Eclipse™ Shoulder Prosthesis

Protocol: 003
Version Date:
August 15, 2019

NCT01790113

A PROSPECTIVE, RANDOMIZED, MULTICENTER STUDY COMPARING THE SAFETY AND EFFECTIVENESS OF ARTHREX'S ECLIPSE™ SHOULDER TO THE UNIVERS™ II SHOULDER PROSTHESIS IN PATIENTS WITH A DEGENERATIVE JOINT DISEASE

Investigational Plan

Study Sponsor

ARTHREX INC
1370 Creekside Boulevard
Naples, Florida 34108 USA

Protocol Signature Page

Protocol: 003

A PROSPECTIVE, RANDOMIZED, MULTICENTER STUDY COMPARING THE SAFETY AND EFFECTIVENESS OF ARTHREX'S ECLIPSE™ SHOULDER TO THE UNIVERS™ II SHOULDER PROSTHESIS IN PATIENTS WITH A DEGENERATIVE JOINT DISEASE

I have read this protocol and agree to adhere to the requirements. I will provide copies of this protocol and all pertinent information to the study personnel under my supervision. I will discuss this material with them and ensure they are fully informed regarding the investigational device and the conduct of the study according to FDA regulations for IDE studies including 21CFR 812, 50, 54, 56; this Investigational Plan; HIPAA, Good Clinical Practices and applicable national and local regulations whichever provide the greater protection of the individual. I agree to collect and report all study data according to this protocol.

_____

Investigational Site Name

_____ _____

Primary Clinical Investigator – Print Name

_____ _____

Primary Clinical Investigator Signature **Date (MM – DD – YYYY)**

_____ _____

Sub-Clinical Investigator – Print Name **Date (MM – DD – YYYY)**

_____ _____

Sub-Clinical Investigator Signature **Date (MM – DD – YYYY)**

Table of Contents

Protocol Signature Page **2**

Table of Contents **3**

1 Protocol Summary **6**

2 Introduction **11**

2.1 Shoulder Arthroplasty Background *11*
2.2 Treatment Options: Total Shoulder Arthroplasty *12*
2.3 Investigational Device: Eclipse™ Shoulder Prosthesis *12*
2.4 Control Device: Univers™ II Shoulder Prosthesis *13*

3 Study Design, Objectives and Endpoints **14**

3.1 Study Design *14*
3.2 Objectives and Study Endpoints *14*
3.2.1 Primary Safety and Effectiveness Objective *14*
3.2.2 Primary Endpoint *14*

4 Study Population: Inclusion and Exclusion Criteria **16**

4.1 Study Population *16*
4.1.1 Intention to Treat (ITT) Cohort *16*
4.1.2 Per Protocol (Efficacy Evaluable) Cohort *16*
4.2 Study Subject Eligibility Criteria *16*
4.2.1 Inclusion Criteria *16*
4.2.2 Exclusion Criteria *17*
4.3 Allowed Concomitant and Prohibited Treatments *20*
4.4 Concomitant Analgesic *21*
4.5 Subject Compensation *21*
4.6 DSM- IV -TR® Definitions : *21*
***4.7** Osteoporosis (Moses, 2012)* *25*

5 Risk Analysis **28**

5.1 Risks and Mitigations *28*
5.2 Benefits *30*

6 Study Procedures **32**

6.1 Subject Status: *32*
6.1.1 Subject Recruitment *32*
6.1.2 Consent *32*
6.1.3 Enrollment Status *33*
6.2 Preoperative Evaluation: Visit 1 (-21 to day 0) *34*
6.3 Surgery Procedure: Visit 2 (day 0) *35*
6.4 Post-op Visits: 3 -3 months (90 days +/- 14 days) *36*
6.5 Follow-up: Visit 4 - 6 months (180 days +/- 30 days & Visit 5 -12 Months (360 days +/- 60 days) *36*
6.6 Follow-up and End of Study: Visit 6 - 24 Months (720 days + 60 days) *37*
6.7 Subject Outcomes Procedure *38*

7 Device Description **44**

7.1 Device Materials 44
7.2 Device Description 44
7.3 Principle of Device Operation 44
7.4 Accessory Device Information 45

8 Study Administration 46
8.1 Role of the Study Sponsor 46
8.2 General Duties 46
8.3 Subject Confidentiality 46
8.4 Selection of Investigators 47
8.5 Supplemental Applications 47
8.6 Submitting Reports 47
8.7 Maintaining Records 47
8.8 Institutional Review Board (IRB) Approval 48
8.9 Investigator Agreement and Financial Disclosure 48
8.10 Study Monitors 48
8.11 Investigational Site Qualification 51
8.12 Investigational Site Training 51
8.13 Investigator Responsibility for Study Conduct 52
8.14 Investigational Site Termination 54
8.15 Final Monitoring Visit 54
8.16 Protocol Amendments 55
8.17 Protocol Deviations and Violations 55
8.18 Publication 56
8.19 Audits / Inspections 56

9 Adverse Events Definitions 57
9.1 Definitions 57
9.2 Adverse Event Documentation 59
9.3 Adverse Event and Unanticipated Adverse Device Effect Reporting 60
9.4 Device Complications 61
9.5 Safety Monitoring 61

10 Statistical Method and Sample Size Calculation 62
10.1 Definition of Month 24 Composite Clinical Success (CCS) 62
10.2 Primary Efficacy Hypothesis 67
10.3 Secondary Outcomes 67
10.4 Sample Size Analysis for Primary Non-Inferiority Test 68
10.5 Analysis of Baseline Differences and Poolability 68
10.6 Survival Analysis 69
10.7 Safety Analysis 69
10.8 Treatment of Missing Data 70

11 Bibliography 72

Appendix 2-1 Radiation Dose Estimate 75

Appendix 2-2 Rehabilitation Plan 77

Appendix 2-3 Surgeon Training 79

Appendix 2-4 Schedule of Events 81

Appendix 2-5 Case Report Forms 83

Appendix 2-6 Surgical Technique ECLIPSE 84

Appendix 2-7 Radiographic Evaluation Protocol 85

Appendix 2-9 Constant Shoulder Score Patient Survey.....114

Appendix 2-10 Constant Shoulder Score Physician Investigator Examiner Section 115

Appendix 2-11 Summary of MMT Functions: 118

Appendix 2-11 Constant Score Calculations.....120

1 Protocol Summary

Title:	A Prospective, Randomized, Multicenter Study Comparing the Safety and Effectiveness of Arthrex's Eclipse™ Shoulder Prosthesis to the Univers™ II Shoulder Prosthesis in Patients with a Degenerative Joint Disease
Purpose:	The purpose of this study is to demonstrate non-inferiority of the Arthrex Eclipse™ Shoulder Prosthesis to the Arthrex Univers™ II Shoulder Prosthesis for the treatment of degenerative joint disease in subjects who are candidates for total shoulder replacement. Non-inferiority in terms of safety and effectiveness will be measured by a 2 year composite clinical success (CCS) that requires functional improvement, radiographic success, absence of reoperations and revision, and lack of serious device-related adverse events.
Study Design:	Prospective, randomized, multi-center, clinical study, up to 20 sites will randomize up to 350 subjects who are candidates for a Total Shoulder Arthroplasty, to 2 treatment groups in a 2:1 (Eclipse: Univers II) fashion. This study will cease enrollment and be terminated if the Eclipse Shoulder Prosthesis receives 510 (k) clearance prior to all subjects completing the study.
Study Hypothesis:	The goal of the study is to determine that the Eclipse™ Shoulder Prosthesis is non-inferior to the Univers™ II Shoulder Prosthesis.
Investigational Arm:	Arthrex Eclipse™ Shoulder Prosthesis (Eclipse)
Control Arm:	Arthrex Univers™ II Shoulder Prosthesis (Universe II)

Study Population: The population for this study will consist of males and females 21 years of age and older who are candidates for a total shoulder joint replacement where the humeral head and neck are of sufficient bone stock and the rotator cuff is intact or re-constructible for one of the following indications: Osteoarthritis, avascular necrosis, post-traumatic arthritis, or rheumatoid arthritis.
Additionally, the subject is not a candidate for a hemi-humeral arthroplasty and has continued symptoms in target shoulder despite at least six months of other treatment modalities (anti-inflammatory, physical therapy and steroid injections).

Primary Objective: The primary safety and effectiveness objective for this study is to demonstrate that the expected proportion of patients to achieve a Month 24 Composite Clinical Success (CCS) criterion among patients implanted with the investigational device (Arthrex's Eclipse) is clinically non-inferior to a control device (Arthrex's Univers II). The Composite Clinical Success endpoint contains the following components:

- Functional improvement as reflected in the Adjusted Constant score change from baseline to Month 24 clinical visit,
- Radiographic outcome success at Month 24,
- Absence of reoperations and revisions to the exact two-year anniversary of the index surgery, and
- Lack of serious device related complications to the exact two-year anniversary of the index surgery

Primary Endpoint: The primary safety and effectiveness endpoint is a composite of the following:

- An improvement in the Adjusted Constant Score (for pain, function and range of motion) from baseline (pre-op) to the Month 24 time-point that is ≥10 points and a final Adjusted Constant Score ≥54.
- Radiographic success at the Month 24 time-point, which is defined as absence of clinically significant humeral radiolucency, humeral migration/ subsidence (relative to 3 month time point), glenoid radiolucency, glenoid migration/subsidence (relative to 3 month time point), device disassembly or fracture, and/or periprosthetic fracture, as described in the radiographic protocol.
- No reoperation, removal, or modification of any study component up to the subject's completion of the study.
- No serious device–related complications up to the subject's completion of the study.

For a patient to be considered a success, he or she must meet all the above criteria.

Secondary Endpoints: The secondary endpoints include:

- Adjusted Constant score and radiographic success evaluated at each time point
- The percentage of patients achieving an Adjusted Constant Score ≥70 at each time point.
- SF-36
- VAS

Inclusion Criteria

1. The subject is ≥ 21 years of age
2. The subject has continued symptoms in target shoulder despite at least 3 months of other treatments (e.g.: anti-inflammatory, physical therapy and steroid injections)
3. The subject has a diagnosis in the target shoulder of one or more of the following: osteoarthritis, avascular necrosis, post-traumatic arthritis, or rheumatoid arthritis. The above are defined as follows:

   Osteoarthritis (Kellgren-Lawrence Grade 3 or higher), with clinical history of an absence of major trauma to the joint; symptoms of pain, stiffness, swelling and/or loss of motion; and with radiographic evidence of joint space narrowing, sub-chondral sclerosis, peripheral osteophytes with or without posterior subluxation of the humeral head.

   Avascular Necrosis (Staging System of Cruess Stage IV or higher), with a clinical history of a known risk factor for avascular necrosis; symptoms of pain and loss of motion; and radiographic findings of flattening or collapse of the humeral head and joint space narrowing.

   Post-Traumatic Arthritis (Kellgren-Lawrence Grade 3 or higher)**,** with a clinical history of trauma to the targeted shoulder and subsequent pain, stiffness, swelling and loss of motion; and with radiographic evidence of joint space narrowing, sub-chondral sclerosis, peripheral osteophytes.

   Rheumatoid Arthritis (American College of Rheumatology classification score of 6 or higher), with a clinical history that demonstrates: morning stiffness for at least 1 hour and present for at least 6 weeks, swelling, loss of motion, and/or serum rheumatoid factor; and radiographic findings of narrow joint space, peri-articular osteopenia, and/or peri-articular erosions and medial glenoid erosion.

4. The subject presents with pain and functional impairment in the index shoulder, measured by an Adjusted Constant Score of ≤ 50. Note: The Adjusted Constant Score will be calculated from the raw

Constant Score to establish patient eligibility.

5. The subject is willing to receive implantation of the Arthrex's Eclipse or Univers II total shoulder joint replacement.
6. The subject must be physically and mentally willing and able to comply with all study procedures (including follow-up visits and radiographic assessments) until the conclusion of the study.
7. The subject has been informed of the nature of the study and has provided written consent as approved by the local Institutional Review Board or Ethic Review Board.

Exclusion Criteria

1. The subject is a likely candidate for hemi-humeral arthroplasty (i.e.: Avascular Necrosis of the humeral head without glenoid involvement (Stages 0-3); Rotator Cuff Deficient Shoulder, Glenoid Bone deficiency/deformity that precludes glenoid replacement (Walch Type B2 or C) or fractures of the Proximal Humerus, without Glenoid involvement.
2. The subject has immature bone as defined by the absence of cancellous bone patterning, a mature, thick cortex, and stress lines within the cancellous bone.
3. The subject has obvious defects in bone quality, such as cysts or lesions, in the humeral head of the target shoulder, as demonstrated by radiographic evaluation
4. The subject has on the target shoulder a rotator cuff that is not intact and not reconstructible.
5. The subject has irreducible 3- and 4- part proximal humeral fractures of the target shoulder.
6. The subject has documented history of foreign-body sensitivity.
7. The subject is pregnant, or lactating, or intends to become pregnant during treatment period
8. The subject has documented diagnosis of Schizophrenia, Bipolar Disorder and/or Major Depressive Disorder as defined by DSM IV.
9. The subject is skeletally immature as demonstrated radiographically by incomplete closure of proximal humeral epiphyses.
10. The subject is at high risk for poor healing or confounding outcomes (i.e.; clinically significant renal, hepatic, cardiac, hematologic diseases or endocrine disease).
11. The subject is on immune-stimulating or immunosuppressive agents.
12. The subject has co-morbidities that reduces life–expectancy to less than 36 months.
13. The subject is seeking workman's compensation for shoulder injury.
14. The subject is $\geq$ 350 lbs.
15. The subject engaged in heavy labor (e.g. repetitive lifting in the excess of more than 50 lbs.)
16. The subject has had surgery in the affected shoulder in the last 12 months (with the exception of a diagnostic arthroscopy without any reconstruction or repair procedures)

17. The subject is engaged in active sports participation. (e.g. weight lifting involving upper extremities or involved in contact sports)
18. The subject is taking medication known to potentially interfere with bone/soft tissue healing (e.g. steroids-with the exception of topical and /or inhalers)
19. The subject is a prisoner or ward of the state.
20. The subject has a documented diagnosis of alcohol and/or substance abuse as defined by DSM IV
21. The subject has an active or chronic infection, either systemic or local.
22. The subject has pathologic fractures of the affected shoulder.
23. The subject has acute trauma of the affected shoulder
24. The subject has osteoporosis defined as a bone density T score of $\leq$ -2.5. (A screening Questionnaire for osteoporosis, SCORE (Simple Calculated Osteoporosis Risk Estimation) and MORES (Male Osteoporosis Risk Estimation Score), will be used to screen patients who require a DEXA bone mineral density measurement.

Timeline:	Initial Enrollment:	10/2012
	Last Enrollment:	12/2017
	Last Subject Visit	7/2019
	Last Close-out Visit	10/2019
Study Duration:	The length of the Study will be 24 months post-operative*. V 1 Screening : -21 days to day 0 V2 Surgery: day 0 V3 Post-op: 3 months =90 days +/- 14 days V4 Post-op: 6 months = 180 days +/- 30 days V5 Post-op: 12 months =360 days +/- 60 days V6 Post-op: 24 months = 720 days +/- 60days * If the study is prematurely terminated the investigator will promptly inform active subjects to ensure adequate follow-up for the subjects according to their standard of care practices.	
Monitoring:	Arthrex Clinical Research 1370 Creekside Blvd Naples, FL 34103 Ph.: 239.598.4302	

2 Introduction

2.1 Shoulder Arthroplasty Background

Shoulder replacement surgery started in the 1950's in the United States primarily to treat severe shoulder fractures. Today, shoulder arthroplasty is used to treat many painful conditions of the shoulder such as; degenerative joint disease (Osteoarthritis), Rheumatoid Arthritis, post-traumatic arthritis and avascular necrosis. The most common reason for undergoing shoulder replacement surgery is osteoarthritis. Osteoarthritis, known as a degenerative disease of the shoulder, is characterized by permanent loss of the normal surface of the ball and socket of the shoulder joint. The cartilage that normally provides this smooth surface, known as articular cartilage, degenerates and wears down. This causes loss of comfort and function of the shoulder (pain, weakness, stiffness and grinding). When the symptoms of shoulder arthritis are severe, shoulder joint replacement arthroplasty may be considered. Osteoarthritis most often occurs in people over 50. In younger people, it can result from injury or trauma, such as a fractured or dislocated shoulder, known as posttraumatic arthritis. Shoulder arthritis can also be caused by conditions where blood circulation to the ball and socket is disrupted, such as avascular necrosis. Another common type of shoulder arthritis is rheumatoid arthritis. Rheumatoid arthritis is a systemic condition that causes inflammation of the lining of the joints. This inflammation can, over time, invade and destroy the cartilage and bone.

A person with shoulder arthritis will likely have pain while moving the shoulder as well as after moving the shoulder. Shoulder arthritis is diagnosed by a history of lost shoulder function (often without injury), or during physical exam, where there is stiffness and grinding on movement and a characteristic appearance during X –ray, where the humeral head can be seen contacting the socket without the normal space occupied by the articular cartilage.

2.2 Treatment Options: Total Shoulder Arthroplasty

There are many types of shoulder replacements available today. The purpose of this trial will be to demonstrate the safety and performance of Arthrex's Eclipse™ Total Shoulder Prosthesis.

A Total Shoulder Arthroplasty has the same basic parts; a humeral component and a glenoid component. The humeral component evolved through several generations over the years. The 1st generation "Monoblock", consisted of a single piece, that could not move and had limited sizes. The second generation, "Modular" had independent segments for the head and stem, which therefore could be interchanged and sized for the patient. The third generation, "Anatomical", allows for adjustment of the prosthetic humeral head position in reference to the head and some allow for various degrees of head inclination. The traditional glenoid component is an all-polyethylene implant with a slightly convex backside and a keel to be inserted in the glenoid space. More currently used glenoid components have their keels replaced by two or more pegs. In this trial both glenoid components will be available for either treatment group.

2.3 Investigational Device: Eclipse™ Shoulder Prosthesis

The Arthrex Eclipse™ Shoulder Prosthesis is a unique stem free humeral joint prosthesis that is designed as a humeral replacement device. The Eclipse has three design elements 1) a cobalt chrome humeral head, 2) a titanium plasma spray (TPS) and Calcium phosphate (CaP) coated titanium trunion and 3) a titanium hollow screw. The Eclipse is unique in that it strikes a balance between conventional resurfacing devices and standard stemmed devices with several key advantages such as:

- Humeral head can be positioned independently of the humeral shaft axis, which is especially important in post-traumatic arthritis situations;
- Anatomic reconstruction of the humeral head, as the prosthesis can be adjusted to the cortical rim of the humeral resection at the anatomical neck;
- Nine anatomic head diameters available in 2 mm increments;
- Fenestrated cage screw for enhanced fixation;
- Multiple cage screw lengths account for anatomical variations;
- Unrestricted approach to the glenoid;
- Simplified revision arthroplasty and avoidance of complications associated with humeral shaft osteotomy; and
- Potential for less invasive exposure.

2.3.1 Target Indication for Use

The Arthrex Eclipse Shoulder Prosthesis is indicated as a total joint replacement where the humeral head and neck are of sufficient bone stock and the rotator cuff is intact or re-constructible for the following indications; osteoarthritis, avascular necrosis, post-traumatic arthritis, or rheumatoid arthritis.

This product has CE marking and is Canadian licensed, but does not have FDA clearance in the United States.

2.4 Control Device: Univers™ II Shoulder Prosthesis

The Univers™ II Shoulder Prosthesis humeral component was designed to account for anatomical variation of the proximal humerus commonly encountered by the surgeon. Variable adjustment with respect to the inclination angle, version and head offset are features critical to the reconstruction of the proximal humerus. The simplified design of the Univers™ II Shoulder Prosthesis humeral component allows the surgeon to adapt the humeral stem and articular surface to the position that best represents the patient's normal anatomy. All the adjustments can be made intraoperatively with the implant in the humeral canal. The Arthrex Univers™ II Shoulder Prosthesis consists of a titanium alloy stem for attachment to the humerus, a Chromium-Cobalt spherical head for replacing the humeral head and a titanium trunion construct to connect the stem to the head. The Univers™ II Shoulder Prosthesis has multiple head diameters and heights, along with multiple keeled and pegged glenoid options.

2.4.1 Indication for Use

The Univers™ II Shoulder Prosthesis is indicated in shoulder replacement when conditions indicating severe pain or significant disability resulting from one or more of the following conditions:

- degenerative, rheumatoid, post-traumatic disease
- injury of the glenohumeral joint
- non-union head fracture of long duration
- irreducible 2 and 4 part proximal humeral fractures
- avascular necrosis of the humeral head
- difficult clinical management problem where arthrodesis or resectional arthroplasty is not acceptable.

This product has CE marking, is Canadian licensed and FDA cleared in 510(k) K071032, K010124, K083435 and K120044.

3 Study Design, Objectives and Endpoints

3.1 Study Design

Prospective, randomized, multi-center, clinical study. Up to twenty centers will randomize up to 350 subjects who are candidates for a Total Shoulder Arthroplasty, to 2 treatment groups in a 2:1 (Eclipse: Univers II) fashion. FDA has agreed that randomization of controls may be halted after N=77, with continuing enrollment of Eclipse until the originally planned Eclipse sample size target is reached. Given the timing needed for approval to stop control enrollment, the actually number of evaluable randomized controls may be slightly larger. This study will cease enrollment and be terminated if the Eclipse Shoulder Prosthesis receives 510 (k) clearance prior to all subjects completing the study.

3.2 Objectives and Study Endpoints

3.2.1 Primary Safety and Effectiveness Objective

The primary safety and effectiveness objective for this study is to demonstrate that the proportion of patients expected to achieve a Month 24 Composite Clinical Success (CCS) criterion among patients implanted with the investigational device (Arthrex's Eclipse) is clinically non-inferior to a control device (Arthrex's Univers™ II). The composite clinical success criterion contains the following components:

- Functional improvement as reflected in the Adjusted Constant score change from baseline to the Month 24 clinical visit,
- Radiographic outcome success at Month 24,
- Absence of reoperations and revisions up to the subject's completion of the study, and
- Lack of serious device related complications up to the subject's completion of the study.

3.2.2 Primary Endpoint

The primary safety and effectiveness endpoint is 2 Year Composite Clinical Success requiring the following:

- An improvement in the Adjusted Constant Score (for pain, function and range of motion) from baseline (pre-op) to the Month 24 time-point that is ≥10 points and a final Adjusted Constant Score ≥54.

- Radiographic success at the Month 24 time-point which is defined as absence of clinically significant humeral radiolucency, humeral migration/subsidence (relative to 3 month time point), glenoid radiolucency, glenoid migration/subsidence (relative to 3 month time point), device disassembly or fracture, and/or periprosthetic fracture, as described in the radiographic protocol

- No reoperation, removal, or modification of any study component up to the subject's completion of the study.

- No serious device–related complications up to the subject's completion of the study.

For a patient to be considered a success, he or she must meet all of the above criteria.

3.2.3 Secondary Endpoints

The following will be evaluated as secondary endpoints:

- Adjusted Constant scores and radiographic success evaluated at each time point.

- The percentage of patients achieving an Adjusted Constant Score ≥70 at each time point.

- SF-36

- VAS

4 Study Population: Inclusion and Exclusion Criteria

4.1 Study Population

4.1.1 Intention to Treat (ITT) Cohort

The investigator will invite prospective patients to enroll in the study that meet the inclusion/exclusion criteria and have signed the informed consent. All patients randomized to either the investigational device (Arthrex Eclipse™ Shoulder Prosthesis) or the control device (Arthrex Univers™ II Shoulder Prosthesis) will be included in the ITT cohort. Randomization will take place after patients have been screened for inclusion and exclusion criteria. Patients found prior to randomization to not meet all inclusion and exclusion criteria will be defined as screen failures and will not receive the investigational device. These patients will be excluded from the ITT cohort.

4.1.2 Per Protocol (Efficacy Evaluable) Cohort

Patients included in the ITT cohort but found to have been randomized in error will be excluded from the Per Protocol (Efficacy Evaluable) cohort. A patient will be considered to have been randomized in error if it is determined that the patient has clinically significant violations of the inclusion or exclusion criteria. Because approval and labeling is sought for patients meeting study inclusion and exclusion criteria, primary non-inferiority testing will be conducted in the Per Protocol (Efficacy Evaluable) cohort. Safety endpoints will be summarized for the Per Protocol cohort for the same reason. However, all adverse events that occur in the study will be reported in safety listings based on the ITT cohort.

4.2 Study Subject Eligibility Criteria

Candidates must meet all eligibility criteria to be eligible for study participation:

4.2.1 Inclusion Criteria

1. The subject is ≥21 years of age
2. The subject has continued symptoms in target shoulder despite at least 3 months of other treatment modalities (e.g.: anti-inflammatory, physical therapy and steroid injections)
3. The subject has a diagnosis in the target shoulder of one or more of the following: osteoarthritis, avascular necrosis, post-traumatic arthritis, or rheumatoid arthritis. The above are defined as follows:

Osteoarthritis (Kellgren-Lawrence Grade 3 or higher), with clinical history of an absence of major trauma to the joint; symptoms of pain, stiffness, swelling and/or loss of motion; and with radiographic evidence of joint space narrowing, sub-chondral sclerosis, peripheral osteophytes with or without posterior subluxation of the humeral head.

