Post-market Clinical Follow-up Study to Provide Safety, Performance and Clinical Benefits Data of the ToggleLoc™ 2.9mm and the JuggerLoc™ Soft Tissue Systems (Implants and Instrumentation) in the Shoulder

A Multicenter Retrospective Study

Protocol number: MDRG2017-89MS-70SM

Protocol date: 22.December.2021

NCT number: NCT05584553

Table of Contents

1 Study Synopsis

Title	Post-market Clinical Follow-up Study to Provide Safety, Performance and Clinical Benefits Data of the ToggleLoc™ 2.9mm and the JuggerLoc™ Soft Tissue Systems (Implants and Instrumentation) in the Shoulder - A Multicenter Retrospective Study
Single Identification Number (Clinical Investigational only as per Art. 70 of EU MDR)	N/A
Protocol Number	MDRG2017-89MS-70SM
Study Sponsor Contact Information	Zimmer GmbH Zählerweg 4 6300 Zug, Switzerland +41 (0) 58 854 80 00 Zimmer Biomet Clinical Affairs Department 1800 W. Center St., Warsaw, IN 46580, USA Phone: (800) 613-6131, Fax: (574) 372-4710
Authorized Representative Contact Information, if applicable (Clinical Investigation only as per Annex XV of EU MDR)	N/A
Monitoring Contact Information	Zimmer GmbH Zählerweg 4 6300 Zug, Switzerland +41 (0) 58 854 80 00 Zimmer Biomet Clinical Affairs Department 1800 W. Center St., Warsaw, IN 46580, USA Phone: (800) 613-6131, Fax: (574) 372-4710
Investigational Site Information (Clinical Investigation as per	The study will include up to four sites. Details regarding the sites involved will be maintained in the Sponsor's Trial Master File.

Annex XV of EU MDR)	
External Organizations, if applicable	N/A

2 Abbreviations

The following abbreviations are used throughout this study protocol.

ADE	Adverse Device Effect
AE	Adverse Event
Case ID	Case Identification Number
CE	Conformité Européene (European Conformity)
CI	Confidence Interval
CRF	Case Report Form
CTA	Clinical Trial Agreement
DD	Device Deficiency
DOH	Declaration of Helsinki
EC	Ethics Committee
e-CRF	Electronic Case Report Form
EDC	Electronic Data Capture
EU MDR	European Regulation (EU) 2017/745
FDA	Food and Drug Administration
FUP	Follow-Up
GDPR	General Data Protection Regulation
ICF	Informed Consent Form
IFU	Instructions for Use
ICH	International Conference on Harmonisation (Harmonization)
ID	Identification
IRB	Institutional Review Board
ISO	International Standards Organization
MDCG	Medical Device Coordination Group
N/A	Not Applicable
PMCF	Post-Market Clinical Follow-Up
PROMS	Patient-Reported Outcome Measures
SAE	Serious Adverse Event
SADE	Serious Adverse Device Effect
USADE	Unanticipated Adverse Device Effect

3 Study Rationale and Objectives

This post-market clinical follow-up (PMCF) study, entitled *"Post-market Clinical Follow-up Study to Provide Safety, Performance and Clinical Benefits Data of the ToggleLoc™ 2.9 mm and the JuggerLoc™ Soft Tissue Systems (Implants and Instrumentation) in the Shoulder"* (Protocol No. MDRG2017-89MS-70SM), is sponsored by Zimmer Biomet, with the study devices manufactured by Biomet Sports Medicine. The ToggleLoc™ 2.9 mm and the JuggerLoc™ Soft Tissue Systems are implants specifically designed for soft tissue-to-bone fixation in the shoulder. The purpose of this investigation is to systematically confirm the devices' safety, performance, and clinical benefits.

The primary objective of the study is to evaluate device performance by assessing soft tissue-to-bone healing in the shoulder. Secondary objectives include the assessment of device safety and clinical benefits. Safety will be evaluated by capturing the incidence and frequency of complications and adverse events (AEs), with specification of their relationship to the device, instrumentation, or procedure. Clinical benefits will be assessed using validated patient-reported outcome measures (PROMs), the Oxford Shoulder Score (OSS) and the EuroQol EQ-5D, collected at the longest available follow-up of at least one year postoperatively.

The study is designed as a global, multicenter, retrospective, consecutive series**.** A total of 206 cases will be included: 103 patients operated with the ToggleLoc™ 2.9 mm device and 103 patients with the JuggerLoc™ system. Eligible participants are consecutive patients previously operated with one of the study devices, provided they meet the study's inclusion and exclusion criteria.

