RHEUMATOLOGY ARTHRITIS DATABASE AND REPOSITORY (RADAR)

Version Date: September 11, 2017

Manual of Operations

Table of Contents

Introduction

Purpose of Operations Manual

Welcome to UAB "Rheumatology Arthritis Database and Repository" (RADAR). This Manual of Operations acts as a guide to the Investigators and Coordinators regarding the day-to-day conduct of study protocol. This protocol maintains Human Subjects Research approval, issued by the UAB OIRB (Protocol IRB080317004).

Directory of Study Participants

Principal Investigator:

S. Louis Bridges, Jr., MD, PhD
Professor of Medicine and Microbiology
Division of Clinical Immunology and Rheumatology
Director, UAB Rheumatoid Arthritis Clinic
Phone: 205 934-4616
E-mail: sbridges@uabmc.edu

Co-Investigators:

Winn W. Chatham, MD,
Professor of Medicine
Division of Clinical Immunology and Rheumatology
Phone: 205 934-4212
E-mail: wchatham@uabmc.edu

Jeffrey R. Curtis, MD, MPH
Professor of Medicine
Division of Clinical Immunology and Rheumatology
Phone: 205 934-2130
E-mail: jrcurtis@uabmc.edu

Maria I. Danila, MD
Assistant Professor of Medicine
Division of Clinical Immunology and Rheumatology
Phone: 205 934-2799
E-mail: mdanila@uabmc.edu

Hui-Chen Hsu, PhD

Associate Professor of Medicine and Microbiology
Division of Clinical Immunology and Rheumatology
Phone: 205 934-8909
E-mail: hhsu@uabmc.edu

John D. Mountz, MD, PhD
Professor of Medicine and Microbiology
Division of Clinical Immunology and Rheumatology
Phone: 205 934-8909
E-mail: jdmountz@uabmc.edu

Kenneth G. Saag, MD
Professor of Medicine and Microbiology
Division of Clinical Immunology and Rheumatology
Phone: 205 934-0893
E-mail: ksaag@uabmc.edu

Jasvinder Singh, MD, MPH
Endowed Professor, Division of Clinical Immunology and Rheumatology
Director, Gout Clinic
Phone: 205-934-0315
Email : jsingh@uabmc.edu

David M. Spalding, MD
Professor of Medicine
Division of Clinical Immunology and Rheumatology
Phone: 205 930-8347
E-mail: dspaldin@uabmc.edu

Chander Raman, PhD
Professor of Medicine
Division of Clinical Immunology and Rheumatology
Phone: 205-934-2472
Email: craman@uabmc.edu

Laura B. Hughes, MD, MSPH
Professor of Medicine, Division of Clinical Immunology and Rheumatology
Director, Mercy Cooper Green Hospital Rheumatology Clinic
Phone: 205-934-7995

E-mail: lhughes@uabmc.edu
David M. Spalding, MD
Professor of Medicine
Division of Clinical Immunology and Rheumatology
Phone: 205 930-8347
E-mail: dspaldin@uabmc.edu

Beatriz Y. Hanaoka, MD
Assistant Professor of Medicine
Division of Clinical Immunology and Rheumatology
Shelby Building, Room 210
Phone: (205) 996-0843
Email: bhanaoka@uabmc.edu

Matthew Stoll, MD, PhD, MCSC
Associate Professor of Pediatrics
Division of Pediatric Rheumatology
Phone: 205-638-9438
Email: mstoll@peds.uab.edu

Theiss, Steven M., M.D.
Professor, John D. Sherrill Chair of Orthopaedic Surgery
Director, Division of Orthopaedic Surgery
Phone: 205-930-8339
Email: stheiss@uabmc.edu

Shawn R. Gilbert, M.D.
Professor, Division of Orthopaedic Surgery
Phone: 205-638-9540
Email: srgilbert@uabmc.edu

Ghanem, Elie, M.D.
Assistant Professor, Division of Orthopaedic Surgery
Phone: (205) 930-8545
E-mail: eghanem@uab.edu

Naranje, Sameer M., M.D., M.R.C.S.
Assistant Professor, Division of Orthopaedic Surgery

Phone: (205) 930-8339
E-mail: snaranje@uab.edu

Jean E. Oakes, M.D.
Assistant Professor, Director, Hand Fellowship Program
Division of Orthopaedic Surgery
Phone: 205-930-8339
Email: joakes@uabmc.edu

Brent Ponce, M.D.
Assistant Professor, Division of Orthopaedic Surgery
Phone: 205-930-8339
Email: bponce@uab.edu

Clinical Coordinators:
Laticia Woodruff RN, MSN
Research Nurse Coordinator
University of Alabama at Birmingham
Phone: 205-934-9843
E-mail: lplove@uabmc.edu

Vanessa Hill, BSN, MSN
Nurse Practitioner
Phone: 205-930-8247
E-mail: vkhill@uabmc.edu

Stephanie Biggers, RN
Nurse Coordinator
Phone: 205-934-1444
E-mail: sbiggers@uabmc.edu

Database Manager:
Dongmei Sun, PhD
Phone: 205-934-4867
E-mail: dongmeisun@uabmc.edu

Laboratory Manager:
Keith Wanzeck, MS

Phone: 205-975-9840
E-mail: kwanzeck@uabmc.edu

Program Manager:
Stephanie Ledbetter, MS
Phone: 205-934-7423
E-mail: sledbetter@uabmc.edu

RADAR Study Visit for Rheumatology Patients and Controls
Inclusion and Exclusion Criteria

A. RA Inclusion criteria will be:

1. Age ≥ 18 years

2. Diagnosis of RA, based on the cumulative presence of at least 4 of 7 American College of Rheumatology Criteria.

Exclusion criteria will be:

1. Age under 18 years of age.
2. Diagnosis of:
    - Systemic lupus erythematosus
    - Juvenile arthritis
    - Psoriasis or psoriatic arthritis
    - Chronic hepatitis C infection

B. OA Inclusion criteria will be:

1. Age ≥ 18 years
2. Diagnosis of OA, as determined by treating physician

Exclusion criteria will be:

1. Age under 18 years of age.
2. Diagnosis of:
    - Systemic lupus erythematosus
    - Rheumatoid Arthritis
    - Juvenile arthritis
    - Psoriasis or psoriatic arthritis

C. Gout Inclusion criteria will be:

1. Age ≥ 18 years
2. Diagnosis of Gout

Exclusion criteria will be:

1. Age under 18 years of age.
2. Diagnosis of:
   Systemic lupus erythematosus
   Juvenile arthritis
   Psoriasis or psoriatic arthritis

D. Scleroderma Inclusion criteria will be:
1. Age ≥ 18 years
2. Diagnosis of Scleroderma
Exclusion criteria will be:
1. Age under 18 years of age.
2. Diagnosis of:
   Systemic lupus erythematosus
   Juvenile arthritis

E. Seronegative spondyloarthropathy Inclusion criteria will be:
1. Age > 18 years
2. Diagnosis of Seronegative spondyloarthropathy
Exclusion criteria will be:
1. Age under 18 years of age.
2. Diagnosis of:
   Systemic lupus erythematosus
   Juvenile arthritis

F. Polymyositis/dermatomyositis Inclusion criteria will be:
1. Age > 18 years
2. Diagnosis of Polymyositis/dermatomyositis
   Exclusion criteria will be:
1. Age under 18 years of age.
2. Diagnosis of:
   Systemic lupus erythematosus
   Juvenile arthritis

G. For Controls
Inclusion criteria will be:
   1. Age > 18 years
   2. Self-declared “healthy”
Exclusion criteria will be:

1. Age under 18 years of age.
2. Diagnosis of:
    - Systemic lupus erythematosus
    - Juvenile arthritis
    - Inflammatory Arthritis (OA is not exclusion)
    - Autoimmune Disease
    - Musculoskeletal Disease

Instructions for Obtaining Patient ID Number Assignment

All participants signing an information letter for consent to participate in RADAR must be assigned a unique participant identification number. The clinical coordinator will choose the next consecutive six-digit number to assign to that participant. All data collection forms will include the unique patient identifier (PID). PID digits signify the following information: R-RADAR identifier

Digit #1- site (1-TKC Rheumatology Clinic)

Digit #2-5- consecutive patient number per site

Ex. R-10035- 35th patient enrolled

Digit #2- site (2- UAB Highlands Rheumatology Clinic)

Digit #2-5- consecutive patient number per site

Ex. R-20035- 35th patient enrolled

To ensure that PID's are not duplicated in enrollment efforts, coordinators will each be delegated a "block" of 100 PID's to assign to enrolling participants, accordingly.

Data collection

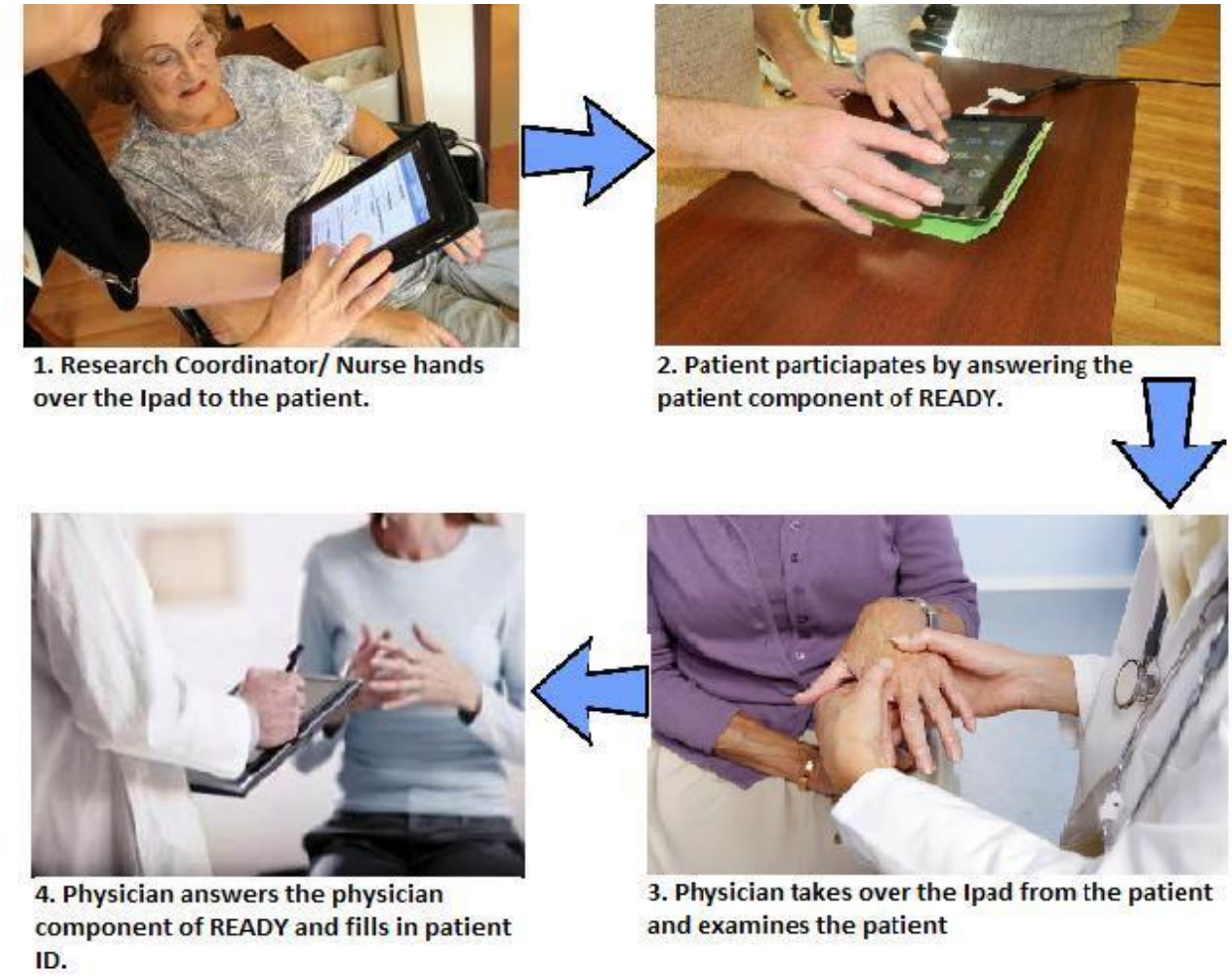
During the first study visit, study coordinators will complete an enrollment form to collect a brief medical history (Appendix III). Following enrollment, clinical data will be collected during the patient's clinic visits using the Gout Note and/or iPAD/tablet PC technology (Appendix V). Data routinely collected on the RADAR subjects includes RA medications, Disease Activity Score based on 28 joints (DAS), Health Assessment Questionnaire, as well as standard demographic and clinical data, including criteria for the diagnosis of RA, extra-articular manifestations, autoantibody status, etc.

UAB Rheumatology clinic has instituted data collection through the RhEumatoid Arthritis Disease activitY (READY) electronic measurement tool, that will collect data from patients using multiple existing, validated PRO instruments via tablet PC (iPad) with internet connection. If the patient is enrolled in RADAR, data collected through READY can be later linked to the medical record number by approved study personnel. Research and clinical staff will be available to provide direction and assistance to patients, if needed, with the iPAD and READY application. After the questionnaire is completed, a "patient assessment score" will be automatically calculated by the READY application, based on the patient's answers; providing data in terms of scores depicting patient reported outcomes. Physicians then enter clinical data, such as joint count, assessed disease activity, and changes in medication, into the READY application. This score and other data collected from the iPad are encrypted using Secure Socket Layer (SSL) technology will be stored in a password protected temporary database, accessible to select RADAR study personnel only.

Work flow for data collection, using the iPAD and READY app

Completion of the survey should take no longer than 5 minutes, presumably less, and will be used for both research and patient care purposes. No compensation will be provided to the participant for completing the survey. However, access to this site is strictly monitored and password protected. No information from which one could identify an individual patient or physician will be transmitted electronically.

Figure 1



Initial Enrollment Visit

Consent by verbal agreement and/or iPAD questionnaire, with signed Information Letter must be obtained before any data are collected for research purposes and before any research related procedures are performed. The participant will be assigned a participant number by the study coordinator. The next available number will be assigned to next participant enrolled in the study. The details regarding assignment of participant number are described above. Participants will be evaluated to ascertain that all entry criteria are fulfilled as detailed above. If the subject meets entry criteria and consents to participate in RADAR, the initial study visit will commence immediately.