Avascular Necrosis (Staging System of Cruess Stage IV or higher), with a clinical history of a known risk factor for avascular necrosis; symptoms of pain and loss of motion; and radiographic findings of flattening or collapse of the humeral head and joint space narrowing.

Post-Traumatic Arthritis (Kellgren-Lawrence Grade 3 or higher), **with** a clinical history of trauma to the targeted shoulder and subsequent pain, stiffness, swelling and loss of motion; and with radiographic evidence of joint space narrowing, sub-chondral sclerosis, peripheral osteophytes.

Rheumatoid Arthritis (American College of Rheumatology classification score of 6 or higher), with a clinical history that demonstrates: morning stiffness for at least 1 hour and present for at least 6 weeks, swelling, loss of motion, and/or serum rheumatoid factor; and radiographic findings of narrow joint space, peri-articular osteopenia, and/or peri-articular erosions and medial glenoid erosion.

4. The subject presents with pain and functional impairment in the index shoulder, measured by an Adjusted Constant Score of ≤50. Note: The Adjusted Constant Score will be calculated from the raw Constant Score to establish patient eligibility.
5. The subject is willing to receive implantation of the Arthrex™ Shoulder Prosthesis or Univers™ II Shoulder Prosthesis.
6. The subject must be physically and mentally willing and able to comply with all study procedures (including follow-up visits and radiographic assessments) until the conclusion of the study.
7. The subject has been informed of the nature of the study and provided written consent as approved by the sites local Institutional Review Board or Ethic Review Board.

4.2.2 Exclusion Criteria

1. The subject is likely a candidate for hemi-humeral arthroplasty (i.e.: Avascular Necrosis of the humeral head without glenoid involvement (Stages 0-3): Rotator Cuff Deficient Shoulder: Glenoid Bone deficiency/deformity that precludes glenoid replacement (Walch Type B2 or C) or Fractures of the Proximal Humerus, without Glenoid involvement.
2. The subject has immature bone as defined by the absence of cancellous bone patterning, a mature, thick cortex, and stress lines within the cancellous bone.

3. The subject has obvious defects in bone quality, such as cysts or lesions, in the humeral head of the target shoulder, as demonstrated by radiographic evaluation.
4. The subject has a target shoulder a rotator cuff that is not intact and not reconstructible.
5. The subject has Irreducible 3- and 4- part proximal humeral fractures of the target shoulder.
6. The subject has documented history of foreign-body sensitivity.
7. Subject with positive pregnancy test, or lactating, or intends to become pregnant during treatment period
8. The subject has documented diagnosis of Schizophrenia, Bipolar Disorder and/or Major Depressive Disorder as defined by DSM IV.
9. The subject is skeletally immature demonstrated radiographically by incomplete closure of proximal humeral epiphyses.
10. The subject is at high risk for poor healing or confounding outcomes (i.e.: clinically significant renal, hepatic, cardiac hematologic or endocrine disease).
11. The subject is on immune-stimulating or immunosuppressive agents
12. The subject has co-morbidity that reduces life expectancy < 36 month.
13. The subject seeking or receiving workman's compensation for shoulder injury,
14. The subject is $\geq$ 350 lbs.
15. The subject engaged in heavy labor (e.g. repetitive lifting in the excess of more than 50 lbs.)
16. The subject has had surgery in the affected shoulder in the last 12 months (with the exception of a diagnostic arthroscopy without any reconstruction or repair procedures)
17. The subject is engaged in active sports participation. (e.g. weight lifting involving upper extremities or involved in contact sports)
18. The subject is taking medication known to potentially interfere with bone/soft tissue healing (e.g. steroids-with the exception of topical and /or inhalers)
19. The subject is a prisoners or wards of the state
20. The subject has a history document diagnosis of alcohol and/or substance abuse as defined by DSM IV
21. The subject has an active or chronic infection, either systemic or local.
22. The subject has Pathologic fractures of the affected shoulder
23. The subject has acute trauma of the affected shoulder
24. The subject has osteoporosis defined as a bone density T score of $\leq$ -2.5. (A screening Questionnaire for osteoporosis, SCORE (Simple Calculated Osteoporosis Risk Estimation) and MORES (Male Osteoporosis Risk Estimation Score), will be used to screen patients who require a DEXA bone mineral density measurement.

Kellgren-Lawrence Scale

Osteoarthritis will be evaluated using the Kellgren-Lawrence Scale (Jacobson, 1996) as follows:

Grade of Osteoarthritis	Description
1	doubtful narrowing of joint space, possible osteophytic lipping
2	definite small osteophytes, possible narrowing of joint space
3	multiple moderately sized osteophytes definite joint narrowing, some sclerotic areas, possible deformation of bone ends
4	Large osteophytes, marked narrowing of joint space

Staging System of Cruess

Avascular Necrosis will be evaluated using the Staging System of Cruess (Cruess 1978)

Stage of Avascular Necrosis	Description
I	Documented only by magnetic resonance imaging or bone scan
II	Localized or mottled sclerosis, osteopenia
III	Crescent sign present, indicating a subchondral fracture
IV	Flattening and collapse of humeral head subchondral bone
V	Degenerative changes extending to glenoid side of joint

American College of Rheumatology

Rheumatoid Arthritis will be evaluated using the American College of Rheumatology (Aletaha 2010)

	Possible Points
Joint Involvement (Choose option in each category)	
1 large joint	0
2-10 large joints	1

1-3 small joints (with or without involvement of large joints)	2
4-10 small joints (with or without involvement of large joints)	3
> 10 joints (at least 1 small joint)	5

Serology (at least 1 test result is needed for classification)

Negative RF *and* negative ACPA	0
Low-positive RF *or* low-positive ACPA	2
High-positive RF *or* high-positive ACPA	3

Acute-phase reactants (at least 1 test result is needed for classification)

Normal CRP and normal ESR	0
Abnormal CRP or abnormal ESR	1

Duration of symptoms

< 6 weeks	0
≥ 6 weeks	1

4.3 Allowed Concomitant and Prohibited Treatments

The Arthrex Eclipse™ and Univers™ II Shoulder Prosthesis are to be performed as a total shoulder arthroplasty. A hemi-arthroplasty is prohibited except when the investigator determines operatively it is the best alternative for the subject. The alternative hemi-arthroplasty must be with a Univers ™ II Shoulder Prosthesis only; the subject will be dropped as a study participant. The Investigational device, "Eclipse™ Shoulder Prosthesis" must never be implanted as a hemi-Arthroplasty.

Subject may not enter any other clinical trial involving medical or surgical intervention, or undergo any elective orthopedic surgery of target upper extremity while enrolled in this study. Observational studies will be considered with the sponsor's approval.

Participation is restricted to having only one shoulder enrolled in this study.

4.4 Concomitant Analgesic

Use of medication for pain management (includes over the counter medications, prescription analgesics, narcotics, anti-inflammatories, muscle relaxants) will be recorded at each study visit. The data collected will include medication name, indication for use and dose.

This data is entered on the Concomitant /Medication form in the EDC. Medication used preoperative, operative and immediate postoperatively (while in recovery room) for target total shoulder replacement will not be collected during the study.

Additionally, concomitant treatment (physical therapy) will be recorded at each study visit. This data is entered on the Post-operative Evaluation Visit form in the EDC.

4.5 Subject Compensation

Each subject who returns for a follow up visit within the protocol required time frame will receive a reasonable compensation to offset the cost of meals, transportation, parking and other such expenses, as approved by the IRB. Compensation is provided to the subject by the investigational site. Compensation amounts are specified in the Informed Consent and the Clinical Trial Agreement.

4.6 DSM- IV -TR® Definitions :

4.6.1 Schizophrenia

Symptoms of Schizophrenia typically begin between adolescence and early adulthood for males and a few years later for females, and usually as a result of a stressful period (such as beginning college or starting a first full time job). Characteristic symptoms: Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated):

(1) Delusions
(2) Hallucinations
(3) Disorganized speech (e.g. frequent derailment or incoherence)
(4) Grossly disorganized or catatonic behavior
(5) Negative symptoms, i.e., affective flattening, alogia or avolition

Note: only one Criterion A symptom is required if delusions are bizarre or hallucinations consist of a voice keeping a running commentary on the person's behavior or thoughts, or two or more voices conversing with each other.

4.6.2 Bipolar Disorders:

Diagnostic criteria Bipolar I:

A. Criteria, except duration are currently (or most recently) met for a Maniac, a Hypomanic, a Mixed, or a Major Depressive Episode.
B. There has previously been at least one Manic Episode or Mixed Episode.
C. The mood symptoms cause clinically significant distress or impairment in social, occupational, or other important areas of functioning.
D. The mood symptoms in Criteria A and B are not better accounted for by Schizoaffective Disorder and are not superimposed on Schizophrenia, Schizophreniform disorder, delusional Disorder, or Psychotic Disorder Not Otherwise Specified.
E. The mood symptoms in Criteria A and B are not due to the direct physiological effects of a substance (e.g., a drug of abuse , a medication or other treatment) or a general medical condition(e.g. hyperthyroidism)

For a diagnosis of Bipolar I disorder, a person must have at least one manic episode. Mania is sometimes referred to as the other extreme to depression. Mania is an intense high where the person feels euphoric, almost indestructible in areas such as personal finances, business dealings, or relationships. They may have an elevated self-esteem, be more talkative than usual, have flight of ideas, a reduced need for sleep, and be easily distracted. The high, although it may sound appealing, will often lead to severe difficulties in these areas, such as spending much more money than intended, making extremely rash business and personal decisions, involvement in dangerous sexual behavior, and/or the use of drugs or alcohol. Depression is often experienced as the high quickly fades and as the consequences of their activities becomes apparent, the depressive episode can be exacerbated.

Diagnostic criteria for Bipolar II:

Presence (or history) of one or more Major Depressive Episode

A. Presence (or history) of at least one Hypomanic Episode
B. There has never been a Manic Episode or a mixed Episode
C. The mood symptoms in criteria A and B are not better accounted for by Schizoaffective Disorder and superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder Not Otherwise Specified.

D. The symptoms cause clinically significant distress or impairment in social, occupational, or other important areas functioning.

Bipolar II: Similar to Bipolar I Disorder, there are periods of highs as described above and often followed by periods of depression. Bipolar II Disorder however is different in that the highs are hypo manic, rather than manic. In other words, they have similar symptoms but they are not severe enough to cause marked impairment in social or occupational functioning and typically do not require hospitalization in order to assure the safety of the person.

4.6.2 Major Depressive Disorder

The essential feature of Major Depressive Disorder is a clinical course by one or more Major Depressive Episodes (see below) without a history of Manic, Mixed, or Hypomanic Episodes. Episodes of Substance-Induced Mood Disorder (due to the direct physiological effect of a drug of abuse, a medication, or toxin exposure) or of Mood Disorder Due to a General Medical Condition do not count toward a diagnosis of Major Depressive Disorder. In addition, the episodes must not be better accounted for by Schizoaffective Disorder and are not superimposed on Schizophrenia, Schizophreniform Disorder, Delusional Disorder, or Psychotic Disorder.

The essential features of a major Depressive Episode is a period of at least 2 weeks (most of the day ,nearly every day) during which there is either depressed mood or the loss of interest or pleasure in nearly all activities. The episode must be accompanied by clinically significant distress or impairment in social, occupational, or other important areas of functioning. The individual must also experience at least four additional symptoms drawn from a list that includes:

- changes in appetite or weight, sleep and psychomotor activity
- depressed energy
- feelings of worthlessness or guilt
- difficulty thinking , concentrating, or making decisions
- recurrent thoughts of death or suicidal ideation, plans or attempts.

4.6.3 Substance abuse

A maladaptive pattern of substance use leading to clinically significant or distress, as manifested by one (or more) of the within a 12 month period: (1) recurrent use resulting in a failure to fulfill major obligations at work, school, or home; (2) recurrent use in situations which are physically

hazardous (e.g., driving while intoxicated); (3) recurrent substance-related legal problems resulting (e.g., arrests for substance –related disorderly conduct) or (4) continued use despite significant social or interpersonal problems caused or exacerbated by the effects of the substance (e.g., arguments with spouse about consequences of intoxication, physical fights) The symptoms do not meet the criteria for substance dependence for this class of substance.

Substance Dependence is a maladaptive pattern of substance use to clinically significant or distress, as manifested by three (or more) of the following, occurring at any time in the same 12 month period:

(1) tolerance as defined by either of the following:
    i. A need for markedly increased amounts of the substance to achieve intoxication or desired effect.
    ii. Markedly diminished effect with continued use of the same amount of the substance
(2) Withdrawal, as manifested by either of the following:
    i. The characteristics withdrawal syndrome for the substance
    ii. The same substance is taken to relieve or avoid withdrawal symptoms.
(3) The substance is often taken in larger amounts or over a longer period than intended.
(4) There is a persistent desire or unsuccessful efforts to cut down or control substance use.
(5) A great deal of time is spent in activities necessary to obtain the substance , use the substance or recover from its effects
(6) Important social, occupational, or recreational activities are given up or reduced because of substance use
(7) The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g. continued drinking despite recognition that an ulcer was made worse by alcohol consumption)

4.6.4 Alcohol Abuse

Alcohol abuse requires fewer symptoms and, thus, may be less severe than Dependence and is only diagnosed once the absence of Dependence has been established. School and Job performance may suffer either from the aftereffects of drinking or from actual intoxication on the job or at school; child care or household responsibilities may be neglected; and alcohol related absences may occur from school or job. The person may use alcohol in physically hazardous circumstances. Legal difficulties may arise because of alcohol use. Finally, individuals with Alcohol Abuse may continue to consume alcohol despite the knowledge that continued consumption poses significant social or interpersonal problems for them. When these problems

are accompanied by evidence of tolerance, withdrawal, or compulsive behavior related to alcohol use, a diagnosis of Alcohol Dependence, rather than Alcohol abuse, should be considered. Since some symptoms of tolerance, withdrawal, or compulsive use can occur in individuals with Abuse but not dependence, one should determine if the full criteria for dependence are met.

4.6.5 Alcohol Dependence

Physiological dependence on alcohol is indicated by evidence of tolerance or symptoms of Withdrawal. Especially if associated with a history of withdrawal, physiological dependence is an indication of a more severe clinical course overall. (e.g. earlier onset, higher levels of intake, more alcohol –related problems) Withdrawal from alcohol can be unpleasant and intense; individuals with Alcohol dependence may continue to consume alcohol, despite adverse consequences, often to avoid or to relieve the symptoms of withdrawal. Some withdrawal symptoms, (e.g. sleep problems) can persist at lower intensities for months. Once a pattern of compulsive use develops, individuals with Dependence may devote substantial periods of time to obtaining and consuming alcoholic beverages. These individuals often continue to use alcohol, blackouts, liver disease, or other sequelae.

Note: Mental health diagnoses are made by psychiatrist, psychologist, or other mental health professionals who is specially trained to diagnose and treat mental illnesses. The mental health professional uses specially designed interview and assessment tools to evaluate a person for a mental illness. For the purposes of this study subjects with documented diagnosis according to the DSM IV, by a psychiatrist, psychologist or other mental health professional would be required to exclude a subject's with a history of Schizophrenia, Bipolar Disorder , Major Depressive Disorder , alcohol and/substance abuse.

4.7 Osteoporosis (Moses, 2012)

4.7.1 Dual X-ray absorptiometry (DXA)

DXA is a diagnostic test used to assess bone density. Dual-energy X-ray absorptiometry (DXA, previously DEXA) is a means of measuring bone mineral density (BMD). Two X-ray beams with different energy levels are aimed at the patient's bones. When soft tissue absorption is subtracted out, the BMD can be determined from the absorption of each beam by bone. Dual-energy X-ray absorptiometry is the most widely used and most thoroughly studied bone density measurement technology. The DXA scan is typically used to diagnose and follow osteoporosis

Upon completion of a DXA scan, the bone density if the patient is then compared to the average peak bone density of adults of same sex and race. This score is called the "T score and it expresses the bone density in terms of the number of standard deviations (SD) below peak young adult bone mass.

Note: Generally the DEXA Scan will have a reading from the spine, the hip and the forearm. The lowest most negative score should be use to qualify the subject for enrollment and enter into the EDC.

4.7.2 T-score

The World Health Organization has defined the following categories based on bone density in white women:

Normal bone	T-score greater than -1
Osteopenia	T-score between -1 and -2.5
Osteoporosis	T-score less than or equal to -2.5
Severe (established) osteoporosis	T-score less than -2.5 and 1+ osteoporotic fractures

Note: in this study a T-score of ≤ -2.5 is considered Osteoporosis and the subject is excluded.

4.7.3 Simple calculated osteoporosis risk estimation

The following risk assessments have been reported to appropriately identify women (SCORE) and men (MORES) who are likely to be at risk for osteoporosis.

Women: Simple Calculated Osteoporosis Risk Estimation (SCORE)

A risk assessment instrument, the "simple calculated osteoporosis risk estimation" (SCORE), has been reported to appropriately identify women likely to have low (t score ≤−2 SD) bone mineral density (BMD) and who should be referred for bone densitometry. The majority of Osteoporosis risk is predicted by age, weight and ethnicity. The criteria for the SCORE questionnaire are as follows:

a. Race not black : 5 points
b. Rheumatoid Arthritis : 4 points
c. Fracture after age 45 on wrist , hip or rib: 4 points per Fracture
d. Age over 65; calculate 3 x (1st digit of age) Example for age 70 :21 points

e. Weight: calculate (-1 x weight in pounds)/10. Example for weight 200 pounds: -20 point
f. Estrogen therapy never use: 1 point

A result of 6 or above on the SCORE Questionnaire is associated with T-score below-2 SD. Osteoporosis testing with Dexa Scan is recommended if score of 6 or above. (Lydick 1998)

For Men: Male Osteoporosis Risk Estimation Score (MORES)

A risk assessment instrument, the "male osteoporosis risk estimation score" (MORES) has been reported to appropriately identify men who are likely to have low (t score ≤−2 SD) BMD and who should be referred for bone densitometry. The majority of osteoporosis risk in males is predicted by age, weight, and a chronic obstructive pulmonary disease (COPD) diagnosis. The criteria for the MORES questionnaire are as follows:

a. Age:
    1. 55 Years or younger (0 points)
    2. 56 to 74 years: 3 points
    3. 75 years or older: 4 points
b. Confirmed COPD Diagnosis: 3 points
No COPD Diagnosis: 0 points
c. Weight:
    1. 154 pounds or less: 6 points
    2. 155 to 176 pounds: 4 points
    3. Greater than 176 pounds (0 points)

A result of 6 or above on the MORES Questionnaire is associated with T-score below-2 SD. Osteoporosis testing with DEXA Scan is required if score of 6 or above. (Shepherd 2007)

5 Risk Analysis

5.1 Risks and Mitigations

Shoulder replacement surgery started in the United States in the 1950s. Because of the vast amounts of clinical experience available, the risk and adverse events associated with shoulder arthroplasty are well understood. The risk profile has improved over time with advances in technology and surgical techniques. The risks from implantation of the Eclipse™ Shoulder Prosthesis (including the device and the procedure) are described below. In addition to the risk mitigation described, subject selection criteria, study methods, evaluations, follow-up periods, facilities and investigator selection are intended to minimize risk to subjects participating. In this study, subjects will be monitored throughout the study (day 0 to 24 Months following the procedure) for the detection of adverse events. If the study is prematurely terminated the investigator will promptly inform active subjects to assure appropriate follow-up for the subjects as per their standard of care practices. Subjects will be advised that the standard of care visits may vary from the scheduled study visits. Furthermore, subjects will be informed of how and whom they should follow up with if they have any issues or adverse events related to the study device. Subjects randomized to the comparator device will be treated in compliance with its indication and instructions for use, adding no additional risk to subjects.

The investigation is designed to compare the Eclipse Shoulder to an FDA cleared standard of care for shoulder arthroplasty (Arthrex Univers™ II), and the number of patients to be enrolled provides the necessary number of subjects to statistically demonstrate the Eclipse Shoulder is non-inferior to the current standard of care for shoulder arthroplasty patients. The age, sex, and condition of the study population are consistent with the standard of care, and the inclusion and exclusion criteria have been designed to prevent the enrollment of study subjects for whom shoulder arthroplasty would not be the standard of care.

Furthermore, any risks associated with participation in this study will be minimized and managed in accordance and full compliance with 21 CFR 50 Protection of Human Subjects, CRF 56 Institutional Review Boards and 21 CFR 812 Investigational Device Exemptions.

The risks to patients from the radiation (postoperative X-rays of the device) a person will receive during this study are expected to be minor, as, based on a review of the literature, each patient would receive 0.015 mSv per visit, and 0.075 mSv for all visits up to and including the 24 month visit. Based on a large study of cancer risk associated with exposure to radiation, it was estimated that the excess relative risk for cancer is 0.97 per Sv (Cardis et al. 2005), leading to an excess relative risk of 0.00007 for radiographs utilized in this study. (Appendix 2-1 Radiation Dose).

Pregnant females may not participate due to potential risks to the fetus. Any female patient who may potentially become pregnant prior to the onset of the study must take pregnancy test prior to the surgery.

As with any surgical procedure, risks and complications are possible. The surgical staff routinely makes every effort to minimize these complications. Some potential complications that may occur as a result of any surgical procedure are listed below:

As with any invasive procedure, both deep and superficial infections may occur with an overall prevalence 0.7% (Bohsali, 2006). All procedures will be performed aseptically, and surgeons are instructed to never reuse or re-sterilize the device.

As with all surgeries, there is a potential for temporary or permanent nerve damage as a result of trauma which is reported 0.8 % (Bohsali, 2006). In addition, joint pain, stiffness, and swelling following the surgery can occur. These can be managed by following the Postoperative Total Shoulder Arthroplasty Rehabilitation Plan described in Appendix 2-2.

Delayed wound healing and wound hematomas are possible with any surgery and are reported to be 12.8% (Amirfeyz). However, the Inclusion/Exclusion criteria excludes those patients who might be more at risk for delayed healing (i.e. patients at a higher risk for poor healing, patients on immunostimulating agents, patients with poorly controlled diabetes or clinically significant/actively being treated renal, cardiac, liver or hematologic disease).

Additional surgical complications may include cardiovascular events such as venous thrombosis, pulmonary embolism and cardiac arrest. Subjects are monitored for these complications and instructed to contact their surgeon if any problems are detected.

As with any foreign body implant, allergies and other reactions to device material may occur. Patients will be queried about allergies and previous implants; where material sensitivity is suspected, appropriate tests should be made to rule out sensitivity prior to implantation. The Eclipse Shoulder Prosthesis is manufactured from known materials such as Titanium and Cobalt Chrome and coated with Titanium plasma spray (TPS) and Calcium phosphate (CaP); the glenoid component is also manufactured from a known material, Ultra High Molecular Weight Polyethylene (UHMWPE). All of these materials have a long history of clinical use, including in similar medical devices. As the glenoid component is comprised of UHMWPE, there is no risk of metal-on-metal wear, which has recently been determined to cause long-term adverse biologic reactions with certain metal-on-metal hip prosthesis.

Loosening of the implant as a result of changed conditions in load transfer, fatigue wear disassociation of the components, or tissue reaction has been reported to occur (7% aseptic loosening of humeral head). Patients will be assessed for sufficient quantities or quality of humeral head and/or humeral neck bone stock prior to implant via radiograph. Loosening of the implant may also

be caused by inadequate anchoring technique. These risks are mitigated by assuring that the surgeons are properly trained on the specifics of the device, as well as the corresponding surgical procedure.

Specific surgeon training will help mitigate the risks of extreme weakening of the bone structure in the preparation the bone bed, unsuitable implant size selection, inadequate cleaning of the bone bed prior to implantation, excessive use of force in placing or anchoring the implant, creation splintering factures, or development of bones tears. Additional training regarding the use of only the associated Arthrex delivery system, instruments, and trial prosthesis for implantation will mitigate the risks of dislocation, subluxation, and inadequate scope of movement as a result of failure to achieve optimum positioning of the implant. In addition, proper training on the surgical technique and the positioning of the implants will mitigate the risk of temporary or permanent nerve damage. Surgeon training on the implant utilize will be required of all surgeons in the study, and documentation of surgeon training will be recorded in the site binders (Appendix 2-3 Surgeon Training).

Comprehensive bench and clinical experience outside the US (included in the Report of Priors) demonstrates that there is minimal risk of device fractures. To mitigate the risk of bone fractures as a result of one-sided overload or weakened bone structure, the fixation provided by this device needs to be protected, postoperatively, until healing is complete. The postoperative regimen prescribed by the physician should be strictly followed to avoid adverse stresses applied to the implant.

