Regeneron Protocol R475-OA-1611

Quick Reference Guide for MR Image Acquisition of Hips, Knee and Shoulder Joints

1.5T MRI Scanners

MRI VISITS

Screening - An MRI must be performed for the index joint and contralateral joint as well as any knee or hip joint that has a baseline K-L score ≥3

JR Pre-Operative

Post-Op Week 20

Unscheduled

Event Driven - Any imaging done outside of regular study visits, requested by the PI for any joint following a report of clinically significant worsening or exacerbation of pain in that joint

MR IMAGING PROTOCOL: Hips

The imaging exam should be carried out as follows:

Left and Right Hips*

1. **3-Plane Localizer(s)**
2. **Coronal 2D T1-w FSE**
3. **Coronal 2D STIR**
4. **Axial PD-w FSE fat sat**

The order of acquisitions and should be the same for each subject-visit. The entire protocol should be programmed into your scanner and saved as ***Regeneron R475-OA-1611*** at the beginning of this clinical trial. Once approved by BioClinica, this protocol should be recalled and used without alteration for each examination. To ensure consistency, review the subject's **Screening** exam before scanning for a follow up visit.

**When scanning the subject with an artificial hip joint, do not include the replaced joint in the Field of View (FOV). This applies to all sequences of the protocol. Prescribe the Field of View (FOV) for unilateral joint coverage, do not image the artificial hip!*

SUBJECT PREPARATION AND POSITIONING: Hips

Hips

- The pelvic or body (phased-array) coil should be used for imaging.
- The feet should be strapped to provide immobility and correct positioning.
- When moving the table inside the scanner, use laser lights to zero in on the hip joint.

ANATOMICAL COVERAGE AND SLICE PRESCRIPTION: Hips - 1

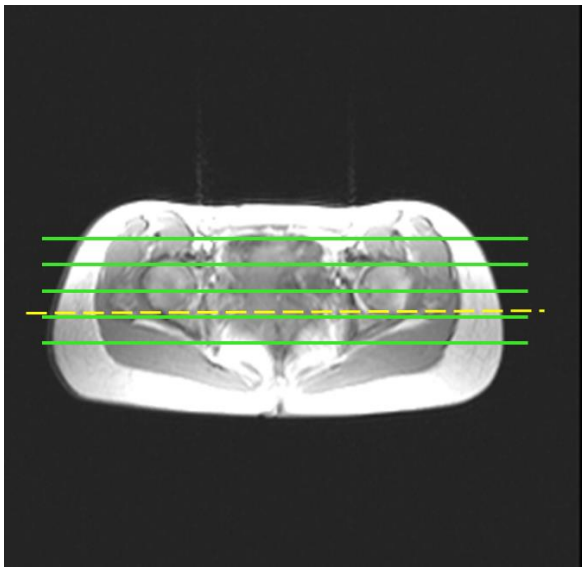
Coronal 2D T1-w FSE (Sequence 2) and 2D STIR (Sequence 3)

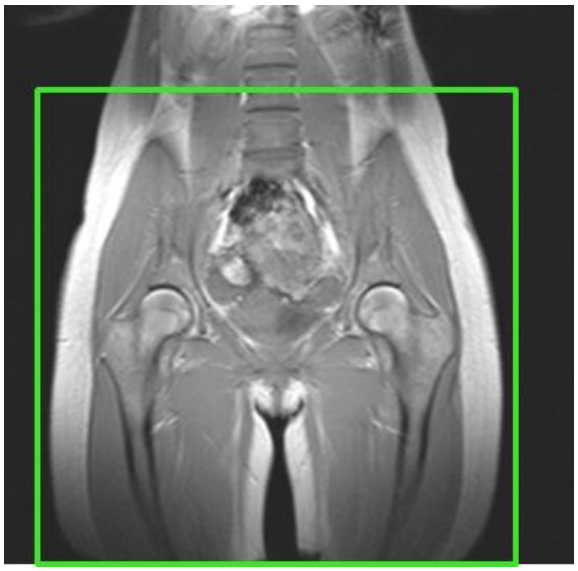
Based on the axial localizer

- ✓ Find the image with the largest cross-section through femoral heads and angulate the slices parallel to the line through inferior margins of the femoral heads.
- ✓ Be sure to completely cover both acetabulofemoral joints in R-L direction.
- ✓ The stack should be centered over the femoral heads and acetabular sockets in A-P direction
- ✓ Both hip joints should be completely covered within the stack. For large joints add slices as needed to attain the required coverage. For smaller joints the recommended number of slices should still be acquired.