To be completed by Coordinator Prior to Initial Visit:

1. Obtain a blank copy of the information letter for consent to participate in RADAR
2. Obtain labels and tubes for the blood samples
3. Pre-fill lab order for study blood draw (unless circumstances dictate otherwise)

To be completed by Coordinator During Initial Visit:

1. Review and confirm patient meets inclusion/exclusion criteria
2. Obtain consent using Information Letter (first visit only)
3. Copy Information letter and give participant and original is kept in RADAR folder, stored in a locked file cabinet.
4. Complete study blood collection. If collected in TKC clinic lab. Specimens will be picked up by coordinator.
5. Complete the following:

RADAR Enrollment Form *Variables* (first visit only):

Patient ID Number: to be assigned as above.

Visit Date: date subject enrolled in RADAR should be documented

Date of Onset of Polyarthralgias/Diagnosis: month and year.

Consent for Future Specimen Research and Future Contact

Height and weight: weight (in pounds) and height (in inches) in the participant's street clothes will be obtained at each visit.

Demographics and Participant Information: gender, date of birth, race and ethnicity (as declared by the participant)

RA Study Enrollment: Was participant enrolled in CLEAR or TEAR?

Autoantibodies: documentation of rheumatoid factor results (positive or negative, plus units and date obtained) and anti-CCP antibody results (positive or negative, plus units and date obtained). Only the most recent result for each should be recorded.

ACR/EULAR Criteria: questionnaire to be completed by coordinator or physician. (Gout Note)

Physical Examination and Health Questionnaire

Data collection via Gout Note or READY app on clinic iPAD (enrollment and subsequent visits)

Patient ID Number: To be assigned as above.

Visit Date: Each visit date for the subject should be clearly documented

Height and weight: Weight (in pounds) and height (in inches) in the participant's street clothes will be obtained at each visit.

Tender Joint (TNDRJNTS) and Swollen Joint (SWLNJNTS) Count: Joint tenderness on palpation or passive range of motion and examination for swelling will be assessed on 28 joints (0-28).

Modified Health Assessment Questionnaire (mHAQ): patient self-reported functional questionnaire filled out by patient and scored by physician or nurse coordinator. The total mHAQ score (0-8) is the mean of the score for the eight responses (total score count/24).

Patient Numeric Rating Scale (PATNRS): patient self-reported pain level based on the question "How active is your RA today". Patient as asked to choose from 1 to 10 (severity of RA increasing from left to right) to signify their answer to the question. 1 = Very well. 10 = Very poorly.

Physician Numeric Rating Scale (MDNRS): physician assessed RA severity level, signified by choice of number from 1 to 10 (severity of RA increasing from left to right). 1 = Very well. 10 = Very poorly.

Clinical Disease Activity Index (CDAI): the CDAI score (0-76) is the sum of the TNDRJNTS, SWLNJNTS, the PATVAS and the MDVAS.

Medication List: documentation of past and current RA medications, including most recent dosage.

Autoantibodies: documentation of rheumatoid factor results (positive or negative, plus units and date obtained) and anti-CCP antibody results (positive or negative, plus units and date obtained). Only the most recent result for each should be recorded.

Blood samples for isolation and storage of DNA, RNA, PBMC's and serum/plasma:

For specimen receipt in the lab, extensive QC protocols are in place to ensure proper handling, labeling and storage of specimens and specimen derivatives. All specimens received in the lab are required to have legible labels showing the study ID associated with the participant. This information, together with the date and study, are entered into secure password protected database systems to record proper receipt of the specimen, what was done with the specimen and how/where it was stored. Data entry is independently checked every week to ensure that the correct information has been recorded. Written standard operating procedures are available for all routine specimens handling in the laboratory. In addition, each staff member is trained in general laboratory safety, BSL2 level biosafety including training in blood borne pathogens, GCP and chemical safety.

All stored specimens are assigned a unique location in an appropriate freezer. As part of ongoing quality control, randomly picked boxes within the freezers are regularly audited.

All freezers are inspected visually each business day and a regular maintenance schedule is followed that includes the cleaning of filters and gaskets and removal of excess ice. In addition, all freezers are remotely monitored 24 hours a day for any alarm state and a call list is in place to notify appropriate staff when an alarm occurs.

Specimens collected from RA participants at enrollment visit and once annually:

- ☐ 1 x 8 ml purple top (BD P100 plasma protein preservation) tubes (for buffy coat, DNA, and plasma)
- ☐ 1 x 8 ml red/gray top (BD Vacutainer SST tubes, plastic, polymer gel with clot activator) (for serum)
- ☐ 1 x 9.5 ml green top EDTA tube (for peripheral blood cell isolation by Ficoll-Hypaque).

If requested, 2 green tops will be collected for RADAR ancillary studies.

- ☐ 1 x 2.5 ml PreAnalytiX PAXgene RNA tube

Synovial Fluid: collected at each visit for each participant, if synovial fluid is obtained during joint aspiration:

Synovial fluid (2 ml minimum, 50 ml maximum, per joint) from up to four joints will be obtained for isolation of cell types and stored.

Instructions for obtaining, handling, processing and storage of the SF samples can be found in Appendix II.

To be completed by Coordinator after the study visit:

1. Complete data collection and data entry (enrollment and other visits, as needed)
2. Deliver specimens to Dr. Bridges Lab. Notify Keith Wanzeck of delivery.
3. Confirm lab results for clinical blood testing: CRP and ESR tests (if available)
4. Confirm lab results for clinical synovial fluid testing: Cell count with differential, crystals, gram stain with cell culture (if available)

Subsequent RADAR Study Visits

We will obtain serial samples from multiple patients. Rather than mandate how often RADAR visits will occur, we will capture data and samples from patients on the days of the scheduled visits to their rheumatologist. Blood specimens are collected up to 4 visits annually, including enrollment visit. After the first 4 visits, blood specimens are collected once annually.

At all clinic visits, data is collected using iPAD (includes HAQ, Joint Count, MDAS, and PDAS).

Synovial fluid will be collected if joint aspiration if part of the patient's routine clinical care.

Specimens collected at each subsequent visit, up to four visits annually, including enrollment:

1 x 8 ml purple top (BD P100 plasma protein preservation) tubes (for buffy coat, DNA, and plasma)

1 x 8 ml red/gray top (BD Vacutainer SST tubes, plastic, polymer gel with clot activator) (for serum)

Withdrawal from the Study

The only reasons the participant will have follow-up discontinued are death, the participant withdraws consent, or if the participant is lost to follow-up. In these instances the Withdrawal form will be completed.

RADAR Patient Enrollment Case Report Form

Participant ID: _____ Weight: _____ VISIT DATE: _____

Diagnosis/ICD 9_____ Age at draw: _____ Gender: M F

Patient has completed information letter for consent to participate in RADAR for use of sample and information in research. Y N

Subject agrees to have specimen samples used in additional research in relation to other medical conditions, including but not limited to lupus, heart diseases, cancer and diabetes. Y N

Ethnicity: Hispanic or Latino ☐

Not Hispanic or Latino ☐

Unknown (not reporting) ☐

Race: American Indian/Alaskan Native ☐

Asian ☐

Native Hawaiian/Pacific Islander ☐

Black or African American ☐

White ☐

More than one race ☐

Unknown (not reporting) ☐

Have you been diagnosis with having inflammatory arthritis? Y N
(Includes Rheumatoid Arthritis, Psoriatic Arthritis, Ankylosing Spondylitis, Gouty Arthritis, other)

Have you been diagnosed with having autoimmune disease? Y N
(Includes Systemic Lupus Erythematosus, Crohns, Ulcerative Colitis, Myositis, Scleroderma, other)

Have you been diagnosed with having Osteoarthritis? Y N

Are you currently being treated for chronic illness? Y N
(Includes Multiple Sclerosis, Cystic Fibrosis, Cancer, Chronic Hepatitis, Diabetes Mellitus, other)

Have you been enrolled as a participant in another study?

CLEAR Y N U/NA **Profile** Y N U/NA **Other**_____

Patient Numerical Rating Scale

Considering all the ways in which illness and health conditions may affect you at this time, please indicate below how you are doing:

0 .5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0 8.5 9.0 9.5 10

Very Well — Not Very Well

Health Assessment Questionnaire

Please select fields, which best describes your abilities over the past week:

1. Dress yourself, including shoelaces and buttons?

☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do

2. Get in and out of bed?

☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do

3. Lift a full cup or glass to your mouth?

☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do

4. Walk outdoors on flat ground?

☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do

5. Wash and dry your body?

☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do

6. Bend down to pick up clothing from the floor?

☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do

7. Turn facets on and off?

☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do

8. Get in and out of a car, bus, train, or airplane?

☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do

9. Walk two miles or three kilometers, if you wish?

☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do

10. Participate in recreational activities and sports as you would like, if you wish?

☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do

Your PAIN:

How much pain have you had because of your condition OVER THE PAST WEEK?

On a scale of 1-10 (where zero represents 'no pain' and 10 represents 'severe pain': _____

Do you drink alcoholic beverages?

☐ Not at all ☐ On occasion ☐ 1-3 per week ☐ 1-2 per day ☐ 3 or more per day

---

Do you currently smoke cigarettes?

☐ No, never ☐ Not now, but I did in the past ☐ Yes, currently

---

RA participants only

	Tender (Right)	Swollen (Right)	Tender (Left)	Swollen (Left)
Shoulder	☐	☐	☐	☐
Elbow	☐	☐	☐	☐
Wrist	☐	☐	☐	☐
MCP-1	☐	☐	☐	☐
MCP-2	☐	☐	☐	☐
MCP-3	☐	☐	☐	☐
MCP-4	☐	☐	☐	☐
MCP-5	☐	☐	☐	☐
PIP-1	☐	☐	☐	☐
PIP-2	☐	☐	☐	☐
PIP-3	☐	☐	☐	☐
PIP-4	☐	☐	☐	☐
PIP-5	☐	☐	☐	☐
Knee	☐	☐	☐	☐

MD Numerical Rating Scale Disease Activity:

0 .5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0 8.5 9.0 9.5 10

RA Medications-Biologics

Drug Name	*Started Using Date	**Current Users		***Past but not current user		‡Start, Stop or change drug	†Reason
		Current Dose	Frequency	Most Recent Dose	Date of Most Recent Use		
Actemra							
Cimzia							
Enbrel							
Humira							
Kineret							
Orencia							
Remicade							
Rituxan							
Simponi							
Other Biologic							

RA Medications-DMARDS

Drug Name	*Started Using Date	**Current Users		***Past but not current user		‡Start, Stop or change drug	†Reason
		Current Dose	Frequency	Most Recent Dose	Date of Most Recent Use		
Arava							
Azulfidine							
Cyclosporine							
Imuran							
Minocin							
MTX							
Plaquenil							
Prednisone							

Pain Medications and NSAIDs

Drug Name	*Started Using Date	**Current Users		***Past but not current user		Start, Stop or change drug	Reason
		Current Dose	Frequency	Most Recent Dose	Date of Most Recent Use		

OA Participants Only

Affected Joints	**Left**	**Right**	**X-ray w/in the last year?**
Shoulder	☐	☐	☐
Elbow	☐	☐	☐
Wrist	☐	☐	☐
Hip	☐	☐	☐
Knee	☐	☐	☐
Hand	☐	☐	☐

Joint Surgeries

Joint /Year	**TR**	**ARTH**	**FUSION**
_____	☐	☐	☐
_____	☐	☐	☐
_____	☐	☐	☐
_____	☐	☐	☐
_____	☐	☐	☐

NOTES:

LAB RESULTS:

Lab Date: _____

CRP (mg/L): _____

ESR (mm/hr): _____

HSCRP (mg/L): _____

Synovial Fluid collected: ☐ No ☐ Yes

SF Cell count with diff: _____

Crystals present: ☐ No ☐ Yes

Gram stain with Cell culture: _____

RADAR Control Enrollment Case Report Form

Participant ID: _____ Registration DATE: _____

Age at draw: _____ Gender: M F

Patient has completed informed consent for use of sample and information in research. Y N

Subject agrees to have specimen samples used in additional research in relation to other medical conditions, including but not limited to lupus, heart diseases, cancer and diabetes. Y N

Ethnicity:

- Hispanic or Latino ☐
- Not Hispanic or Latino ☐
- Unknown (not reporting) ☐

Race:

- American Indian/Alaskan Native ☐
- Asian ☐
- Native Hawaiian/Pacific Islander ☐
- Black or African American ☐
- White ☐
- More than one race ☐
- Unknown (not reporting) ☐

Do you have inflammatory arthritis, such as RA, PsA, Gouty Arthritis, etc? Y N

Do you have autoimmune disease, such as SLE, Myositis, AnkSpon, Crohns, etc? Y N

Do you have OA? Y N

Are you being treated for chronic illness, such as MS, Cancer, Diabetes, ALS, CF, etc? Y N

Are you enrolled as a control in:

CLEAR Y N U/NA **Profile** Y N U/NA **Other**_____

Information Letter for Consent to participate in "Rheumatology and Arthritis Database and Repository (RADAR)"

You are invited to participate in a research study to identify genetic (inherited) and other factors that determine the severity of different rheumatic diseases. This study is being conducted under the direction of Dr. S. Louis Bridges, Jr., in the University of Alabama at Birmingham Department of Medicine. You were selected as a possible participant because you are age 18 years or older, a current patient at the UAB Rheumatology Clinic; or you may have been selected as a possible "control" (healthy) participant.

What will be involved if you participate? Your participation is completely voluntary. If you decide to participate in this research study, you will be asked to complete a series of questions and blood will be collected to obtain DNA, blood cells and serum samples which will be used for research. If synovial fluid is collected from your joint(s), a portion will be retained for this study. In some special cases, a stool specimen may be requested by your rheumatologist. If you agree, you will be provided with a stool collection kit and will obtain stool specimens personally at the most convenient time for you, with provided instructions and collection tools. This study does not involve medications or any other intervention, apart from your routine clinical care. Your total time commitment to participate in this study will be approximately 20 minutes.

Are there any risks or discomforts? Your participation in this study involves drawing blood by needle-stick, which may possibly cause minor discomfort, bruising of puncture site, or light-headedness. In most cases, blood will be drawn at the same time that blood tests are done for your routine care or treatment.

Are there any benefits to yourself or others? There is no direct benefit to you from this study, but the information gained may advance our understanding and treatment of persons with rheumatologic disease.

Will you receive compensation for participating? There will be no compensation for participation in this study.

Are there any costs? If you decide to participate, you will incur no cost.

If you change your mind about participating, Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in the study. You have the right not to participate and it will not jeopardize your medical care or result in a loss of benefits.