In the United States, 12,758 Total Shoulder Arthroplasty procedures were performed from 1990-2000, with 61.3 % females and 38.7% males; 8 % were under the age of 50; 12.3% were between 50 to 59, 10.5% were between 60-64, 54.6% were between 65-79 and 14.7% were older than 80. Additionally, in regards to diagnosis for that 12, 758 Arthroplasty procedures, there were 64.6% diagnosed with Osteoarthritis of shoulder region, 10.3% with Fractures of upper end of humerus, 6.5% with Rheumatoid arthritis, 13.9% with Aseptic necrosis of humeral head and 4.7% with missing data (Jain NB, 2006).

The US Department of Health and Human Services (HHS) reports that between 1997-2005 the number of shoulder arthroplasty or total shoulder replacements increased by 145%.

The trends demonstrate that the number of Total Shoulder Arthroplasty performed, the subject population and the suggested indication will be appropriately represented by adherence to the Inclusion/Exclusion Criteria.

5.2 Benefits

Arthrex Inc. firmly believes that the values of the knowledge to be gained by conducting this clinical study to demonstrate the safety and efficacy of this device outweigh the potential risks posed to participating subjects. The need for the data from such a study together with the benefit of receiving a Total

Shoulder Arthroplasty in a controlled setting balances the risks related to participation in the study.

6 Study Procedures

6.1 Subject Status:

The investigator or designee should review all prospective subjects' medical histories to screen for eligibility. (Appendix 2-4 Schedule of Events)

6.1.1 Subject Recruitment

The investigator will provide all patients who present to his practice and are candidates for a total shoulder joint replacement where the humeral head and neck are of sufficient bone stock and the rotator cuff is intact or re-constructible for one of the following indications: Osteoarthritis, avascular necrosis, post-traumatic arthritis, or rheumatoid arthritis, the opportunity to participate in this clinical trial

6.1.2 Consent

The investigator will prepare an informed consent form in accordance with this study protocol and all regulatory requirements (21 CFR Part 50) using the sample informed consent form provided in this investigational plan. The informed consent form must be submitted to the IRB and a copy of the final IRB-approved consent form must be submitted to Arthrex Clinical Research prior to the start of the study at the investigational site.

The subject candidate will be introduced to the study by the investigator. Interested patients will have the study thoroughly explained to them by the investigator and/or site coordinator. Additionally, an informed consent form will be provided to the patient so they may take home and review with significant others if desired. The informed consent process includes ensuring all of the patient's questions are answered. Once the subject decides if they want to participate in the clinical trial, the site will obtain a signed consent from the subject and make arrangements to schedule them for their pre surgical visit.

Prior to any study procedures, all subjects must document their consent for study participation and authorization for use and disclosure of health information by signing the IRB-approved Informed Consent form.

6.1.3 Enrollment Status

Screening Status:
Subject's that have signed the informed consent and have data collected at Visit 1 will be considered Screened.

Randomized:
Only those patients who meet the inclusion and exclusion criteria.

Treated:
Once implanted the subject status will update to either Implanted - Eclipse or Implanted - Univers II.

Screen Failed:
Screen failures are those subjects who have signed the informed consent and data has been collected at visit 1, but are not eligible or not able to start treatment. Subjects that were screened and randomized but had to have a non study total shoulder replacement will be consider a Screen Fail.
Once the subject is determined to be a "Screen Fail" and the End of Study form is completed (with the reason) in the EDC, the subject status will update to Screen Fail. An enrollment log of all subjects screened for the study. The reason(s) for screen failure will be recorded on the log.

Early Termination:
Subjects that are screened, randomized, and implanted with the Univers II or the Eclipse but drop out prior to 24 months (720 days +/- 60days) will be considered Early Termination.

Potential reasons for "Early Termination" may include, but are not limited to:

- Subject participation in a clinical trial is voluntary. The subject may discontinue participation (refuse all subsequent testing and follow-up procedures) at any time without penalty or loss of benefits.
- The investigator may terminate the subject's participation without regard to the subject's consent if the investigator believes it is medically necessary and in the best interest of the subject.
- Lost to Follow-up: The subject does not complete the 24 month follow-up but has not "officially" withdrawn from the study.
    - Failure to return for follow-up visits is not a criterion for withdrawal.
    - In order to consider a subject lost to follow-up, site personnel should make all reasonable efforts to locate and establish communication with the study subject. All attempts should be

documented within the source documents, indicating date, time, method, and site personnel.

- A minimum of three documented attempts should be made without response from the study subject in order to classify a subject as lost to follow-up.

Should subject discontinuation occur the reason(s) for discontinuation must be documented in the source documents along with notification to Arthrex Clinical Research. Once the End of Study form is completed in the EDC, the subject status will update to "Early Termination"

Subjects who are determined to be "Early Termination" from the study will not be replaced.

Complete:
Subjects that are screened, randomized, implanted with the Univers II or the Eclipse and completed the 24 month (720 days +/- 60ays) follow up Visit 6 will be considered Complete.

- Once the data for visit 6 is entered in the EDC and the End of Study form, the subject status will update to complete.

6.2 Preoperative Evaluation: Visit 1 (-21 to day 0)

Once the subject has signed the informed consent and prior to surgery, they will have the following data collected and procedures conducted: (Appendix 2-5 Case Report Forms)

- Demographics /History CRF
  - Kellgren-Lawrence Scale
  - Staging System of Cruess
  - American College of Rheumatology
  - SCORE/MORES questionnaire
- Concomitant Medication & Therapy CRF (pain management only)
- Subject Report Survey's:

Note: Subject surveys are to be completed prior to the Physical, The survey should be QC'd for completeness, discrepancies, signed or initialed and dated, during the visit.

  - SF36
  - VAS
  - Constant Score:
    - Subject will be asked to fill out the subject section regarding activities of daily living (sleep, work, recreation / sport).
    - Clinician completes objective section by assessing range of motion and strength
- Physical Exam/Shoulder Exam includes sensory and motor testing

- Radiograph(s)

Note:

- Serum or urine Pregnancy test if applicable
- Enrollment Checklist
- Patient Education regarding Total Shoulder Prosthesis, post-operative procedures and the follow-up study schedule.
  - Inform subjects that they will return post-op within 3 months, 6 months, 12 Months and 24 Months for follow-up.
  - Deviations
- Note: Screening procedures may be done on different days within the screening window.

6.3 Surgery Procedure: Visit 2 (day 0)

Prior to surgery the following should be reviewed to confirm eligibility;

- Pre-op lab (Pregnancy test if applicable)
- Enrollment Checklist Review (Occurs prior to subject randomization)
- Concomitant Medication/Therapy Review (pain management only)
- Deviations

Post-operative care for both groups will follow the Postoperative Total Shoulder Arthroplasty Rehabilitation Plan (Appendix 2- 2).

Surgery

- Eclipse ™ Shoulder Prosthesis refer to Surgical Technique # IDE-LT0715B (Appendix 2-6)

Post-operative Data Collection

- Surgical /Operative details
- Adverse Event Review
- Concomitant Medication/Therapy Review (pain management only)
- Radiographs may be completed at Standard of Care post-operative visits within 72 hours of surgery. (Appendix 2-8 Radiographic Evaluation Protocol)
- Rehabilitation (Appendix 2-2)
- Patient Education regarding Total Shoulder Prosthesis, post-operative procedures and the follow-up study schedule.
- Inform subjects that they will return post-op within 3 months, 6 months, 12 Months and 24 Months for follow-up.
- Deviations

Follow-up Visits:

- Prior to discharge from the hospital the study follow –up visit is scheduled at the investigative site for 3 months post-op visit.

6.4 Post-op Visits: 3 -3 months (90 days +/- 14 days)

During the post op visit the subject will have the following:

- Concomitant Medication/Therapy Review (pain management only)
- Subject Report Survey's:
- Note: Subject surveys are to be completed prior to the Physical, The survey should be QC'd for completeness, discrepancies, signed or initialed and dated, during the visit.
    - SF36
    - VAS
    - Constant Score:
        - Subject will be asked to fill out the subject section regarding activities of daily living (sleep, work, recreation / sport).
        - Clinician completes objective section by assessing range of motion and strength
- Shoulder Exam includes sensory and motor testing.
- Adverse Event Review
- Surgical Radiograph: Refer to Radiographic Evaluation Protocol (Appendix 2-8)
- Postoperative evaluation
- Deviations
- The follow –up schedule review: Subjects will be scheduled to return at 6 months (180 $\pm$ 30 days), 12 Months (360 $\pm$ 60 days) and 24 Months (720 $\pm$ 60 days) for follow-up Radiographs, Constant Score, Adverse Event review and medication/therapy assessment.

6.5 Follow-up: Visit 4 - 6 months (180 days +/- 30 days & Visit 5 -12 Months (360 days +/- 60 days)

During each follow up visit the subject will be interviewed and have the following data collection:

- Concomitant Medication/Therapy Review (pain management only)
- Subject Report Survey's:
    - Note: Subject surveys are to be completed prior to the shoulder exam, the survey should be QC'd for completeness, discrepancies, signed or initialed and dated, during the visit.

      .
    - SF-36
    - VAS
    - Constant Score
        - Subject will be asked to fill out the subject section regarding activities of daily living (sleep, work, recreation / sport).

- Clinician completes objective section by assessing range of motion and strength.
- Shoulder Exam includes sensory and motor testing
- Adverse Event Review
- Radiographs: Refer to Radiographic Evaluation Protocol (Appendix 2-8)
- Postoperative evaluation
- Deviations
- The follow –up schedule review: Subjects will be scheduled to return at Visit 6 -24 Months (720 days +/- 60 days) for follow-up Radiographs, Constant Score, and Adverse Event review and medication/therapy assessment.

6.6 Follow-up and End of Study: Visit 6 - 24 Months (720 days ± 60 days)

All subjects enrolled in the study will have the following data collection at Visit 6 or End of Study Visit if it occurs prior to 24 Months (720 days +/- 60 days).

- Concomitant Medication/Therapy Review (pain management only)
- Subject Report Survey's:
  - Note: Subject surveys are to be completed prior to the shoulder exam. The survey should be QC'd for completeness, discrepancies, signed or initialed and dated, during the visit.
  - SF-36
  - VAS
  - Constant Score
    - Subject will be asked to fill out the subject section regarding activities of daily living (sleep, work, recreation / sport).
    - Clinician completes objective section by assessing range of motion and strength
- Shoulder Exam includes sensory and motor testing
- Adverse Event Review
- Radiographs: Refer to Radiographic Evaluation Protocol (Appendix 2-8)
- Postoperative evaluation
- Deviations
- End of Study Form

6.7 Subject Outcomes Procedure

6.7.1 Constant Shoulder Score

"The Constant score was devised by Christopher Constant with the assistance of Alan Murley during the years 1981-1986. The score was first presented in a university thesis in 1986 (Constant CR) and the methodology published in 1987(Constant CR). The functional assessment score was conceived as a system of assessing the overall value, or functional state, of a normal, a diseased, or a treated shoulder" (Constant CR)

Constant Shoulder Score is a widely used shoulder specific scoring system. The Constant Score uses subjective and objective measures to determine whether a certain functional movement is possible (e.g. forward elevation, external rotation, and internal rotation of the shoulder). As an outcome tool, the Constant score includes an analysis of pain, shoulder motion, strength, and function. From a perfect score of 100, it reserves 35 points for patient-reported subjective assessment, including the pain and the ability to perform basic activities of daily living and 65 points for objective measurements (40 points for ROM and 25 points for strength). See Table 1(Constant C.R.)

Table 1: Scoring for Individual Parameter	
Pain	15
Activities of daily living	20
Range of Motion	40
Power	25
Total	100

6.7.2 Constant Score Procedure:

Patients are instructed to complete a one page questionnaire that assesses subjective pain and Activities of Daily Living (ADLs). (Appendix 2.9 Constant Shoulder Score /1 –Patient Survey)

Pain:

Pain is allotted 15 points;
"The assessment is made on the most severe pain experienced during all ordinary activities of daily living, such as work, recreation, rest and pain affecting sleep.
Pain is graded as none, mild, moderate or severe. Severe pain is allotted 0 Points, Moderate pain 5 points, mild pain 10 points and 15 points is allotted for none or no pain. See Table 2" (Constant C.R.)

Table 2: Scoring for Pain

None	15
Mild	10
Moderate	5
Severe	0
Total	

Activities of daily living:

"The subjective ability to perform all activities of the patient's wishes scores 20 points. This includes 10 points for full work and recreational activities and unaffected sleep and a further ten points for positioning of the hands tasks from below the waist to above the head levels, with proportional lower scores for less ability. See Table 3"

Table 3: Scoring for Activities of Daily Living

Activity level	
Full work	4
Full recreation/sport	4
Unaffected Sleep	2
Positioning	
Up to waist	2
Up to xiphoid	4
Up to neck	6
Up to top of head	8
Above head	10
Total for activities of daily living:	20*

"During positioning, only one of the five positions is found in each patient. The maximal points attainable by a normal individual in the section of the assessment can be only 20 points. This is a subjective assessment, especially with regards to the first ten points. The ten points for positioning are separate from the assessment of active range.

Range of Motion:

Constant Shoulder Score /2-Physcian-Investigator Examiner Section (Appendix 2-10)

"The total points allocated for full normal active ranges of movement to be assessed are 40. This consists of a maximum of ten points for each of forward flexion and lateral elevation and each of functional composite external and internal rotation. For forward and lateral elevation, a goniometer is used to measure the angle of active motion in these planes". (Constant C.R.)

A goniometer is placed between the arm and upper part of the thorax. Table 4 Shows the allocation of ten points for varying degrees of forward and lateral elevation achieved.

Table 4: Points for Forward Flexion and Lateral Elevation

Flexion /Elevation (▫)	*Points*
0-30	0
31-60	2
61-90	4
91-120	6
121-150	8
151-180	10

"Allocation of points to external and internal rotation (Table 5 and 6) is based on allocation of points for composite rotational maneuvers that place the hand into certain positions relative to the head, neck, and trunk. The main elements of the composite motion are external rotation combined with extension. There is some degree of overlap in the assessment of the various active motions with the subjective positioning earlier in the evaluation. This has the effect of a more sensitive overall indication of function" (Constant C.R.)

Table 5: External Rotation Scoring

Position	*Points*
Hand behind head with elbow held forward	2
Hand behind head elbow held back	2
Hand on top of head with elbow held forward	2
Hand on top of head with elbow held back	2
Full elevation from top of head	2
Total	10

Table 6: Internal Rotation Scoring

Position	*Points*
Dorsum of hand to lateral thigh	0
Dorsum of hand to buttock	2
Dorsum of hand to lumbosacral junction	4
Dorsum of hand to waist 93rd lumbar vertebra)	6
Dorsum of hand to 12th dorsal vertebra	8
Dorsum of hand to interscapular region (DV 7)	10

The Constant Strength/Power; "Strength of Abduction" is tested using the method described by Moseley with scoring based on the number of pounds pull the patient can resist in abduction, up to a maximum of 90▫. A normal shoulder in a 25-year old man resists 25 pounds without difficulty. (Constant C.R.)

A hand held dynamometer/manual muscle test system (MMT) is small and light enough for measuring the power of the shoulder, especially for diseased shoulder's and will not cause modification of the technique or positioning.

For setup of the MMT see Appendix 2.11-"Summary of the MMT Functions needed for the Constant Score Test for Strength of Abduction and Preparing the MMT System for Shoulder Test"

The examiner should stand with one foot placed in the smaller looped end of adjustable pull strap, with the curved padded attachment facing toward
the floor. The examiner should adjust the strap so that the bottom of the curved padded attachment is level with the subject's AC joint. The subject is to place the hand through the loop so that the back of the wrist is against the curve padded attachment (palm facing down). The MMT unit is placed between the examiner's hand and the limb being assessed. The hand is placed under the strap and around the body of the MMT.
The examiner will not apply pressure to the MMT and will release his or her hand when the subject starts the test. This allows the examiner easy access to the TOP buttons with the thumb. Buttons should be pressed accordingly using the examiners opposite hand. The MMT is activated by pressing the Menu/Select button (1).

The subject's arm is positioned to 90 degree abduction to the body and slightly in front of the body. The examiner adjusts foot position to align the strap perpendicular (plumb) with respect to the floor. If patient cannot achieve the test position, a force measurement of "0" should be recorded.

The MMT is activated by pressing the Menu/Select button (1).
The first trial should be for practice at 50% of maximum safe effort. Subject should rest for at least 30 seconds, and then conduct the assessment. The subject exert the maximum for "5" seconds. The MMT will beep when the "5" seconds are completed.

"The strength of the normal shoulder may differ and deteriorate with age; the constant score will also decrease, although the score may be normal for the patient's age and gender." (Katolik LI 2005)

The Adjusted Constant Score utilized in this study was presented by Katolik in 2005. Table '7 "below shows normal Constant score based on age and sex. (Katolik LI 2005)

To calculate a normalized or adjusted score: The Normalized or Adjusted Score =The raw Constant Score is divided by the normal score as provided in Table 7 (Katolik 2005) then multiplied by 100. For example if a 52 year old female had a raw Constant score of 50, her Adjusted Constant Score would be 68.5 (i.e., 50/84 100= 59.5).

Table 7: Normal Constant Score		
Age (y)	**Gender Adjustment**	
	Male	**Female**
18-29	95	88
30-39	95	87
40-49	96	86
50-59	94	84
60-69	92	83
≥ 70	88	81

This algorithm will be employed during the collection of the pre-operative raw Constant Score so that an Adjusted Constant Score can be calculated and documented on source document similar to Table 7 for the purpose of determining a subject's eligibility with respect to the study's inclusion/exclusion.

6.7.3 SF-36

The SF-36 is a multi-purpose, short-form health survey with only 36 questions. It yields an 8-scale profile of functional health and well-being scores as well as psychometrically-based physical and mental health summary measures and a preference-based health utility index. It is a generic measure, as opposed to one that targets a specific age, disease, or treatment group. Accordingly, the SF-36 has proven useful in surveys of general and specific populations, comparing the relative burden of diseases, and in differentiating the health benefits produced by a wide range of different treatments.

6.7.4 VAS

Shoulder and arm pain will be measured via a 100mm (0-100) Visual Analog Scale (VAS). The Visual Analog Scale will be used to rate the subject's pain. The subjects will be asked to rate average shoulder and arm pain they have

experienced over the past week, based on the questions asked. They will be asked to respond to the worksheet. The VAS scale is a 100 mm horizontal line, where the far left side of the scale equals no pain and the far side of the scale equals the worst possible pain.

6.7.5 Radiograph

All post-operative radiographs will be obtained and forwarded to the study core radiologist. Upon receipt of the radiographs, a qualified technologist will review the image data for adequacy issues and if appropriate notify Arthrex and site to resolve issue, and repeat images within the protocol specific time-point windows. In the event that a patient requires additional x-rays related to an adverse device effect, the X-rays will also be forward to the Core Radiologist. Each site will be provided image data transmittal forms, imaging guidelines, site procedures for handling data and instructions data transfer.

6.7.6 Physical Exam

A physical examination will be conducted and an assessment of the shoulder including circulation, motor and sensory outcomes, deformity and wound healing. The motor function evaluation includes an assessment of the strength of the operated and contralateral shoulder with scores ranging from 0 for "No contraction" to 5+ for "Normal or active movement, against full resistance." The sensation evaluation includes an assessment of C5 to T1 with grades of "Absent," "Impaired," or "Normal."

7 Device Description

7.1 Device Materials

Humeral Head: Cobalt-chrome molybdenum alloy, ISO 5832-12

Trunion: Titanium alloy (Ti 6Al 4V alloy), ISO 5832-3, with titanium plasma (TPS) / calcium phosphate (CaP) coating

Hollow Screw: Titanium alloy (Ti 6Al 4V alloy), ISO 5832-3

7.2 Device Description

The ***Arthrex Eclipse™ Shoulder Prosthesis*** is designed to be used as a Total Shoulder Replacement device. Its unique design allows for use in those instances where a traditional stemmed device is not required, or where a "Cap-type", or resurfacing device is not indicated. It also allows for much easier placement of a glenoid during the primary surgery, or in the case of a revision surgery caused by progression of the disease in the glenoid region. The device allows easier access to the glenoid as compared to a "resurfacing" device, as the humeral head is removed, as it is with a stemmed device, creating greater access to the glenoid. The Eclipse device is a bone-sparing device, and is easily converted to a stemmed device if required due to disease progression.

The Arthrex Eclipse™ Shoulder Prosthesis is a shaft-free humeral joint prosthesis that is designed as a humeral head replacement device. The shaft-free humeral joint implant has three design elements 1) a cobalt chrome humeral head; 2) a titanium plasma spray (TPS) and Calcium (CaP) coated titanium trunion; and 3) a titanium hollow screw.

The Arthrex Eclipse™ Shoulder Prosthesis is to be mated with an Arthrex Univers ™ II Shoulder Prosthesis, glenoid device, FDA cleared in 510(k) K010124, K083435 and K120044.

The part numbers and general descriptions of the Arthrex Eclipse ™ Shoulder Prosthesis are listed in the Surgical Technique.

7.3 Principle of Device Operation

The Arthrex Eclipse™ Shoulder Prosthesis is anatomically designed to have a contoured articulating surface that simulates the normal humeral head articulation of the proximal humerus in the shoulder. The operation of the device is accomplished by the articulation of the Arthrex Eclipse ™ Shoulder Prosthesis (on the humeral side) with a glenoid device as in a total shoulder arthroplasty.

The patient's humeral head is resected along the anatomical neck of the humerus. The Eclipse humeral head is placed on the trunion, which is supported

on the cortical margin of the humeral head. The trunion itself is fixed to the proximal humerus by the hollow screw. The forces are applied uniformly to the cortical shaft bone of the proximal humerus via the trunion. The pressure on the resected surface of the humeral head in the anatomical neck is transferred uniformly to the cancellous bone. The pressure and shear forces applied to the humeral head are thus transferred both cortically and over the cancellous bone via the pressure disc.

The shaft-free humeral head prosthesis allows implantation without having to take the geometry of the humeral shaft into account. In the case of older humeral head fractures, the broken head cap is often displaced in relation to the humeral shaft. In such instances, the humeral shaft is often displaced forwards and medially and the head segment is offset upwards and backwards. "Conventional" shaft prosthesis is frequently not level with the cap. This renders implantation of the classic stem prosthesis considerably more difficult. It is sufficient with the Eclipse shaft-free humeral head prosthesis to resect the necrotic or arthritic head cap and to fix the trunion with the hollow screw, with the prosthetic humeral head placed over it. The Eclipse shaft-free humeral head prosthesis enables positioning of the humeral head (cap) independently of the humeral shaft.

The Eclipse™ Shoulder Prosthesis is distributed with the Univers glenoid device (K010124, K083435, K120044) as the articulating partner. This device has a major advantage compared to conventional resurfacing cup prostheses. The Eclipse shaft-free humeral head prosthesis requires the entire humeral head to be resected, thus providing access to the glenoid, as in arthroplasty performed with shaft prostheses.

Another advantage of the Eclipse device compared to conventional resurfacing cup prostheses it is relatively easy handling, safe and mechanically proven cement less anchoring with the hollow screw.

The minimal bone loss during implantation of the Eclipse shaft-free humeral head prosthesis enables, insofar as the anatomical conditions allow a shaft prosthesis to be subsequently implanted should revision surgery be necessary.

7.4 Accessory Device Information

The Arthrex Eclipse Instrument set consists of all the instruments used for placement and removal of implants and manipulation of components, as well as cutting, drilling and reaming instruments for preparing the implant site. The instruments are manufactured of stainless steel and plastics that have acquitted themselves well in this type of use. The use of such instruments is the state of the art for placement of endoprostheses.

The part number for the Arthrex Eclipse Instrumentation Set is IDE-RAR-9400S. The instruments included in this set are listed in The Surgical Technique.

8 Study Administration

8.1 Role of the Study Sponsor

As the study sponsor of this clinical study, Arthrex, Inc., has the overall responsibility for the conduct of the study, including assurance that the study meets and is conducted within the regulatory requirements specified by each reviewing regulatory authority. In this study, Arthrex Inc. will have certain direct responsibilities and may delegate other responsibilities to other designees.

8.2 General Duties

Arthrex Inc. will be responsible for submitting the IDE application to FDA and ensuring IRB approval prior to shipping study product to sites. Additionally, Arthrex Inc. is responsible for ensuring investigators are properly trained on the study product, conducting and ensuring proper clinical site monitoring and subject informed consent is obtained. Arthrex Inc. will also supply qualified clinical sites with study devices that obtain IRB approval for this study.

As the study sponsor of this clinical study, Arthrex Inc. will be responsible to monitor it for safety. In the circumstance where unanticipated adverse device event or serious adverse events occur due to a procedure, Arthrex, Inc. will convene a review committee which will determine any unreasonable risk to subject or if the study should be reviewed for modification or early termination.

Arthrex or designee is responsible for providing quality data that satisfies regulations and informing the study investigators of unanticipated adverse device events and deviations from the protocol as appropriate.

Arthrex will promptly notify Investigators if the Eclipse Shoulder Prosthesis receives 510 (k) clearance and to cease enrollment and terminate the study.