Based on the coronal localizer

- ✓ Find the image with the largest cross section through the femoral heads and prescribe the Field of View (FOV) so that both acetabulofemoral joints are in the center if the Field of View (FOV) in S-I direction.
- ✓ Make sure the Field of View (FOV) is well centered and incorporates both hip joints in R-L direction.





ANATOMICAL COVERAGE AND SLICE PRESCRIPTION: Hips - 2

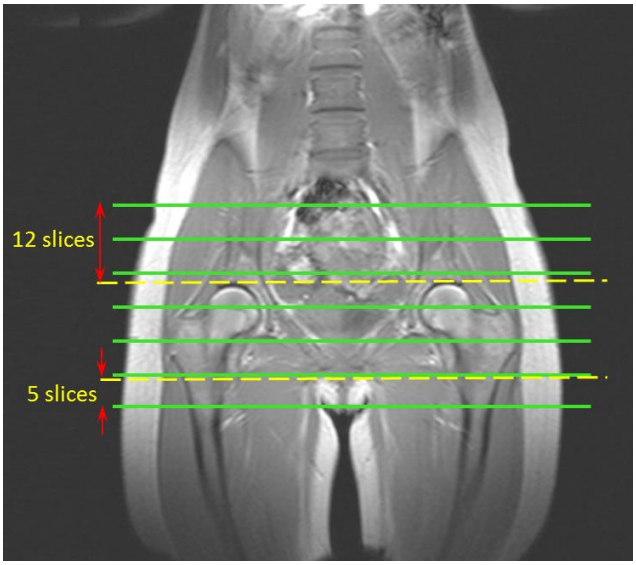
Axial PD-w FSE fat sat (Sequence 4)

Based on the coronal localizer

- ✓ Find the image with the largest cross section through the femoral heads and angulate the slices parallel to the line through superior margins of the femoral heads.
- ✓ Make sure to prescribe the most superior slice above the superior margins of the femoral heads by 12 slices (~50mm). Check the position of the most inferior slice. Make sure it is below the lesser trochanters by at least 5 slices (~20mm). If necessary add more slices to provide the required coverage in S-I direction.
- ✓ Make sure the stack is well centered and incorporates both hip joints in R-L direction.

Based on the axial localizer

- ✓ Find the image with the largest cross section through the femoral heads and make sure the Field of View (FOV) is well centered and incorporates both hip joints in A-P and R-L directions.



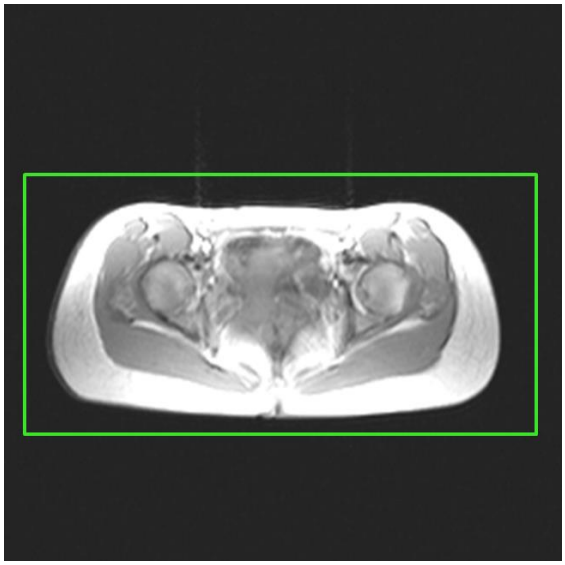


IMAGE ACQUISITION PARAMETERS: Hips

To setup and save each sequence please refer to the table below. The sequences are based on suggested acquisition parameters that are typical for 1.5T MRI scanners. Depending on specific hardware/software versions, some settings may vary. Start with your routine clinical sequences and modify settings as indicated below. The imaging protocol for your scanner should be saved at study initiation and subsequently used for all subjects. Consistency in acquisition across all visits is especially important!