You are free to withdraw from this research study at any time. If you choose to withdraw, you may request that your biological samples be disposed of according to standard medical research procedures. Your choice to leave the study will not affect your relationship with this institution.

Any data and biological samples obtained in connection with this study will remain anonymous. We will protect your privacy and the data you provide will be de-identified before it is shared with other investigators, so that it cannot be linked back to you. Part of your blood samples will be used to identify genes and proteins that may be a sign someone may develop rheumatologic disease, influence how severe the disease is, and affect how well someone will respond to treatment. Information collected through your participation may be published in a professional journal and or presented at a professional meeting. However, your personal information will not be shared.

Proposed future research may require you to be contacted to ask for your consent to allow your specimens to be used.

Your consent to this study indicates that you will donate the specimens and data for medical research purposes. Your donation does not entitle you to compensation from any commercial use of the products that may be derived from the specimen.

_____ Yes, I agree to have my study specimens and or study data used in additional research in relation to other medical conditions, including but limited to, heart disease, cancer, or diabetes, as long as all personal identifying information is removed.

_____ No, I do not agree to have my study specimens and or study data used in additional research in relation to other medical conditions, including but limited to, heart disease, cancer, or diabetes, as long as all personal identifying information is removed.

If you have questions about this study, please contact Dr. S. Louis Bridges, Jr. or his associates at UAB at 205-934-7000.

If you have questions about your rights as a research participant, you may contact the University of Alabama at Birmingham Office of Institutional Review Board for Human Use by phone at (205) 934-3789 or 1-800-822-8816. If calling the toll-free number, press the option for "all other calls" or ask the operator for extension 4-3789. Regular hours for the Office of the IRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday. You may also call this number in the event the research staff cannot be reached or you wish to talk to someone else.

HAVING READ THE INFORMATION ABOVE, YOU MUST DECIDE IF YOU WANT TO PARTICIPATE IN THIS RESEARCH PROJECT. IF YOU DECIDE TO PARTICIPATE, PLEASE CLICK ON THE LINK BELOW.

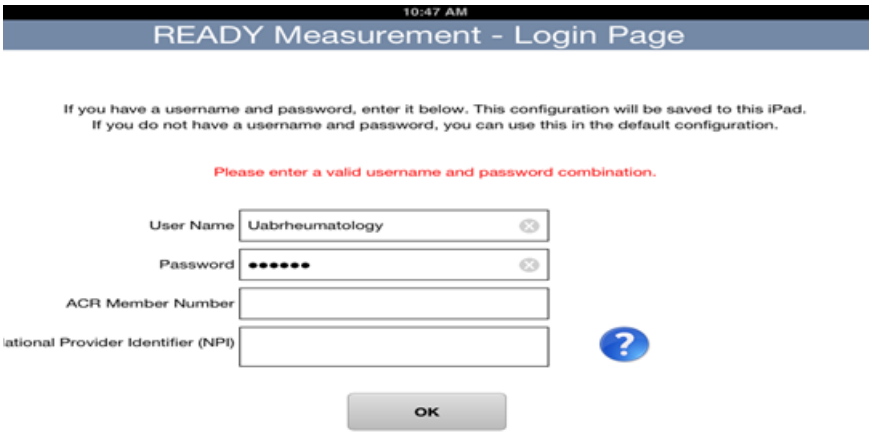
YOU MAY PRINT A COPY OF THIS LETTER TO KEEP.

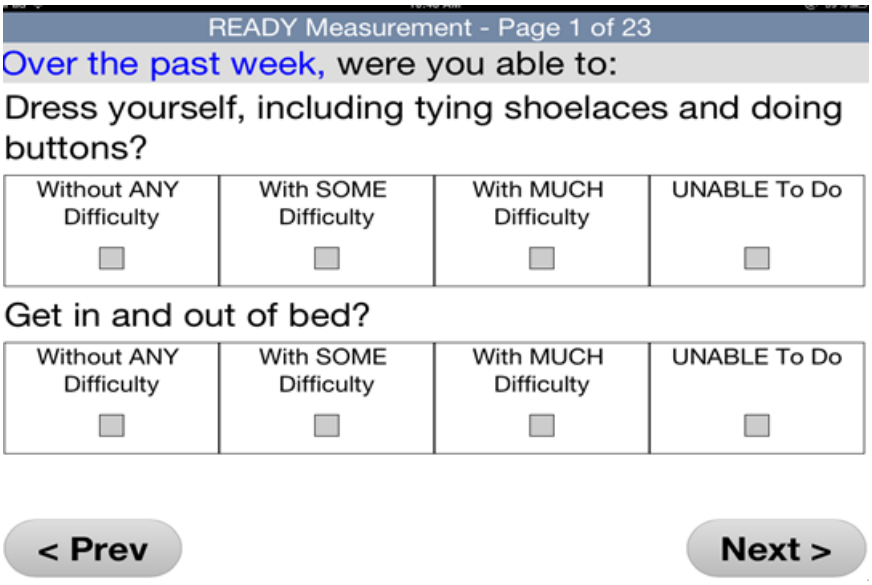
S. Louis Bridges, Jr, MD, PhD December 29, 2016

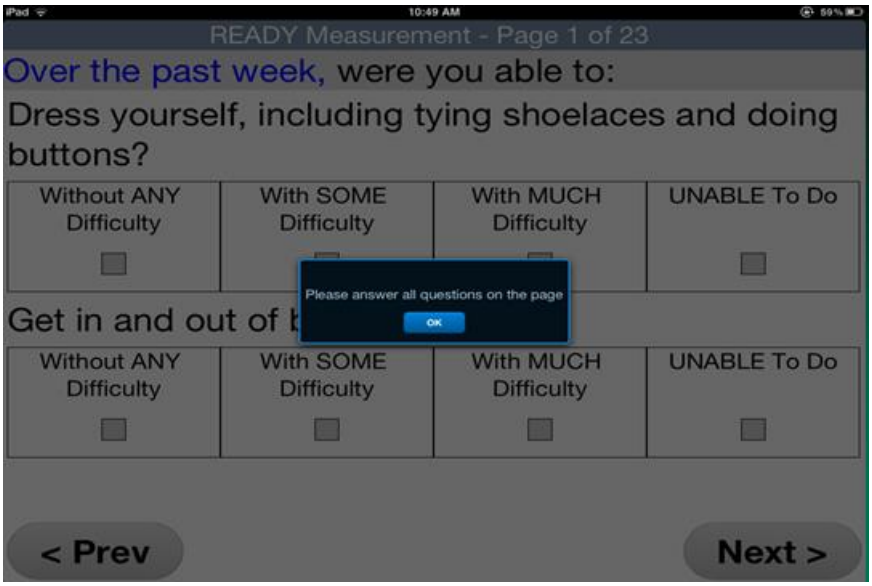
Investigator Date

The University of Alabama at Birmingham Institutional Review Board has approved this document for use from _____ to _____. Protocol #X080317004

Rheumatoid Arthritis Disease Activity (READY) Measurement



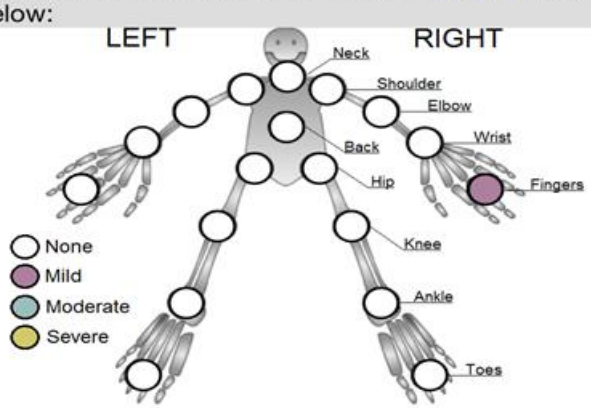

READY Measurement - Page 1 of 23
Over the past week, were you able to:
Dress yourself, including tying shoelaces and doing buttons?
Without ANY Difficulty
With SOME Difficulty
With MUCH Difficulty
UNABLE To Do
Get in and out of bed?
Without ANY Difficulty
With SOME Difficulty
With MUCH Difficulty
UNABLE To Do
< Prev
Next >


READY Measurement - Page 1 of 23
Over the past week, were you able to:
Dress yourself, including tying shoelaces and doing buttons?
Without ANY Difficulty
With SOME Difficulty
With MUCH Difficulty
UNABLE To Do
Please answer all questions on the page
OK
Get in and out of b
Without ANY Difficulty
With SOME Difficulty
With MUCH Difficulty
UNABLE To Do
< Prev
Next >

iPad 10:50 AM 58%

READY Measurement - Page 8 of 23

Please indicate the amount of pain you are having today in each of the joints listed below:



< Prev

Next >

iPad 10:51 AM 58%

READY Measurement - Page 9 of 23

How much pain have you had because of your arthritis over the past week? Indicate on the scale how severe your pain has been:

No Pain — Pain as bad as could be

0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0 8.5 9.0 9.5 10.0

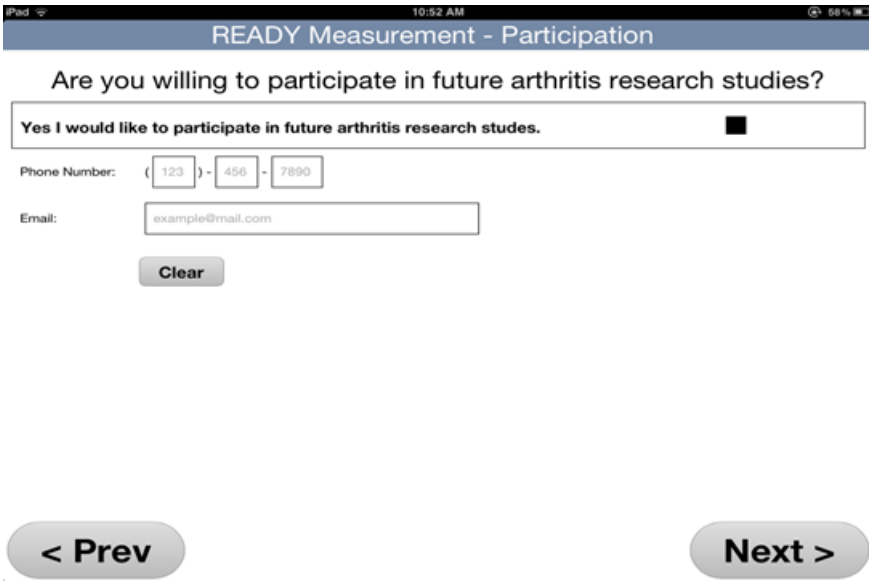
How much of a problem has unusual fatigue or tiredness been for you in the past week? Indicate on the scale how severity of your fatigue:

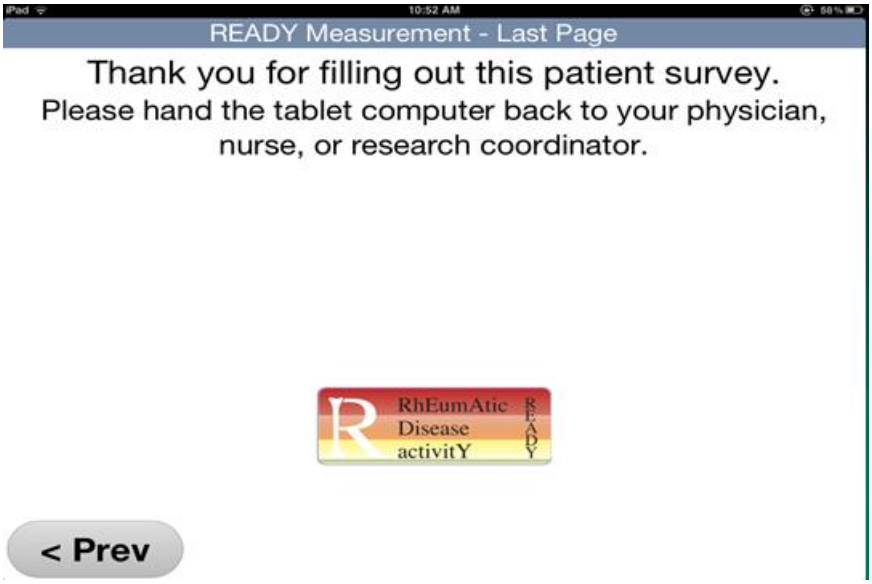
No Pain — Pain as bad as could be

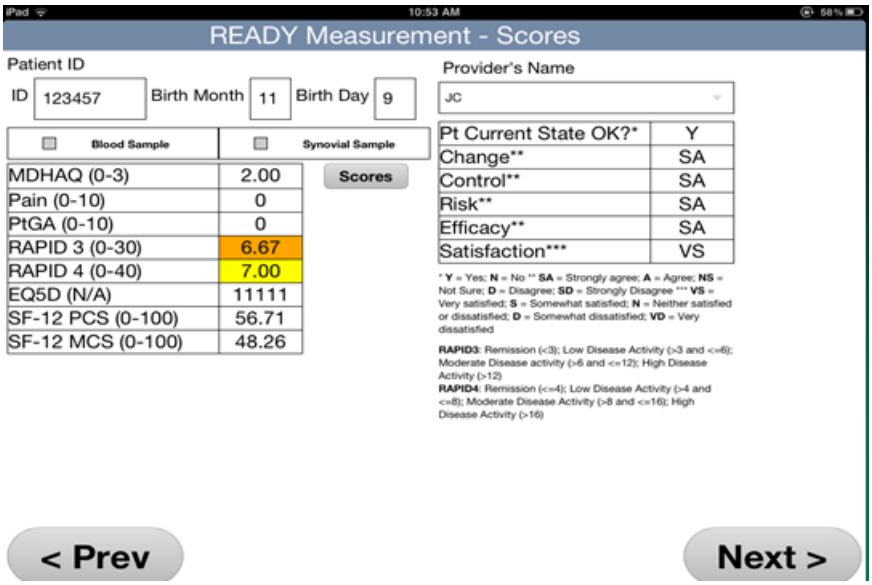
0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0 8.5 9.0 9.5 10.0