Arthrex Inc. or designee will ensure all investigational devices are returned to the sponsor upon completion of enrollment or if study is terminated prematurely. Arthrex Inc. or designee will prepare written reports and a final report

8.3 Subject Confidentiality

During the investigation, confidentiality shall be observed by all parties involved. All data shall be secured against unauthorized access. Subject confidentiality will be maintained throughout the clinical study in a way that assures that data can always be tracked back to the source data. For this purpose, a unique subject identification number and will be used that allows identification of all data reported for each subject. Subject names should be maintained separately from case report forms whenever possible.

Data relating to the study might be made available to third parties (for example in case of an audit performed by regulatory authorities) provided the data are treated as confidential and that the subject's privacy is guaranteed.

8.4 Selection of Investigators

Arthrex, Inc. will select qualified investigators, ship investigational product only to participating investigators who have documented IRB approval of the protocol, obtain signed study agreements, and provide the investigators with the information necessary to conduct the study.

In the selection of study investigators, the Sponsor requires each investigator to have adequate experience with the investigational product, and to demonstrate a commitment to subject safety and consistency through adherence to study protocols. The Sponsor will closely monitor compliance with the protocol throughout the study.

8.5 Supplemental Applications

As appropriate, Arthrex, Inc. will submit changes in the Investigational Plan to the appropriate regulatory authorities and investigators to obtain IRB re-approval.

8.6 Submitting Reports

Arthrex Inc. will submit all applicable reports required by the FDA. This includes serious unanticipated adverse device effects, withdrawal of IRB or regulatory approval, current investigators list, annual progress reports, recall information, and final reports.

Investigative site personnel will notify Arthrex within 24 hours of any unanticipated serious adverse device effects or death; and within 5 days for any withdrawal of IRB approval. Arthrex will submit annual progress reports and a final report to FDA.

8.7 Maintaining Records

Arthrex, Inc., and/or its designees will maintain copies of correspondence, data, shipment of devices, adverse device effects, and other records related to the clinical trial. Arthrex Inc. and/or its designees will maintain records related to the signed Investigator Agreements.

Investigational site will maintain records related to the clinical trial for a period no less than 2 years following the date a marketing application is approved for the device for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified. The

investigational site shall notify Arthrex, Inc. before disposing of the clinical trial records.

8.8 Institutional Review Board (IRB) Approval

The protocol, Informed Consent Form and Authorization for the Use and Disclosure of Health Information (HIPAA) (US sites), or country specific requirement) must be reviewed and approved by the respective IRB and Arthrex Clinical Research before subject enrollment. Changes to the protocol must be approved in writing by Arthrex Clinical Research and the IRB (as applicable) before the change is implemented.

Prior to subject enrollment, a signed copy of the IRB approval letter addressed to the investigator must be submitted to the Arthrex Clinical Research, certifying trial approval. Investigators are responsible for submitting and obtaining initial approval and continuing approval from the IRB and forwarding copies of the approval letters to Arthrex Clinical Research. The original letters are to be kept in the investigational center's Regulatory Binder designated for this study.

The investigator will notify the Arthrex Clinical Research within five (5) working days of withdrawal of IRB approval.

The investigator will promptly provide written notification to the reviewing IRB if the study is terminated prematurely.

8.9 Investigator Agreement and Financial Disclosure

The Principal investigator at each site will sign the Investigator's Agreement before beginning the study, as required by Federal Regulations. The principal investigator agrees to be responsible for conducting the investigational study in accordance with the signed agreement, the investigational protocol, and applicable FDA regulations.

In accordance with Federal Regulations, all Investigators will be required to sign a Financial Disclosure form, which certifies the Investigator's and his/her immediate family's financial interest in Arthrex Inc. and study outcomes. Investigators must inform Arthrex Clinical Research of any changes to the information within the financial disclosure throughout the course of the study and for a period of one year after the device is approved by the FDA or the study is terminated, whichever is later.

8.10 Study Monitors

Monitors for this study must be qualified by education, experience, and training to serve in the role of a Study Monitor. The qualifications of monitors will be on file at Arthrex Clinical Research. Study Monitors will follow Arthrex Clinical

Research standard operating procedures and the written Monitoring Plan for this study. All monitors (Arthrex Clinical Research or contracted) will have training on the monitoring plan, monitoring plan amendments, associated documents (Arthrex Quality documents , documents reference in monitoring plan , Clinical Investigational plan)

Arthrex Clinical Research or designee monitoring activities objective is to prevent or mitigate issues with study conduct, data collection/reporting and subject safety.

Arthrex Clinical Research monitor will review critical data remotely via the EDC and/or data reports routinely. Critical data includes:

- protocol eligibility including medical history, physical and enrollment.
- safety assessments / Adverse Events/device effects
- investigational product accountability
- study endpoints
- concomitant medications
- deviations

Arthrex Clinical Research team will review site trial file in eTMF (e.g. VEEVA) ongoing basis. Sites will be required to upload all regulatory site files in the Arthrex Clinical Research team will review/quality checks on all uploaded site completeness, accuracy and version control. The eTMF will contain the following documents:

- Clinical trial agreement (executed initially and all amendments)
- Curriculum vitae for each research team member on delegation log will be signed and updated every 2 years.
- Delegation of authority log-for each member of the research team performing study related activities.
- Financial disclosure statement
- Investigation product accountability logs, labels, DFUs and packing slips
- Good Clinical Practice Certificate/CITI (e.g. initial and updates) for all members of research team.
- IRB Documentation (initial approvals, continuing reviews, change in research, ICF , advertisement and reporting requirements)
- Medical license (investigators, nurses, PA current with all renewals)
- Enrollment logs, Protocol signature page
- Research team training documents (investigator meeting, procedure training, Veeva, EDC Certificate, protocol updates)

Arthrex Clinical Research monitors or designees will visit each clinical site routinely (after the 1st subject is enrolled and every12-16 weeks) to perform on site monitoring. The monitors will be reviewing 100% of the critical data in the EDC database and verifying with source documents (i.e. the electronic medical record, professional notes, laboratory reports, study-specific worksheets, etc.).
In the event that information in the EDC database does not match the corresponding information on the source document, the study monitor will generate an electronic data query for site resolution. The study monitor may request further documentation, such as clinic notes or lab reports, when adverse events or complications are identified and reported.

Critical data includes:

- Informed consent process
- Protocol eligibility including medical history, physical and enrollment-see section
- Randomization process
- Safety assessments / Adverse Events/device effects
- Investigational product accountability
- study endpoints
- deviations

Additionally, the study site will be evaluated for study conduct, timeliness of data form completion and data accuracy.

Arthrex Clinical Research monitors or designees review findings with Investigator, /research team during site visits. These findings will include study updates, training as needed, action items and at a minimum if present., "identified non-compliance" (e.g., ICF process issues, protocol eligibility issues, AE reporting issues, data collection of critical endpoint issue and deviations).
Repeated site non-compliance will be documented and subject to a corrective action plan. If a corrective action plan is not followed, the clinical site may be withdrawn from the study by the sponsor.

Arthrex's site monitor will forward a follow up letter with findings to site's investigator and research team from monitoring visit, open action items and pending issues that should be addressed before the next monitoring visit when possible.

The Monitoring Plan will specify the relative frequency, scope, and general conduct of monitoring visits as well as identify any relevant study-specific Study Monitor responsibilities.

8.11 Investigational Site Qualification

Investigational sites will be qualified and selected by Arthrex's Clinical Affairs, Manager based on investigator qualification, research staff expertise and availability, subject availability and overall site reputation. The site qualification will be scheduled to include time with the Investigator, study coordinator and other study personnel. Areas of discussion include review of personnel training, investigator qualifications, adequacy of potential subject pool, FDA-regulated study experience, and this study's specific requirements for procedures and equipment, and a review of staffing and equipment, availability and appropriateness. A written follow up letter will be submitted to the Investigator documenting any concerns and/or completion of study activities during the pre-study visit.

8.12 Investigational Site Training

Study conduct-specific training of clinical trial personnel is the responsibility of Arthrex's CRA, the study monitor and the Investigator. Study training will occur before the first device use. The investigator is responsible for ensuring that his/her staff conducts the study according to protocol. To ensure compliance with the Investigational Plan and regulatory requirements as well as accurate data collection, site training will include a detailed review of this Investigational Plan, Electronic Data Collection (EDC), adverse event reporting, device handling and inventory, monitoring logistics, and regulatory requirements.

Arthrex's CRA or the study monitor will ensure that study personnel:

- Submit this Investigational Plan to their IRB for appropriate review and obtain written approval for the conduct of the study prior to consenting any subject for this study;
- Maintain all study correspondence, this Investigational Plan, and all related and required records on file at their facility, and
- Confirm the investigator understands his/her full responsibility for the study investigation at their individual medical practices, clinics, or medical facilities.

Procedure and Training

All Investigators and site personnel participating in the study will receive device-specific detailed training from Arthrex personnel.

Physician Hands-on Training

All Investigators will have experience with arthroplasty surgery, in addition to being instructed on the specifics of the Eclipse™ and the Univers™ II Shoulder Prosthesis. After instruction from a qualified Arthrex trainer, the physician will demonstrate successful application of the study device either in Sawbones or

cadaver specimen. In addition, an Arthrex "corporate team member" or designee will be present for the each Investigator's first surgical case.

All training will be documented prior to first use of the study device.

8.13 Investigator Responsibility for Study Conduct

Study investigators will ensure that all work and services they provide will be conducted in compliance with the signed agreement, the investigational plan and applicable federal regulations for investigational device exemption studies and HIPAA (US sites), for protecting the rights, safety, and welfare of subjects under the investigator's care and for control of investigational devices/product. It is the responsibility of each site principal investigator to provide the current study protocol to all sub-investigators and other staff responsible for study conduct, as well as provide for the training of all sub-investigators or other staff involved in the conduct of this research. Specific responsibilities are listed in the Investigator Agreement and include:

- That informed consent is obtained in accordance with 21CRF Part 50.
- That there is Institutional Review Board (IRB) approval prior to commencement of study activities at the site.
- That investigational device/product is only to be used with subjects under the investigator's supervision.
- That they disclose to sponsor sufficient accurate financial information to allow applicant to submit accurate disclosure statement under 21 CFR Part 54.
- To prepare and submit to Arthrex Clinical Research and IRB complete, accurate and timely reports on this investigation when necessary, according to 21 CFR 812.50. Types of reports to be submitted include reports pertaining to unanticipated adverse device effects, withdrawal of IRB approval and deviations from the investigational plan. The investigator is required to submit an annual report to his/her IRB with a copy to Arthrex Clinical Research.
- That upon completion or termination of the clinical investigation at sponsor's request, investigator shall return remaining supply of investigational product/device or otherwise dispose of the device as the sponsor directs.
- That upon completion of the trial, a final written report to the reviewing IRB, within three (3) months of completion or termination of the study. The final report must include;
    - Device name
    - Number of subjects screened, enrolled, withdrawn and completed
    - Number of devices received, used and returned
    - Summary of all adverse effects (anticipated and unanticipated)
    - Summary of serious adverse events

- Summary of all protocol deviations
- Brief statement of results, outcomes and conclusions.

- Maintain records and reports (see Records below) on file at the investigational site for a minimum of two years after the later of either the completion/termination of the investigational study or the date the Eclipse ™ Shoulder Prosthesis receives market approval for the indication being studied. They may be discarded only upon approval from Arthrex. The Principal Investigator must contact Arthrex's CRA before destroying any records and reports pertaining to the study to ensure that they no longer need to be retained. In addition, Arthrex must be contacted if the investigator plans to leave the investigational site to ensure that arrangements for a new investigator or records transfer are made prior to investigator departure.

- Records

Records are to be maintained by the Investigator in the designated Investigational center's Regulatory Binder include:

- Investigational plan and all amendments
- Signed Investigator Agreement
- Signed Financial Disclosure
- IRB approval letter including all versions of the consent and HIPAA authorization form(s)
- IRB Membership list or Letter of Assurance
- All correspondence relating to the study between the site and Arthrex.
- CVs and professional licenses for all investigators
- Site personnel signature and responsibility list
- Clinical monitor sign-in log
- Subject Screening/Enrollment log
- Investigational device inventory log including: date, quantity, and lot numbers of all devices, identification of all persons the device was used on and final disposition.

The following records must be maintained for each subject enrolled in the study:

- Signed Consent Form and Authorization for the Use and Disclosure of Health Information
- Compete, accurate and current data collection forms
- Adverse effect reports and any supporting documentation

- Protocol deviations
- Complete medical records, including procedure reports, lab reports, professional notes, etc.
- Records pertain to subject death during the investigation (including death records, death certificate, and autopsy report if performed).

Arthrex reserves the right to secure data clarification and additional medical documentation on subjects enrolled in this study at any time.

8.14 Investigational Site Termination

Arthrex reserves the right to terminate an investigational site for any of the following reasons:

- Failure to secure subject informed consent or Authorization for the Use and Disclosure of Health Information prior to study enrollment
- Failure to report unanticipated adverse device effects within 24 hours of discovery to sponsor or monitor and ten days (to the IRB) of learning of the effect
- Failure to report serious adverse device effects within 24 hours of discovery to Arthrex.
- Repeated investigational plan violations
- Repeated failure to appropriately complete case report forms
- Failure to enroll an adequate number of subjects
- Loss of or unaccounted for investigational product inventory
- Administrative decision by the company

8.15 Final Monitoring Visit

Upon completion of the clinical study (when all subjects enrolled have completed the follow-up visits, the data collection and queries have been completed, and no additional information is required of the site for data management / statistical review), a final study close-out visit will be conducted by the Study Monitor. The study monitor will verify disposition of investigational devices and review regulatory documents to confirm that the investigator's regulatory files are current and complete, and that any outstanding issues from previous visits have been resolved. Other issues that will be reviewed at this visit include, but are not limited to: long-term retention of study files, possibility of site audits, publication policy, and verification that the investigator will notify the IRB regarding study closure. A final follow-up letter will be drafted and submitted to the Investigator to document that all investigational plan-related activities have been completed and that the clinical study is completed and may be closed at the site.

The monitor may conduct close out activities remotely if the Eclipse Shoulder Prosthesis receive 510 (k) clearance and this study is terminated prematurely.

8.16 Protocol Amendments

All protocol amendments must be approved by Arthrex Inc. All amendments must have FDA approval in addition to IRB approval.

8.17 Protocol Deviations and Violations

Protocol deviations are defined as any event where the clinical investigator or site personnel did not conduct the study according to the protocol.

Any protocol deviations undertaken to protect the life or physical well-being of a subject in an emergency situation must be reported to the

Arthrex Clinical Research within 48 hours of occurrence and the respective IRB as soon as possible, but in no event later than five calendar days after the emergency occurs.

Departures to protocol are often situations where unforeseen circumstances are beyond the investigator's control (e.g., subject did not attend scheduled follow-up visit, blood sample lost by laboratory, etc.); however, the event is still considered a protocol deviation and requires documentation as such.

Subject-specific deviations will be reported in the EDC.

Study deviations are classified as follows:

- Informed Consent Form (ICF)
  - Wrong ICF version signed
  - Other deviation related to informed consent version.
- Protocol
  - Study procedure not done per protocol
  - Study procedure or visit not done
  - Study procedure or visit Out of study window
  - Other procedure not done per protocol
- Eligibility
  - Subject did not meet eligibility criteria
  - Other deviation related to eligibility criteria
- Source Document
  - Missing or incomplete source document
  - Other deviation related to source document
- Regulatory
  - Subject enrolled without IRB approval

- Other deviations related to Regulatory

Non-subject specific deviations or violations, (e.g. unauthorized use of an investigational device outside the study, unauthorized use of an investigational device by a physician who has not signed an investigator agreement, etc.), will also need to be reported to Arthrex Clinical Research via EDC. Investigators will also adhere to procedures for reporting study deviations and violations to their IRB in accordance with their specific IRB reporting policies and procedures.

Regulations require that investigators maintain accurate, complete and current records, including documents showing the dates of and reasons for each deviation from the protocol.

8.18 Publication

The publication of the principal results from any single center experience within the trial is not permitted, and any exceptions to this rule require the prior approval from Arthrex, Inc.

8.19 Audits / Inspections

In the event that audits are initiated by the sponsor, its designee, or FDA, the investigator will allow access to the original medical records and provide all requested information.

9 Adverse Events Definitions

9.1 Definitions

9.1.1 Adverse Events

An adverse event (AE) is any undesirable experience (e.g., sign, symptom, illness, clinically significant abnormal laboratory value, or other medical event) occurring in a subject during the course of the study, whether or not it is related to the investigational device or procedure.

An AE does include a/an:

- Exacerbation of a pre-existing illness
- Increase in frequency or intensity of a pre-existing episodic event or condition
- Condition detected or diagnosed after study device use even though it may have been present prior to the start of the study
- Continuous persistent disease or symptoms present at baseline that worsen following the start of the study

An AE does not include a/an:

- Medical or surgical procedure (e.g., surgery, endoscopy, transfusion); the condition that leads to the procedure is considered an AE
- Pre-existing diseases or conditions present or detected at the start of the study that do not worsen
- Situations where an untoward medical occurrence has not occurred (e.g., hospitalizations for cosmetic elective surgery, social and/or convenience admissions)
- The disease or disorder being studied, or sign or symptom associated with the disease or disorder, unless the disease, sign or symptom is more severe than expected based on the subject's condition and/or requires intervention.

9.1.2 Serious Adverse Events

A Serious adverse event is an adverse event that:

- led to death,
- led to serious deterioration in the health of a subject that
  - resulted in a life-threatening illness or injury,
  - resulted in permanent impairment of a body structure or body function,

- required inpatient hospitalization or prolongation of existing hospitalization,
- resulted in medical or surgical intervention to prevent permanent impairment to a body structure or a body function.

- led to fetal distress, fetal death or a congenital anomaly or birth defect.
- The following clarifications are provided for the serious adverse events:
  - Life-threatening means that the subject was, in the view of the investigator, at immediate risk of death from the event as it occurred. The definition does not include an event that, had it occurred in a more severe form, might have caused death.
  - Hospitalization for elective treatment of a pre-existing condition that did not worsen during the study is not considered a serious adverse event.
  - "Inpatient" hospitalization means the subject has been formally admitted to a hospital for medical reasons. This may or may not be overnight. It does not include presentation at a causality or emergency room.
  - Important medical events that may not result in death, or be life-threatening, however based upon appropriate medical judgment, may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed in this definition.
  - Is significant for any other reason.

9.1.3 Anticipated Adverse Events:

Anticipated adverse events are those events that are reasonably expected to occur as a result of the subject's disease state or treatment. For this study, anticipated adverse events associated with the procedure or post-procedure include, but are not limited to, the following;

- Infections, both deep and superficial
- Allergies or other reaction to device materials
- Temporary or permanent nerve damage as a result of surgery, pressure or hematoma.
- Bruising (hematoma)
- Cardiovascular complications including venous thrombosis, pulmonary embolism, and cardiac arrest.
- Delayed wound healing.

Device-related adverse events are those events that can be directly attributed to the study device and are adjudicated as such by the investigator. These events may include, but are not limited to:

- Infections, both deep and superficial
- Allergies or other reaction to device materials
- Loosening of the implant as a result of changed condition in load transfer, respectively fatigue wear or tissue reaction to implant or as result of inadequate anchoring technique.
- Dislocation, subluxation or inadequate scope of movement as a result of failure to achieve optimum positioning of the implant.
- Joint stiffness, pain, and swelling
- Bone fractures as a result of one-sided overload or weakened bone structure.
- Temporary or permanent nerve damage as a result of pressure or hematoma.
- Bruising (hematoma) and delayed wound healing.

9.1.4 Unanticipated Serious Adverse Device Effects

An Unexpected Serious Adverse Device Effect (USADE) is defined as any serious adverse effect on the study subject's health or safety, or any life-threatening problem or death caused by or associated with the device. Also, the effect must not have been previously identified in this Investigational Plan or Instructions for Use in its nature, frequency or severity. UADEs may also include other serious problems associated with the device that affect the rights or welfare of study subjects.

9.2 Adverse Event Documentation

Adverse event information will be collected on all subjects. All adverse events must be reported in the source documents and in the EDC. Adverse events will be evaluated by the investigator and differentiated by:

- Seriousness, as defined in Section 9.1.2
- Severity of the event, defined below.
    - **Mild:** Awareness of signs and symptoms, but easily tolerated; are of minor irritant type, causing no loss of time from normal activities; symptoms would not require medication or a medical evaluation; signs and symptoms are transient.

- **Moderate:** Discomfort severe enough to cause interference with usual activities; requiring treatment, but not extended hospitalization or intensive care for the subject.
- **Severe:** Incapacitating with inability to do work or usual activities; signs and symptoms may be systemic in nature or require medical evaluation and/or treatment; requiring additional hospitalization or intensive care (prolonged hospitalization).

- Relatedness to the device or procedure, defined as:
  - **Unrelated:** AE is due to the underlying disease state or concomitant medication or therapy not related to the study-specific devices or procedures.
  - **Probably not Related:** AE had minimum or no temporal relationship to the study-specific devices or procedures and/or more likely alternative etiology exists.
  - **Possibly Related:** AE had a strong temporal relationship to the study-specific devices or procedures and alternative etiology is equally or less likely compared to the potential relationship to the study-specific devices or procedures.
  - **Probably Related:** AE had a strong temporal relationship to the study-specific devices or procedures and another etiology is unlikely.
  - **Unknown:** Relationship of the AE to the study-specific devices or procedures and alternative etiology is unknown.

9.3 Adverse Event and Unanticipated Adverse Device Effect Reporting

At every subject encounter, the investigator will determine if there has been an adverse event since the last encounter.

For this study, serious adverse events must be reported immediately (within 24 hours) directly to Arthrex, Inc. by completing the Adverse Event form and entering it into EDC. At the time of the initial report, the outcome (resolution status) may not be known. Updated information must be entered into EDC until final resolution of the event.

Unanticipated Serious Adverse Device Effects must also be reported by the investigator to the approving IRB as soon as possible, but not later than 10 working days after the investigator first learns of the effect. The sponsor must report to the FDA, all reviewing IRBs and participating investigators within 10 working days of notification from the investigator of a USADE.

The medical monitor will provide medical surveillance on adverse events and will evaluate all Serious Adverse Events (SAEs).

9.4 Device Complications

For this study all device complication including; damaged parts, cracked parts, packaging –device component missing, packaging-broken in package, piece broke from device, frozen or other will be collected and reported in EDC.

9.5 Safety Monitoring

As the study sponsor of this clinical study, Arthrex Inc. will be responsible to monitor it for safety. In the circumstance where unanticipated adverse device event or serious adverse events occur due to a procedure, Arthrex, Inc., will convene a review committee which will determine any unreasonable risk to subjects, or if the study should be reviewed for modification or early termination.

10 Statistical Method and Sample Size Calculation

10.1 Definition of Month 24 Composite Clinical Success (CCS)

A literature search was conducted to estimate expected post-operative Constant scores and subjective success rate of TSA procedures. Fifteen (15) articles were found [1-15]. Four (4) articles were excluded due to data that appeared to be from the same data base and may contain the same subjects. The 11 included articles contained data on a total of 1095 subjects. All 11 of the articles contained post-operative Constant Scores, and 6 contained standard deviation associated with the post-operative Constant Score. Four (4) of the articles contained age/sex Adjusted Constant Scores and 3 out of those 4 contained standard deviation associated with the age/sex adjusted Constant Score. Four (4) of the 11 articles contained subjective satisfaction scores. The entire compilation can be seen in Appendix 2-12. Weighted averages based on sample size were calculated for Constant Scores, standard deviations, and percent satisfied using the compiled literature. The data is summarized in Table 1.

Table 1: Summarized weighted averages

Constant Score	66.2 ± 16.2
Adjusted Constant Score	87.6 ± 22.8
% Good/Satisfied or Better	93%
# of Subjects	1095

The data suggest that 93% of subjects were satisfied or better with the outcomes of TSA. Any pass/fail criterion for minimum acceptable Constant Score should produce an over-all success rate for non-investigation devices similar to those reported in literature (93%). To estimate the range of Constant Scores that would include 93% of the subjects, an 86% prediction interval was calculated. The results of the prediction interval can be seen in Table 2, and the calculation is illustrated in

Figure 1.

Table 2: Calculated prediction interval

	86% PI	Minimum Score
Constant Score	23.9	42.3
Adjusted Constant Score	33.7	53.9

Based on the literature available, a minimum Adjusted Constant score of 53.9 (or ≥54) should produce a pass rate of approximately 93%.