Sequence #	2	3	4
Sequence name	**Coronal 2D T1-w FSE**	**Coronal 2D STIR**	**Axial 2D PD-w FSE fat sat**
Sequence type/ technique	*tse2d1 – Siemens; FSE-XL – GE; TSE - Philips	*tirm2d1_7 – Siemens; IR –GE; TSE IR - Philips	*tse2d1_7 – Siemens; FSE-XL – GE; TSE - Philips
Image orientation	Coronal	Coronal	Axial
Scan Mode	2D	2D	2D
Imaging options	fast, EDR, VBW, NPW - GE; Fast imaging YES and MS – Philips		The same as for sequence 2 and 6
FOV (freq. × phase) [mm×mm]	380 × 380	380 × 380	380 × 280
Acquisition Matrix (frequency × phase)	512×50% - Siemens; 512×256 - GE; Voxel size (mm): 0.74×1.48 and Recon voxel size (mm): 0.74×0.74 - Philips		512×50% - Siemens; 512×256 - GE; Voxel size (mm): 0.74×1.09 - Philips
TR [ms]	400 – 650	4000 – 5000	4000 – 5000
TE [ms]	8 - 12	25 - 35	35 - 45
TI [ms]	NA	150 - 170	NA
Flip angle [deg.]	Default	NA	Default
Slices	24	24	42
Slice thickness [mm]	3	3	4
Slices gap [mm]	0.3 (10%)	0.3 (10%)	0.4 (10%)
Ave/NEX/NSA	1 (2 for GE)	1 (2 for GE)	1 (2 for GE if NPW is used)
Phase/Foldover direction	R-L	R-L	A-P
Oversampling (Phase)	Phase oversampling 50-70% - Siemens; NPW - GE; Foldover suppression ON - Philips		As needed
ETL/Turbo factor	3	5 - 9	7 - 9
Bandwidth/ water-fat shift	120-150Hz/px - Siemens; 15.6kHz - GE; User defined 1.8px - Philips		
Fat saturation	None		Fat Sat - Siemens; Fat – GE; SPAIR - Philips
Acquisition time [min:sec]	4:30	4:30	7:00

MRI VISITS

Screening - An MRI must be performed for the index joint and contralateral joint as well as any knee or hip joint that has a baseline K-L score ≥3

JR Pre-Operative

Post-Op Week 20

Unscheduled

Event Driven - Any imaging done outside of regular study visits, requested by the PI for any joint following a report of clinically significant worsening or exacerbation of pain in that joint

MR IMAGING PROTOCOL: Knee

The imaging exam should be carried out as follows:

Left and Right Knee

1. **3-Plane Localizer(s)**
2. **Coronal 2D T1-w FSE**
3. **Coronal 2D PD-w FSE fat sat**
4. **Sagittal 2D PD-w FSE fat sat**

The order of acquisitions and should be the same for each subject-visit. The entire protocol should be programmed into your scanner and saved as ***Regeneron R475-OA-1611*** at the beginning of this clinical trial. Once approved by BioClinica, this protocol should be recalled and used without alteration for each examination. To ensure consistency, review the subject's **Screening** exam before scanning for a follow up visit.

If left and right knee scans are to be acquired, upon completion of the above protocol on one knee, the contralateral knee should also be scanned.