The inclusion criteria require that patients:

- Have received the ToggleLoc™ 2.9 mm and/or the JuggerLoc™ device for shoulder soft tissue-to-bone fixation;
- Are skeletally mature adults, aged 18 years or older;
- Are capable of understanding the surgeon's explanations, willing and able to comply with follow-up instructions, and have provided informed consent to participate.

The exclusion criteria disqualify patients who:

- Present with infection;
- Have poor bone or soft tissue quality, or limited blood supply;

- Have mental or neurological conditions that prevent adherence to postoperative care instructions;
- Demonstrate foreign body sensitivity, unless pre-implant testing was performed;
- Are unwilling or unable to provide informed consent or comply with follow-up requirements;
- Have any condition that, in the investigator's judgment, poses undue risk or interferes with study participation;
- Are considered vulnerable subjects, including prisoners, individuals unable to understand study participation, patients with substance abuse, or those expected to be non-compliant;
- Have undergone off-label use of the device.

Clinical data will be obtained retrospectively from hospital and clinic databases, including preoperative and intraoperative records. In addition, a final follow-up visit**,** conducted at least one year after the initial operation, will be performed either on-site to collect PROMs and confirm clinical outcomes. All protocol deviations and adverse events will be systematically recorded throughout the study. Data will be collected using both paper and electronic formats and subsequently analyzed by Zimmer Biomet or its designee. Results will be summarized and shared with participating investigators.

The study duration is expected to be 18 months. The outcomes will be reported using statistical methods appropriate for retrospective case series, with particular focus on safety events, performance, and PROMs.

This PMCF study adheres to the highest international standards, including ISO 14155:2020 (Good Clinical Practice for medical device trials), the Declaration of Helsinki, European Medical Device Regulation (EU) 2017/745, and MDCG 2020-10/1 safety reporting guidelines. Study funding is fully provided by Zimmer Biomet, covering clinical data collection, IRB/EC fees, and associated study expenses, as outlined in the executed Clinical Trial Agreement.

4 Introduction and Purpose

The musculoskeletal system functions through the coordinated action of multiple tissue types. These include, among others, specialized organized connective tissues such as tendons, ligaments, capsule and fascia. These connective tissues are attached to bone through a specialized interface called an insertion site or enthesis [5] [6]. Entheses integrate tendon or ligament structures to bone and facilitate joint motion [6]. Because entheses link soft to hard tissue, they are regions of high-stress concentration. As a result, they are susceptible to chronic and acute injury [5] [7].

Complete or partial detachment of ligaments, tendons and/or other soft tissues from their associated bones are common orthopedic injuries. The number and incidence of these types of injuries have increased substantially during the last few decades, especially the number of sports related injuries [8] [9].

Rotator cuff disorders are the most common causes of shoulder pain or disability, but other soft tissue injuries can also occur, requiring surgical techniques such as Bankart lesion repairs S.L.A.P. lesion repair, acromio-clavicular repair, capsular shift/ capsulolabral reconstruction, deltoid repair, biceps tenodesis and pectoralis major repair.

The rotator cuff consists of four muscles (supraspinatus, infraspinatus, teres minor, and subscapularis), with the supraspinatus most commonly injured [10]. The etiology of rotator cuff tears is multifactorial and likely a combination of micro/macro trauma and age-related degenerative changes [11]. Athletes engaged in sports that involve overhead motions such as throwing, tennis, or swimming are more susceptible to overuse injury. The prevalence of symptomatic rotator cuff tears increases with increasing age [10] [12]. Full-thickness rotator cuff tears are present in approximately 13% of individuals in their 50s and 50% of individuals in their 80s [13]. Surgical management of massive rotator cuff tears remains challenging, with failure rates ranging from 20% to 90% [14].

When partial detachment of soft tissue structures from bone occurs, the injury may heal itself with conservative measures. However, in the case of complete detachment or when the conservative treatment has failed, surgical repair is required for restoration of function. Optimal fixation devices should confer immediate stability, resist gap formation, promote biologic healing, and restore the anatomic footprint of the native tendon or ligament [15]. From an evolutionary point of view, there has been a lot of advancement in shoulder repair. In the last decades, rotator cuff surgery has developed from open surgery to an all-arthroscopic procedure. Arthroscopic repair of rotator cuff led to decreased immediate post-operative pain, decreased surgical insult to the deltoid and decreased post-operative stiffness [12] and is now an established method of treatment with reproducible results.