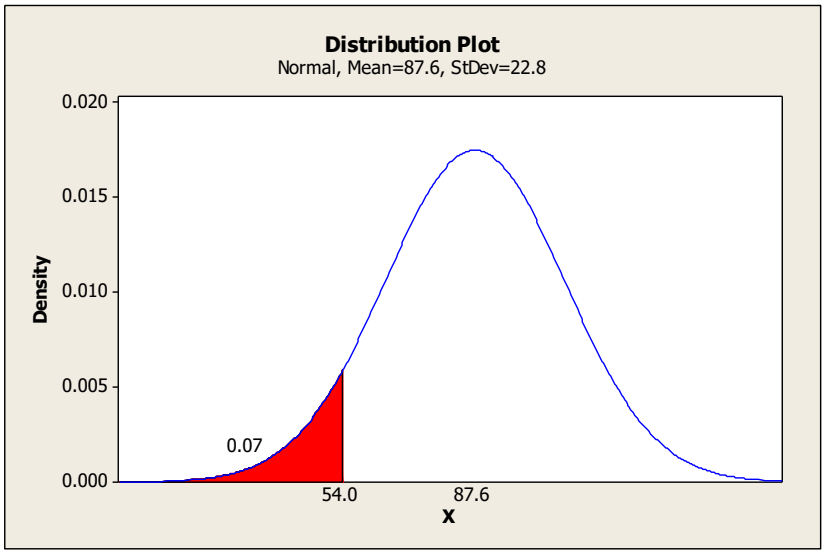


Figure 1: Adjusted constant score distribution plot

10.2 Determining the Adjusted Constant Score for Inclusion Criteria:

A literature search was conducted to estimate the expected Pre-operative Constant scores for Inclusion Criteria. To our knowledge there is no definitive statement regarding the use of pre-operative Constant Score as an inclusion/exclusion criterion; however, the range of expected pre-operative Constant scores can be derived. Fifteen (15) articles were found [1-15]. Of those, 4 were excluded due to data that appeared to be from the same data base and may contain the same subjects [1, 12, 13, and 14]. Ten (10) of the remaining eleven (11) articles contained pre-operative Constant Scores, and of those ten, three (3) reported standard deviation. Four (4) of the articles contained age/sex Adjusted Constant Scores and 3 out of those 4 contained standard deviation associated with the age/sex adjusted Constant Score. The entire compilation can be seen in the Appendix 2-13. Weighted averages based on sample size were calculated for Constant Scores and standard deviations using the compiled literature. The data is summarized in Table 3.

Table 3: Summarized weighted averages

Constant Score	28.2 ± 11.7 (n = 752)
Adjusted Constant Score	37.3 ± 15.6 (n = 619)

A 95% prediction interval suggests 95% of the subjects enrolled had pre-operative Adjusted Constant Scores between 6.6 and 67.9. A conservative Adjusted Constant Score of ≤ 50 for Inclusion Criteria was chosen to eliminate the possibility of biases.

The goal of the study is to determine non-inferiority of the Eclipse ™ Shoulder Prosthesis compared to the Arthrex's Univers ™ II Shoulder Prosthesis. Non-inferiority will be evaluated by the 2 year Composite Clinical Success (CCS) and is based on:

1. Adjusted Constant score change ≥ 10. This is based off the minimum clinically relevant difference (Brorson S, 2009) (Haahr JP, 2005) (Pfahler M, 2006)
2. Adjusted Constant Score ≥54. This is based on ~~the above~~ calculations in Table 2.
3. Radiographic Outcomes Success: Patient meets acceptance criteria for humeral radiolucency, humeral migration/subsidence, glenoid radiolucency, glenoid migration/subsidence device condition, and periprosthetic fracture.

Investigational Group (Eclipse)

Radiolucency will be evaluated in each of nine Zones from the Neutral Rotation AP and Axillary views.

- **Acceptance Criterion:** Radiolucency > 2 mm in ≤ 3 zones (out of 9 zones)
- **Rationale**: The methods used are based off the 3/8 ratio presented by Sperling as a risk for implant loosening. With nine zones for the investigational humeral implant, 3/8 of 9 = 3.375. As such, radiolucency in 3 zones falls below the criterion for radiolucency established by Sperling, and, as such is the acceptable amount of radiolucency for this device (Sperling JW, 2000).

Control Group

Radiolucency will be evaluated in each of the 15 Zones adapted from Sperling et al. for the humeral component of the *control* device from the Neutral Rotation AP and Axillary views (Sperling JW, 2000).

- **Acceptance Criterion:** Radiolucency > 2 mm in ≤ 5 zones (out of 15 zones)
- **Rationale**: The methods used are based off the 3/8 ratio presented by Sperling as a risk for implant loosening. With nine zones for the investigational humeral implant, 3/8 of 15 = 5.625. As such, radiolucency in 5 zones falls below the criterion for radiolucency

established by Sperling, and, as such is the acceptable amount of radiolucency for this device (Sperling JW, 2000).

Humeral Migration/Subsidence

Humeral Migration/Subsidence will be graded as 'Absent' or 'present'

- **Absent:** Humeral component displacement ≤3 mm relative to the baseline time point
- **Present:** Humeral component displacement > 3 mm relative to the baseline time point

Humeral Migration/Subsidence Endpoints will be assessed for change relative to month 3 image.

***Success Criterion for Humeral Migration*:** Absent Humeral Migration/Subsidence

Glenoid Radiolucency

Glenoid Radiolucency (Keeled & Pegged) will be graded as described per the method of Lazarus et al. (2002). As the geometry of the pegged and keeled components is different, Lazarus developed and validated a grading schema that would provide a means to compare the two different designs of glenoid components.

Keeled Glenoid Component

Grade 0: No radiolucency

Grade 1: Radiolucency at superior and/or inferior flange

Grade 2: Incomplete radiolucency at keel

Grade 3: Complete radiolucency (≤2 mm around keel)

Grade 4: Complete radiolucency (>2 mm around keel)

Grade 5: Gross loosening

Pegged Glenoid Component

Grade 0: No radiolucency

Grade 1: Incomplete radiolucency around one or two pegs

Grade 2: Complete radiolucency (≤2 mm wide) around one peg only, with or without incomplete radiolucency around one other peg

Grade 3: Complete radiolucency (≤2 mm wide) around 2 or more pegs

Grade 4: Complete radiolucency (>2 mm wide) around 2 or more pegs

Grade 5: Gross loosening

***Success Criterion for Glenoid Radiolucency*:** Grade ≤ 3 glenoid Radiolucency

- **Rationale:** Previously, researchers have utilized a glenoid lucency of ≥4 (per criteria of Lazarus 2002) to determine those patients "at risk" for device malfunction due to glenoid lucency as 24 Months post-op. Haines et al. (2006) observed, in a prospective clinical trial of shoulder arthroplasties (n=124 shoulders, n=113 patients), 14% of patients at > 24 Months had a glenoid lucency score ≥4 (per criteria of Lazarus 2002). These patients, having what the authors describe as "at risk" implants, demonstrated a 78% survival rate at seven years, but only a 46% survival rate at ten years, compared to a survival rate of 84% at 10 years for the entire patient cohort. (Haines et al. 2006)

Glenoid Migration/Subsidence

Glenoid Migration/Subsidence will be graded as 'Absent' or 'Present'

- **Absent:** Glenoid component displacement ≤3 mm relative to the baseline time point
- **Present:** Glenoid component displacement > 3 mm relative to the baseline time point

Glenoid Migration/Subsidence Endpoints will be assessed for change relative to month 3 image.

***Success Criterion for Glenoid Migration*:** Absent Glenoid Migration/Subsidence

Device Condition

Device Condition will be evaluated to assess the condition and integrity of the device. Device Condition will be graded as 'Intact', 'Disassembly' or 'Fracture' in accordance with the following definitions:

- **Intact:** No evidence of fractured or disassembled hardware. The hardware is intact.
- **Disassembly:** Presence of device component disassembly
- **Fracture:** Presence of fracture or breakage of one or more device components

***Success Criterion for Device Condition*:** Intact device condition

Periprosthetic Fracture

Periprosthetic fracture will be graded as 'Absent', 'Present – Humeral' in accordance with the following definitions:

- **Absent:** No evidence of periprosthetic fracture(s) about the humeral or glenoid components

- **Present – Humeral:** Presence of periprosthetic fracture(s) about the humeral component that is not present on the relative baseline time point

***Success Criterion for Periprosthetic Fracture*:** Absence of device-related Periprosthetic fracture

4. No reoperation, removal, or modification of any study component up to the subject's completion of the study

5. Lack of serious device related complications (defined as a severe device-related adverse event) up to the subject's completion of the study.

Per the World Health Organization Definition of adverse events, a Grade 3 (or severe) adverse event significantly limits the patient's ability to perform routine activities despite symptomatic therapy.

10.2 Primary Efficacy Hypothesis

The primary efficacy hypothesis for this study is formulated in terms of clinical non-inferiority and is consistent with the Blackwelder approach (Blackwelder, 1982). Symbolically, the null and alternative hypotheses may be expressed as follows:

Ho: $\pi_{\text{Eclipse™}} - \pi_{\text{Univers II™}} \leq -\delta$ **(investigational device inferior)**

Ha: $\pi_{\text{Eclipse™}} - \pi_{\text{Univers II™}} > -\delta$ **(investigational device not inferior)**

The π represents the proportion (or probability) of devices expected to achieve Month 24 Composite Clinical Success. Thus, this study is designed to demonstrate that π for investigational device is no more than δ less than π among control devices. For $\delta = 0.10$, these hypotheses may be written as:

Ho: $\pi_{\text{Eclipse™}} - \pi_{\text{Univers II™}} \leq -0.10$

Ha: $\pi_{\text{Eclipse™}} - \pi_{\text{Univers II™}} > -0.10$

10.3 Secondary Outcomes

Descriptive analyses will be performed on the secondary efficacy endpoint. Continuous variables including function scores will be summarized for each device group pre-operatively and at each planned follow-up visit (Post-op, Month 3, Month 6, Month 12, and Month 24) using means, SDs, medians, minimum, and maximum values. Standardized effect sizes (mean difference divided standard deviation of differences) will be computed at each time point for each continuous measure in order to facilitate assessment of group differences across measures as well as time. Pooled t-tests and Wilcoxon rank sum tests will be provided as additional descriptive measures. Categorical secondary efficacy endpoints will be compared between groups

using counts and percentages. Descriptive chi-square tests will be provided for secondary categorical efficacy endpoints. There will be no imputation of missing values for secondary endpoints and no control for type I error in the set of secondary endpoints. Graphical displays of selected endpoints will be provided to provide visual assessments of group differences over time.

10.4 Sample Size Analysis for Primary Non-Inferiority Test

Given the above criteria, the Sponsor expects a success rate of 88% for both the Eclipse and control group.

To determine the required sample size, it was assumed that the above primary hypotheses will be tested using 1-sided α=0.05 at a statistical power of at least 80%. Under these assumptions, nQuery Advisor 7.0 module PTE0U-1 produces the following:

"When the sample sizes in the groups are 98 and 196, a two-group large-sample normal approximation test of proportions with a one-sided 0.05 significance level will have 80% power to reject the null hypothesis that the test and the standard are not equivalent (the difference in proportions, p_T - p_S, is -0.10 or farther from zero in the same direction) in favor of the alternative hypothesis that the proportions in the two groups are equivalent, assuming that the expected difference in proportions is 0.00 and the proportion in the standard group is 0.88.

Therefore, the total number of Per Protocol (Efficacy Evaluable) patients required under these assumptions are N=294. The number of protocol violations of inclusion / exclusion criteria (i.e., randomized in error) is expected to be small. The randomized sample size is adjusted up by 15% to account for both loss-to-follow-up and exclusions due to protocol violation to N=347.

10.5 Analysis of Baseline Differences and Poolability

10.5.1 Description of demographics and baseline characteristics

Demographic and baseline characteristics will be tabulated and compared between the investigational group and control group. Variables to be compared will include baseline shoulder assessment, disease severity, age, gender, limb dominance, primary diagnosis, Body Mass Index (BMI), weight, and height. Descriptive p-values will be determined using Wilcoxon rank sum tests for continuous measures and chi-square or exact tests for categorical variables. However, focus will be on clinical significance of group differences and only secondarily on p-values, since these p-values are not associated with planned comparison. If there are clinically significant group differences for any baseline variable, then multiple logistic regression will be used to assess the impact of controlling for the baseline variable on conclusion. Specifically, the odds ratio for achieving Month 24 CCS

comparing investigational group to control group will be computed with and without including the baseline variable in question. If the odds ratio changes by less than 15%, it will be concluded that the primary results are not confounding by device group imbalance for that variable (Mickey RM, 1989).

10.5.2 Description of site differences at baseline

Demographic data, primary diagnosis, and summary clinical measures will tabulated by investigative site. Interval measures will be compared among sites using analysis of variance (ANOVA) (Scheffe, 1959). Frequency distributions will be compared among sites using chi-square statistics or generalized exact tests (Mehta CR, 1983), as appropriate. For statistical comparisons only, sites contributing less than 10 eligible procedures will be combined.

10.6 Survival Analysis

For each relevant cohort, life-tables will be tabulated indicating the number of device failures and the number of at-risk procedures over time. Since the number of patients at risk (i.e., those being followed) diminishes over time, Peto's method (Peto T, 1977) will be used to determine standard errors for estimates of cumulative survival. Kaplan-Meier survival curves (Kaplan EL, 1958) will be plotted for investigational and control devices on the same graph to facilitate graphical comparisons of survivorship over time. The secondary hypothesis of equal survival distributions between groups will be tested using a log-rank statistic (Mantel N, 1959). Comparisons among sites in device survival will be performed using log-rank statistics (Mantel, 1966) and Cox regression (Cox, 1972). In some analyses, sites contributing fewer than 10 patients will be combined.

10.7 Safety Analysis

All safety endpoints will be summarized separately for investigational and control groups. Similarly, listings with details of the specific complications will be summarized separately as well.

The CCS Component Safety endpoint is any serious, definitely device-related adverse event within 24 Months of surgery. This will be evaluated at the exact two year anniversary (i.e., relative day 730) after the implantation surgery. The safety hypothesis of investigational verses control equality in the likelihood of serious device-related adverse event will be tested using a two-sided Fisher's Exact Test with Type I error rate set to α=0.05.

10.7.1 Adverse events counts over time

The numbers of specific adverse events occurring pre-discharge and for each study interval will summarized separately for each relevant cohort. Counts

of systemic adverse events will be summarized on a per patient basis. All other adverse events will be summarized on a per procedure basis.

10.7.2 Adverse event detail listings

Adverse events listings will be provided for all patients in the ITT cohort and will provide details regarding adverse event type, relation to shoulder procedure, action taken, and clinical outcome. Separate listings will be constructed for adverse events with "definite" relationship to the device, "severe" adverse event, "severe device-related", serious adverse events, and for all adverse events. The listing for all adverse events will be sorted by adverse event type.

Additional listings will be provided that include all adverse events among procedures requiring revision, removal, or replacement and all adverse events among patients who died.

10.8 Treatment of Missing Data

As previously described, patient success will be defined at Month 24 postoperatively on the basis of a Composite Clinical Success (CCS) criterion. If the Month 24 CCS endpoint is missing due to a clinical evaluation (i.e., Constant score or radiographic results) unavailable at the Month 24 interval but available at a later date (i.e., after the end of the Month 24 interval), the later clinical evaluations will be used to impute missing values. The roll-back imputation is typically considered conservative since in most orthopedic study, maximum recovery is achieved earlier than 24 Months.

It is expected that there will be at least a few patients with missing Month 24 CCS despite the use of Month 24+ roll-back for clinical and radiographic components of the Month 24 CCS. A tipping point analysis will be performed in order to assess the impact of missing data on primary non-inferiority comparisons. Sequentially, at each stage of the tipping point analysis, one missing Month 24 CCS in the investigational device group will be considered as a failure while at the same time one missing value in the control group will be considered a success. Tipping point stages will be sequentially assessed until there are no more missing CCS values in either group.

If the percentage of missing CCS is more than small, e.g., >10%, then the primary sensitivity analysis will involve multiple imputation (Rubin DB, 1991) (MI) rather than tipping point analysis.

MI minimizes the effects of selection bias on the estimates of the proportions achieving Month 24 CCS. A logistic regression method for monotone missing data using SAS procedure Proc.MI (SAS Institute INC, 2006) will be employed to produce multiply imputed outcome determinations for patients missing Month 24 CCS. This method first fits a

logistic regression model for the outcome variable based on covariates using complete cases. Then, based on the fitted regression model, a new logistic regression model is simulated from the posterior predictive distribution of the parameters which is then used to impute the missing outcome variables. This is done by using the model to compute the expected probability of clinical success for each patient missing the outcome. A uniform random number from 0 to the patient specific expected probability is then generated and if the value is less than the expected probability, the outcome is imputed as a success, otherwise impute the outcome as failure. After all missing outcomes are imputed, the estimated proportion and its standard error will be determined in the usual way. This process will be repeated 20 times. The final point estimate will be determined as the mean value over these 20 multiple imputations. The final standard error used to construct the 95% confidence interval needed for the primary non-inferiority test will be determined from the pooled variance (within imputation variance) plus a term reflecting variability among the 20 multiply imputed point estimates (between imputation variance) (Rubin DB, 1986). The final estimate and 95% confidence interval will be computed by the SAS procedure Proc.MIANALYZE using this approach. By imputing the missing values among patients with missing Month 24 CCS, bias is reduced since the inference is to the entire population that includes patients both missing and not missing Month 24 CCS. The standard error of the final estimate accounts for the statistical uncertainty present in the imputed outcomes and so confidence intervals tend to have the correct coverage rates.

11 Bibliography

Aletaha D, Neogi T, Silman AJ, et al. 2010 Rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Arthritis Rheum. 2010;62(9):2569-81.

Blackwelder, W. (1982). Proving the null hypothesis. *Controlled Clinical Trials*, 3:345-353.

Bohsali KI, W. M. (2006). Complications of total shoulder arthroplasty. *J Bone Joint Surg , 88*, 2279-2292

Boileau, P., et al., *Cemented polyethylene versus uncemented metal-backed glenoid components in total shoulder arthroplasty: a prospective, double-blind, randomized study.* J Shoulder Elbow Surg, 2002. **11**(4): p. 351-9.

Brorson S, O. B. (2009). Effect of osteosynthesis, primary hemiarthroplasty, and non surgical management for displaced four-part fractures of the proximal humerus in elderly: a multi-centre, randomized clinical trial. *Trials , 8*, 10-51.

Collin, P., et al., *A ten-year radiologic comparison of two-all polyethylene glenoid component designs: a prospective trial.* J Shoulder Elbow Surg, 2011. **20**(8): p. 1217-23.

Constant CR, A Clinical Method of Functional assessment of the Shoulder. Clinical Orthopaedics and Related Research. 161-165

Cox, D. (1972). Regression models with life-tables (with discussion). *Journal of the Royal Statistical Society, B* , 66:188-90.

Cruess RL. Experience with steroid-induced avascular necrosis of the shoulder and etiologic considerations regarding osteonecrosis of the hip. Clin Orthop 1978; 130:86-93.

Devinney DS, F. M. (2005). *Surgery of Shoulder Arthritis. In: Arthritis and Allied Conditions: A Textbook of Rheumatology* (15th Ed ed.). (W. Koopman, Ed.)

Edwards, T.B., et al., *A comparison of hemiarthroplasty and total shoulder arthroplasty in the treatment of primary glenohumeral osteoarthritis: results of a multicenter study.* J Shoulder Elbow Surg, 2003. **12**(3): p. 207-13.

Haahr JP, Ø. S. (2005). Exercise versus arthroscopic decompression in patients with subacomial impingement: A randomized, controlled study in 90 cases with a 1-year follow-up. *Ann Rheum Dis , 64* (5), 760-4.

Habermeyer P, et al. Classifications and Scores of the Shoulder, Springer 2006; 199-212. Jacobson. (1996). Definitions of osteoarthritis in the knee and hand. *Ann Rheum Dis, 55* (9), 656-658.

Jain NB, H. L. (2006). Trensd in the epidemiology of total shoulder arthroplasty in the United States from 1990-2000. *Arthritis Rheum* , 55(4);591-7.

Kaplan EL, M. P. (1958). nonparametric estimation from incomplete observations. *Journal of the American Statistical Association* , 53;457-481.

Katolik LI, R. A. (2005). Normalization of Constant Score. *J Shoulder Elbow Surg , 14*(3), 279-85.

Lafosse, L., et al., *Primary total shoulder arthroplasty performed entirely thru the rotator interval: Technique and minimum two-year outcomes.* J Shoulder Elbow Surg, 2009.

Levy, O. and S.A. Copeland, *Cementless surface replacement arthroplasty (Copeland CSRA) for osteoarthritis of the shoulder.* J Shoulder Elbow Surg, 2004. **13**(3): p. 266-71.

Levy, O., et al., *Copeland surface replacement arthroplasty of the shoulder in rheumatoid arthritis.* J Bone Joint Surg Am, 2004. **86-A**(3): p. 512-8.

Lo, I.K., et al., *Quality-of-life outcome following hemiarthroplasty or total shoulder arthroplasty in patients with osteoarthritis. A prospective, randomized trial.* J Bone Joint Surg Am, 2005. **87**(10): p. 2178-85.

Mantel N, H. W. (1959). Statistical Aspects of the analysis of Data from Retropective Studies of Diseases. *J. Nat. Cancer Inst.,* , 22:719-748.

Mantel, N. (1966). Evaluation of survival data and two new rank order statistics arising in its consideration. *Cancer Chemotherapy Rep.* , 50:163-170.

Mehta CR, P. N. (1983). A algorithm for performing Fisher's exact test in r x c contingency tables. *Journal of the American Statistical Association* , 78:472-434.

Mickey RM, G. S. (1989). The impact of confounder selection critieria on effect estimation. *American Journal of Epidemiology* , 129:1:125-133.

Moses, S. (2012). *Osteoporosis SCORE Estimation*. Retrieved from Family Practice Notebook: http://www.fpnotebook.com/rheum/exam/OstprsScrEstmtn.htm

Peto T, P. M. (1977). Desgin and analysis of radnomization clinical trials requiring prolonger observation of exh patient ii: Analysis and examples. *British Journal of Cancer* , 35;1-39

Nuttall, D., J.F. Haines, and Trail, II, *A study of the micromovement of pegged and keeled glenoid components compared using radiostereometric analysis.* J Shoulder Elbow Surg, 2007. **16**(3 Suppl): p. S65-70.

Pfahler M, J. F. (2006). Hemiarthroplasty versus total shoulder prosthesis: Results of cemented glenoid components. *Shoulder Elbow Surg , 15* (2), 154-63.

Rahme, H., et al., *Stability of cemented in-line pegged glenoid compared with keeled glenoid components in total shoulder arthroplasty.* J Bone Joint Surg Am, 2009. **91**(8): p. 1965-72.

Rubin DB, S. N. (1991). Mulitple imputation in health-care databases: an overview and some applications. *Statistics in Medicine*, 10:585-598.

Rubin DB, S. N. (1986). Multiple imputation for interval estimation from random samples with ignorable nonresponse. *Journal of the American Statistical Association*, 81:394:366-374.

SAS Institute Inc. (2006). http://support.sas.com/onlinedoc/913/docMainpage.jsp

Schumann, K., et al., *Sports activity after anatomical total shoulder arthroplasty.* Am J Sports Med, 2010. **38**(10): p. 2097-105.

Scheffe, H. (1959). *The analysis of variance.* Chichester: John wiley & Sons.

Shepard, A (2007) Development and Internal Validation of the Male Osteoporosis Risk Estimation Score. Annals of Family Medicine www.ANNFAMMED.ORG Vol 5, No.6

Sperling JW, C. R. (2000). Radiographic assessment of ingrowth total shoulder arthroplasty. *J Shoulder Elbow Surg*, 507-13.

Walch, G., et al., *The influence of glenohumeral prosthetic mismatch on glenoid radiolucent lines: results of a multicenter study.* J Bone Joint Surg Am, 2002. **84-A**(12): p. 2186-91.

Yian, E.H., et al., *Radiographic and computed tomography analysis of cemented pegged polyethylene glenoid components in total shoulder replacement.* J Bone Joint Surg Am, 2005. **87**(9): p. 1928-36.

Young, A., et al., *A multicentre study of the long-term results of using a flat-back polyethylene glenoid component in shoulder replacement for primary osteoarthritis.* J Bone Joint Surg Br, 2011. **93**(2): p. 210-6.

Young, A.A., et al., *Secondary rotator cuff dysfunction following total shoulder arthroplasty for primary glenohumeral osteoarthritis: results of a multicenter study with more than five years of follow-up.* J Bone Joint Surg Am, 2012. **94**(8): p. 685-93.

Appendix 2-1 Radiation Dose Estimate

Medical Metrics, Inc.
2121 Sage Road, Suite 300
Houston, Texas 77056

P 713-850-7500
F 713-850-7527
www.medicalmetrics.com

Radiation Dose Estimate for the Arthrex Eclipse IDE Study

Summary

An estimate of the radiation dose that will be received by patients in the Arthrex Eclipse shoulder study was prepared based on the available scientific literature. This estimate assumes that standard x-ray positioning and x-ray set-up is used at all sites. There can be substantial site-to-site differences due to the type of equipment and how it is used. This radiation estimate is based on the schedule of radiographic studies as described in the radiographic evaluation protocol.