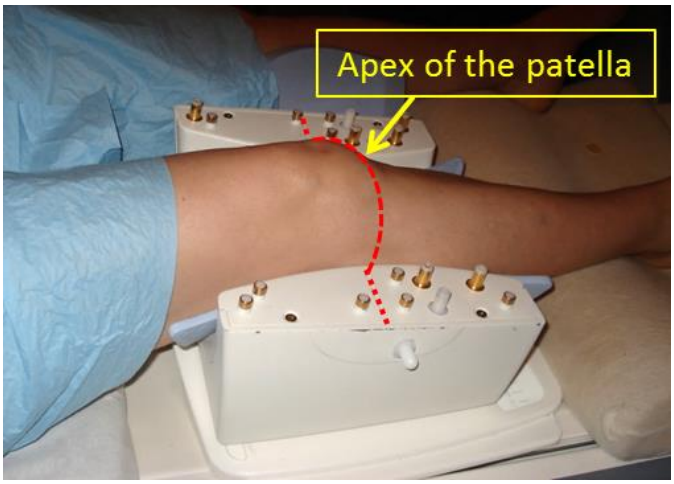
If the contralateral joint has a total joint replacement please do not scan and indicate in the comment section of the transmittal form which joint has a total replacement.

SUBJECT PREPARATION AND POSITIONING: Knee

Proper subject preparation is critical for obtaining high-quality images. Follow these guidelines and make sure to consistently cover all preparatory steps during each subject-visit.

- All loose metal objects should be removed as well as metal-containing jewelry and clothing (zippers, belts, snaps). It is recommended that the subject be dressed in a hospital gown.
- The head-phones should be used if available. Alternatively, provide the subject with earplugs and make sure he/she can hear your comments during imaging.
- Provide the subject with a blanket(s) and pads, as needed, to ensure comfort and immobility during imaging.
- Subject positioning inside the scanner should normally be Feet-First Supine (FFS).
- During imaging monitor the subject at all times.

- The laterality of the knee being imaged should correctly be entered through the scanner console.
- In the coil the knee should be positioned so that apex of the patella is aligned with the center of the coil.
- The leg should be in a relaxed, neutral position. The most comfortable (and sustainable) one is attained when the knee is slightly flexed. Many coils are designed to accommodate this. However, if the base of your coil is flat, use the pad(s) to slightly elevate and flex the knee to attain optimal positioning.
- Never insert a cushion or pad under the heel (ankle).
- Once the knee is comfortably placed and centered inside the base of the coil, attach the top. Use pads as needed to immobilize the knee.
- Position the coil as close as possible to the center of the table. To achieve this, offset the patient toward the contralateral side.
- When moving the table inside the scanner, use laser lights to zero in at the center of the coil (apex of the patella).



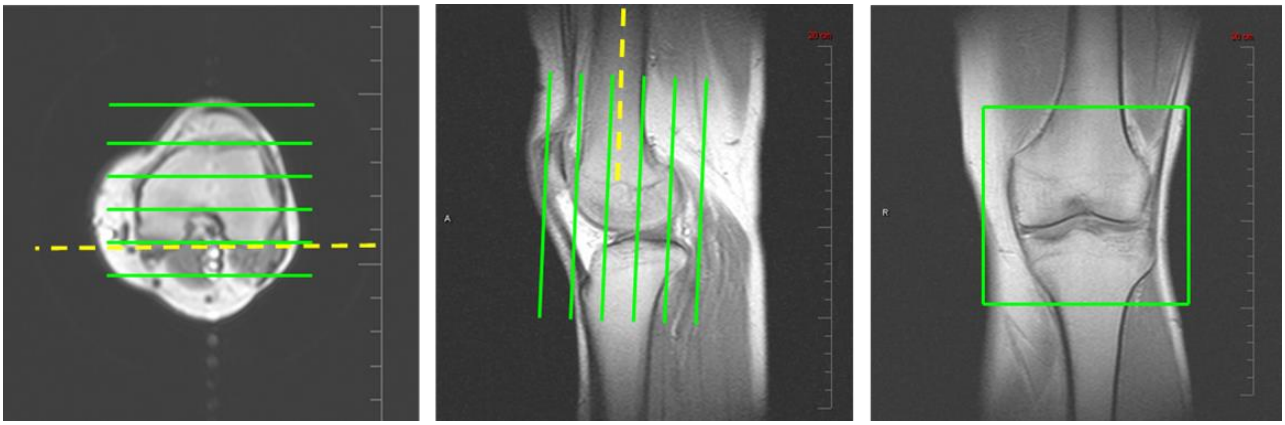
ANATOMICAL COVERAGE AND SLICE PRESCRIPTION: Knee

Coronal 2D T1-w FSE (Sequence 2) and 2D PD-w FSE fat sat (Sequence 3)

Based on the axial localizer find the slice with the largest cross-section through femoral condyles and identify the line connecting the posterior surfaces of the condyles. The slices should be parallel to this line.