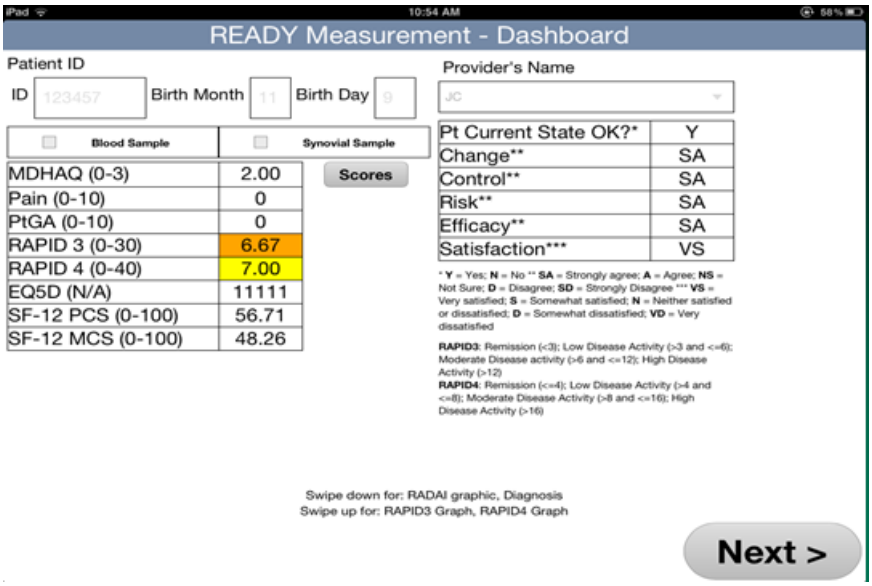
< Prev

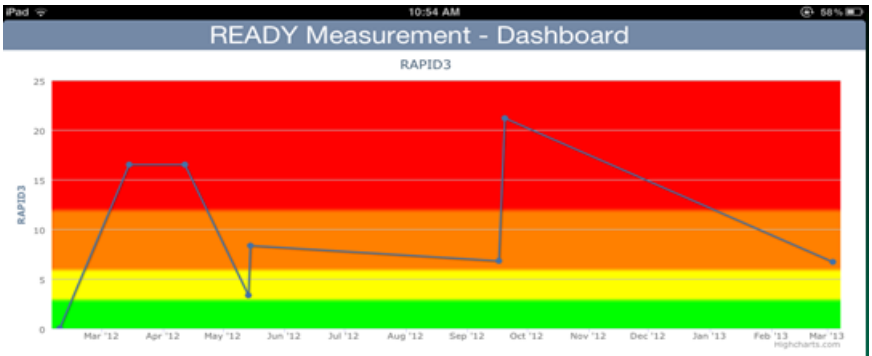
Next >

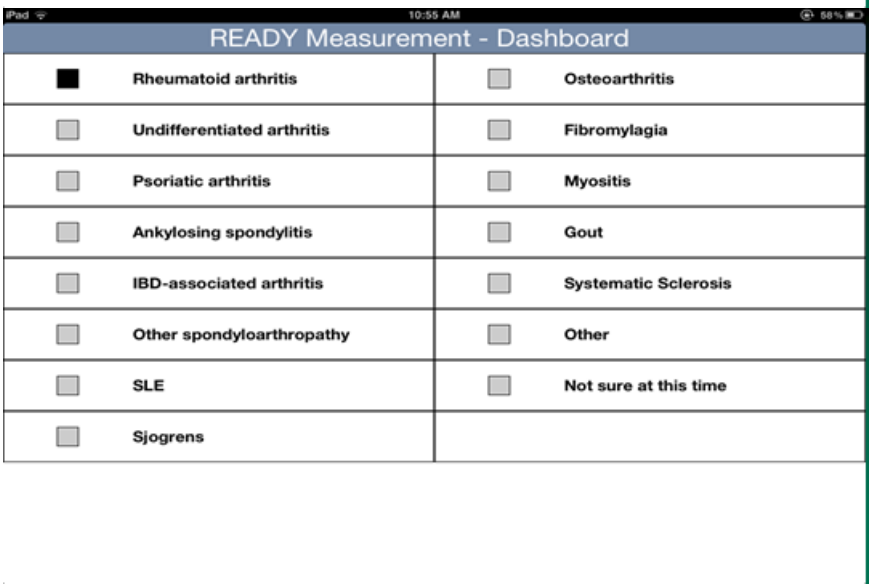

iPad
10:52 AM
58%
READY Measurement - Participation
Are you willing to participate in future arthritis research studies?
Yes I would like to participate in future arthritis research studes.
Phone Number:
(123) - 456 - 7890
Email:
example@mail.com
Clear
< Prev
Next >

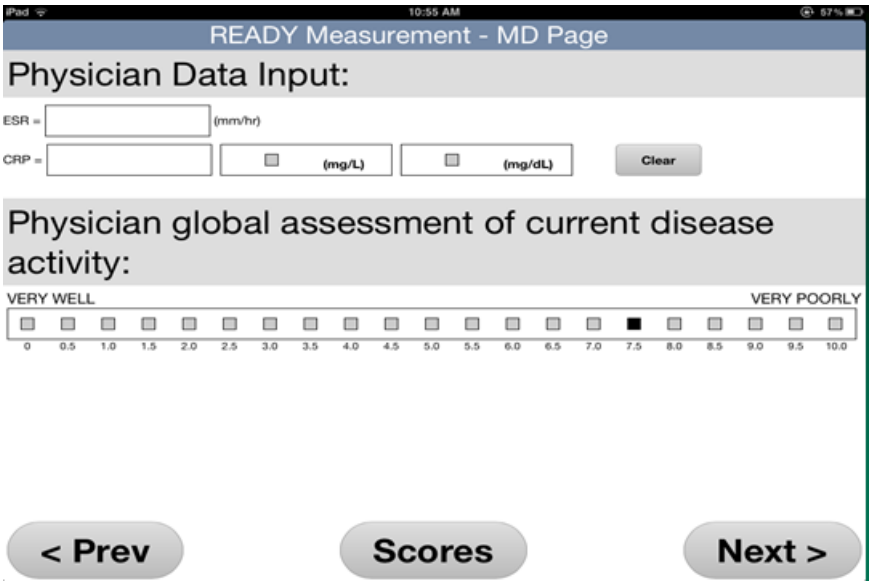

iPad
10:52 AM
58%
READY Measurement - Last Page
Thank you for filling out this patient survey.
Please hand the tablet computer back to your physician, nurse, or research coordinator.
RhEumAtic Disease activitY
READY
< Prev

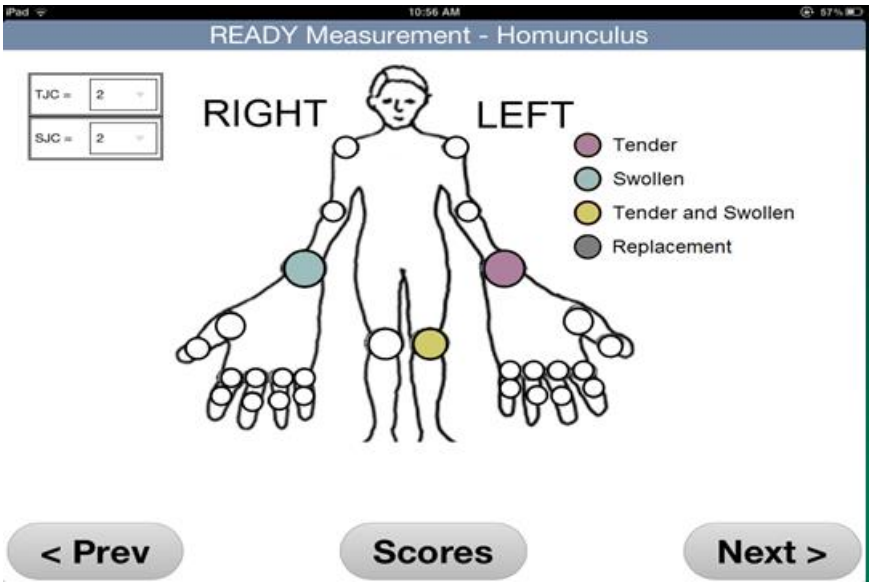

iPad
10:53 AM
58%
READY Measurement - Scores
Patient ID
ID 123457
Birth Month 11
Birth Day 9
Provider's Name
JC
Blood Sample
Synovial Sample
MDHAQ (0-3) 2.00
Scores
Pain (0-10) 0
PtGA (0-10) 0
RAPID 3 (0-30) 6.67
RAPID 4 (0-40) 7.00
EQ5D (N/A) 11111
SF-12 PCS (0-100) 56.71
SF-12 MCS (0-100) 48.26
Pt Current State OK?* Y
Change** SA
Control** SA
Risk** SA
Efficacy** SA
Satisfaction*** VS
* Y = Yes; N = No ** SA = Strongly agree; A = Agree; NS = Not Sure; D = Disagree; SD = Strongly Disagree *** VS = Very satisfied; S = Somewhat satisfied; N = Neither satisfied or dissatisfied; D = Somewhat dissatisfied; VD = Very dissatisfied
RAPID3: Remission (<3); Low Disease Activity (>3 and <=6); Moderate Disease activity (>6 and <=12); High Disease Activity (>12)
RAPID4: Remission (<=4); Low Disease Activity (>4 and <=8); Moderate Disease Activity (>8 and <=16); High Disease Activity (>16)
< Prev
Next >

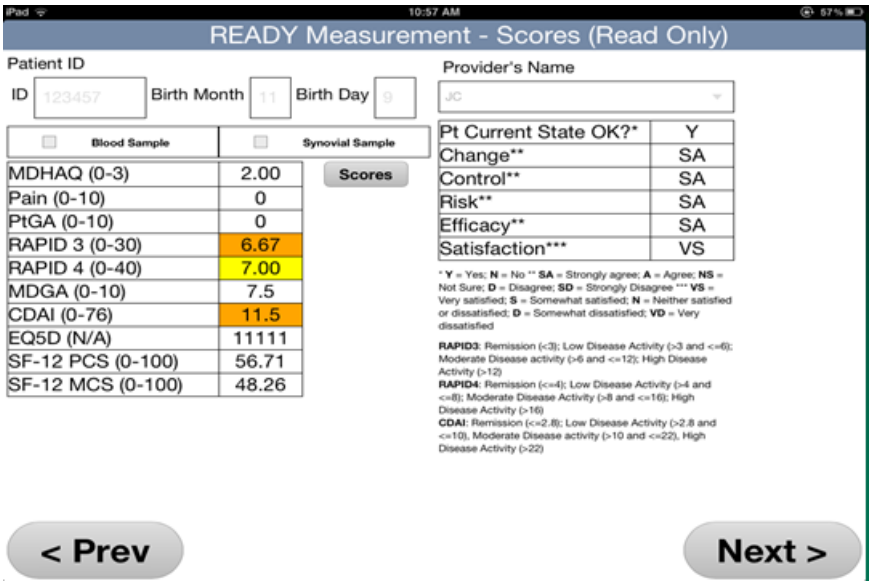

iPad
10:54 AM
58%
READY Measurement - Dashboard
Patient ID
ID 123457
Birth Month 11
Birth Day 9
Provider's Name
JC
Blood Sample
Synovial Sample
MDHAQ (0-3) 2.00
Scores
Pain (0-10) 0
PtGA (0-10) 0
RAPID 3 (0-30) 6.67
RAPID 4 (0-40) 7.00
EQ5D (N/A) 11111
SF-12 PCS (0-100) 56.71
SF-12 MCS (0-100) 48.26
Pt Current State OK?* Y
Change** SA
Control** SA
Risk** SA
Efficacy** SA
Satisfaction*** VS
* Y = Yes; N = No ** SA = Strongly agree; A = Agree; NS = Not Sure; D = Disagree; SD = Strongly Disagree *** VS = Very satisfied; S = Somewhat satisfied; N = Neither satisfied or dissatisfied; D = Somewhat dissatisfied; VD = Very dissatisfied
RAPID3: Remission (<3); Low Disease Activity (>3 and <=6); Moderate Disease activity (>6 and <=12); High Disease Activity (>12)
RAPID4: Remission (<=4); Low Disease Activity (>4 and <=8); Moderate Disease Activity (>8 and <=16); High Disease Activity (>16)
Swipe down for: RADAI graphic, Diagnosis
Swipe up for: RAPID3 Graph, RAPID4 Graph
Next >

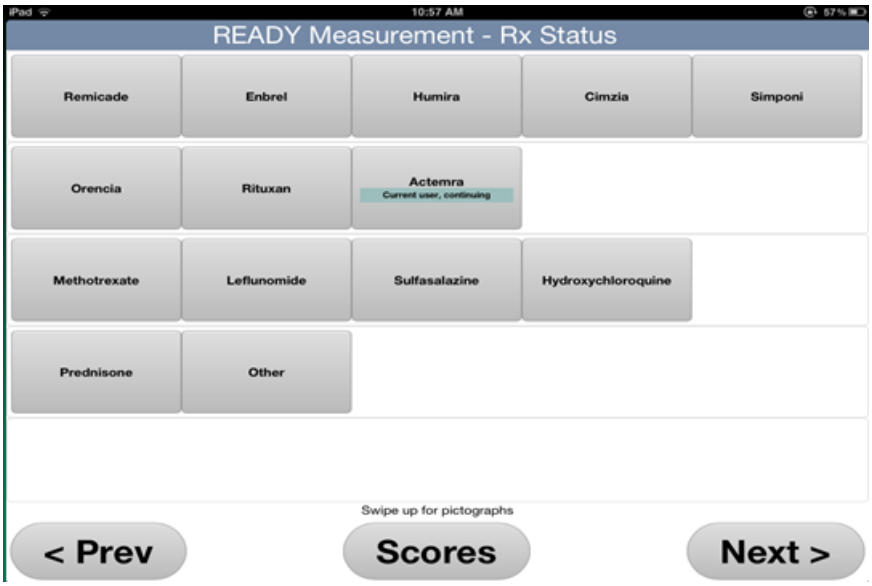

iPad
10:54 AM
58%
READY Measurement - Dashboard
RAPID3
RAPID3
25
20
15
10
5
0
Mar '12
Apr '12
May '12
Jun '12
Jul '12
Aug '12
Sep '12
Oct '12
Nov '12
Dec '12
Jan '13
Feb '13
Mar '13
Highcharts.com