Numerous devices are currently available to re-attach soft tissue to bone. Among others, suture anchors are one of the most important innovations in arthroscopic shoulder surgery for tendon or ligament fixation to bone [15].

Many designs of suture anchors are available, with individual characteristics that influence the appropriateness of its usage including size, shape, composition, and holding strength.

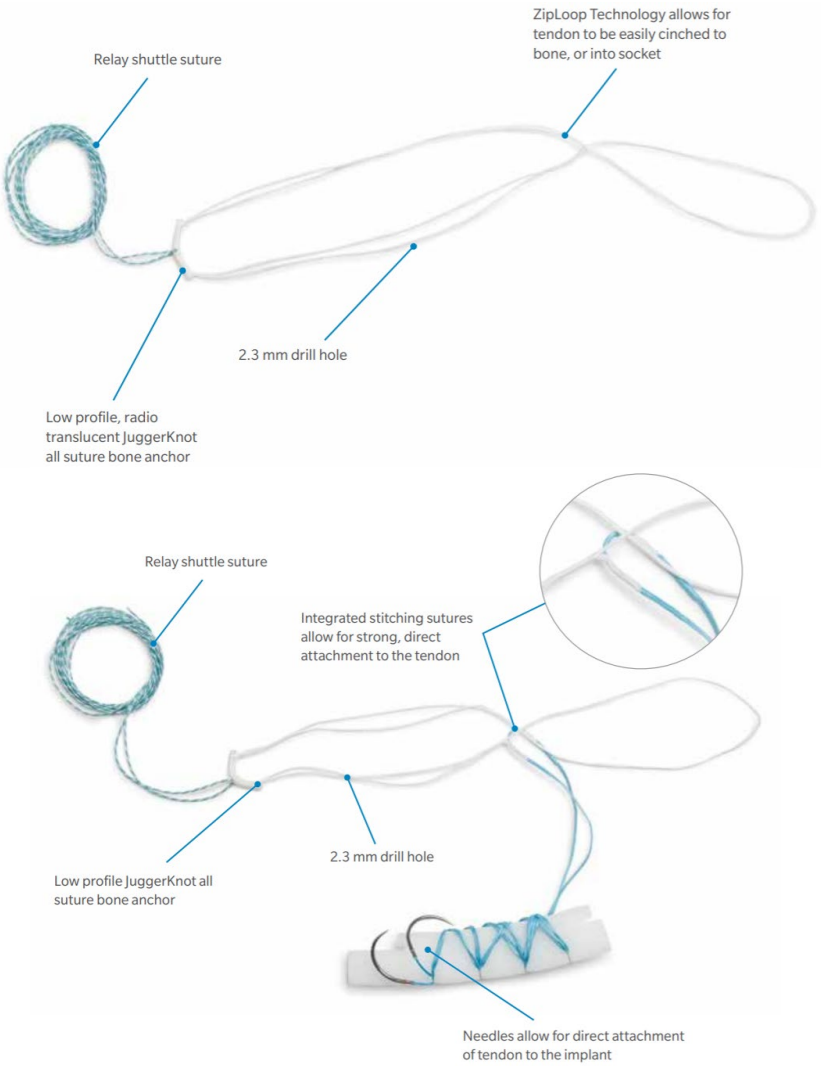
The aim of this retrospective post-market clinical follow-up study is to confirm performance, clinical benefits and safety of the ToggleLoc 2.9mm and the JuggerLoc Soft Tissue Systems when used for soft tissue to bone fixation in the shoulder.

5 Study Device Information

5.1 Study Device

The ToggleLoc 2.9 mm and JuggerLoc Soft Tissue devices consist of non-resorbable devices intended to aid in arthroscopic and orthopaedic reconstructive procedures requiring soft tissue to bone fixation. The clinical purpose is to restore the function and flexibility of the specific anatomical area requiring soft tissue to bone fixation and to relieve pain that cannot be controlled by other treatments. These Systems have been in clinical use since 2015 and are currently CE marked. The ToggleLoc 2.9 mm and JuggerLoc Soft Tissue Systems are FDA cleared implants intended for soft tissue to bone fixation in the shoulder, knee, and elbow.