Based on the mid-sagittal localizer prescribe the slices parallel to the femoral shaft. Make sure to also include the patella.

Based on the coronal localizer the knee joint should be in the center of the Field of View (FOV).



Sagittal 2D PD-w FSE fat sat (Sequence 4)

Based on the axial localizer find the image with the largest cross-section through femoral condyles and identify the line connecting the posterior surfaces of the condyles. The slices should be perpendicular to this line. Make sure the joint is well centered within the stack.

Based on the mid-sagittal localizer the Femoral-Tibial joint should be in the center of the Field of View (FOV) and the patella should also be included.

Based on the coronal localizer prescribe the slices parallel to the femoral shaft. The knee joint should be completely covered within the stack. For a large knee add slices as needed to attain the required coverage. For a smaller knee the recommended number of slices should still be acquired.

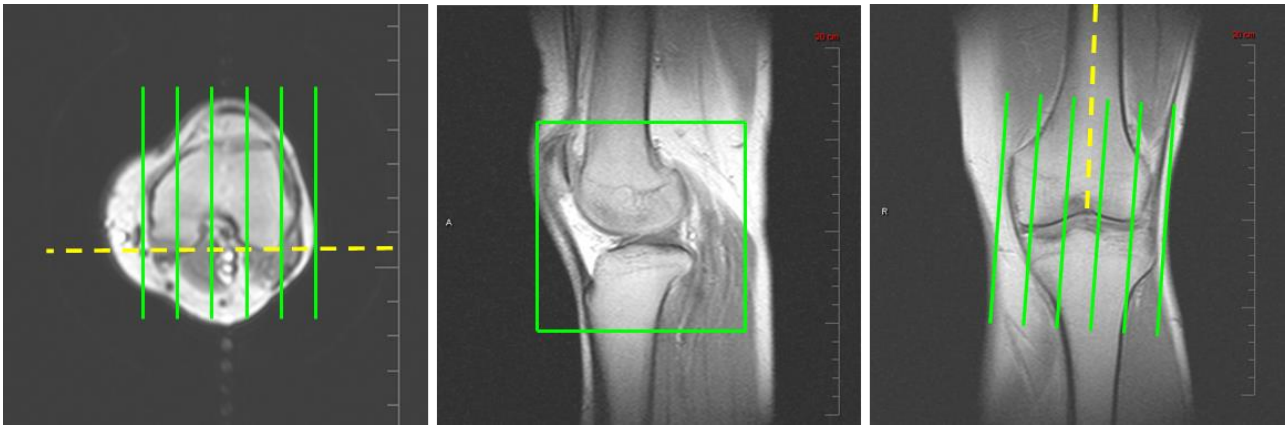


IMAGE ACQUISITION PARAMETERS: Knee

To setup and save each sequence please refer to the table below. The sequences are based on suggested acquisition parameters that are typical for 1.5T MRI scanners. Depending on specific hardware/software versions, some settings may vary. Start with your routine clinical sequences and modify settings as indicated below. The imaging protocol for your scanner should be saved at study initiation and subsequently used for all subjects. Consistency in acquisition across all visits is especially important!