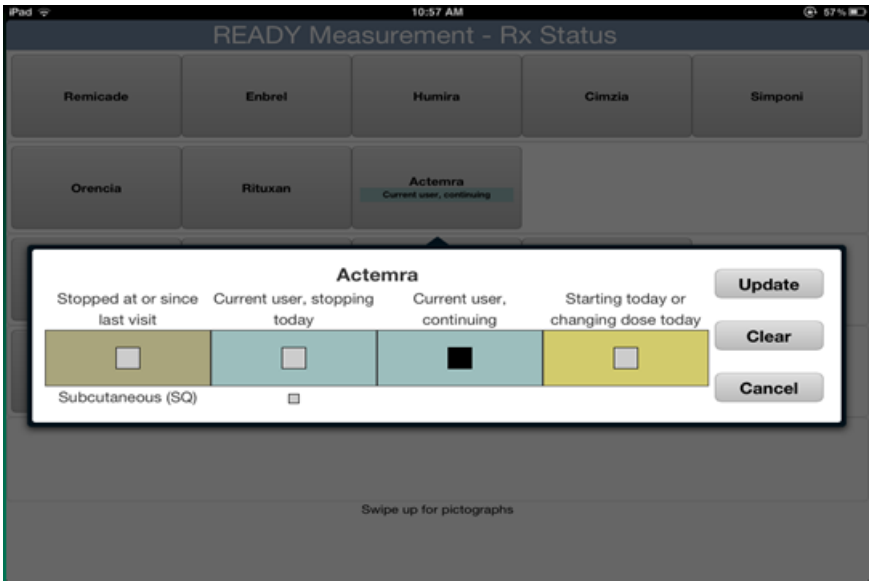

iPad
10:55 AM
58%
READY Measurement - Dashboard
Rheumatoid arthritis
Osteoarthritis
Undifferentiated arthritis
Fibromylagia
Psoriatic arthritis
Myositis
Ankylosing spondylitis
Gout
IBD-associated arthritis
Systematic Sclerosis
Other spondyloarthropathy
Other
SLE
Not sure at this time
Sjogrens

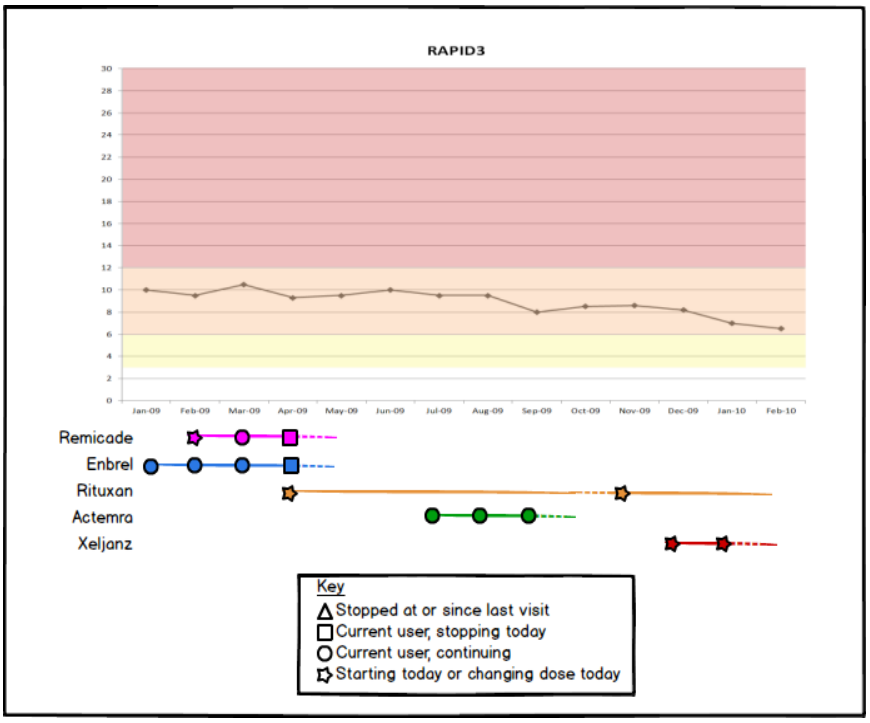

iPad
10:55 AM
57%
READY Measurement - MD Page
Physician Data Input:
ESR =
(mm/hr)
CRP =
(mg/L)
(mg/dL)
Clear
Physician global assessment of current disease activity:
VERY WELL
VERY POORLY
0 0.5 1.0 1.5 2.0 2.5 3.0 3.5 4.0 4.5 5.0 5.5 6.0 6.5 7.0 7.5 8.0 8.5 9.0 9.5 10.0
< Prev
Scores
Next >

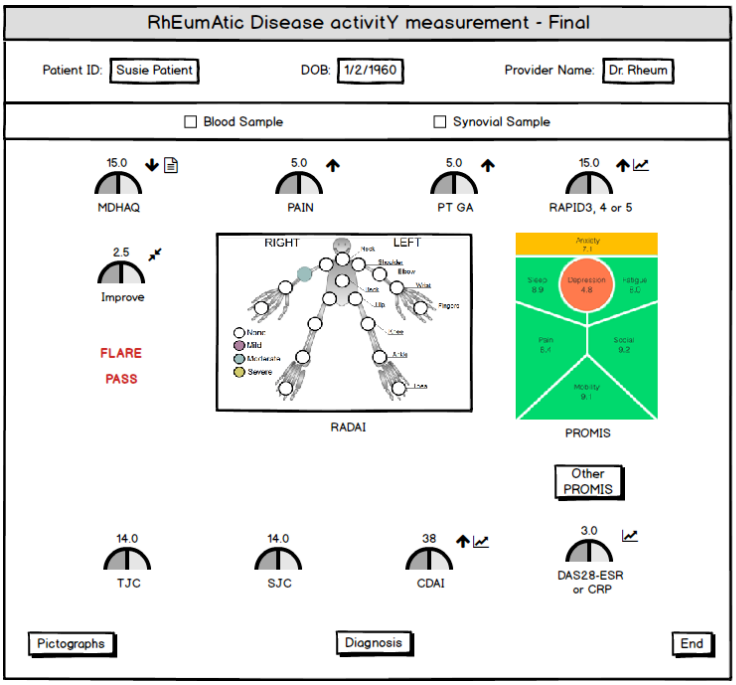

iPad
10:56 AM
57%
READY Measurement - Homunculus
TJC =
2
SJC =
2
RIGHT
LEFT
Tender
Swollen
Tender and Swollen
Replacement
< Prev
Scores
Next >


iPad
10:57 AM
57%
READY Measurement - Scores (Read Only)
Patient ID
ID 123457
Birth Month 11
Birth Day 9
Provider's Name
JC
Blood Sample
Synovial Sample
Scores
MDHAQ (0-3) 2.00
Pain (0-10) 0
PtGA (0-10) 0
RAPID 3 (0-30) 6.67
RAPID 4 (0-40) 7.00
MDGA (0-10) 7.5
CDAI (0-76) 11.5
EQ5D (N/A) 11111
SF-12 PCS (0-100) 56.71
SF-12 MCS (0-100) 48.26
Pt Current State OK?* Y
Change** SA
Control** SA
Risk** SA
Efficacy** SA
Satisfaction*** VS
* Y = Yes; N = No ** SA = Strongly agree; A = Agree; NS = Not Sure; D = Disagree; SD = Strongly Disagree *** VS = Very satisfied; S = Somewhat satisfied; N = Neither satisfied or dissatisfied; D = Somewhat dissatisfied; VD = Very dissatisfied
RAPID3: Remission (<3); Low Disease Activity (>3 and <=6); Moderate Disease activity (>6 and <=12); High Disease Activity (>12)
RAPID4: Remission (<=4); Low Disease Activity (>4 and <=8); Moderate Disease Activity (>8 and <=16); High Disease Activity (>16)
CDAI: Remission (<=2.8); Low Disease Activity (>2.8 and <=10), Moderate Disease activity (>10 and <=22), High Disease Activity (>22)
< Prev
Next >


iPad
10:57 AM
57%
READY Measurement - Rx Status
Remicade
Enbrel
Humira
Cimzia
Simponi
Orencia
Rituxan
Actemra
Current user, continuing
Methotrexate
Leflunomide
Sulfasalazine
Hydroxychloroquine
Prednisone
Other
Swipe up for pictographs
< Prev
Scores
Next >

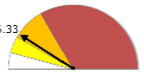

iPad
10:57 AM
57%
READY Measurement - Rx Status
Remicade
Enbrel
Humira
Cimzia
Simponi
Orencia
Rituxan
Actemra
Current user, continuing
Actemra
Stopped at or since last visit
Current user, stopping today
Current user, continuing
Starting today or changing dose today
Update
Clear
Cancel
Subcutaneous (SQ)
Swipe up for pictographs


RAPID3
30
28
26
24
22
20
18
16
14
12
10
8
6
4
2
0
Jan-09
Feb-09
Mar-09
Apr-09
May-09
Jun-09
Jul-09
Aug-09
Sep-09
Oct-09
Nov-09
Dec-09
Jan-10
Feb-10
Remicade
Enbrel
Rituxan
Actemra
Xeljanz
Key
Stopped at or since last visit
Current user, stopping today
Current user, continuing
Starting today or changing dose today



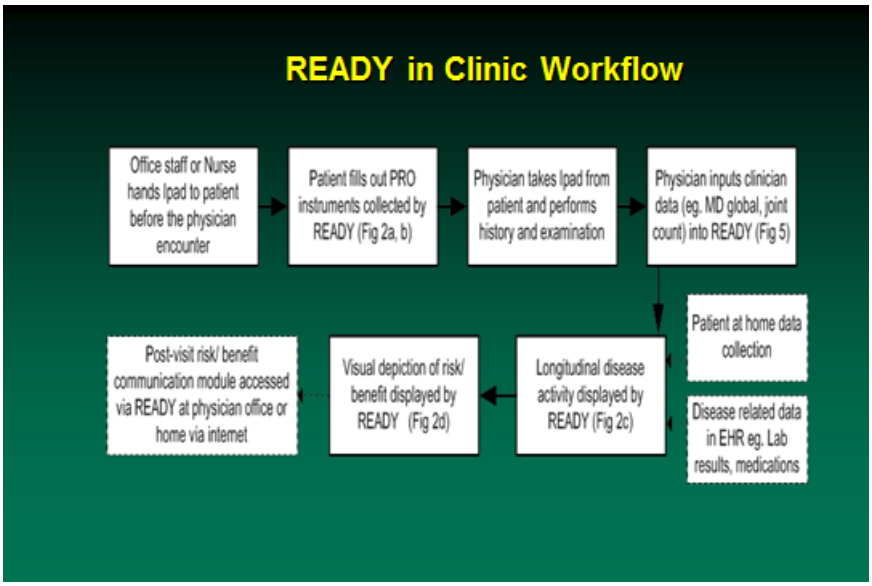
Notes: This is the last screen of the app and shows all possible scores with the ability to see the pictographs and diagnosis. What scores are displayed will be based on the configuration profile.

KEY



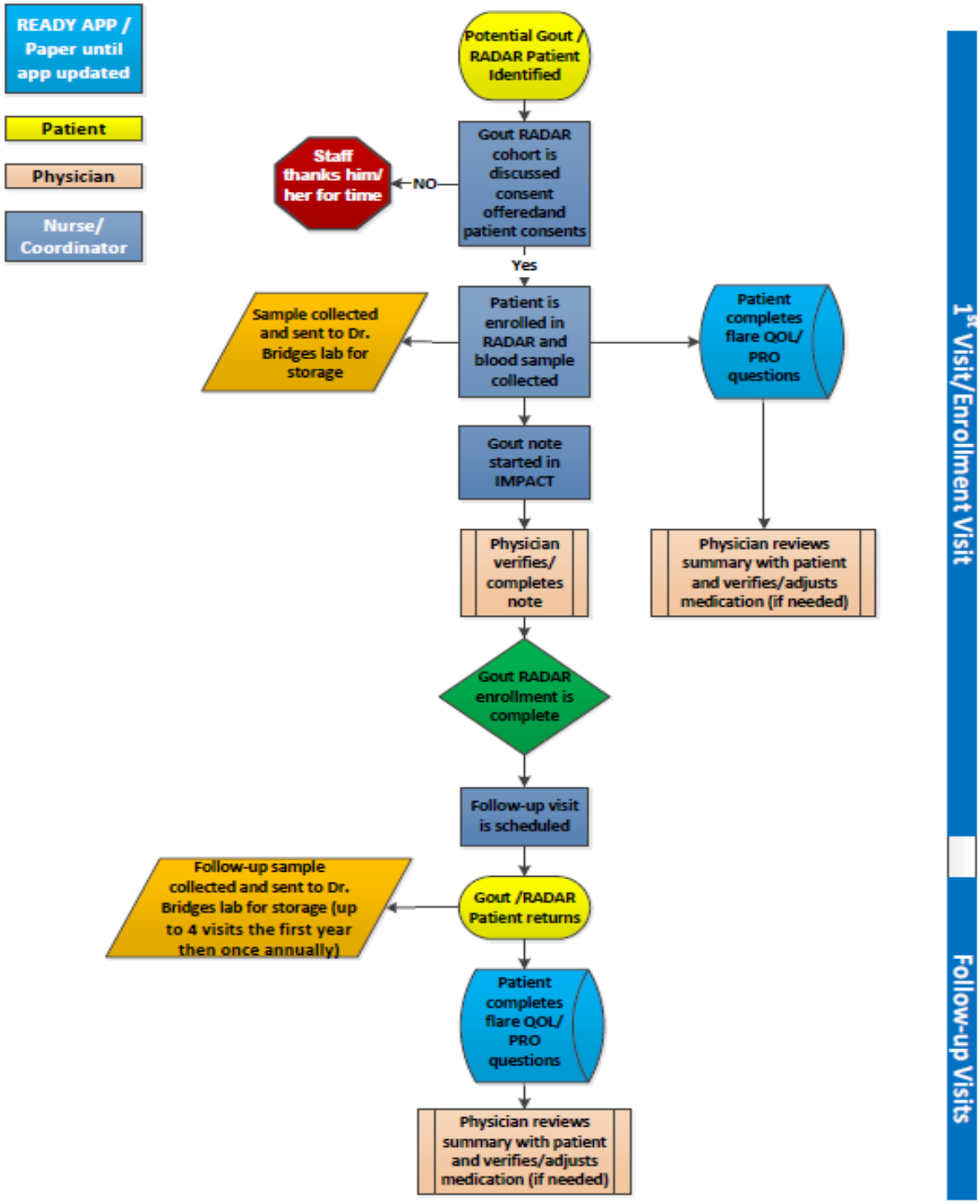
Gauge color-coded based on disease activity thresholds (i.e., remission, low, moderate, and high) and needle points to value of score.