Literature Estimates

Several peer-reviewed publications provide typical doses for shoulder x-rays. Teeuwisse et al performed an inter-hospital comparison of patient doses[1]. X-ray doses were collected following standardized protocols at 11 hospitals in The Netherlands. Effective doses were reported. They report a median dose of 0.005 mSv for both Neutral AP and AP x-rays of the externally rotated shoulder. The coefficient of variation was 71 to 88% (standard deviation/ mean X 100). This is the only publication with view-specific doses. Based on this study, it is assumed that the dose is similar for each of the three x-ray views that will be collected in the Eclipse study. George et al reported typical x-ray doses based on analysis of patient x-ray equipment details collected from six hospitals in the UK[2]. The calculations were verified by comparison to entrance skin dose measurements. They reported suggested dose levels of 0.5 mGy for typical shoulder exams. This dose is expressed in terms of absorbed dose. It is converted to effective dose by multiplying by the weighting factor (1.0) and then by the tissue weighting factor (0.01 for bone). The suggested absorbed dose would therefore result in an effective dose of 0.005 mSv, which is the same as in the Teeuwise et al study. Mettler et al have published a catalog of effective doses[3]. They provide data for x-ray procedures and this includes all views in a standard exam. They report that the average effective dose is 0.01 mSv for a shoulder procedure. A basic shoulder series consists of AP x-rays with the humerus in neutral as well as in internal and external rotation[4]. The average dose per view would therefore be 0.00333 mSv.

Radiation Dose Estimates for the Study

Based on the publications reviewed, 0.005 mSv will be used as the typical effective dose per x-ray. Each patient would receive 0.015 mSv per visit, and 0.075 mSv for all visits up to and including the 24 month visit. Based on a large study of cancer risk associated with exposure to radiation, it was estimated that the excess relative risk for cancer is 0.97 per Sv[5]. The excess relative risk of the radiation that each patient would receive from participation in the Eclipse study is therefore 0.97 * 0.075 * 1 Sv/1000mSv = 0.000073. To help place the radiation estimate for the Eclipse study into perspective, a person will be exposed to 0.03 mSv of radiation during a typical coast-to-coast round-trip airplane flight (http://www.radiologyinfo.org/en/safety/index.cfm?pg=sfty_xray). The public is exposed to approximately 3 mSv/y from background radiation[6].

medicalmetrics INC.
Insight from Imaging

Table 1: Schedule of Radiographic Studies and Examination Intervals and the Typical Doses Expected for each Exam and for the Study Overall (mSV)

RADIOGRAPHIC STUDIES	POSTOP	3 MONTHS	6 MONTHS	12 MONTHS	24 MONTHS	PATIENT TOTAL
AP – Internal Rotation	0.005	0.005	0.005	0.005	0.005	**0.025**
AP – Neutral Rotation	0.005	0.005	0.005	0.005	0.005	**0.025**
Axillary	0.005	0.005	0.005	0.005	0.005	**0.025**
Visit Total	0.015	0.015	0.015	0.015	0.015	**0.075**

Reference List

1. Teeuwisse W, Geleijns J, Veldkamp W. An inter-hospital comparison of patient dose based on clinical indications. European Radiology. 2007;17(7):1795-805.
2. George J, Eatough J, Mountford P, Koller C, Oxtoby J, Frain G. Patient dose optimization in plain radiography based on standard exposure factors. British Journal of Radiology. 2004;77(922):858.
3. Mettler FA, Huda W, Yoshizumi TT, Mahesh M. Effective Doses in Radiology and Diagnostic Nuclear Medicine: A Catalog1. Radiology. 2008;248(1):254.
4. Frank ED, Long BW, Smith BJ. Merrill's atlas of radiographic positioning & procedures: Mosby/Elsevier; 2007.
5. Cardis E, Vrijheid M, Blettner M, et al. Risk of cancer after low doses of ionising radiation: retrospective cohort study in 15 countries. BMJ. 2005;331(7508):77.
6. Huda W, Vance A. Patient radiation doses from adult and pediatric CT. American Journal of Roentgenology. 2007;188(2):540-6.

Appendix 2-2 Rehabilitation Plan

Postoperative Total Shoulder Arthroplasty Rehabilitation Plan:

Note: The rehabilitation activities and /or schedule may be adjusted as determined by the surgeon.

1. Postoperatively the arm (of target shoulder) is placed in a sling supported by a form-fitting pillow with a waist strap, which immobilizes the upper extremity.
2. Begin wrist, hand, and finger range of motion and grip strengthening on the evening of surgery.
3. Postoperative day one, initiate passive and active-assisted range of motion exercises.
    a. These activities will include pendulum exercises in a standing position, as well as assisted forward elevation exercises in a supine position with a limitation of 90°,
    b. Active-assisted external rotation exercises in the supine position are allowed up to 20° of external rotation and again adjusted based on the surgeon's evaluation at the completion of the subscapularis repair.
    c. The focus of the rehabilitation program is to teach the patient exercises that they can conduct three to four times per day on their own. Assisted devices such as a pulley or a physical therapy baton can be valuable.
4. Provide education to the patient regarding their home exercise program and schedule outpatient physical therapy program prior to discharge.
5. Active exercise is likely to start 10 -14 days after the surgical procedure.
    a. The major restriction to physical therapy, within the first six weeks, is prohibiting resisted internal rotation or other activities that would put stress on the subscapularis repair such as passive unprotected external rotation performed by the physical therapist.
    b. If the patient is allowed independent active-assisted external rotation, the subscapularis repair will not be jeopardized.

c. For the first six weeks the focus is on stretching and improving active range of motion.

6. Once the subscapularis tendon has had adequate time to heal, at approximately six weeks.
    a. All range of motion including internal rotation are advanced as tolerated.
    b. The strengthening program is balanced to include both the anterior rotator cuff (subscapularis) and posterior rotator cuff (primarily supraspinatus and infraspinatus).
    c. Deltoid strengthening as well as scapular muscle strengthening (shoulder shrugs, scapular protraction, scapular retraction, rows, front pull downs) can be gradually incorporated into the patient's rehabilitation program.
7. By three months, it is likely that the patient should be independent with a rehabilitation program. Continued physical therapy after this time period would be a clinical decision by the surgeon.
8. Encourage subjects to pursue both the stretching and strengthening program throughout the entire first year.
9. It is likely that the patients will continue to improve with regards to strength and function for 18-24 months postoperatively.
10. Strength should allow all activities of daily living as well as light recreational activities such as golf, light fitness training, household chores, gardening and swimming in select patients.
11. The final weight-restriction includes no repetitive lifting activities greater than 20 pounds and no repetitive work activities at shoulder level or above on a routine basis.

Appendix 2-3 Surgeon Training

The training program begins with an In-Class session at an Arthrex training center. Training will include didactic and hands-on experience through sawbones and /or cadaveric workshops. During the In-Class session, Trainees will be supervised and mentored by Instructors experienced in the product and surgical Technique. To reinforce the techniques the surgeon has learned, the newly trained investigator/surgeons will have unlimited access to the web-based training materials and access to written material included in the Investigator Training binder.

The objectives that must be met in order to be credentialed on the Eclipse Shoulder are:

1. Attendance at an In-Class Training Session,

AND

2. Completion of two (2) supervised shoulder replacements on sawbones,

OR

3. Completion of two (2) supervised shoulder replacements on cadavers.

AND

4. Demonstrates understanding on the surgical Technique as documented on the Surgical Training Checklist.

Below is a breakdown of the elements of the Surgeon Training Program:

I. <u>In-Class Training Session</u>
- Discussion about Clinical Protocol
  - Patient Selection
  - Indications, Precautions & Contraindications
  - Surgical considerations, implications, perils, pitfalls & recommendations
  - Complications
  - Review of Surgical Video or Cadaver demonstration
- Hands-on Introduction/Review of Instrumentation
- Hands-on Training
  - Sawbones workshop and/or
  - Cadaver lab for bone

II. <u>Training Materials Available at All Times</u>

III. Online access available to all accepted Trainees
    - "DFU" Indications for Use
    - Report of Priors
    - Eclipse Surgical Brochure
    - Surgical Video
    - In-Class materials (updated and available after each training session)

IV. <u>In-Class Training Session</u>
- Discussion about Clinical Protocol
    - Patient Selection
    - Indications, Precautions & Contraindications
    - Surgical considerations, implications, perils, pitfalls & recommendations
    - Complications
    - Review of Surgical Video or Cadaver demonstration
- Hands-on Introduction/Review of Instrumentation

Hands-on Training

Appendix 2-4 Schedule of Events

Arthrex Eclipse Shoulder Prosthesis IDE		Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Unscheduled
CRF #	Schedule of Events	Day -21 to -2	Day 0	3 months± 2 weeks[1]	6 months ± 1 month	12 months ± 2 months	24 months ± 2months or End of Study	
	Informed Consent[1]	X	X	X	X	X	X	X
01	Demo & History • Kellgren Lawrence • Staging System of Cruess • American College of Rheumatology • SCORE	X						
02	Medication & Therapy	X[2]	X	X	X	X	X	X
03	SF 36	X		X	X	X	X	X[3]
04	VAS	X		X	X	X	X	X[3]
05	Constant Score	X		X	X	X	X	X[3]
06	Physical Exam (VS) • Shoulder Exam • Sensory & Motor Testing	X		X	X	X	X	X
	Pre-op labs·Pregnancy[4]	X	X					
07	Enrollment form[5]	X						
	Patient Education	X	X					
08	Surgery/Operative detail		X[7]					X
09	AE		X[8]	X	X	X	X	X
10	Post-operative evaluation			X	X	X	X	X
11	Radiograph[9]	X[10]	X[11]	X	X	X	X	X
	Rehabilitation		X[12]	X	X	X	X	X
12	Hospital Discharge		X					X
13	Deviation Form	X	X	X	X	X	X	X

14	**End of Study**						**X[13]**	

1 A Month =30 days

2 Informed Consent (ICF) is obtained and signed prior to any study related procedures and a revised is ICF is signed at the next study visit prior to any new or revised study related procedures.

3 Medication /Therapy Form will document at least 3 months of conservative treatment as required per Inclusion Criteria

4 SF 36, VAS and Constant may be done during unscheduled visit only if one of the required time points was missed, must document in deviation log

5 The only Pre-op laboratory require for the study is a pregnancy test if female and with child bearing potential. Pregnancy test may be done at V1 and or V2.

6 Data for Enrollment is collected at screening and confirmed at Visit 2 prior to Randomization

7 Randomization will occur on visit 2 after Inclusion/Exclusion criteria is confirmed

8 Operative detail is collected at Visit 2

9 Adverse Events are collected after subject has received treatment

10 All Radiographs must be done as per Radiographic Protocol inadequate Radiographs should be repeated within the time point window.

11 Radiographs must be available in medical record to validate Inclusion/Exclusion Criteria, if ordered during screening and results available to confirm eligibility prior to Randomization

12 The post-operative Radiographs must be done per Radiographic protocol and within 72 hours of surgery.

13 The Rehabilitation Plan is initiated on the evening of surgery –Refer to Appendix 2-2

14 If subject terminates prior to 24 months all end of study procedure and form are completed as if the subject completed 24 months.

Appendix 2-5 Case Report Forms

Appendix 2-6 Surgical Technique ECLIPSE

Appendix 2-7 Radiographic Evaluation Protocol

A PROSPECTIVE, RANDOMIZED, MULTICENTER STUDY TO EVALUATE THE SAFETY AND EFFICACY OF ARTHREX'S ECLIPSE PROSTHESIS

Protocol Number: 003

Radiographic Evaluation Protocol
Revision C

Sponsor: **Arthrex, Inc.**
1370 Creekside Boulevard
Naples, Florida 34108 USA
Telephone: (800) 933-7001

Core Lab: **Medical Metrics, Inc.**
2121 Sage, Suite 300
Houston, Texas 77056
Tel: (713) 850-7500
Fax: (713) 850-9996

Table of Contents

SIGNATURE PAGE 3
HISTORY OF REVISIONS 4
ABBREVIATIONS 5

1 STUDY DESIGN 6
2 RADIOGRAPHIC IMAGING 6
3 ASSESSMENT METHODS 6
3.1 Data Collection 6
3.2 Independent Evaluator 7
3.3 Qualitative Radiographic Assessments 7
4.4 Classification System for the Qualitative Assessments 8
4.4.1. Humeral Radiolucency 8
4.4.2. Humeral Migration/Subsidence 9
4.4.3. Device Condition 10
4.4.4. Periprosthetic Fracture 10
4.4.5. Glenoid Radiolucency (Keeled) 10
4.4.6. Glenoid Radiolucency (Pegged) 11
4.4.7. Glenoid Migration/Subsidence 12
4.4.8. Other Radiographic Observations 13
5 RADIOGRAPH TRANSMITTAL 13
6 DATA MANAGEMENT AND QUALITY CONTROL 13

APPENDIX 1: RADIOGRAPHIC ASSESSMENT SUMMARY 15
APPENDIX 2: RADIOGRAPHIC IMAGE ACQUISITION PROTOCOL 16
Checklist for AP Oblique X-rays of the Shoulder (Grashey View) 17
Internal and External Rotation 17
Checklist for Axillary X-ray of the Shoulder 18
Checklist for Labeling the X-rays 19
APPENDIX 3: IMAGE TRANSFER PROTOCOL 20
A. Subject Identification Code 20
B. Image Transmittal Form 20
C. Electronic Transfer (FTP) 22
D. Non-Electronic Transfer (CD/DVD or Plain Film) 25
APPENDIX 4: RADIOGRAPHIC DATA COLLECTION TEMPLATE 29

SIGNATURE PAGE

By signing this document, the individuals named below agree that they have read the protocol and agree to follow the procedures outlined herein.

Protocol Title	A Prospective, Randomized, Multicenter, Study to Evaluate the Safety and Efficacy of Arthrex's Eclipse™ Prosthesis – Radiographic Evaluation Protocol
Revision / Date	C / 20-Dec-2012
Sponsor Protocol Number	003
Device Name	Eclipse™ Shoulder Prosthesis
Study Sponsor	_____ _____ Melissa Hirschberg RN Date Clinical Research Associate 1370 Creekside Blvd Naples Florida 34108 Tel: (800)933-7001 ext. 1122 Fax: (800) 643-9310 Email: Melissa.Hirschberg@Arthrex.com
Imaging Core Lab	_____ _____ Brian Pikkula, Ph.D. Date Manager of Technical Services Medical Metrics, Inc. 2121 Sage Road, Suite 300 Houston, TX 77056 USA Tel: (713) 850-7500 Fax: (713) 850-9996 Email: bpikkula@medicalmetrics.com

HISTORY OF REVISIONS

The following table summarizes the history of revisions to this protocol:

Revision	Release Date	Significant Revisions Since Previous Version
A	29-Jun-2012	N/A
B	03-Aug-2012	• Remove PostOp time point from assessments of Humeral Radiolucency, Glenoid Radiolucency (Keeled) and Glenoid Radiolucency (Pegged) • Replace Neutral rotation with External rotation in AP view
C	20-Dec-2012	• Added alternate (seated) view of Axillary View and modified supine angulation.

ABBREVIATIONS

AP	Antero-Posterior
CRF	Case Report Form
DICOM	Digital Imaging and Communications in Medicine
IDE	Investigational Device Exemption
ITF	Image Transmittal Form
kVp	Peak Kilo Volts
mAs	Milli-Ampere Second
MMI	Medical Metrics, Inc.
SAE	Serious Adverse Event
SID	Source Image Distance
SOP	Standard Operating Procedures

1 STUDY DESIGN

This is a multi-center, prospective, randomized, controlled study to evaluate the safety and effectiveness of the Arthrex Eclipse™ compared to the Arthrex Univers II™. Candidates for total shoulder arthroplasty will be randomized in a 2 to 1 ratio into the investigational and control arms, respectively. Please refer to the Clinical Investigational Plan for additional information regarding the study design.

2 RADIOGRAPHIC IMAGING

Subjects will undergo standard evaluations at specified post-operative time points. The radiographic imaging schedule is presented in Table 1 below. The radiographic imaging protocol for collecting required views is described in **Appendix 2**.

Table 1: Schedule of Radiographic Studies and Examination Intervals

RADIOGRAPHIC STUDIES	POSTOP	3 MONTHS ±2 WEEKS	6 MONTHS ±2 WEEKS	12 MONTHS ±1 MONTH	24 MONTHS ±1 MONTH	AV[†]
AP – Internal Rotation	x	x	x	x	x	–
AP – External Rotation	x	x	x	x	x	–
Axillary	x	x	x	x	x	–

[‡] Additional and unscheduled visits will be stored if collected.

The radiology technologist will ensure that the views exhibit minimal out-of-plane effects; that all relevant anatomy is visible; and that the films are properly labeled. The plain films will be used to evaluate device condition and to detect the presence of device-related complications.

3 ASSESSMENT METHODS

3.1 Data Collection

The investigational sites will produce the films identified in the Schedule of Radiographic Studies and Examination Intervals (Table 1) above. The investigational sites will send the films or digital images to Medical Metrics, the imaging core lab for this study. Medical Metrics will digitize the films to a minimum resolution of 150 dpi (dots per inch). The digital images will be maintained in a secure, clinical database.

The investigational sites will transfer the radiographic images to Medical Metrics in accordance with the image transfer protocol identified in **Appendix 3**. A radiograph transmittal form will be attached with the films or digital images. This form will provide the following information to identify each shipment of radiographic images: Subject ID Number (which includes the Site Number), Visit Designation, Visit Date, and Radiographic Views present.

Access to films and associated study data will be restricted to authorized personnel only. All data and materials shall be considered the exclusive, confidential property of Arthrex. The analysis and management of the radiographic images and data will be performed by Medical Metrics in accordance with their established and audited Standard Operating Procedures (SOPs).

3.2 Independent Evaluator

The following qualitative assessments shall be performed by two, independent reviewers (the "primary reviewers") and an adjudicator. The primary reviewers will be blinded to each other's assessments. Disagreements between the two primary reviewers will be resolved by the adjudicator. Adjudication shall be performed on a per-assessment basis, so that only those assessments with a disagreement shall be graded by a third reader. Each reviewer (primary and adjudicator) shall be a board-certified, practicing, radiologist with musculoskeletal fellowship-training. The reviewers shall be paid consultants to MMI and have no financial interest in Arthrex.

The radiographic reviewers shall be fully trained on the schedule of assessments and grading system for each assessment. The reviewers shall also be trained on the features of the device, its design and the indications for its use. The radiologists will not have access to the clinical outcomes data during the investigation.

3.3 Qualitative Radiographic Assessments

The following qualitative, visual assessments will be performed by trained, independent radiologists at Medical Metrics:

1. Humeral Radiolucency
2. Humeral Migration/Subsidence
3. Device Condition
4. Periprosthetic Fracture
5. Glenoid Radiolucency (Keeled)
6. Glenoid Radiolucency (Pegged)
7. Glenoid Migration/Subsidence
8. Additional Radiographic Observations

The qualitative assessments will be conducted for both the investigational and control groups at the time points indicated in Table 2 below.

Table 2: Schedule of the Qualitative Assessments

Assessment	*Component*	*Time Points*
Humeral Radiolucency	Humeral	3M, 6M, 12M, 24M, AV†
Humeral Migration/Subsidence	Humeral	6M, 12M, 24M, AV†
Device Condition	Humeral & Glenoid	PostOp, 3M, 6M, 12M, 24M, AV†
Periprosthetic Fracture	Humeral	PostOp, 3M, 6M, 12M, 24M, AV†
Glenoid Radiolucency (Keeled)	Glenoid	3M, 6M, 12M, 24M, AV†

Glenoid Radiolucency (Pegged)	Glenoid	3M, 6M, 12M, 24M, AV[†]
Glenoid Migration/Subsidence	Glenoid	6M, 12M, 24M, AV[†]
Additional Observations	Humeral & Glenoid	PostOp, 3M, 6M, 12M, 24M, AV[†]

[‡] Additional and unscheduled visit imaging will be evaluated if collected.

4.4 Classification System for the Qualitative Assessments

A detailed classification system for each qualitative assessment is provided below. In cases where an assessment cannot be made from the available images due to technical factors (e.g. obscured anatomy, poor contrast or high parallax) the assessment will be graded as 'Indeterminate'. If an assessment cannot be made due to missing films, the assessment will be graded as 'Unable to Assess'. In cases where the assessment is not relevant at a given time point, it will be graded as 'NA'.

4.4.1. Humeral Radiolucency

Humeral Radiolucency will be graded as 'Absent' or 'Present' in accordance with the following definitions:

0. **Absent:** No evidence of radiolucency at the bone implant interface exceeding 2 mm
1. **Present:** Presence of radiolucency at the bone implant interface exceeding 2 mm

The radiolucency will be measured as a distance perpendicular to the bone implant interface and will be evaluated in both the Investigational and Control groups. Presence of progressive radiolucency will be noted by the radiologist in the comments section. If multiple radiolucencies are observed, the greatest radiolucency will be reported.

a. Humerus (Investigational) – Radiolucency will be evaluated in each of nine zones from the External Rotation AP and Axillary views as follows (Figure 1):
   i. External Rotation AP: Zone 1 – Lateral screw
   ii. External Rotation AP: Zone 2 – Distal end of screw
   iii. External Rotation AP: Zone 3 – Medial screw
   iv. External Rotation AP: Zone 4 – Superior head /bone interface
   v. External Rotation AP: Zone 5 – Inferior head /bone interface
   vi. Axillary view: Zone 6 – Anterior screw
   vii. Axillary view: Zone 7 – Posterior screw
   viii. Axillary view: Zone 8 – Anterior head /bone interface
   ix. Axillary view: Zone 9 – Posterior head /bone interface

b. Humerus (Control) – Radiolucency will be evaluated in each of the 15 Zones adapted from in Sperling et al. (2000)[1] for the humeral component of the *control* device from the External Rotation AP and Axillary views. (Figure 2).

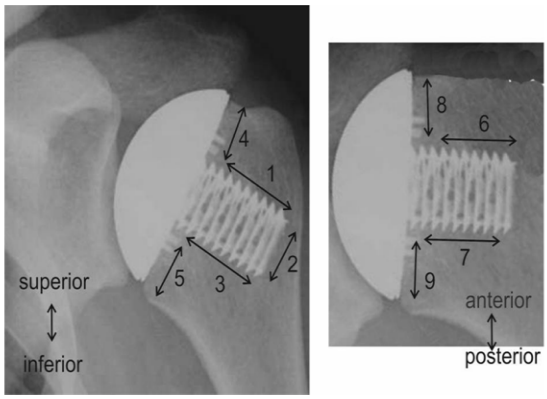


Figure 1 Radiolucency zones for the investigational device in AP view (left) and axillary view (right).

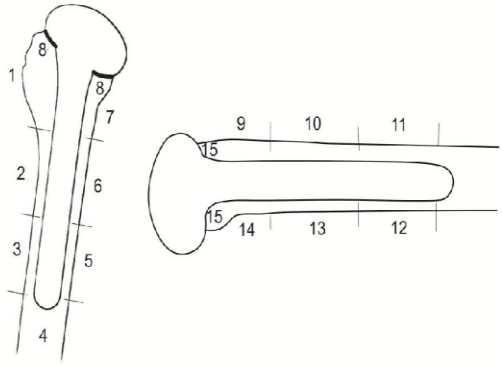


Figure 2 Radiolucency zones for the control device in AP view (left) [from Sperling et al. (2000)] and axillary view (right).

4.4.2. Humeral Migration/Subsidence

Humeral Migration/Subsidence will be graded as 'Absent' or 'Present' in accordance with the following definitions:

0. **Absent:** No evidence of humeral component displacement > 3 mm
1. **Present:** Presence of humeral component displacement > 3 mm

[1] Sperling JW, Cofield RH, O'Driscoll SW, Torchia ME, Rowland CM. Radiographic assessment of ingrowth total shoulder arthroplasty. *J Shoulder Elbow Surg*. 2000;9:507–13.

The assessment of Humeral Migration/Subsidence will be performed by comparing the position of the glenoid component at each visit with its corresponding position on baseline radiographs. Humeral Migration/Subsidence will be assessed from the AP and axillary views for the humeral component relative to the Month 3 baseline. If Month 3 imaging is not available, the Month 6 radiographs will serve as the baseline; and if Month 6 images are not available, the assessment will be graded as 'Unable to Assess'. If an affirmative call of migration/subsidence is recorded, the reader will record the direction in the comments section (i.e., medial, lateral, anterior, posterior or subsidence).

4.4.3. Device Condition

Device Condition will be evaluated to assess the condition and integrity of the device. Device Condition will be graded as 'Intact', 'Disassembly' or 'Fracture' in accordance with the following definitions:

0. **Intact:** No evidence of fractured or disassembled hardware. The hardware is intact.
1. **Disassembly:** Presence of device component disassembly (e.g., head disassembly from the screw)
2. **Fracture:** Presence of fracture or breakage of one or more device components

Additional observations will be documented in the radiologist comments.