Sequence #	*2*	*3*	*4*
Sequence name	**Coronal 2D T1-w FSE**	**Coronal 2D PD-w FSE fat sat**	**Sagittal 2D PD-w FSE fat sat**
Sequence type/ technique	*tse2d1 – Siemens; FSE-XL – GE; TSE - Philips		
Image orientation	Coronal	Coronal	Sagittal
Scan Mode	2D	2D	2D
Imaging options	fast, EDR, VBW - GE; Fast imaging YES and MS – Philips		fast, EDR, VBW, NPW - GE; Fast imaging YES and MS – Philips
FOV (freq. × phase) [mm×mm]	170 × 170	170 × 170	170 × 170
Acquisition Matrix (frequency × phase)	256×100% - Siemens; 256×256 - GE; Voxel size (mm): 0.664×0.664 - Philips		
TR [ms]	400 –650	3500 – 5000	3500 – 5000
TE [ms]	8 - 12	25 - 40	25 - 40
TI [ms]	NA	NA	NA
Flip angle [deg.]	Default	Default	Default
Slices	30	30	30
Slice thickness [mm]	3	3	3
Slices gap [mm]	0.3 (10%)	0.3 (10%)	0.3 (10%)
Ave/NEX/NSA	1		1 (2 for GE)
Phase/Foldover direction	R-L		H-F
Oversampling (Phase)	None		Phase 50-80% - Siemens; NPW - GE; Foldover suppression ON - Philips
ETL/Turbo factor	3	5 - 9	5 - 9
Bandwidth/ water-fat shift	120-150Hz/px - Siemens; 15.6kHz - GE; User defined 1.8px - Philips		
Fat saturation	None	Fat Sat - Siemens; Fat – GE; SPAIR - Philips	
Acquisition time [min:sec]	4:30	4:30	4:30

MRI VISITS

Screening - An MRI must be performed for the index joint and contralateral joint as well as any knee or hip joint that has a baseline K-L score ≥3

JR Pre-Operative

Post-Op Week 20

Unscheduled

Event Driven - Any imaging done outside of regular study visits, requested by the PI for any joint following a report of clinically significant worsening or exacerbation of pain in that joint

MR IMAGING PROTOCOL: Shoulder

The imaging exam should be carried out as follows:

Left and Right Shoulder

1. **3-Plane Localizer(s)**
2. **Oblique coronal 2D PD-w FSE**
3. **Oblique coronal 2D PD-w FSE fat sat**
4. **Oblique sagittal 2D PD-w FSE**

The order of acquisitions and should be the same for each subject-visit. The entire protocol should be programmed into your scanner and saved as ***Regeneron R475-OA-1611*** at the beginning of this clinical trial. Once approved by BioClinica, this protocol should be recalled and used without alteration for each examination. To ensure consistency, review the subject's **Screening** exam before scanning for a follow up visit.

If left and right shoulder scans are to be acquired, upon completion of the above protocol on one shoulder, the contralateral shoulder should also be scanned.

SUBJECT PREPARATION AND POSITIONING: Shoulder

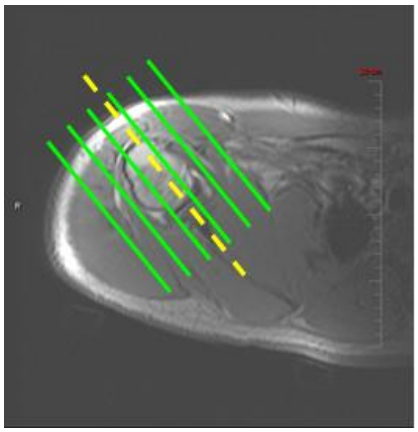
Proper subject preparation is critical for obtaining high-quality images. Follow these guidelines and make sure to consistently cover all preparatory steps during each subject-visit.