The JuggerLoc has a low profile, all suture bone anchor made of woven Ultra-High Molecular Weight Polyethylene (UHMWPE) (Figure 1). It is connected to a Zip loop construct also made from UHMWPE, and may be constructed with or without additional suture strands with needles. The JuggerLoc can be anchored directly into the bone, allowing the soft tissue to be attached directly into the bone without the need for a complete end-to-end bone channel.



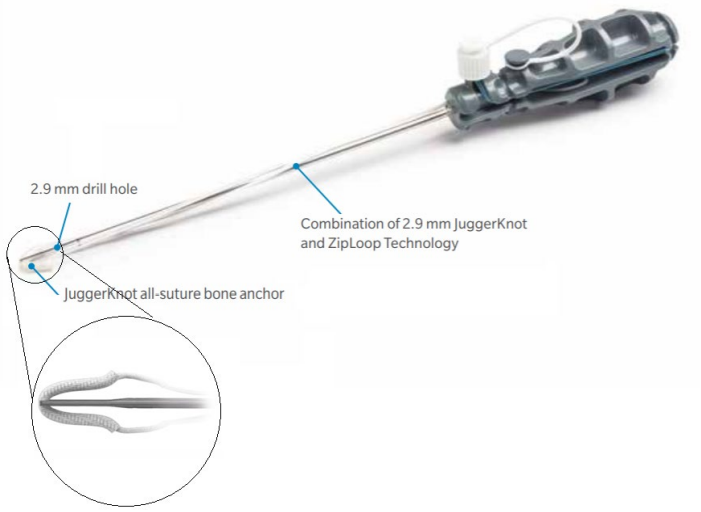


Figure 1. JuggerLoc Soft Tissue Pull Through with (a) and without (b) Needles and JuggerLoc Unicortical Soft Tissue Fixation without Needles (c).

The ToggleLoc 2.9 mm consists of a metallic anchor made of Ti6Al4V connected to a Zip loop construct of UHMWPE. Two configurations to attach soft tissue exist, one with and one without needles (Figure 2). To implant the ToggleLoc 2.9 mm, a hole is drilled through the bone to create a bone channel. The anchor resides on the bone surface, and the suture extends through the bone and around/through the soft tissue, where is it tied (Figure 3).

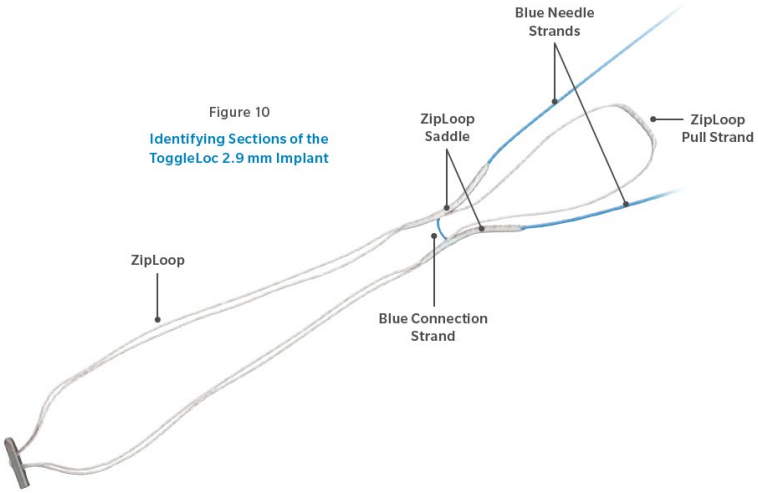


Figure 2. ToggleLoc 2.9 mm Soft Tissue System devices (with and without needles) with metallic hard bone anchor and the Zip loop technology.

