subject is pregnant;
5. Subject is vulnerable (prisoner, mentally incompetent or unable to understand what participation to the study entails, a known alcohol or drug abuser, anticipated to be non-compliant);

6. The subject is unwilling or unable to give consent or to comply with the follow-up program;
7. Subject meets any contraindications of the appropriate Instruction for Use.

5 Study Procedure Flowchart



6 STATISTICAL ANALYSIS PLAN

6.1 Sample Size

The sample size for the study was estimated based on the expected clinical success rate of 90.2%, based on a meta-analysis. The sample size includes a 10% non-inferiority margin (90.2 - 10% = 80. 2%). The expected clinical success rate of the JuggerStitch system is assumed to be 90.2%. A sample size of 83 JuggerStitch patients will provide approximately 80% power for the one-sided exact binomial test at 0.05 significant level to claim non-inferiority to the meta-analysis benchmark of 90.2%. The sample size was calculated by SAS for Windows version 9.4.

Considering an attrition rate of 20%, 104 cases will be enrolled in this clinical study.

The overall success rate will be calculated based on the percentage of subjects who have successful clinical repair. The following hypothesis will be tested by the exact binomial test:

H_0: $E_1 – E_0 \leq - \delta_E$

H_a: $E_1 – E_0 > - \delta_E$

Where:

E0 = 90.2%, the success repair rate of similar devices

E1 = success rate of the JuggerStitch treatment group

δ_E = 0.10, non-inferiority margin for clinical success

In addition, a one-sided 95% exact confidence Interval (CI), lower limit of the success rate, will be calculated.

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