- Score higher than last visit
- Score lower than last visit
- Score the same as last visit
- Click (anywhere on MDHAQ icon) to view score details
- Click (anywhere on RAPIDx icon) to view trend/med chart



RADAR Gout Study Visit

RADAR Gout Study Visit Workflow



Drug Name	NEVER Taken	Dose CURRENTLY Taking	Frequency	Year Started (**MM/DD/YYYY)**	Year Stopped (**MM/DD/YYYY)**	Stopped Medication Reason # (See list below)
Allopurinol	☐	☐ 100 mg ☐ 200 mg ☐ 300 mg ☐ 400mg ☐_____ mg ☐Unknown	☐ q.d. ☐ BID ☐ TID ☐ PRN ☐ Other _____	_ _/ _ _/ _ _ _ _	_ _/ _ _/ _ _ _ _	
Febuxostat (also known as Uloric®)	☐	☐ 40 mg ☐ 80 mg ☐ 120 mg ☐_____ mg ☐Unknown	☐ q.d. ☐ BID ☐ TID ☐ PRN ☐ Other _____	_ _/ _ _/ _ _ _ _	_ _/ _ _/ _ _ _ _	
Probenecid (also known as Benemid ®)	☐	☐_____ mg ☐Unknown	☐ q.d. ☐ BID ☐ TID ☐ PRN ☐ Other _____	_ _/ _ _/ _ _ _ _	_ _/ _ _/ _ _ _ _	
Colchicine (also known as Colcrys®)	☐	☐ 0.6 mg ☐1.2 mg ☐Unknown	☐ q.d. ☐ BID ☐ TID ☐ PRN ☐ Other _____	_ _/ _ _/ _ _ _ _	_ _/ _ _/ _ _ _ _	

Col-Benemid (also known as Colchicine-Probenecid)	☐	☐ 0.5 mg and 500 mg ☐Unknown	☐ q.d. ☐ BID ☐ TID ☐ PRN ☐ Other _____	_ _/ _ _/ _ _ _ _	_ _/ _ _/ _ _ _ _	
Lesinurad (also known as Zurampic®	☐	☐ 200 mg ☐Unknown	☐ q.d. ☐ BID ☐ TID ☐ PRN ☐ Other _____	_ _/ _ _/ _ _ _ _	_ _/ _ _/ _ _ _ _	
Anakinra (also known as Kineret®)	☐	☐ 100 mg/0.67 mL		_ _/ _ _/ _ _ _ _	_ _/ _ _/ _ _ _ _	
Krystexxa® (also known as pegloticase)	☐	☐ 8 mg/mL		_ _/ _ _/ _ _ _ _	_ _/ _ _/ _ _ _ _	
Cherry extract / Cherry juice	☐	☐_____ mg ☐Unknown		_ _/ _ _/ _ _ _ _	_ _/ _ _/ _ _ _ _	

Gout Clinic Survey

(Provider/Nurse/ Research assistance Administered Module on iPad:)

Provider Last Name: _____

Participant Last Name: _____ Participant First Name: _____

DOB _ _/ _ _/ _ _ _ _
MM DD YYYY

Sex : ☐Male ☐Female

Ethnicity/Race: Hispanic or Latino ☐Yes ☐No

Race: ☐American Indian or Alaska Native
☐Asian
☐Black or African American
☐Native Hawaiian or Other Pacific Ilander
☐White

Patient has completed informed consent for use of blood sample and health information for research.
☐Yes ☐No
Subject agrees to have biospecimen samples used in additional research in relation to other medical conditions, including but not limited to cardiovascular disease, cerebrovascular disease, hyperlipidemia, kidney disease, cancer and diabetes.
☐Yes ☐No

Blood Sample Collection: ☐ Yes ☐ No ☐ Already Collected Date: _ _/_ _/_ _ _ _

Form completed by coordinator last names: _____ Visit Date: _ _/ _ _/ _ _ _ _

Have you **EVER** used or taken a prescription medication for gout?
☐Yes ☐No

Reason Stopped Codes
From the list below, select the number that corresponds to the reason for each listed drug that has been stopped.
1 – No efficacy
2 – Side effects/other medical condition
3 – Cost concerns
4 – Recommended by healthcare provider
5 – Other reasons/Unknown (please specify)

Has a doctor or other health care provider **EVER** told you that you have any of the following?

Metabolic Syndrome	☐Yes ☐No
Type 2 DM	☐Yes ☐No
Hypertension	☐Yes ☐No
CAD	☐Yes ☐No
PVD	☐Yes ☐No
CVA	☐Yes ☐No
CKD	☐Yes ☐No
Nephrolithiasis	☐Yes ☐No
Kidney Transplant	☐Yes ☐No

CURRENT or PAST participation in the following study(s):

	Currently enrolled in study	Eligible for study following chart/lab review for I/E	Contacted/discussed study opportunity, added to study/patient list
AMPEL - Pegloticase	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No
Amgen- Denosumab Gout Erosions Study	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No
UAB Gout Patient Registry - RADAR	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No
AZ Fitbit Study	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No
Horizon- Pegloticase Study	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No
SOBI- Anakinra	☐Yes ☐No	☐Yes ☐No	☐Yes ☐No

Synovial fluid analysis: ☐ MSU negative / ☐ MSU Positive / ☐ Not done

Location of aspirate:

- ❑ 1st MTP joint
- ❑ Ankle
- ❑ Foot
- ❑ Knee
- ❑ Elbow
- ❑ Hand
- ❑ Wrist
- ❑ Other

Date: _ _/ _ _/ _ _ _ _

MM DD YYYY

MSU Crystal identified by UAB rheumatology ❑

MSU Crystal result documented by review of synovial fluid report ❑

Patient reported MSU crystal result

Rheumatology Arthritis Database and Repository (RADAR) Joint

This study will collect joint tissue and peripheral blood from patients with arthritis and from unaffected controls for current and future IRB-approved research studies.

Contact Information:

Principal Investigator: S. Louis Bridges, Jr., MD, PhD
Phone: 205 934-4616 (Direct Line); 205 266-6997 (Cell); email: sbridges@uabmc.edu

Program Manager: Stephanie Ledbetter
Phone: 205 934-7423 (Direct Line); 205 410-8480 (Cell); email: sledbetter@uabmc.edu

Laboratory Manager: Keith Wanzeck
Phone: 205 975-9840 (Direct Line), kwanzeck@uabmc.edu

RADAR Joint Inclusion and Exclusion Criteria

Patients	Controls
Inclusion Criteria: Sex: Male or Female Race/Ethnicity: All Age: >18 years Health status: Arthritis (Rheumatoid arthritis, psoriatic arthritis, osteoarthritis)	**Inclusion Criteria:** Sex: Male or Female Race/Ethnicity: All Age: >18 years Health status: Undergoing joint surgery for a clinically indicated reason other than arthritis (trauma, cancer, etc.)
Exclusion Criteria: Age under 18 years Diagnosis of: Systemic lupus erythematosus or Juvenile arthritis, idiopathic arthritis	**Exclusion Criteria:** Age under 18 years Diagnosis of arthritis of any type

RADAR Joint Study Visit Checklist

- ☐ **Obtain Informed Consent:**

- RADAR Joint Consent to be completed
- Must be signed by participant prior to blood and data collection

- ☐ **Assign PID**

- Ex. R-30001 (R=RADAR; 3=joint study; 0001=part. #1 of 9999)

- ☐ **Data Collection:**

- RADAR Joint CRF to be completed

- ☐ **Blood Collection:**

- 3 tubes*, collected in the following order:
- 1 SST/tiger top
- 1 purple top EDTA
- 1 PAXGene
- Store upright at room temperature until pickup

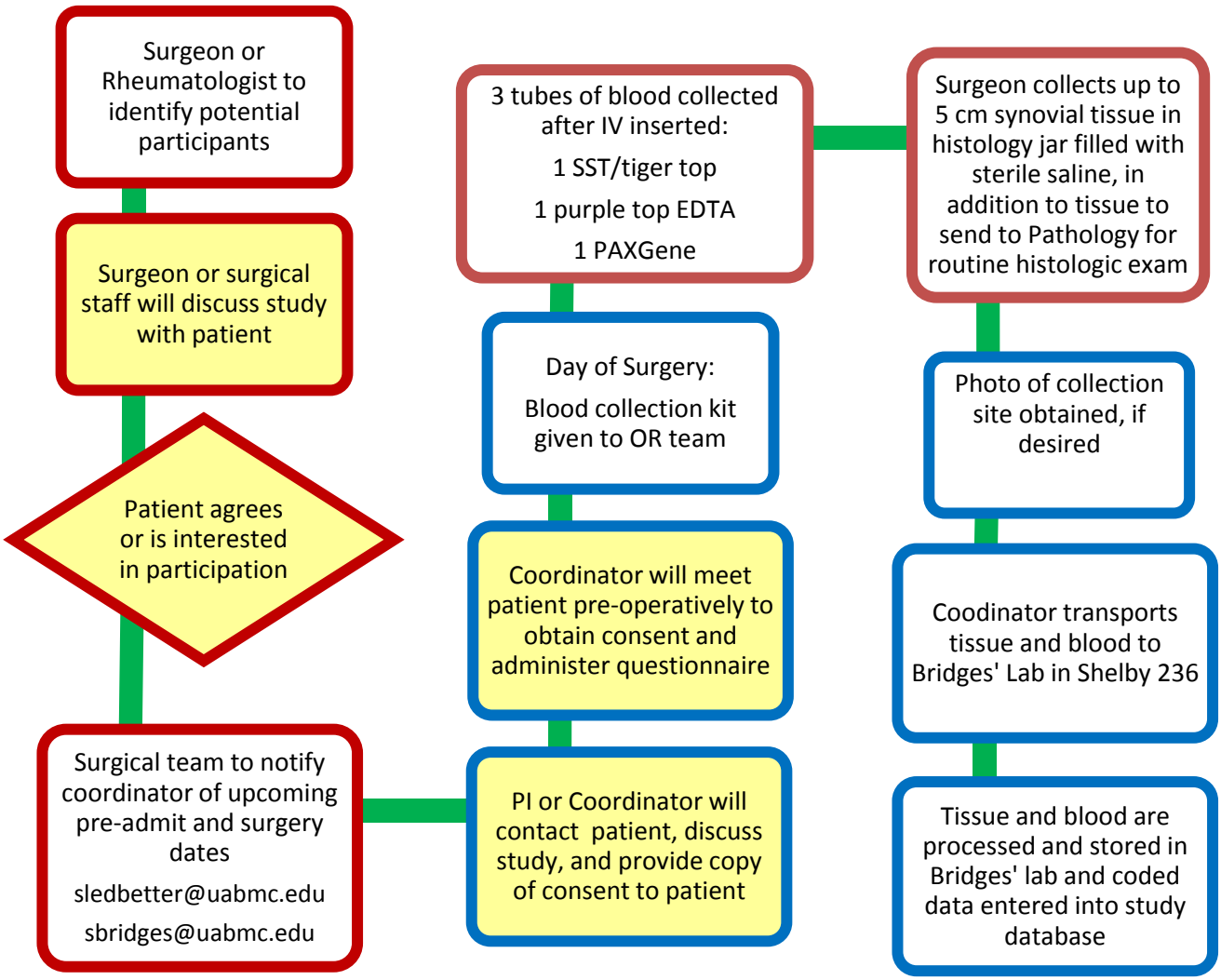
- ☐ **Joint Tissue Collection:**

- Collect up to 5 cm piece of synovial tissue; smaller fragments acceptable
- Place tissue in histology jar (sterile saline)
- Store at 4 degrees (refrigerator) until processed

*We will supply blood collection tubes

RADAR Joint Study Visit Work Flow:

Yellow: patient interaction; Red Outline: Surgeon or Surgery Team; Blue Outline: RADAR Joint team, coordinator



RADAR Joint Consent Form

INFORMED CONSENT FOR PARTICIPATION IN A CLINICAL RESEARCH STUDY

TITLE OF RESEARCH: Rheumatology Arthritis Database and Repository (RADAR) Joint

IRB PROTOCOL NUMBER: X170302004

INVESTIGATORS: S. Louis Bridges, Jr., MD, PhD

SPONSOR: UAB Division of Clinical Immunology and Rheumatology

Purpose of the Research

The purpose of the study is to examine the cells and proteins and other features in the joint tissues of patients with arthritis. We hope that, by studying this tissue, we may learn information that may help lead to the development of new treatments for these diseases. You are being considered for this study because you have recently undergone a procedure on your joint that has been deemed necessary by your surgeon.

The goal of this study is to develop new diagnostic tests and therapeutic options for patients with arthritis, and to reduce the time and cost of developing new treatments by sharing data broadly and quickly to the greater biomedical research community. More details are included under the headings "Use and Storage of Blood Samples" and "Confidentiality."

Explanation of Procedures

This study is considered a registry or specimen repository, in which data and specimens are collected for the purpose of doing a wide variety of research. Some of the possible research that your specimen(s) may be used for include biomarkers for diseases, such as arthritis; genetic studies; immunology and antibody studies, gene expression studies for arthritis.

If you choose to participate, we will utilize tissue for the purpose of research that would have otherwise been discarded, which was removed during a procedure on your joint, deemed necessary by your surgeon. Only tissue that was removed for clinically-indicated reasons determined by your surgeon, will be used for research. If you chose to not participate in this study, your tissue will be discarded. As a subject in this study, your part of the study would take up to 30 minutes, and there may be up to 4 parts to your participation.

1. Your medical history will be reviewed and we will collect clinical and demographic data from your medical records, such as your age and weight, as well as clinical data associated with your joint surgery.

2. You will be asked to complete some questionnaires regarding your health, functional ability, family, education and work history.

3. Up to two and a half tablespoons of blood will be taken from a vein in your arm. You will have blood drawn to obtain DNA, blood cells, and serum samples for a specimen repository. This will be collected in conjunction with normally scheduled blood draw or, if this is not convenient for you, by a nurse or doctor involved with the study.

As part of this study, we would like to store some of the blood and joint tissue specimens collected from you for future research in arthritis and related studies. The future research may be conducted by the study doctor or by other researchers that obtain IRB approval for their research. The specimens will be labeled with a code that only the study doctor or coordinator can link back to you. Results of any future research will not be given to you or your doctor. The specimens obtained from you in this research may help in the development of a future commercial product. There are no plans to provide financial compensation to you should this occur.

You may request at any time that your specimens be removed from storage and not be used for future research. If you decide you want your specimens removed, you may contact the study doctor. Once the request is received, and if your specimens have not already been used for other research, they will be destroyed. If you do not make such a request, your specimens will be stored indefinitely or until used.

Risks and Discomforts

There are minimal physical risks associated with your participation by donating joint tissue for this study. The tissue is being removed for clinically indicated purposes. If you have any complications from the procedures of this study, please contact Dr. S. Louis Bridges, Jr. at 205-934-0897. Dr. Bridges may also be reached after hours by paging him at 205-934-3411 (beeper 3187).