4.4.4. Periprosthetic Fracture

Periprosthetic Fracture will be graded as 'Absent' or 'Present' in accordance with the following definitions:

0. **Absent:** No evidence of periprosthetic fracture(s) about the humeral component
1. **Present:** Presence of periprosthetic fracture(s) about the humeral component

4.4.5. Glenoid Radiolucency (Keeled)

Glenoid Radiolucency (Keeled) will be graded per Franklin et al.[2] as 'Grade 1' thru 'Grade 5' or 'N/A' in accordance with the following definitions:

0. **Grade 0:** No evidence of radiolucency at the bone-glenoid implant interface
1. **Grade 1:** Presence of radiolucency at superior and/or inferior flange
2. **Grade 2:** Presence of incomplete radiolucency at keel
3. **Grade 3:** Presence of complete radiolucency (≤ 2 mm wide) around keel

[2] Franklin JL, Barrett WP, Jackins SE, Matsen FA 3rd. Glenoid loosening in total shoulder arthroplasty. Association with rotator cuff deficiency. *J Arthroplasty*. 1988; 3:39-46.

4. **Grade 4:** Presence of complete radiolucency (> 2 mm wide) around keel
5. **Grade 5:** Presence of gross loosening
6. **N/A:** Not Applicable (Pegged component implanted)

Presence of progressive radiolucency (i.e., increase in radiolucency width) will be noted by the radiologist in the comments section. Figure 3 illustrates Grade 0 to Grade 5 for the keeled glenoid component. If more than one grade is applicable, the most severe category will be reported. If 'Grade 5' (gross loosening) is recorded, the radiologist will record the direction of migration of the glenoid component associated with the loosening.

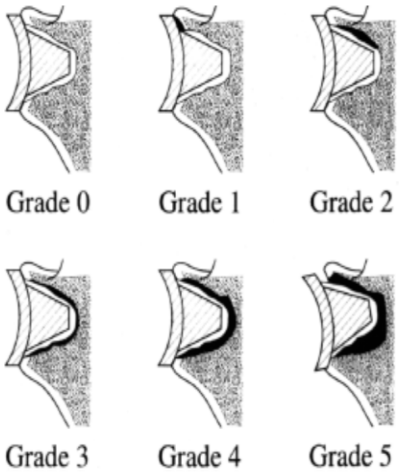


Figure 3 Illustration depicting the grading system used to assess radiolucencies about keeled glenoid components

4.4.6. Glenoid Radiolucency (Pegged)

Glenoid Radiolucency (Pegged) will be adapted from Lazarus et al.[3] as 'Grade 1' thru 'Grade 5' or 'N/A' in accordance with the following definitions.

0. **Grade 0:** No evidence of radiolucency at the bone-glenoid implant interface
1. **Grade 1:** Presence of incomplete radiolucency around one or two pegs
2. **Grade 2:** Presence of complete radiolucency (≤ 2 mm wide) around one peg only, with or without incomplete radiolucency around one other peg
3. **Grade 3:** Presence of complete radiolucency (≤ 2 mm wide) around two or more pegs

[3] Lazarus MD, Jensen KL, Southworth C, Matsen FA. The radiographic evaluation of keeled and pegged glenoid component insertion. *J Bone Joint Surg Am.* 2002; 84-A:1174-1182.

4. **Grade 4:** Presence of complete radiolucency (> 2 mm wide) around two or more pegs
5. **Grade 5:** Presence of gross loosening
6. **N/A:** Not Applicable (Keeled component implanted)

Presence of progressive radiolucency (i.e., increase in radiolucency width) will be noted by the radiologist in the comments section. Illustration of the pegged glenoid component Grade 0 to Grade 5 is given in Figure 4. If more than one grade is applicable, the most severe category will be reported. If 'Grade 5' (gross loosening) is recorded, the radiologist will record the direction of migration of the glenoid component associated with the loosening.

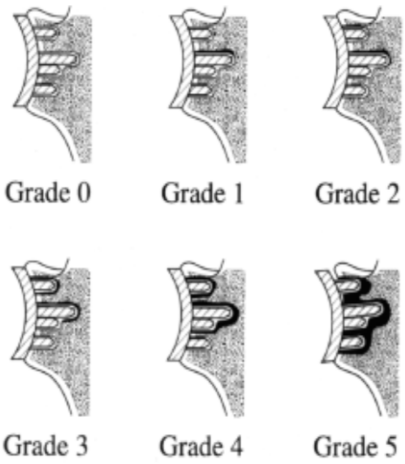


Figure 4 Illustration depicting the grading system used to assess radiolucencies about pegged glenoid components

4.4.7. Glenoid Migration/Subsidence

Glenoid Migration/Subsidence will be graded as 'Absent' or 'Present' in accordance with the following definitions:

0. **Absent:** No evidence of glenoid component displacement > 3 mm
1. **Present:** Presence of glenoid component displacement > 3 mm

The assessment of Glenoid Migration/Subsidence will be performed by comparing the position of the glenoid component at each visit with its corresponding position on baseline radiographs. Glenoid Migration/Subsidence will be assessed from the AP and axillary views for the glenoid component relative to the Month 3 baseline. If the Month 3 imaging is not available, the Month 6 radiographs will serve as the baseline; and if Month 6 images are not available, the assessment will be graded as 'Unable to Assess'. If an affirmative call of migration/subsidence is recorded, the reader will record the direction (i.e., medial, lateral, anterior, posterior or subsidence).

Medical Metrics will maintain compliance with all standard operating procedures and data management practices including:

1. Restricting access to digital information and images to authorized personnel only.
2. Maintaining audit trails of modifications made to the client data (such as corrections to the subject demographics and/or visit information).
3. Performing routine quality audits and process inspection.
4. Performing routine data backup and data validation procedures.
5. Maintaining all films in a secure manner while in MMI's possession.
6. Promptly returning original (or copies of) films and digital media to the clinical sites.

A validated software system will be used to record the radiologist's assessments, store the data and images, and produce the radiographic deliverables.

1. Qualitative radiographic assessments will be captured through a validated software interface. The assessments will be digitally signed and dated at the time the assessments are produced.
2. User authentication will validate the identity of the software operator.
3. Automated error detection tools will assist in error avoidance.
4. The radiographic assessments will be stored in a proprietary database and linked with the images used to produce the assessments.
5. Electronic audit trails of modifications made to the data will be recorded in accordance with good clinical practices and the provisions of 21 CFR Part 11.
6. During the production of deliverables, data will be automatically extracted from the database using a validated software tool that produces summary electronic deliverables in a standard format.
7. A set of quality control checks will be applied to the deliverable to confirm accuracy of the reported data.
8. Each electronic deliverable will be password-protected against subsequent editing prior to shipment to the Arthrex and/or their designee.

An example radiographic case report form that summarizes the complete set of radiographic assessments to be produced during the study is provided in **Appendix 4.** The assessments summarized in this form will be captured electronically and stored in digital form.

Medical Metrics will regularly submit an inventory report of images received to date. Each interim report shall include a list of images received by subject, by time point and by view. Each report will be cumulative and up-to-date. Medical Metrics will support database queries related to each inventory report as requested.

APPENDIX 1: RADIOGRAPHIC ASSESSMENT SUMMARY

Qualitative Assessments	Evaluations/Comparisons
1. Humeral Radiolucency	• Humeral Radiolucency will be evaluated in each treatment group beginning with the 3 Month time point. • Humeral Radiolucency in the Investigational group will be evaluated in 9 zones separately and the Control group will consist of 15 zones evaluated separately.
2. Humeral Migration/Subsidence	• Humeral Migration/Subsidence will be evaluated in each treatment group beginning with Month 6 relative to the Month 3 time point. • Humeral Migration/Subsidence will be graded as 'Absent' or 'Present'.
3. Device Condition	• Device Condition will be evaluated at each post-operative visit beginning with the PostOp time point. • Device Condition will be graded as 'Intact', 'Disassembly', or 'Fracture'
4. Periprosthetic Fracture	• Periprosthetic Fracture will be evaluated in each treatment group beginning with the PostOp time point. • Periprosthetic Fracture will be graded as 'Absent' or 'Present'.
5. Glenoid Radiolucency (Keeled)	• Glenoid Radiolucency (Keeled) will be evaluated in each treatment group beginning with the 3 Month time point. • Glenoid Radiolucency (Keeled) will be graded as 'Grade 1 to Grade 5' or 'N/A'.
6. Glenoid Radiolucency (Pegged)	• Glenoid Radiolucency (Pegged) will be evaluated in each treatment group beginning with the 3 Month time point. • Glenoid Radiolucency (Pegged) will be graded as 'Grade 1 to Grade 5' or 'N/A'.
7. Glenoid Migration/Subsidence	• Glenoid Migration/Subsidence will be evaluated in each treatment group beginning with Month 6 relative to the Month 3 time point. • Glenoid Migration/Subsidence will be graded as 'Absent', or 'Present'
8. Additional Radiographic Observations	• Additional observations will be documented at the discretion of the radiologist at all post-operative time points.

APPENDIX 2: RADIOGRAPHIC IMAGE ACQUISITION PROTOCOL

The guidelines for the X-ray image acquisition protocol are found on the next page.

Checklist for AP Oblique X-rays of the Shoulder (Grashey View) Internal and External Rotation

EQUIPMENT SETUP

- ❑ Set up the X-ray system according to your standard protocol.
  - Insert a cassette loaded with a 10'' x 12'' film. Position lengthwise to capture entire humeral stem.
  - Set the mAs and kVp based on your technique chart and the size of the subject.
  - 34" SID
- ❑ Note any deviations from the standard settings in the patient record.
- ❑ Tube is perpendicular to plate

SUBJECT PREPARATION

- ❑ Subject should be standing and rotate body posteriorly 30º - 45º toward the affected shoulder.
- ❑ Arm should be at the subject's side, and shoulder relaxed.
- ❑ Turn face away from affected shoulder.
- ❑ Position the Central Ray at the mid-glenohumeral joint.

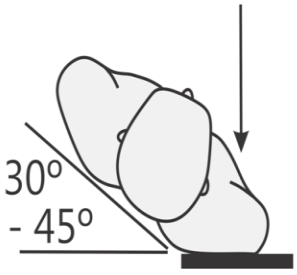
VIEWS

- ❑ AP Oblique Internal Rotation
  - At the immediate post-operative time point, the subject should only rotate the arm to the extent possibly without pain.
  - Arm is maximally *internally* rotated

- ❑ AP Oblique External Rotation
  - At the immediate post-operative time point, the subject should only rotate the arm to the extent possibly without pain.
  - Arm is maximally *externally* rotated
  - Ensure full rotation of the humerus and absence of any abduction of the arm from the body

QUALITY

- ❑ X-ray should demonstrate:
  - Entire prosthesis
  - Glenoid cavity in profile
  - Observation of the subacromial space
  - Adequate trabecular detail of glenoid and humerus

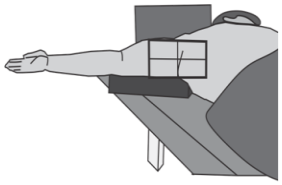


Checklist for Axillary X-ray of the Shoulder

EQUIPMENT SETUP

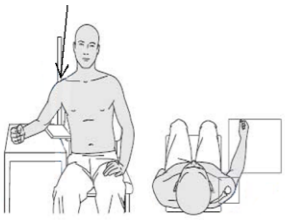
- ❑ Set up the X-ray system according to your standard protocol.
  - Insert a cassette loaded with a 10'' x 12'' film.
  - Set the mAs and kVp based on your technique chart and the size of the subject.
  - 40" SID
- ❑ Note any deviations from the standard settings in the patient record.

SUBJECT PREPARATION – SUPINE (RECOMMENDED)



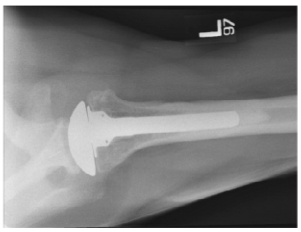
- ❑ At the immediate postoperative time point, the subject should only abduct the arm to the extent possibly without pain.
- ❑ Subject should be in the supine position.
- ❑ Abduct arm 90º from body and humerus, elbow and ulna/radius parallel with table
- ❑ Hand is supinated.
- ❑ Sponge support may be needed under the humerus and distal arm may be supported with chair or other support.
- ❑ Turn face away from affected shoulder.
- ❑ Position the Central Ray at the mid-glenohumeral joint.
- ❑ Angle beam 15º - 30º medially.

SUBJECT PREPARATION – SEATED (ALTERNATE)



- ❑ At the immediate postoperative time point, the subject should only abduct the arm to the extent possible without pain
- ❑ Subject should be seated with forearm resting comfortably on table
- ❑ Place cassette on table between the torso and the subject's elbow
- ❑ Turn face away from affected shoulder
- ❑ Position the central beam at the mid-glenohumeral joint

QUALITY



- ❑ X-ray should demonstrate:
  - Entire prosthesis
  - Glenohumeral joint profiled
  - Coracoid process pointing anteriorly
  - Lesser tubercle in profile directed anteriorly
  - Adequate trabecular detail of glenoid and humerus

Checklist for Labeling the X-rays

- ❑ Be sure that you have correctly noted the subject and visit information on each film, in particular, the Subject ID, the visit ID (e.g. PostOp, Month 3, Month 6, etc), the visit date, and the view (APExt, APInt, Axillary)
- ❑ The subject and visit information should be documented on a self-adhesive film label (provided by the study sponsor or their designee) and attached to the film.
  - Each film label should be attached to the film in such a way that it is correct-reading and does not obscure the anatomy.
  - If possible, the film label should be placed over the subject information to mask (or redact) this information.
  - It may be necessary to redact the subject information by other means if the film label fails to achieve this purpose.
- ❑ Be sure that you have labeled each view accordingly. You may label the exam date and/or view with radiographic markers or stick-on labels in addition to using the standard film label provided by the sponsor or their designee.
- ❑ Be sure that you have identified the subject's right and left side.

APPENDIX 3: IMAGE TRANSFER PROTOCOL

A. Subject Identification Code

Subjects will be identified using a unique subject identification code consisting of site number, subject number and subject initials. The format of this identification code is provided below:

003 – □□ – □□□
Study# Site # Subject #

Examples: 003–01–001 003-12–024 003–10–045

Notes: Include leading zeros in the site and subject numbers

Note: Deviations from the protocol described on the following pages may be permitted to accommodate certain imaging systems, PACS systems and IT constraints. Please contact Medical Metrics for details.

B. Image Transmittal Form

All digital images and plain films sent to Medical Metrics (via FTP or courier) must be accompanied by an **Image Transmittal Form** (ITF). The ITF provides an inventory of all images contained within the shipment. The ITF also provides a mechanism for documenting the shipment, receipt and return of the radiographic images. An example of the ITF is provided on the following page.

If the images sent to Medical Metrics are transmitted via FTP, the ITF must be faxed. If CD/DVDs or plain films are transmitted via courier, the ITF must be included in the parcel in triplicate form.

Pink: Retained by Investigational Site at the time of film shipment
White: Retained by Medical Metrics after receipt of films
Canary: Returned with films to Site by Medical Metrics

It is recommended that the clinical sites forward all images to Medical Metrics, Inc. within two weeks of collection to ensure timely record-keeping and a continuous flow of images. The radiographic films will be promptly returned to the sites after they have been imported into the Medical Metrics database.

Eclipse IDE Study – Image Transmittal Form

Arthrex, Inc., 1370 Creekside Boulevard, Naples, Florida 34108 - Telephone: (800) 933-7001

Sent Date: ___ - ____ - ____ (dd - mmm - yyyy) Method of Transfer: ☐ Courier ☐ FTP

If courier, Tracking #: _____

Person Preparing Shipment/Transfer:

Name: _____ Email: _____

Phone: _____ Fax: _____

Subject ID 003 - __ (Site) - ___ (Subject)	Visit Designation	Visit Date (DD-MMM-YY)	Indicate Views Enclosed with an 'X'			
			AP Internal	AP External	Axillary	Other

Core Lab:
Medical Metrics, Inc.
Attn: Eclipse IDE Study #336
2121 Sage Road, Ste 300
Houston, Texas 77056
Ph: (713) 850-7500

Address to Return Images: (N/A for FTP)
_____
_____
_____
_____
_____

(To Be Completed by Medical Metrics Personnel)

Date of Return: ___ - ____ - ____ (dd - mmm - yyyy) Tracking #: _____ (N/A for FTP)

Return Prepared By: _____

Pink Copy – Investigational Site. Send White and Canary copies to Medical Metrics with films.
Medical Metrics returns Canary copy to site with films.
3-part NCR not applicable for FTP transfers

C. Electronic Transfer (FTP)

1. Preparation and Labeling of Images for Electronic Transfer (FTP)

Digital images must be organized in descriptively-named folders or files that **clearly identify** the subject ID and visit label when uploaded to the FTP site. Acceptable file types and labeling conventions are as follows:

DICOM: *Unrestricted*

Windows® compatible graphics formats:

An adequate descriptive file path is described below. Other folder structures and filenames are acceptable provided each image can be uniquely identified by subject ID, visit designation and view.

[Subject ID_Visit Designation]/[Filename.ext]

Examples: /003-04-001_Month 3/APInt.bmp
/003-10-130_PostOp/APExt.jpg

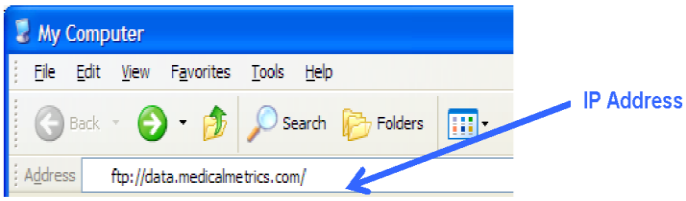
An **Image Transmittal Form** must be faxed to Medical Metrics, Inc. once the images have been uploaded to FTP. The fax number is 713-850-9996.

When MMI receives the fax, the images will be downloaded from the FTP site to MMI's servers, and the images will be removed from the site to show they have been processed. The transmittal form will then be verified and faxed back to the site for their records.

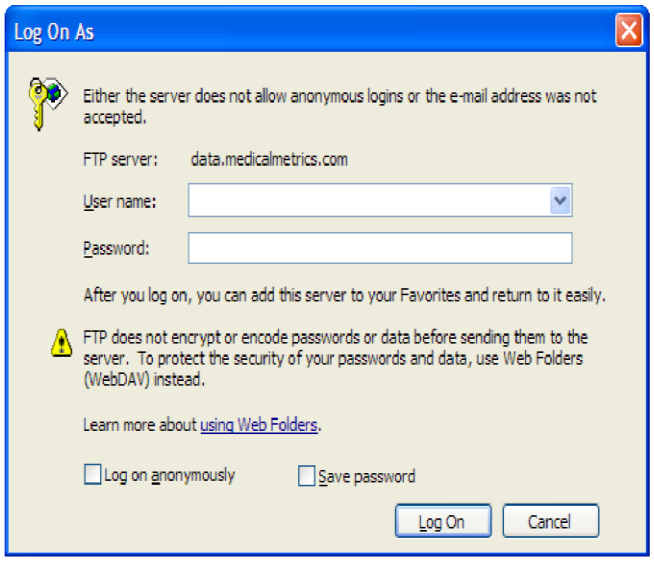
Each site will receive a unique user ID and password for FTP transfer from their facility to MMI.

2. Instructions to Connect to the Medical Metrics FTP Server

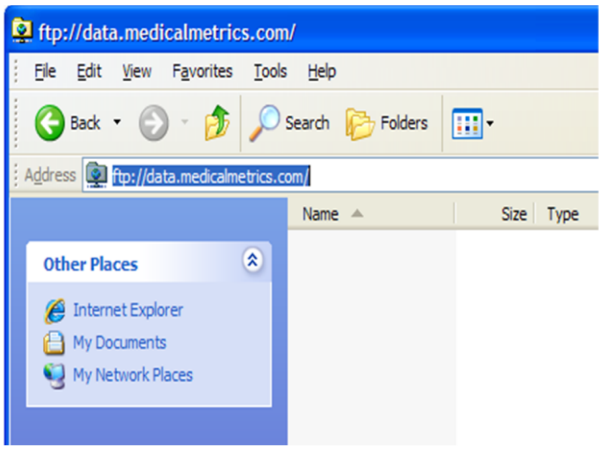
1. Open "My Computer" ( ). Click "Start" → " My Computer"
2. Enter the IP address of the Medical Metrics FTP server (ftp://data.medicalmetrics.com/).



3. When the "Log On As" dialog box appears, type in the user ID and password supplied to you by Medical Metrics. Optionally, you may want to check the "Save Password" box if you will be the only user on the computer.



4. After you have logged in, you will be connected to the Medical Metrics FTP server. The screen will appear similar to that shown below. The actual files and folders listed will depend on the data available to you.

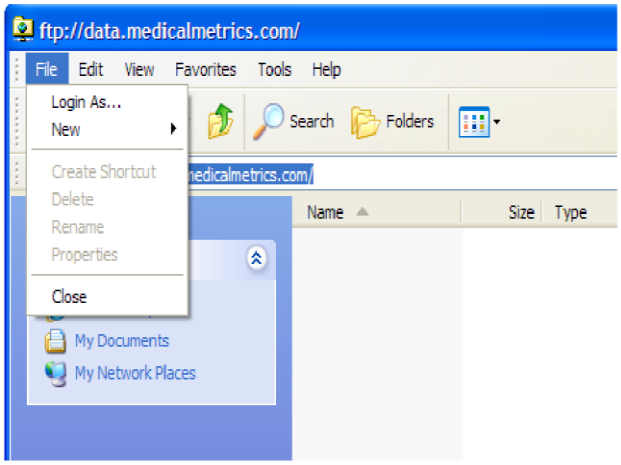


5. To transfer data to Medical Metrics, find the files on your computer and drag them to this window, or copy the items on your computer and paste them in this window.

6. To download data from Medical Metrics, click and drag the items from this window to your computer, or copy them in this window and paste them in some folder on your computer.

7. If you have multiple accounts on the Medical Metrics FTP Server. You will need to make sure you are connected to the correct ftp account. Do the following to login to another account:

   Click "File" → "Login As"



8. Once images are transferred, fax the transmittal form to 713-850-9996. Ensure that the transmittal form is complete prior to sending the fax.

   If you experience any difficulties, please contact the designated project manager or call (713) 850-7500.

D. Non-Electronic Transfer (CD/DVD or Plain Film)

Investigational sites transferring plain films and/or digital images on a CD/DVD will send all imaging exams to the core lab at the following address:

Medical Metrics, Inc.
Attn: Eclipse IDE Study #336
2121 Sage Road, Ste 300
Houston, TX 77056

Phone: (713) 850-7500
Fax: (713) 850-9996

All imaging exams will be sent via courier service (e.g. FedEx, UPS or DHL) so that shipments may be tracked. An **Image Transmittal Form** (ITF) must accompany the shipment. The ITF provides an inventory of the shipment and should be placed inside the packing container.

1. Preparation and Labeling of Images for CD/DVD Transfer

Images for a specific subject visit should be stored on a single CD or DVD. **If possible, a single CD/DVD should contain only the images obtained during a single visit (PostOp, Month 3, etc.) for a single subject.** Placing digital images for multiple subjects and/or multiple visits on a single CD or DVD should be avoided. It is recommended that images be stored to CD/DVD in DICOM format.

Digital images must be organized in descriptively named folders or files that **clearly identify** the subject ID and visit label when uploaded to the FTP site. Acceptable file types and labeling conventions are as follows:

DICOM: *Unrestricted*

Windows® compatible graphics formats:

An adequate descriptive file path is described below. Other folder structures and filenames are acceptable provided each image can be uniquely identified by subject ID, visit designation and view.

[Subject ID_Visit Designation]/[Filename.ext]

Examples: /003-04-001_Month 3/APInt.bmp
/003-10-130_PostOp/APExt.jpg

CD/DVD Label

If images are sent to Medical Metrics on CD/DVD, a **CD/DVD Label** must be affixed to the CD/DVD. The CD/DVD Label is a permanent-adhesive label with pre-printed fill-in-the-blank and check-box information. The label is used to identify the subject ID, visit date, visit designation, and views of the images stored on the CD or DVD.

An example **CD/DVD Label** is provided below:

Eclipse IDE Study – CD/DVD Label

Subject ID: 003 – __ __ – __ __ __
Site # Subject #

Visit Designation: _____

Visit Date: __ __ – __ __ __ – __ __
dd mmm yy

Group: ☐ **Investigational** ☐ **Control**

Notes: Include leading zeros in the site and subject numbers
Use standard Visit Designations *(e.g. PostOp, Month 3, etc.)*
Use DD-MMM-YY date format (*e.g. '01-Jan-12*')

2. Preparation and Labeling of Images for Film Transfer

Film Label

If plain films are sent to Medical Metrics, a **Film Label** must be affixed to the film. The Film Label is a permanent-adhesive address label with pre-printed fill-in-the-blank information. The label is placed directly on each film and is used to identify the subject ID, visit designation, visit date and view. An example **Film Label** is provided below:

Eclipse IDE Study – Film Label

Subject ID: 003 – __ __ – __ __ __
Site # Subject #

Visit Designation: _____

Visit Date: __ __ – __ __ __ – __ __
dd mmm yy

View: _____

The radiology technologist or site coordinator will complete the label and adhere it to a corner of the film in such a manner that it can be correctly read when viewing

the film, does not obscure the study anatomy and, if possible, covers the protected health information (PHI) of the subject.