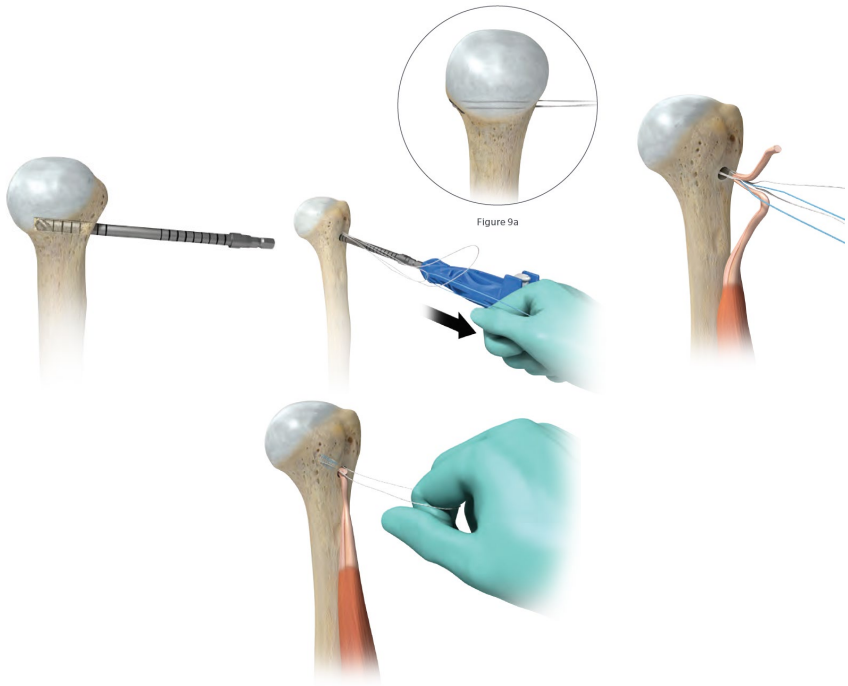


Figure 3. ToggleLoc 2.9 mm Soft Tissue Systems requires a bone channel for fixation of soft tissue to bone.

The two systems and their attached sutures are long-term implants that directly contact bone, soft tissue, and body fluids. Whereas these devices are designed for permanent implantation, the necessary functional lifetime is until healing has occurred, as the intended purpose of these devices is to provide internal fixation while the body heals naturally, typically 6 weeks to 1 year.

5.2 Instrumentation

The ToggleLoc 2.9 mm and JuggerLoc Soft Tissue devices are intended to be used only with the JuggerLoc Instruments. The use of instruments or implant components from other systems can result in inaccurate fit, incorrect sizing, excessive wear and device failure. Further information on the clinical use of the instruments is available in the relevant surgical technique.

5.3 Compatibility

To determine whether devices have been authorized for use in a proposed combination with Zimmer and/or Biomet products, please contact your sales representative or visit the Zimmer Electronic Labeling Service (eLabeling) website: https://labeling.zimmerbiomet.com/

5.4 Accountability of Devices

Device accountability is not required for this study. The devices used in the study are commercially available via FDA 510(k) # K141263 and CE O2271.

6 Statistical Methods

6.1 Sample Size Calculation

The overall success rate will be calculated based on the percentage of subjects who have had successful soft tissue to bone healing in the shoulder. The following hypotheses will be tested by exact binomial test:

H_0: $E_1 - E_0 \leq -\delta_E$

H_a: $E_1 - E_0 > -\delta_E$

Where:

E_0 = 85 % the expected success rate of similar devices when used in the shoulder

E_1 = the success rate in the ToggleLoc 2.9 mm Soft Tissue System treatment group in the shoulder

δ_E = 0.10, non-inferiority margin for soft tissue to bone healing in the shoulder

and

H_0: $E_1 - E_0 \leq -\delta_E$

H_a: $E_1 - E_0 > -\delta_E$

Where:

E_0 = 85 % the expected success rate of similar devices when used in the shoulder

E_1 = the success rate in the JuggerLoc Soft Tissue System treatment group in the shoulder

δ_E = 0.10, non-inferiority margin for soft tissue to bone healing in the shoulder

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

Based on the hypothesis test above, 103 subjects operated with the ToggleLoc 2.9 mm and 103 subjects operated with the JuggerLoc Soft Tissue Systems in the shoulder will provide approximately 80% power for the one-sided exact binomial test at 0.05 significant level. The sample sizes were calculated using SAS version 9.4.

6.2 General Statistical Methods and Data Analysis

Data collected in the study will be summarized descriptively. Descriptive summaries will be the basis of study reports to participants, as well as to generate an overall summary of the of the clinical evaluation of the ToggleLoc 2.9 mm and the JuggerLoc Soft Tissue Systems and their instrumentation when used in the shoulder.

Continuous data (e.g. age) will be summarized through means, medians, standard deviation, minimum, maximum and 95% confidence intervals (CIs) over time periods of interest. Categorical data (e.g. gender) will be summarized using counts, percentages and 95% confidence limits over time periods of interest. Summaries of complication data will be presented as frequencies and percentages. Subgroup summaries will be generated as needed either by strata within the study population (e.g. male vs. female, preop diagnosis) or by different cut-points (e.g. body mass index (BMI) ranges). Patient confidentiality will be protected at all times, and patient identifiers will not be included in data summaries.

7 References

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