The risks associated with blood draw include pain, a bruise at the site of vein puncture, inflammation of the vein and infection. Every care will be taken to avoid these complications.

The risks of electronic data storage include a data security breach. The files/data will be encrypted and stored on computers located in Drs. Bridges' laboratory for indefinite time period. Every care will be taken to avoid these risks. Your information and results for this study will be labeled with a study code and NOT with any identifying information, in order to minimize the risk that results can be linked to you. The key to the code linking your samples to your name will be maintained in confidential files with standard security precautions, and will never leave UAB. Genetic information or other data derived from your samples may be stored off site and in data repositories for broad sharing with the research community, but will only be identified by your unique study number.

Information for Women of Childbearing Potential and/or Men Capable of Fathering a Child

There is no added risk of participating in this study if you could become pregnant or are capable of fathering a child.

Benefits

There is no direct benefit to you from this study, but the information gained may advance our understanding of rheumatoid arthritis and its treatment.

Alternatives

This study does not involve medications or any other intervention. The alternative is to not participate in the study.

Confidentiality

Information obtained about you for this study will be kept confidential to the extent allowed by law. However, research information that identifies you may be shared with the UAB Institutional Review Board (IRB) and others who are responsible for ensuring compliance with laws and regulations related to research, including people on behalf of National Institutes of Health and the Office for Human Research Protections (OHRP).

If you receive services in University Hospital as part of this trial, this informed consent document will be placed in and made part of your permanent medical record at this facility. When choosing to take part in this study, you are giving us the permission to use your personal health information that includes health information in your medical records and information that can identify you. For example, personal health information may include your name, address, or phone number.

You are also giving permission to the following groups of people to give information about you (described above) to the researchers for this study:

- Government agencies and public health authorities, such as the Food and Drug Administration (FDA) and the Department of Health and Human Services (DHHS).
- Members of the NIH-funded Accelerating Medicines Partnership (AMP) initiative. The AMP initiative is a collaboration among the National Institutes of Health (NIH), biopharmaceutical companies, and non-profit organizations. The goal of the AMP is to develop new diagnostic tests and therapeutic options for patients, and to reduce the time and cost of developing new treatments by sharing data broadly and quickly to the greater biomedical research community.
- Pharmaceutical or biotechnology companies who may provide financial sponsorship of research studies.

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.

- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.

- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that this new federal law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance, nor does it protect you against genetic discrimination by all employers.

Voluntary Participation and Withdrawal

Whether or not you take part in this study is your choice. There will be no penalty if you decide not to be in the study. If you decide not to be in the study, you will not lose any benefits you are otherwise owed.

You are free to withdraw from this research study at any time. Your choice to leave the study will not affect your relationship with this institution.

If you are a UAB student or employee, taking part in this research is not a part of your UAB class work or duties. You can refuse to enroll, or withdraw after enrolling at any time before the study is over, with no effect on your class standing, grades, or job at UAB. You will not be offered or receive any special consideration if you take part in this research.

Costs of Participation

There will be no costs to you from participation in the research. The costs of your standard medical care will be billed to you and/or your insurance provider in the usual manner.

Payment for Participation in Research

There is no payment for participation in this study.

Significant New Findings

You will be told by the study doctor or the study staff if new information becomes available that might affect your choice to stay in the study.

Optional Research

Please note: This section of the consent form is about optional research that is being done with people who are taking part in this study. You may take part in this optional research if you want to. You can still be a part of this study even if you say no to taking part in any of the optional research.

You can say "yes" or "no" to each of the following studies. Please mark your choice for each study.

Genomic Data Sharing (GDS)

Genetic and other relevant study data, such as health information, may be shared broadly in a coded form for future research or analysis. We may give this data about you to other researchers or companies not at UAB, including other approved investigators in our research networks, or at pharmaceutical or biotechnology companies, who have the expertise required to perform the analyses. We will not give them your name, address, phone number, or any other identifiable information. Research results from these studies will not be returned to you.

Your information may be put in controlled-access databases. This means only researchers who apply for and get permission to use the information for a specific research project will be able to access the information. Your information stored in these databases will not include any identifying information. We will replace identifying information with a code number. We will keep a master list that links your code number to your identifying information here at the UAB. Only certain study personnel for this study at UAB will have access to this master list. Researchers approved to access information in the controlled-access database will agree not to attempt to identify you.

Risks: The risk of sharing your genomic data is that someone could link the information stored in the databases back to you. If your information suggested something serious about your health, it could be misused. For example, it could be used to make it harder for you to get or keep a job or insurance or be used to discriminate against you or your family. There may also be other unknown risks.

Benefits: There is no direct benefit to you from sharing your genomic data. Allowing researchers to use your data may lead to a better understanding of how genes affect health. This may help other people in the future.

Initial your choice below:

___ I agree for my genetic and other relevant study data, such as health information, to be shared broadly in a coded form for future research or analysis.

___ I do not agree for my genetic and other relevant study data, such as health information, to be shared broadly in a coded form for future research or analysis.

Questions

If you have any questions, concerns, or complaints about the research or a research- related injury including available treatments, you may contact Dr. S. Louis Bridges, Jr. He will be glad to answer any of your questions. Dr. Bridges' number is 205-934-0897. Dr. Bridges may also be reached after hours by paging him at 205-934-3411 (beeper 3187).

If you have questions about your rights as a research participant, or concerns or complaints about the research, you may contact the UAB Office of the IRB (OIRB) at (205) 934-3789 or toll free at 1-855-860-3789. Regular hours for the OIRB are 8:00 a.m. to 5:00 p.m. CT, Monday through Friday. You may also call this number in the event the research staff cannot be reached or you wish to talk to someone else.

Legal Rights

You are not waiving any of your legal rights by signing this consent form.

Signatures

Your signature below indicates that you have read (or been read) the information provided above and agree to participate in this study. You will receive a copy of this signed consent form.

_____

Signature of Participant Date

_____

Signature of Person Obtaining Consent Date

University of Alabama at Birmingham
AUTHORIZATION FOR USE/DISCLOSURE OF
PROTECTED HEALTH INFORMATION (PHI) FOR RESEARCH

Participant Name: _____ **UAB IRB Protocol Number:** X170302004
Research Protocol Rheumatology Arthritis Database and Repository (RADAR) Joint (RADAR-Joint) **Principal Investigator:** S. Louis Bridges, Jr., MD, PhD
Sponsor: UAB Division of Clinical Immunology & Rheumatology

What is the purpose of this form? You are being asked to sign this form so that UAB may use and release your protected health information for research. Participation in research is voluntary. If you choose to participate in the research, you must sign this form so that your protected health information may be used for the research.

Why do the researchers want my protected health information? The researchers want to use your protected health information as part of the research protocol listed above and as described to you in the informed consent.

What protected health information do the researchers want to use? All medical information, including but not limited to information and/or records of any diagnosis or treatment of disease or condition, which may include sexually transmitted diseases (e.g., HIV, etc.) or communicable diseases, drug/alcohol dependency, etc.; all personal identifiers, including but not limited to your name, social security number, medical record number, date of birth, dates of service, etc.; any past, present, and future history, examinations, laboratory results, imaging studies and reports and treatments of whatever kind, including but not limited to drug/alcohol treatment, psychiatric/psychological treatment; financial/billing information, including but not limited to copies of your medical bills, and any other information related to or collected for use in the research protocol, regardless of whether the information was collected for research or non-research (e.g., treatment) purposes.

Who will disclose, use and/or receive my protected health information? All Individuals/entities listed in the informed consent documents, including but not limited to, the physicians, nurses and staff and others performing services related to the research (whether at UAB or elsewhere); other operating units of UAB, HSF, UAB Highlands, Children's of Alabama, Eye Foundation Hospital, and the Jefferson County Department of Health, as necessary for their operations; the IRB and its staff; the sponsor of the research and its employees and agents, including any CRO; and any outside regulatory agencies, such as the Food and Drug Administration, providing oversight or performing other legal and/or regulatory functions for which access to participant information is required.

How will my protected health information be protected once it is given to others? Your protected health information that is given to the study sponsor will remain private to the extent possible, even though the study sponsor is not required to follow the federal privacy laws. However, once your information is given to other organizations that are not required to follow federal privacy laws, we cannot assure that the information will remain protected.

How long will this Authorization last? Your authorization for the uses and disclosures described in this Authorization does not have an expiration date.

Can I cancel this Authorization? You may cancel this Authorization at any time by notifying the Principal Investigator, in writing, referencing the research protocol and IRB Protocol Number. If you cancel this Authorization, the study doctor and staff will not use any new health information for research. However, researchers may continue to use the protected health information that was provided before you cancelled your authorization.

Can I see my protected health information? You have a right to request to see your protected health information. However, to ensure the scientific integrity of the research, you will not be able to review the research information until after the research protocol has been completed.

Signature of participant: _____ Date: _____

or participant's legally authorized representative: _____ Date: _____

Printed Name of participant's representative: _____

Relationship to the participant: _____

RADAR Joint Case Report Form

Participant ID: _____ Weight: _____ VISIT DATE: _____

Diagnosis/ICD 9_____ DOB: _____ Gender: ☐ M ☐ F

Patient has completed informed consent for use of sample and information in research. ☐ No ☐ Yes

Subject agrees to have specimen samples used in additional research in relation to other medical conditions, including but not limited to lupus, heart diseases, cancer and diabetes. ☐ No ☐ Yes

---

Ethnicity: Hispanic or Latino ☐
Not Hispanic or Latino ☐
Unknown (not reporting) ☐

Race: American Indian/Alaskan Native ☐
Asian ☐
Native Hawaiian/Pacific Islander ☐
Black or African American ☐
White ☐
More than one race ☐
Unknown (not reporting) ☐

Have you been diagnosis with inflammatory arthritis? ☐ No ☐ Yes
(Includes Rheumatoid Arthritis, Psoriatic Arthritis, other)

Have you been diagnosed with autoimmune disease? ☐ No ☐ Yes
(Includes Systemic Lupus Erythematosus, Crohns, Ulcerative Colitis, Myositis, Scleroderma, other)

Have you been diagnosed with osteoarthritis? ☐ No ☐ Yes

Health Assessment Questionnaire

Please select fields, which best describes your abilities over the past week:

1. Dress yourself, including shoelaces and buttons?
   ☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do
2. Get in and out of bed?
   ☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do

3. Lift a full cup or glass to your mouth?
   ☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do
4. Walk outdoors on flat ground?
   ☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do
5. Wash and dry your body?
   ☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do
6. Bend down to pick up clothing from the floor?
   ☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do
7. Turn facets on and off?
   ☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do
8. Get in and out of a car, bus, train, or airplane?
   ☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do
9. Walk two miles or three kilometers, if you wish?
   ☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do
10. Participate in recreational activities and sports as you would like, if you wish?
    ☐ Without any difficulty ☐ With some difficulty ☐ With much difficulty ☐ Unable to do

---

Your PAIN:

How much pain have you had because of your condition OVER THE PAST WEEK?
On a scale of 1-10 (where zero represents 'no pain' and 10 represents 'severe pain':

_____

Do you drink alcoholic beverages?

☐ Not at all ☐ On occasion ☐ 1-3 per week ☐ 1-2 per day ☐ 3 or more per day

---

Do you currently smoke cigarettes?

☐ No, never ☐ Not now, but I did in the past ☐ Yes, currently

---

Affected Joints	Left	Right	X-ray w/in the last year?
Shoulder	☐	☐	☐
Elbow	☐	☐	☐
Wrist	☐	☐	☐
Hip	☐	☐	☐
Knee	☐	☐	☐
Hand	☐	☐	☐

Joint Surgeries

Joint	Year	TR	ARTH	FUSION
_____		☐	☐	☐
_____		☐	☐	☐
_____		☐	☐	☐
_____		☐	☐	☐
_____		☐	☐	☐

TO BE COMPLETE BY STUDY STAFF

Synovial Tissue collected: ☐ No ☐ Yes

List Current RA Medications: Biologics: _____

DMARDs: _____

Prednisone: _____

Autoantibody Status: CCP: _____ RF: _____

RADAR Blood Processing

Laboratory Test	Procedures

Serum Sample		Collect blood into **<u>one 10 ml (SST tube) red/black tiger top tube</u>** Label tube with subject information Invert the tube gently 8 times Store at room temperature until delivered to Bridges' Lab
DNA, Plasma, Buffy Coat		Collect blood into **<u>one purple top 10 ml (EDTA) tube</u>** ♦ Label tube with subject information ♦ Invert the tube gently 8 times ♦ Store at room temperature until delivered to Bridges' Lab
Sodium Heparin Tubes		Collect blood into ***<u>one 9.5 ml green top (Sodium Heparin) tube (annual visit only)</u>** ♦ Label tube with subject information ♦ Invert the tube gently 8 times ♦ Store at room temperature until delivered to Bridges'Lab ♦ ***2 green tops may be requested as needed for RADAR ancillary studies**
Paxgene Tube		Collect blood into **<u>one 2.5 ml PAXgene tube (annual visit only)</u>**. ♦ Allow each tube at least 10 seconds for a complete blood draw. ♦ Gently invert tube 10 times immediately after blood draw. ♦ Label tube with subject information ♦ Store at room temperature until delivered to Bridges'Lab

For each participant on each visit, the coordinator will prepare a biohazard bag containing the needed blood collection tubes, each labeled with the study PID and visit date. Coordinators will also complete a clinical lab order form, which includes the RADAR IRB protocol #. A pre-printed label requesting the

draw is to be affixed to the bottom of the clinical lab order form, which is then folded and placed within the outer pocket of the biohazard bag.

Transportation to Dr. Bridges' Lab

At the end of clinic, coordinators will pick up blood samples from the clinic lab and bring to Keith Wanzeck in Dr. Bridges' laboratory in Shelby Room 236.

Processing in Dr. Bridges' Lab
Upon receipt of blood, Dr. Bridges' research assistant(s) will process the blood as follows:

Document receipt of blood samples including number of each type of tube, and date, on the RADAR Specimen Processing Sheet.