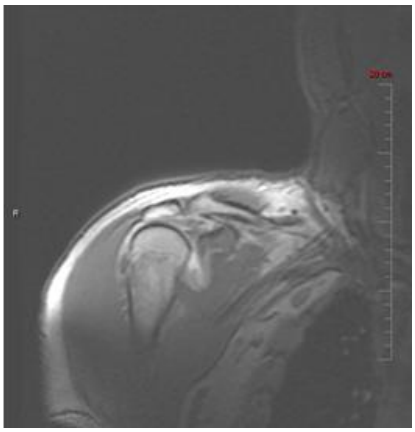
- The laterality of the target shoulder for imaging should correctly be entered through the scanner console.
- All loose metal objects should be removed as well as metal-containing jewelry and clothing (zippers, belts, snaps). It is recommended that the subject be dressed in a hospital gown.
- The head-phones should be used if available. Alternatively, provide the subject with earplugs and make sure he/she can hear your comments during imaging.
- The subject should be positioned supine with the hand extended by the side of the torso or on the stomach.
- A dedicated shoulder coil should be used for imaging.
- The target shoulder should be as close as possible to the center of the magnet bore.
- The padding should be used to elevate the elbow and align the humerus parallel to the table.
- Provide the subject with blanket(s) and pads, as needed, to ensure comfort and immobility during imaging.
- When moving the table inside the scanner, use laser lights to zero in on the shoulder joint.
- During imaging monitor the subject at all times.

ANATOMICAL COVERAGE AND SLICE PRESCRIPTION: Shoulder

Oblique Coronal Scans (sequences 2 and 3)

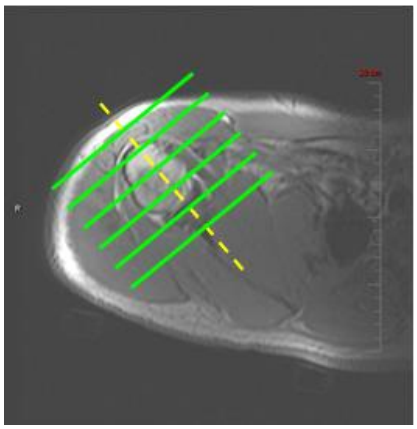
- On an axial localizer identify the slice on which the humeral head and the scapula can be well observed. Identify the axis of the scapula (parallel to the supraspinatus tendon).
- Prescribe the slices parallel to the axis of the scapula.





Oblique Sagittal Scan (sequence 4)

- On an axial localizer identify the slice on which the humeral head and the scapula can be well observed. Identify the axis of the scapula (perpendicular to the supraspinatus tendon).
- Prescribe the slices perpendicular to the axis of the scapula.



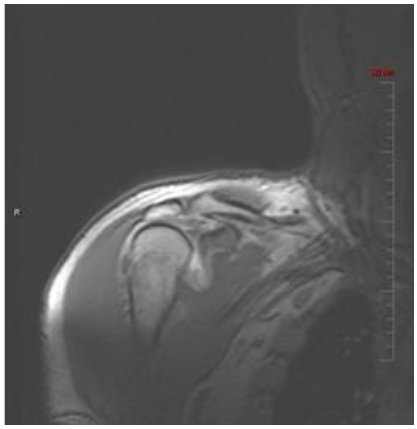


IMAGE ACQUISITION PARAMETERS: Shoulder

To setup and save each sequence please refer to the table below. The sequences are based on suggested acquisition parameters that are typical for 1.5T MRI scanners. Depending on specific hardware/software versions, some settings may vary. Start with your routine clinical sequences and modify settings as indicated below. The imaging protocol for your scanner should be saved at study initiation and subsequently used for all subjects. Consistency in acquisition across all visits is especially important!

	Sequence 2	*Sequence 3*	*Sequence 4*
Sequence name	**Oblique coronal 2D PD-w FSE**	**Oblique coronal 2D PD-w FSE fat sat**	**Oblique sagittal 2D PD-w FSE**
Sequence type/technique	*tse2d1_7 – Siemens; FSE-XL – GE; TSE - Philips		
Image orientation	Oblique coronal	Oblique coronal	Oblique sagittal
Scan Mode	2D	2D	2D
Imaging options	fast, EDR, NPW, VBW - GE; Fast imaging YES and MS – Philips		
FOV (freq × phase) [mm × mm]	190 × 190	190 × 190	190 × 190
Acquisition Matrix (frequency × phase)	256 × 100% - Siemens; 256 × 256 - GE; Voxel size (mm): 0.742 × 0.742 - Philips		
TR [ms]	4000 – 5000	4000 – 5000	4000 – 5000
TE [ms]	35 - 45	35 - 45	35 - 45
Slices	20	20	24
Slice thickness [mm]	3	3	3
Slices gap [mm]	0 (0%)	0 (0%)	0 (0%)
Averages/NEX/NSA	2	2	2
Phase/Foldover direction	H-F	H-F	H-F
Oversampling (Phase)	As needed - Siemens; NPW - GE; Foldover suppression ON - Philips		
ETL/Turbo factor	5 - 9	5 - 9	5 - 9
Bandwidth/water-fat shift	120-150Hz/px - Siemens; 12kHz - GE; Max - Philips		
Fat suppression	None	Fat Sat - Siemens Fat - GE SPAIR - Philips	None
Flow comp.	Yes	Yes	Yes
Sat band (anterior)	Sat band - Siemens/GE; Rest slab - Philips		
Acquisition time [min:sec]	4:30	4:30	4:30

ENTERING SUBJECT DATA IN ELECTRONIC HEADER

In order to ensure patient confidentiality, please enter the following information into the electronic MRI header:

- "**Patient Information**" enter the 3-digit Country Code, 3-digit Site Number followed by the 3-digit Subject Number

  EXAMPLE: 123-101-001

- "**Date of Birth**" enter: **DD-MMM-YYYY**

  EXAMPLE: 07-MAY-1945

Example for countries not allowed to record DOB*:

01-JAN-1945*

- "**Patient History**" enter: **Visit and Laterality if applicable**

  EXAMPLE: Screening, Left

The possible entries for Visit identification:

Screening
Event Driven
Unscheduled
JR Pre-Operative
Post-OP Week 20

Please enter the date of birth as indicated. If regulations prohibit your site from entering the day and month of the date of birth please enter 01 JAN and the correct Year of Birth for the subject. The Year of Birth must be the actual year for the subject.

SUBMITTING DATA TO BIOCLINICA

The data to be sent from the imaging site should include both the imaging study and the transmittal form. Submitting data electronically via the secure FTP website: https://smart.bioclinica.com/ is the required method of submission for this protocol. If your site cannot submit data electronically after attempts have been made to submit a test image, courier services can be utilized.

Electronic Data Transfer Using SMART submit

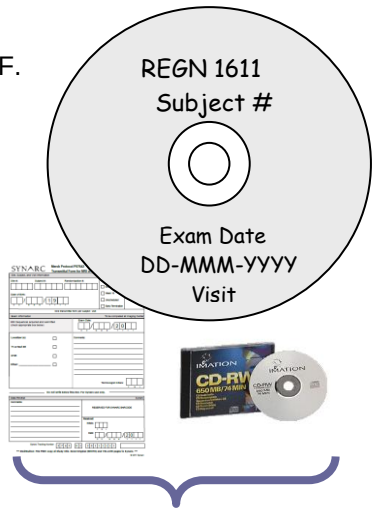
SMART submit is a web-based portal that allows sites to submit images via secure file transfer protocol (FTP). It eliminates delays and expenses associated with shipping images via courier. The Transmittal Form (TF) is completed and submitted electronically as well. Access to SMART submit or technical support may be requested by emailing the study team at Regeneron1611@BioClinica.com.

Sending Data Using Courier Service

The complete package should contain a CD with imaging data and the completed TF.

Export the data to the CD in **uncompressed DICOM** format. Use an indelible marker to label directly on the CD with:

- Study Protocol Number (Regeneron Protocol R475-OA-1611)
- Subject Identifiers (Site Number and Subject Number)
- MRI Exam Date (DD-MMM-YYYY)
- Visit Name



Sending a Package to BioClinica

1. Complete the sender sections of the air waybill, keeping a copy for tracking purposes.
2. Place the white and yellow copies of the TF and the CD for each patient into a shipping envelope. **Please keep pink copy at site.**
3. Call courier to schedule package pick-up.

Ship data to: Regeneron 1611 (9034) Study Team
BioClinica Inc.
7707 Gateway Blvd., Third Floor
Newark, CA 94560 USA
Email: Regeneron1611@BioClinica.com
Office: +1-415-817-8900

Courier
to Bioclinica