Notes: Include leading zeros in the site and subject numbers
Use standard Visit Designations *(e.g.PostOp, Month 3, etc.)*
Use DD-MMM-YY date format (*e.g. '01-Jan-12'*)
Use Standard View designations *(e.g. APInt, APExt, Axillary)*

After labeling each film, all films will be collected and stored in a film jacket or envelope. One film jacket is used to store all the films associated with a single visit. There is one film jacket per subject visit. Each film jacket will be labeled with a **Film Jacket Label**.

Film Jacket Label

All films for a specific subject visit should be placed in a single film jacket or envelope. **A single jacket or envelope should contain only the films obtained during a single visit (PostOp, Month 3, Month 6, etc.) for a single subject.** Differentiating specific subjects and/or visits with paperclips, staples or paper dividers is not permitted.

When plain films are sent to Medical Metrics, a **Film Jacket Label** must be affixed to the jacket or envelope containing the films. The Film Jacket Label is a permanent-adhesive address label with pre-printed fill-in-the-blank and checkbox information. The label is used to identify the subject ID, visit date, treatment group, designation and views enclosed within the film jacket or envelope. An example of the **Film Jacket Label** is provided below:

Eclipse IDE Study – Film Jacket Label

Subject ID: 003 – __ __ (Site #) – __ __ __ (Subject #)
Group (*check only one*):
☐ Investigational
☐ Control

Visit Date: __ __ (dd) – __ __ __ (mmm) – __ __ (yy)

Treatment Side: ☐ Left ☐ Right

Visit Designation (*check only one*):

☐ PostOp ☐ Month 3 ☐ Month 6 ☐ Month 12
☐ Month 24 ☐ Other: _____

View (*check all that apply*):

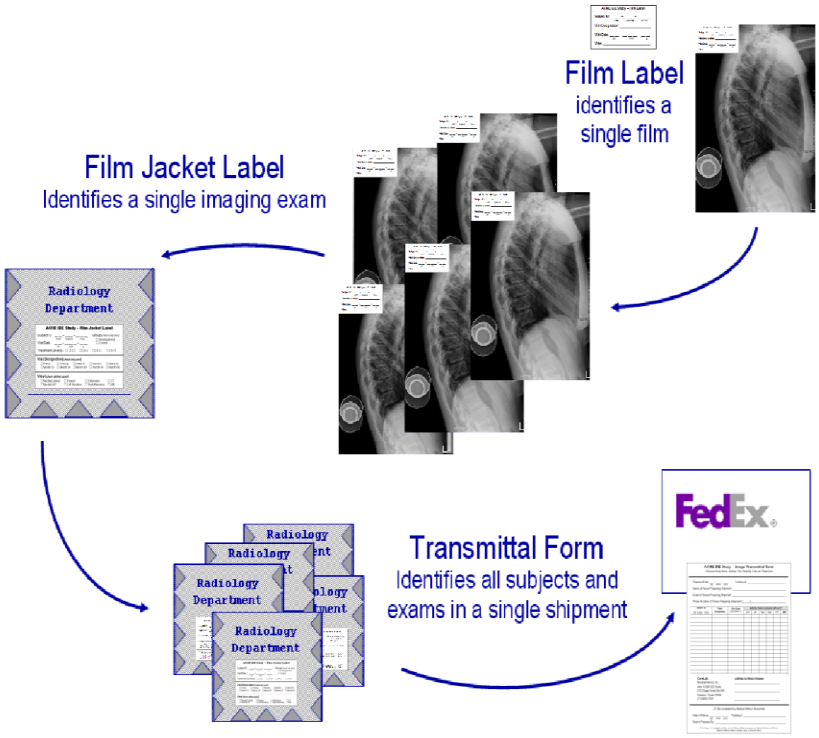
☐ AP Internal ☐ AP External
☐ Axillary ☐ Other: _____

The radiology technologist or site coordinator will complete the **Film Jacket Label** and adhere it to the jacket or envelope.

Notes: Include leading zeros in the site and subject numbers
Use DD-MMM-YY date format (*e.g. '01-Jan-12'*)

Summary

A summary of the **film labeling and packaging sequence** is illustrated below:



APPENDIX 4: RADIOGRAPHIC DATA COLLECTION TEMPLATE

The radiographic data collection template for this study is found on the following page. This template is intended to summarize, in graphical form (similar to a CRF), the list of quantitative and qualitative assessments produced for the study. A validated, electronic data capture system will be used to capture and record the assessments summarized in this template. All recorded assessments will be digitally signed and dated, and maintained in accordance with good clinical practices and the provisions of 21 CFR Part 11.

Arthrex – Eclipse IDE Study – Protocol# 003

Sample Radiographic Case Report Form

Subject Information

Subject ID □□-□□□-□□□ Visit Date □□-□□□-□□ (dd mmm yy)

Visit ID ☐ PostOp ☐ 3 Month ☐ 6 Month ☐ 12 Month ☐ 24 Month ☐ Addl. Visit

Side ☐ Right ☐ Left Group: ☐ Investigational ☐ Control

Qualitative Assessments

Humeral Radiolucency	☐ 0 - Absent	1 - Present	2 - Indeterminate	3 - Unable to Assess	Zone _____
Humeral Migration/Subsidence	☐ 0 - Absent	1 - Present	2 - Indeterminate	3 - Unable to Assess	
Device Condition	☐ 0 - Intact	1 - Disassembly	2 - Fracture	3 - Indeterminate	4 - Unable to Assess
Periprosthetic Fracture	☐ 0 - Absent	1 - Present	2 - Indeterminate	3 - Unable to Assess	0 -
Glenoid Radiolucency (Keeled)	☐ 0 - Grade 0	1 - Grade 1.	2 - Grade 2.	3 - Grade 3	4 - Grade 4
	5 - Grade 5	6 - N/A	7 - Indeterminate	8 - Unable to Assess	
Glenoid Radiolucency (Pegged)	☐ 0 - Grade 0	1 - Grade 1.	2 - Grade 2.	3 - Grade 3	4 - Grade 4
	5 - Grade 5	6 - N/A	7 - Indeterminate	8 - Unable to Assess	
Glenoid Migration/Subsidence	☐ 0 - Absent	1 - Present	2 - Indeterminate	3 - Unable to Assess	

Additional Radiographic Observations / Comments:

Reviewer's Signature: _____ Date: _____

This is a *sample* Radiographic Case Report Form. All assessments will be collected via a validated, electronic data capture system, digitally signed, and maintained in accordance with good clinical practices.

medicalmetrics INC.

Appendix 2-8 Constant Shoulder Score Patient Survey

CONSTANT SHOULDER SCORE / 1-PATIENT SURVEY

Date of Survey: ☐☐-☐☐-☐☐☐☐ Subject Identification Number: ☐☐-☐☐-☐☐☐☐

Answer all questions, selecting just one unless otherwise stated.

During the past 4 weeks:

01. What is your shoulder pain level?

(Consider maximum level of pain)

- ❑ None -15 points
- ❑ Mild -10 points
- ❑ Moderate -5 points
- ❑ Severe – 0 points

02. Activities of Daily Living (Choose all that apply)

- ❑ Full work *(Consider activities of daily life if retired) – 4 points*
- ❑ Full recreation/sport – 4 points
- ❑ Unaffected Sleep – 2 points

03. What is your arm positioning in daily life? (Choose only one)

(Consider demonstrating this to examiner if you do not routinely perform the task)

- ❑ Up to Waist (e.g., washing dishes, cutting meat, typing) – 2 point
- ❑ Up to Xiphoid (e.g., driving, opening a closed door) – 4 points
- ❑ Up to Neck (e.g., drinking with a glass, tying a tie, hanging a jacket) – 6 points
- ❑ Up to Top of Head (e.g., washing hair, combing hair) – 8 points
- ❑ Above Head (e.g., changing a light bulb in a ceiling light) – 10 points

Initialed and dated by Subject: _____ /_____

Initialed and dated by Examiner: _____ /_____

Appendix 2-9 Constant Shoulder Score Physician Investigator Examiner Section

ARTHREX ECLIPSE SHOULDER PROTHESIS #003/G110128

CONSTANT SHOULDER SCORE / 2-PHYSICIAN-INVESTIGATOR-EXAMINER SECTION

Date of Survey: ☐☐-☐☐-☐☐☐☐ Subject Identification Number: ☐☐-☐☐-☐☐☐☐

This section should be completed by the examiner Answer all questions, selecting just one unless otherwise stated.

Instructions: Subject is to reach his or her maximum elevation **but without pain.** Use a handheld goniometer to perform measurements.

04. Forward Flexion (Degrees, °)

Surgical Shoulder*	***Points***	**Contralateral Shoulder**	***Points***
❑ 0-30	0	❑ 0-30	0
❑ 31-60	2	❑ 31-60	2
❑ 61-90	4	❑ 61-90	4
❑ 91-120	6	❑ 91-120	6
❑ 121-150	8	❑ 121-150	8
❑ 151-180	10	❑ 151-180	10
Total:		Total:	

05. Lateral Elevation (Degrees, °)

Surgical Shoulder*	***Points***	**Contralateral Shoulder**	***Points***
❑ 0-30	0	❑ 0-30	0
❑ 31-60	2	❑ 31-60	2
❑ 61-90	4	❑ 61-90	4
❑ 91-120	6	❑ 91-120	6
❑ 121-150	8	❑ 121-150	8
❑ 151-180	10	❑ 151-180	10
Total:		Total:	

06. External Rotation (Choose all that apply)

Instructions: Have subject perform each movement, check box if patient achieves movement without pain. Ask the subject to hold hands slightly detached from head when performing motion.

Surgical Shoulder*		**Contralateral Shoulder**	
❑ Hand behind Head, with elbow held forward	2	❑ Hand behind Head, with elbow held forward	2
❑ Hand behind Head, with elbow held back	2	❑ Hand behind Head, with elbow held back	2
❑ Hand to top of Head, with elbow held forward	2	❑ Hand to top of Head, with elbow held forward	2
❑ Hand to top of Head, with elbow held back	2	❑ Hand to top of Head, with elbow held back	2
❑ Full elevation from on top of head	2	❑ Full elevation from on top of head	2
Total:		Total:	

Initialed and dated by examiner: _____/_____

ARTHREX ECLIPSE SHOULDER PROTHESIS #003/G110128

CONSTANT SHOULDER SCORE / 2-PHYSICIAN-INVESTIGATOR-EXAMINER SECTION

Date of Survey: ☐☐-☐☐-☐☐☐☐ Subject Identification Number: ☐☐-☐☐-☐☐☐☐

7. Internal Rotation. Dorsum of hand to:

Instructions: Have subject stand. Ask the subject to reach his or her maximum internal rotation but without pain. Consider the tip of the thumb as the indicator of the level.

Surgical Shoulder*		Contralateral Shoulder	
❑ Lateral Thigh	0	❑ Lateral Thigh	0
❑ Buttock	2	❑ Buttock	2
❑ Lumbosacral junction	4	❑ Lumbosacral junction	4
❑Waist (3rd lumbar vertebra)	6	❑Waist (3rd lumbar vertebra)	6
❑ 12th dorsal vertebra (T12)	8	❑ 12th dorsal vertebra (T12)	8
❑ Interscapular Region (T7)	10	❑ Interscapular Region (T7)	10
Total:		Total:	

08. Strength of Abduction (Pounds)

Instructions:

- *For setup of the MMT see Appendix -"Summary of the MMT Functions Needed for the Constant Score Test for Strength of Abduction and Preparing the MMT System for Shoulder Test"*
- *The examiner should stand with one foot placed in the smaller looped end of adjustable pull strap, with the curved padded attachment facing toward the floor. The examiner should adjust the strap so that the bottom of the curved padded attachment is level with the subject's AC joint.*
- *The subject is to place the hand through the loop so that the back of the wrist is against the curve padded attachment (palm facing down). The MMT unit is placed between the examiner's hand and the limb being assessed. The hand is placed under the strap and around the body of the MMT.*
- *The examiner will not apply pressure to the MMT and will release his or her hand when the subject starts the test. This allows the examiner easy access to the TOP buttons with the thumb. Buttons should be pressed accordingly using the examiners opposite hand. The MMT is activated by pressing the Menu/Select button (1).*
- *The subject's arm is positioned to 90 degree abduction to the body and slightly in front of the body. The examiner adjusts foot position to align the strap perpendicular (plumb) with respect to the floor. If patient cannot achieve the test position, a force measurement of "0" should be recorded.*
- *The MMT is activated by pressing the Menu/Select button (1).*
- *The first trial should be for practice at 50% of maximum safe effort. Subject should rest for at least 30 seconds, and then conduct the assessment. The subject exert the maximum for "5" seconds. The MMT will beep when the "5" seconds are completed.*
- *Record pounds below 1 point /pound up to 25 pounds,*

Initialed and dated by Examiner: _____ /_____

ARTHREX ECLIPSE SHOULDER PROTHESIS #003/G110128

CONSTANT SHOULDER SCORE / 2-PHYSICIAN-INVESTIGATOR-EXAMINER SECTION

Date of Survey: □□-□□-□□□□ Subject Identification Number: □□-□□-□□□□

Constant Test Scoring Table :	Sum of Points
01. What is your shoulder pain level?	
02. Activities of daily living?	
03. What is your arm positioning in daily life?	
04. Forward Flexion	
05. Lateral Elevation	
06. External Rotation	
07. Internal Rotation	
08. Strength of Abduction (1 point per pound up to maximum of 25 points)	
Total Raw Constant Score (Sum of above points)	
Adjusted : _____ (Total Raw above) / _____ (Normal Score from "Table 7 below") X 100 =	

Raw score from questions 01-08 are directly entered into Electronic Data base (EDC)

EDC will calculate Adjusted Constant Score and confirm calculations above

Table 7: Normal Constant Score bases on age and sex (Katolik LI 2005)		
Age (y)	Gender Adjustment	
	Male	Female
18-29	95	88
30-39	95	87
40-49	96	86
50-59	94	84
60-69	92	83
≥ 70	88	81

Initialed and dated by Examiner: _____ /_____

Appendix 2-10 Summary of MMT Functions:

Summary of the MMT Functions Needed for the Constant Score Test for Strength of Abduction

Please make sure to read the MMT manual for full function descriptions and instructions. Below is a summary to set-up the MMT for the Constant Score test for Strength of Abduction in Pounds.

Open MMT Pelican case and remove the MMT device. Using a Phillips head screw driver remove the removable door in the face of the device and install the battery provided. Make sure the battery is secure in the holder and replace the battery door and the screw. Activate the MMT by sliding the power switch to the "ON" position. This will bring you to the Main Measurement Screen.

Set the range to high:

1. In the Main Measurement Screen, press the RANGE button. "H" or "L" will be indicated on the Main Measurement Screen. Set the Range to "H". Note: the MMT is automatically reset when the range is changed.

Set the measurement scale to pounds:

1. In the Main Measurement Screen, press the LB/KG button. "LB" or "KG" will be indicated on the Main Measurement Screen. Set the measurement scale to "LB".

Activate the beep function:

1. Enter the Main Menu by pressing the MENU button.
2. Press the SCROLL button two times to move the cursor to BEEP.
3. Press enter to turn on BEEP.
4. Press SCROLL button four times to move the cursor to END.
5. Press ENTER to exit the menu.

Set the test time to 5 seconds:

1. Enter the Main Menu by pressing the MENU button.
2. Press the SCROLL button three times to move the cursor to TIME.
3. Press ENTER until the time is set at 5 seconds. Note: the time loops back to 1 second after 10 seconds is reached.
4. Press the SCROLL button three times to move the cursor to END.
5. Press ENTER to exit the menu.

Data Storage

The MMT has the ability to store test data in memory. This data can then be reviewed, analyzed or downloaded at a convenient time. If you choose to store data it is recommended that you manually

store test data. The Auto-Store function will store all test data including unwanted data such as test trials. It is recommended to use the STORE functions as only a back-up for test data.

Guidelines for test storage are:

1. The MMT can store up to 52 tests.
2. Only peak force and peak time are stored in memory.
3. The MMT can store data manually and automatically.
4. To manually store data, press the STORE button. This will place the reading on the Main Measurement Screen into storage. A single beep indicates successful storage.
5. To store automatically, the AUTO STORE function must be enabled. See the function description for Auto-Store in the MMT User's Manual. No beep is given in AUTO STORE mode.
6. When the 52 test capacity is reached, a warning screen is displayed every time storage is attempted. Store data must be emptied by deleting data using the clear all data registers procedure or by downloading the data registers. Refer to the MMT User's Manual for these functions.

Reset Function:

The reset function clears the display screens and sets the MMT for a new measurement. A reset is also required whenever a Diagnostic Error message is displayed. A reset can be triggered by several different functions.

Reset Guidelines:

1. The MMT is automatically reset when the power is applied.
2. A reset is also required whenever a Diagnostic Alert Message is displayed.
3. The MMT is automatically reset when the range is changed.
4. The MMT is automatically reset when the Calibration Routine is completed.
5. The Battery Saver Mode does not cause a Reset to occur.
6. Running the Main Menu does not cause a Reset to occur.
7. The MMT automatically resets on the application of a new force.
8. Pressing the RESET button will clear the display and set the MMT for a new measurement.
9. Pressing the RESET button also sets the zero point for measurements.

Caution: Since the RESET button re-zeros the MMT, force should not be applied while the RESET Button is pressed.

Note:

1. When performing repeated tests, inconsistent placement of the MMT will affect scores.
2. Extreme temperature, especially heat, may affect the values obtained.
3. The MMT cannot tolerate the stress of being used as a floor scale.
4. Care should be taken not to drop the MMT, as it may affect the calibration.
5. Exceeding the force limit (300lbs) may permanently damage the MMT.

Appendix 2-11 Constant Score Calculations

	Author	Title	Implant	# of patients	Age	Women	Pre-Op	Pre-Op Std Dev	Post-Op	Post-Op Std Dev	Difference	Adjusted Pre-Op	Adjusted Pre-Op Std Dev	Adjusted Post-Op	Adjusted Post-Op Std Dev	Difference	Mean follow up time (months)	% Good / Satisfied or Better
1	Pfahler	J Shoulder and Elbow Surg. 2006; 15:156-63	Tornier, Aequalis	705	64.3 (15-90)	74%	28.6		65.7	16.9	37.1	38.4		88.3	23.5	49.9	43	92%
2	Levy	J Shoulder and Elbwo Surg. 2004; 13:266-71	Copeland	42	71.5 (50-87)	69%	20		61.9		41.9	33.8		94		60.2	91	90%
3	Levy	J Bone Joing Surg Am, 2004; 86-A:512-8	Copeland	42	na	na	6	2.5	53.4	13.6	47.4	9	6.3	76	13.4	67	78	96%
4	LaFosse	J Shoulder Elbow Surg. 2009; 18(6): p. 864-73	Depuy Global	17	66.5 (45-81)	59%	25.1		68.5		43.4	28.8	11.7	79	17	50.2	28.7	100%
5	Lo	J Bone Joint Surg Am, 2005; 87-2178-2186	Neer Series 2	20	70.4	50%	28.7	16.4	70.8	17.2	42.1						24	
6	Rahme	J Bone Joint Surg Am, 2009; 91:1965-1972	Zimmer	26	64 (42-81)	64%	25		70		45						24	
7	Nutall	J Shoulder and Elbow Surg. 2007; 16:565-70	Depuy Global Keeled	10	71	30%	20		65		45						24	
			Depuy Global Pegged	10	63	30%	32		62		30							
8	Schumann	Am J Sports Med, 2010. 38(10): p. 2097-105	Promos	45	66.2	61%			70.8	13.8							33.6	
				49					77.2	10.6								
				6					69.3	9.7								
9	Boileau	J Shoulder Elbow Surg. 2002. 11(4): p. 351-9	Tornier, Aequalis	20	69 (59-77)	85%	25		67								24	
10	Collin	J Shoulder Elbow Surg. 2011. 20(8): p. 1217-23.	Tornier, Aequalis (flat)	32	na	na			63									
			Tornier, Aequalis (concave)	24					67									
11	Yian	J Bone Joint Surg Am, 2005. 87(9): p. 1928-36	Zimmer Anatomic	47	57	51%	39		70					85			40	
			Total	1095	Weighted Average		27.4	7.0	66.2	16.2	38.3	36.4	7.9	87.6	22.8	51.3	44.3	93%
12	Edwards	J Shoulder and Elbow Surg. 2003; 12:207-13	Tornier, Aequalis	601	67.3 (42-90)	75%	31.1		70.3		39.2	42.4		96.3		53.9	44	93%
13	Walch	J Bone Joing Surg Am, 2002;84-A:2186-91	Tornier, Aequalis	319	66.4 (54-90)	72%			68.6								53.5	
14	Young	J Bone Joint Surg Br, 2011. 93(2): p. 210-6	Tornier, Aequalis	226	66.9 (40-90)	69%	26.8	10.3	57.6	20	30.8	36.2	13.8	83	29.6	50.2	122.7	76%
15	Young	J Bone Joint Surg Am, 2012. 94(8): p. 685-93	Tornier, Aequalis	518	68 (35 to 90)	69%	30.1	12.3	65.2	16.8	35.1	40.1	16.5	93.8	25.3	50.2	103.6	90%

	Author	Title	Implant	# of patients	Age	Women	Pre-Op	Pre-Op Std Dev	Post-Op	Post-Op Std Dev	Difference	Adjusted Pre-Op	Adjusted Pre-Op Std Dev	Adjusted Post-Op	Adjusted Post-Op Std Dev	Difference	Mean follow up time (months)	% Good / Satisfied or Better
15	Young	J Bone Joint Surg Am, 2012. 94(8): p. 685-93	Tornier, Aequalis	518	68 (35 to 90)	69%	30.1	12.3	65.2	16.8	35.1	40.1	16.5	93.8	25.3	50.2	103.6	90%
2	Levy	J Shoulder and Elbow Surg, 2004; 13:266-71	Copeland	42	71.5 (50-87)	69%	20		61.9		41.9	33.8		94		60.2	91	90%
3	Levy	J Bone Joing Surg Am, 2004; 86-A:512-8	Copeland	42	na	na	6	2.5	53.4	13.6	47.4	9	6.3	76	13.4	67	78	96%
4	LaFosse	J Shoulder Elbow Surg, 2009. 18(6): p. 864-73	Depuy Global	17	66.5 (45-81)	59%	25.1		68.5		43.4	28.8	11.7	79	17	50.2	28.7	100%
5	Lo	J Bone Joint Surg Am, 2005; 87-2178-2186	Neer Series 2	20	70.4	50%	28.7	16.4	70.8	17.2	42.1						24	
6	Rahme	J Bone Joint Surg Am, 2009; 91:1965-1972	Zimmer	26	64 (42-81)	64%	25		70		45						24	
7	Nutall	J Shoulder and Elbow Surg, 2007; 16:365-70	Depuy Global Keeled	10	71	30%	20		65		45						24	
			Depuy Global Pegged	10	63	30%	32		62		30							
8	Schumann	Am J Sports Med, 2010. 38(10): p. 2097-105	Promos	45	66.2	61%			70.8	13.8							33.6	
				49					77.2	10.6								
				6					69.3	9.7								
9	Boileau	J Shoulder Elbow Surg, 2002. 11(4): p. 351-9	Tornier, Aequalis	20	69 (59-77)	85%	25		67								24	
10	Collin	J Shoulder Elbow Surg, 2011. 20(8): p. 1217-23.	Tornier, Aequalis (flat)	32	na	na			63									
			Tornier, Aequalis (concave)	24					67									
11	Yian	J Bone Joint Surg Am, 2005. 87(9): p. 1928-36	Zimmer Anatomic	47	57	51%	39		70					85			40	
			Total	908	Weighted Average		28.2	11.7	66.0	15.9	37.1	37.3	15.6	91.7	24.2	52.0	84.5	90%
12	Edwards	J Shoulder and Elbow Surg, 2003; 12:207-13	Tornier, Aequalis	601	67.3 (42-90)	75%	31.1		70.3		39.2	42.4		96.3		53.9	44	93%
13	Walch	J Bone Joing Surg Am, 2002;84-A;2185-91	Tornier, Aequalis	319	66.4 (54-90)	72%			68.6								53.5	
14	Young	J Bone Joint Surg Br, 2011. 93(2): p. 2104-6	Tornier, Aequalis	226	66.9 (40-90)	69%	26.8	10.3	57.6	20	30.8	36.2	13.8	83	29.6	50.2	122.7	76%
1	Pfahler	J Shoulder and Elbow Surg, 2006; 15:456-63	Tornier, Aequalis	705	64.3 (15-90)	74%	28.6		65.7	16.9	37.1	38.4		88.3	23.5	49.9	43	92%