1.) Purple top tubes:

a. Extract genomic DNA from one 500µl aliquot of whole blood using the Gentra PureGene Kit:

(Cell Lysis)

- Add 500ul whole blood to a 2.0ml microfuge tube containing 1500ul RBC Lysis Solution. Invert to mix and incubate 10 minutes at room temp; invert again once during incubation
- Centrifuge for **1 minute at 13K-16K x g**. Remove supernatant with a micropipette leaving behind visible white cell pellet and 5-10ul of residual liquid
- Vortex tube vigorously to resuspend white blood cells in the residual supernatant
- Add 300ul Cell Lysis Solution to tube and pipet up and down to lyse cells. If clumps are visible after mixing, incubate at **37ºC** or room temp until solution is homogenous. Samples are stable in Cell Lysis Solution at room temp for at least 18 months

(Rnase A Treatment)

- Add 1.5ul RNase A Solution to the cell lysate
- Mix the sample by inverting the tube 25 times and incubate at **37ºC for 15 minutes**

(Protein Precipitation)

- Cool sample to room temp
- Add 100ul Protein Precipitation Solution to the cell lysate

- Vortex vigorously at high speed for 20 seconds to mix
- Centrifuge at **13K-16K x g for 3 minutes**. The precipitated proteins will form a tight, dark brown pellet

(DNA Precipitation)

- Pour supernatant containing DNA (leaving behind the protein pellet) into a clean 1.5ml microfuge tube containing 300ul **100% Isopropanol**
- Mix sample by inverting gently 50 times until the white threads of DNA form a visible clump
- Centrifuge at **13K – 16K x g for 1 minute**; the DNA will be visible as a small white pellet
- Pour off supernatant and drain tube on clean absorbent paper. Add 300ul **70% Ethanol**. Invert tube several times to wash DNA pellet
- Centrifuge at **13K – 16K x g for 1 minute**. Carefully pour off the ethanol. Pellet may be loose so pour slowly and watch pellet.
- Drain tube on clean absorbent paper and allow to air dry at room temp for 15 minutes

(DNA Hydration)

- Add 150ul **DNA Hydration Solution**
- Allow DNA to rehydrate by heating at **65ºC for 1 hour**
- Determine [DNA] with spectrophotometer and store at –70ºC

b. Let the tube stand in a rack for 30 minutes at room temperature.

c. Spin in Hamilton tabletop centrifuge for 15 minutes. The three portions are plasma, buffy coat at interface, and red blood cells on the bottom.

d. Transfer with a pipet 2 ml aliquots of plasma into 2 – 4 cryovials.

e. Label vials with bar-coded FreezerWorks labels. Discard any volume of plasma more than 7.2 ml (enough to fill 4 cryovials).

f. Isolate the buffy coat layer from the remaining blood and aliquot into two cryovials. Label all vials with bar-coded FreezerWorks labels.

g. Isolate 1 ml of Red blood Cells from the bottom of the purple top tube and aliquot into one cyrovial. Add 500ul of saline to the tube and spin at 1500 rpm for 1 min. Discard supernatant. Label tube with packed RBCs or pRBCs and store in -70° C.

h. Store the plasma, genomic DNA, and buffy coat (for future DNA extraction) at -70º C.

i. Enter the location of all tubes in the Freezer Works database.

2.) PAXgene tubes:

a. Incubate blood sample in the PAXgene Blood RNA Tube for a minimum of 2 hrs at room temperature in order to achieve complete lysis. Centrifuge the PAXgene Blood RNA Tube for 10 min at 3000–5000 x g using a swing-out rotor.

b. Remove the supernatant by decanting or pipetting. Add 5 ml RNase-free water to the pellet, and close the tube using a fresh secondary Hemogard closure. If the supernatant is decanted, dry the rim of the tube with a clean paper towel.

c. Thoroughly resuspend the pellet by vortexing, and centrifuge for 10 min at 3000–5000 x g Remove and discard the entire supernatant.

d. Thoroughly resuspend the pellet in 360 µl Buffer BR1 by vortexing.

e. Pipet the sample into a 1.5 ml or 2 ml microfuge tube. Add 300 µl Buffer BR2 and 40 µl Proteinase K. Mix by vortexing, and incubate for 10 min at 55°C using a shaker–incubator **with the speed set to maximum.**

f. Centrifuge for 3 min at maximum speed in a microcentrifuge. Transfer the supernatant to a fresh 1.5 ml or 2 ml microfuge tube.

g. Add 350 µl 100% ethanol. Mix by vortexing, and centrifuge for a maximum of 2 seconds at 1000 x g to remove drops from the inside of the tube lid.

h. Apply 700 µl sample to the PAXgene column sitting in a 2 ml processing tube, and centrifuge for 1 min at 10,000 rpm. Place the PAXgene column in a new 2 ml processing tube, and discard the old processing tube containing flow-through.

i. Apply the remaining sample to the PAXgene column, and centrifuge for 1 min at 10,000 rpm. Place the PAXgene column in a new 2 ml processing tube, and discard the old processing tube containing flow-through.

j. Pipet 350 µl Buffer BR3 into the PAXgene column. Centrifuge for 1 min at 10,000 rpm. Either discard the flow-through, or transfer the PAXgene column to a new processing tube.

k. Add 10 µl DNase I stock solution to 70 µl Buffer RDD. Mix by gently flicking the tube, do not vortex, and centrifuge briefly to collect residual liquid from the sides of the tube. Buffer RDD is supplied with the RNase-Free DNase Set.

l. Pipet the DNase I incubation mix (80 µl) directly onto the spin-column membrane, and place on the benchtop (20–30°C) for 15 min.

m. Pipet 350 µl Buffer BR3 into the PAXgene spin column, and centrifuge for 1 min at 10,000 rpm. Place the PAXgene column in a new 2 ml processing tube, and discard the old processing tube containing flow-through.

n. Apply 500 µl Buffer BR4 to the PAXgene column, and centrifuge for 1 min at 10,000 rpm. Place the PAXgene column in a new 2 ml processing tube, and discard the old processing tube containing flow-through.

o. Add another 500 µl Buffer BR4 to the PAXgene column. Centrifuge for 3 min at maximum speed to dry the PAXgene column membrane.

p. Discard the tube containing the flow-through, and place the PAXgene column in a new 2 ml processing tube. Centrifuge for 1 min at full speed.

q. To elute, discard the tube containing the flow-through, transfer the PAXgene column to a 1.5 ml elution tube, and pipet 40 µl Buffer BR5 directly onto the PAXgene column membrane. Centrifuge for 1 min at 10,000 rpm.

r. Repeat the elution step (step q) as described, using 40 µl Buffer BR5.

s. Incubate the eluate for 5 min at 65°C in a heating block or water bath. Following incubation, chill immediately on ice. It is not necessary to denature samples more than once, and samples remain denatured after freezing and thawing. Store at -80°C.

t. Record the location of tubes in the FreezerWorks database.

3.) Red/gray SST tube:

a. Centrifuge sample for 15 minutes at room temperature. Transfer with a pipet 2 ml aliquots of serum into 2 – 4 cryovials with preprinted, bar-coded WrapAround labels. Discard any volume of serum more than 7.2 ml (enough to fill 4 cryovials).

b. Store the serum samples at –80C.

c. Record the location of all tubes in the FreezerWorks database.

4.) Green top Sodium Heparin tube: Purification and Cryopreservation of Peripheral Blood Mononuclear Cells (PBMC):

1. Remove all buffers, media, and Ficoll-Paque from 4^{o}C and allow to equilibrate to ambient temperature.

2. Determine the number of specimens to be processed and label the appropriate number of 15 ml or 50 ml conical tubes.

3. The buffy coat is obtained from the sodium heparin tube (green top) via the Ficoll underlay. Dilute the peripheral blood as follows:

3.1. For volumes less than 3 mls - bring total volume to 5 mls with ambient temperature unsupplemented RPMI.

3.2. For volumes 3 mls or greater – dilute 1:1 with ambient temperature, unsupplemented RPMI.

4. Transfer sample to appropriate 15 ml or 50 ml conical tube according to the following –

4.1. <7.5 mls, transfer to 15 ml conical tube

4.2. 7.5 – 15 mls, divide equally into two 15 ml conical tubes

4.3. 15 – 22.5 mls, divide equally into three 15 ml conical tubes

5. Insert a 9” Pasteur pipette into the sample tube.

6. Slowly pipette ambient temperature Ficoll-Paque into the Pasteur pipette to generate the ficoll layer under the sample at a volume ratio of 1.5:1 (sample to Ficoll-Paque).

7. Place sample tubes into a swinging bucket centrifuge and spin 30 – 40min @ 400 x *g.*

8. Using a transfer or Pasteur pipette, carefully aspirate/remove the upper layer to ~0.5" above the mononuclear cell containing interface.

9. Using a transfer or Pasteur pipette, carefully remove the white "fluffy" interface containing the mononuclear cells and transfer to a clean 15 ml conical per sample. Multiple tubes from the same donor may be consolidated into a 50 ml conical tube (maximum of 4). Dispose of the Pasteur pipettes in a biohazard sharps container.

10. Dilute 1:1 with ambient temperature RPMI + 1% FBS, invert 5x, and spin 10min @ 400 x *g.*

11. After spin, decant, and resuspend cells in 10mls per sample of RPMI + 10%FBS and count resuspended cells.

12. Spin remaining cells 5min @ 400 x g.

13. Decant tube, gently rack rake to resuspend cells, and resuspend in 1ml of freshly prepared PBMC freeze media (90% FBS/10% DMSO) if cell count is ≤ 10×10^6. If the cell count is > than 10×10^6 then resuspend in 1.5ml of freshly prepared PBMC freeze media (90% FBS/10% DMSO).

14. Transfer 1ml aliquots of PBMCs to 1.8ml Nunc cryovials and label with PBMC label supplied within kit immediately transfer cryovials to a Nalgene *Mr. Frosty* and place at -80^0C for a minimum of 12 hours.

15. Transfer cryovials to liquid nitrogen storage after overnight freeze and no more than 48 after -80^0C freeze in *Mr. Frosty*.

RADAR Specimen Processing Log

Dr. Bridges' Lab

Patient ID Number _____

Date of Processing _____

Visit No. _____

Number of blood tubes received:

Purple _____

SST/Tiger _____

Extended RADAR

Green _____

PaxGene _____

Aliquots of plasma from purple top tube:

Number of cryovials _____

Barcode Freezer location

Aliquots of buffy coat from purple top tube:

Number of cryovials _____

Barcode Freezer location

Genomic DNA extracted from 500 microliters whole blood from purple top tube

Yield of DNA _____

Barcodes Freezer location

Aliquots of serum from red/gray top tubes:

Number of cryovials _____

Barcode Freezer location

Extended RADAR

PBMC extraction from green top tube

Number of Aliquots _____

Cell Count Obtained by Using Hemocytometer __ __. __ x 10^6 cell/ml

Viability __ __.__%

Barcodes

Freezer location

RNA extracted from PAXgene tubes

Yield of RNA _____

Barcodes Freezer location

Synovial Fluid Specimen Processing

For each participant on each visit when synovial fluid is collected, clinic personnel will complete a clinical lab slip requesting lab tests the physician wants performed. In addition, study personnel will place syringe containing unused portion of synovial fluid into biohazard bag provided by coordinating lab. The bag is to be labeled with the patient id number (PID), date of visit and any other study information. The clinical personnel should contact Keith Wanzeck at the Bridges coordinating lab at 205-975-9840 and samples will be retrieved by lab personnel. Or at the end of clinic, coordinators will pick up blood samples from the lab and bring to Keith Wanzeck in Dr. Bridges' laboratory in Shelby Room 236.

Collection of Synovial Fluid

Only remnant synovial fluid will be used for these studies. No fluid will be obtained solely for research purposes.

1. Withdraw approximately up to 50 cc of synovial fluid from remnant fluid, using 100 cc syringe (do not collect if <2.0 ml is available)
2. Place syringe containing of synovial fluid into biohazard bag provided.
3. Seal bag and labeled with the patient id number, study name and date of study visit, and delivery to Dr. Bridges laboratory, Shelby 236 (or call 975-9840 for pick up).

Processing in Dr. Bridges' Lab (Shelby 236)

1. Document receipt of synovial fluid samples including patient identifier number, number of tubes collected volume of synovial fluid received, appearance of synovial fluid and date.
2. Transfer approximately ¼ of the synovial fluid (up to 10 ccs for volume > 40 ml) from syringe into sterile 15 ml conical tubes. If the volume is less than 2 ccs, process all for synovial fluid only, no cells collected.
3. Centrifuge the synovial fluid at 1700rpm/min or higher at 4°C for 5 min
4. Collect supernatant and transfer into 1.8 ml cryovial. Label with PID, study name, date, as "fluid fraction." Stored at -80 º C.
5. Set aside the remainder of the synovial fluid, approximately 30 mL, for delivery to Dr. Mountz's lab for processing.
6. (Optional) If cell pellet is contaminated with RBC, treat it with 5ml ACK lysis buffer for 5 min on ice (do not exceed 10 min), stop the lysis by washing twice with culture medium;
7. Resuspend the cell pellet in ~20 ml RPMI1640 medium;
8. Centrifuge at 300-500rpm/min at 4°C for 5 min; (Alternative: isolate mononuclear cells by using Ficoll-paque solution following the manufacturer's manual);

9. Collect the supernatant as cell fraction 1 (major components: mononuclear cells, PMN); use the cells for experiment/RNA/Protein/Culture); cryopreserve the remainders in 10%DMSO in FBS (transfer the tubes to liquid nitrogen for long-term storage)
10. Collect the pellet as cell fraction 2 (major components: tissue fragments, fibroblasts, macrophages). 1) save some for RNA/Protein; 2) process as 7 or 8 indicated below; 3) save the remainders in 10%DMSO in FBS (transfer the tubes to liquid nitrogen for long-term storage);
11. (Optional, for fibroblast isolation) Re-suspend the pellet from 6 in 5ml 0.2mg/ml collagenase D, incubate at 37°C until the desired disaggregation is achieved; filter supernatant through 100µm sieves to remove undigested fragments; Seed the cells in culture dishes with DMEM supplemented with 10% FBS;
12. Save frozen cell pellets from various cell types by labeling each tube with PID, study name, date, as "pellet re-suspension."

Synovial Fluid Specimen Processing Log Bridges Lab

Patient Identifier Number (PID) _____

Date of Processing _____

Total Amount of Synovial Fluid received _____

Aliquots of Synovial Fluid from syringe:

Number of cryovials _____

Approximate amount of each aliquot _____

Physical Appearance of Synovial Fluid _____

Storage Information

Barcode Freezer location

Comments or Notes:

Synovial Fluid Specimen Processing Log Mountz Lab

Patient Identifier Number (PID) _____

Date of Processing _____

Total Amount of Synovial Fluid received _____

Analysis of synovial fibroblasts

Number of cells in the suspension _____

Number of cells in the fragment _____

Storage Information

Barcode Freezer location

Comments or Notes: