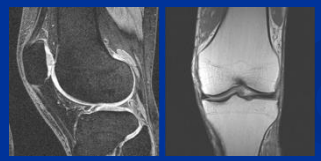
Galapagos/Servier Protocol CL2-201086-002/ GLPG1972-CL-201

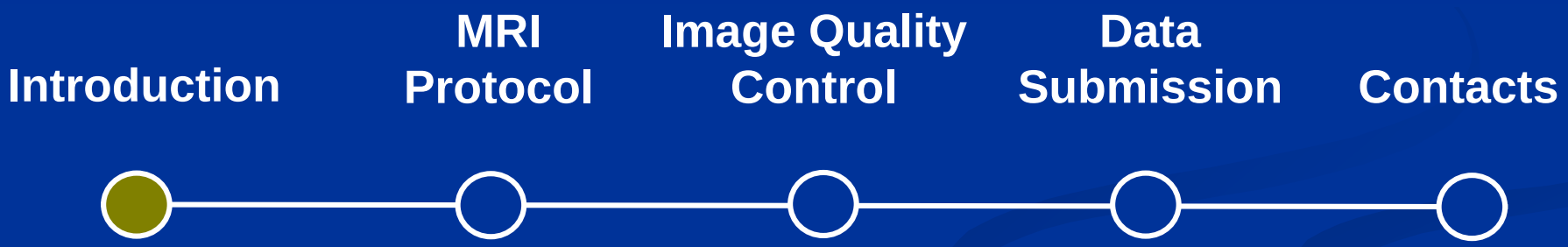
Efficacy and safety of 3 doses of S201086/GLPG1972 administered orally once daily in patients with knee osteoarthritis. A 52-week international, multi-regional, multi-center, randomized, double-blind, placebo-controlled, dose-ranging study.



Training Presentation for Imaging Personnel on MR Image Acquisition of the Knee

Bioclinica, Inc.

Overview


Introduction
MRI Protocol
Image Quality Control
Data Submission
Contacts

Introduction

- Multi-regional, multi-center
- Randomized, double-blind, placebo-controlled
- Efficacy and safety of 3 doses of S201086/GLPG1972 administered orally once daily
- Patients with knee osteoarthritis
- X-ray and MRI
- 110 MRI centers worldwide
- 852 Subjects to be randomized
- Study duration for a subject – 52 weeks

Study Objectives & MR Imaging Endpoints

Primary Objective

- To demonstrate the efficacy of at least one dose (among 3 doses) of S201086/GLPG1972 compared to placebo after 52 weeks of treatment in reducing cartilage loss measured by cartilage thickness using qMRI of the cMTFC of the target knee.

Secondary Objectives

- To assess the safety and tolerability of 3 doses of S201086/GLPG1972.
- To assess efficacy of 3 doses of S201086/GLPG1972 versus placebo after 52 weeks of treatment on:
  - the proportion of “structural progressors*” based on cartilage thickness using qMRI of the cMTFC of the target knee
  - reduction of cartilage loss measured by cartilage thickness using qMRI of the total tibiofemoral compartment (tTFC) of the target knee
- To assess efficacy of 3 doses of S201086/GLPG1972 versus placebo after 28 and 52 weeks of treatment on bone area using qMRI of the medial femoral condyle surface of the target knee.

Schedule of MRI Visits

W000 [Inclusion]

W028

W052

WD [Premature Withdrawal]

If the repeat is needed, it should be done as quickly as possible after the failed exam!

Role of Bioclinica

- Provide expertise in imaging and data management
- Develop and validate imaging protocols
- Create the imaging manual, quick reference guide (QRG), and other study materials
- Qualify imaging centers / train imaging personnel
- Provide technical and logistical support for imaging sites
- Collect and archive locally acquired MRI exams
- Perform image quality control (QC)

Bioclinica Team

Sheena Saighal	*Clinical Project Manager*	*Princeton, NJ*
Vahan Sharoyan, PhD	*MRI Physicist*	*Newark, CA*
Shawn Rezazadeh	*Clinical Operations*	*Newark, CA*
Hien Lam	*Clinical Operations*	*Newark, CA*
Michelle Hebert	*MRI technologist*	*Newark, CA*
Phil Keil	*MRI technologist*	*San Antonio, TX*
Julie Fitzpatrick	*MRI technologist*	*London, UK*
Nuno Lima	*MRI technologist*	*London, UK*

Role of MR Imaging Facility

Acquisition of high quality MR images is critical to the success of this study!

- Perform exams according to the imaging protocol, ensuring consistency across subjects and across visits for each subject
- Submit imaging studies along with accurate demographic information (TF) to Bioclinica within 1 (one) business day after examination.

General Requirements for MRI Sites

- 1.5T (or 3T) scanners
- Siemens/Philips/GE
- Knee RF coil approved by Bioclinica
- Digital archive capability
- No major hardware or software upgrades during study period

It is required that the same scanner and knee coil be used for ALL VISITS!

If you plan to have an upgrade, please contact Bioclinica!

Imaging Site Qualification

Site Qualification Process

- Review of MRI site questionnaire √
- Training of imaging personnel √
- Test dataset acquisition √

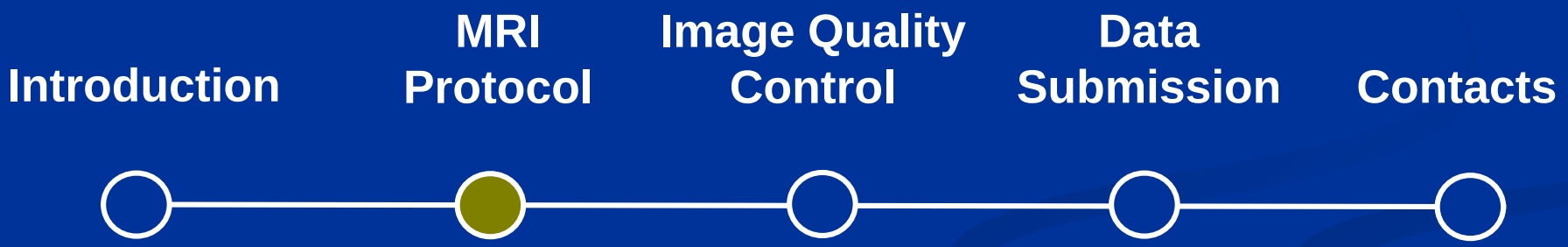
Do not perform scanning of patients until the test dataset is approved by Bioclinica!

Imaging Site Supplies

Reference tools

- MRI procedure manual
- Transmittal forms
- Quick reference guide

Overview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MR Imaging Session: General Information

Subject Safety during the MRI exam is your responsibility!

- Follow Good Clinical Practice. Adhere to your customary procedures for safety screening prior to placing the subject into the scanner.
- Have all study information, study forms, etc. available prior to the exam.

MR Imaging Session: Laterality of the Target Knee

- The laterality of the target knee will be defined for the technologist before MR imaging session
- The imaging personnel should not make the decision regarding laterality
- Target knee will not change during the course of the study
- If in doubt, postpone the MRI exam and contact the PI/Study coordinator for clarification
- Before you start imaging for a follow-up visit, refer to Baseline exam to confirm laterality

Registering the Subject (Labeling the Electronic Header)

- Subject Identification: [4-digit site #]-[5-digit Subject#]
  Example: 0123-00115
- Date of Birth: 01-JAN-YYYY
  Example: 01-JAN-1950
- Subject History: visit and laterality of the
  Example: Baseline, Left

Possible entries for visit name:
W000 [Inclusion]
W028
W052
WD [Premature Withdrawal]

Anonymize, using your PACS, if necessary. Do not give the patient's name or other identifying information, such as Social Security Number, National Health Service Number, or medical record number.

MR Imaging Protocol - 1

Standard Protocol

- at visits W000, W028, W052, WD

1. *3-Plane Localizer(s)*
2. *Sagittal 3D T1-w GRE WE/FS*
3. *Coronal 2D T1-w FSE*

MR Imaging Protocol - 2

Test-Retest Protocol

- one patient only (1st to 3rd) at visits W000, W052 (or WD if the subject discontinues the study). No test-retest protocol at W028.

1. *3-Plane Localizer(s)*
2. *Sagittal 3D T1-w GRE WE/FS*

Take the subject off the table.

3. *3-Plane Localizer(s) retest*
4. *Sagittal 3D T1-w GRE WE/FS retest*
5. *Coronal 2D T1-w FSE*

- Stop image acquisition upon acquiring sequence 2.
- Take the subject off the table.
- Allow the subject to rest for 2-5min.
- Put the subject back on the table and secure the knee inside the knee coil.
- Continue imaging session by acquiring new localizer sequence(s) followed by sequences 4 and 5.
- All acquired sequences (pre- and post-repositioning) should be submitted to Bioclinica as a single imaging exam!

Subject Preparation and Positioning - 1

- The laterality of the target knee 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.
- Subject positioning inside the scanner should be Feet First Supine (FFS).
- In the coil the knee should be positioned so that that the apex of the patella is aligned with the center of the coil (A).
- The leg should be in a relaxed, neutral position. The most comfortable (and sustainable) one is attained when the knee joint is slightly flexed. Many coils are designed to accommodate this. However, if the base of your coil is flat, use the pads/pillows to slightly elevate and flex the knee.

Subject Preparation and Positioning - 2

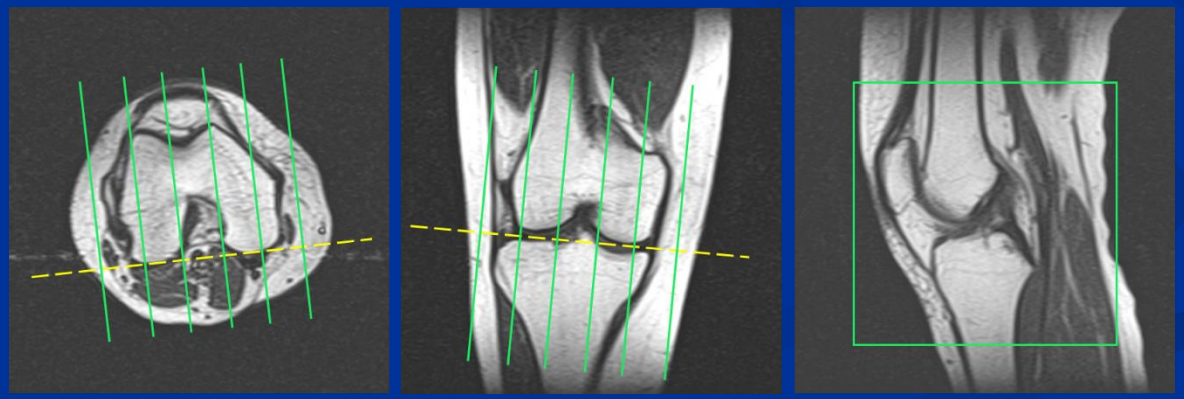
- Once the knee is comfortably oriented and centered inside the base of the coil, attach the top (B). Use pads as needed to immobilize the knee (C).
- Position the coil as close as possible to the center of the table. To achieve this, offset the patient toward the contralateral side.
- Be sure to keep the non-target knee away from the target knee. Have the patient flex and elevate the non-target knee, then put padding under non-target knee to keep it higher (more anterior) than the target knee.
- 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 at the center of the coil (apex of the patella).
- During imaging monitor the subject at all times.

Anatomical Coverage & Slice Prescription - 1

Complete coverage of the knee joint, including patella, is required. If the protocol-recommended number of slices is not enough to attain complete coverage, add as many slices as needed. The protocol-specified FOV dimensions should not be altered!

Sagittal 3D T1-w GRE WE/FS

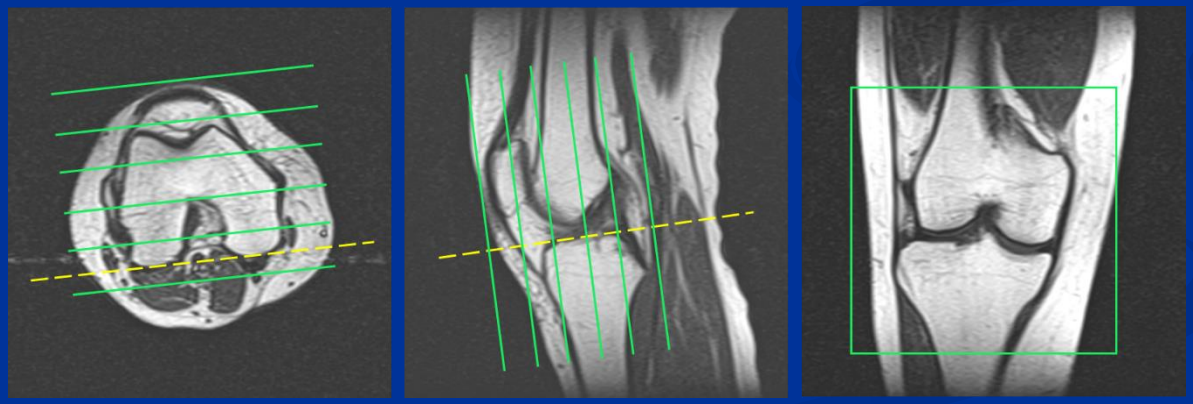
- Based on the axial localizer find the slice with the largest cross-section through femoral condyles and identify the line connecting posterior surfaces of the condyles. The slices should be perpendicular to this line. Make sure the joint is well centered within the stack.
- Based on the coronal localizer prescribe the slices perpendicular to tibial plateau. The knee joint should be in the center of the stack.
- Based on the mid-sagittal localizer make sure the FOV is well prescribed and the knee joint, including patella, is covered. The imaging volume should include both femorotibial and patellar cartilage.



Anatomical Coverage & Slice Prescription - 2

Coronal 2D T1-w FSE

- 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 aligned (parallel) to this line.
- Based on the mid-sagittal localizer prescribe the slices parallel to the tibia. The knee joint should be in the center of the stack.
- Based on the coronal localizer make sure the FOV is well positioned and the femur-tibia joint is in the center of it.



Sequence Settings and Parameters: Siemens 1.5T Scanners - 1

Interface card	Parameter name	Sagittal 3D T1-w FLASH WE/FS	Coronal 2D T1-w FSE
Routine	Sequence file	***fl3d1**	***tse2d1**
	Orientation	Sagittal	Coronal
	Phase encode dir.	A>>P	R>>L
	Phase oversampling [%]	0	0
	Slice oversampling [%]	0	0
	Slice groups	NA	1
	Slices	NA	36
	Slabs	1	NA
	Slices per slab	76	NA
	FOV read [mm]	160	160
	FOV phase [%]	100	100
	Slice thickness [mm]	1.5	3
	Distance factor [%]	NA	10
	TR [ms]	18 - 25	400 - 650
	TE [ms]	6 - 9	8 – 15
	Averages	1	1
	Concatenations	NA	1
Contrast common	Flip Angle [degree]	15	NA
	Water Excitation	On-Fast	NA
	Fat Suppression	OFF	OFF
	Base resolution	512	256
	Phase resolution [%]	100	100
	Slice resolution [%]	100	100
	Phase partial Fourier	Off	Off
	Slice partial Fourier	Off	Off

Sequence Settings and Parameters: Siemens 1.5T Scanners - 2

Interface card	Parameter name	Sagittal 3D T1-w FLASH WE/FS	Coronal 2D T1-w FSE
Contrast iPAT	PAT Mode	None	Default settings
Resolution	Imaging mode	3D	2D
	Filter	Norm	2D Distortion correction
	Interpolation	None	None
Geometry common	Multi-slice mode	NA	Interleave
Sequence Part 1	Bandwidth [Hz/px]	120-180	120-180
	Flow comp	On in frequency direction	None
Sequence Part 2	Turbo Factor	NA	3 - 5
	RF pulse type	Normal (Fast)	Normal (Fast)
	Gradient mode	Normal (Fast)	Normal (Fast)
	Asymmetric echo	On (if available)	OFF
	RF spoiling	Default setting	Default setting
	Scan time [min]	9 – 14	3-4

Sequence Settings and Parameters: Siemens 3T Scanners - 1

Interface card	Parameter name	Sagittal 3D T1-w FLASH WE/FS	Coronal 2D T1-w FSE
Routine	Sequence file	***fl3d1**	***tse2d1**
	Orientation	Sagittal	Coronal
	Phase encode dir.	A>>P	R>>L
	Phase oversampling [%]	0	0
	Slice oversampling [%]	0	0
	Slice groups	NA	1
	Slices	NA	36
	Slabs	1	NA
	Slices per slab	76	NA
	FOV read [mm]	160	160
	FOV phase [%]	100	100
	Slice thickness [mm]	1.5	3
	Distance factor [%]	NA	10
	TR [ms]	15 - 25	500 - 800
	TE [ms]	6 - 9	7-15
	Averages	1	1
	Concatenations	NA	1
Contrast common	Flip Angle [degree]	12	NA
	Water Excitation	On-Fast	NA
	Fat Suppression	OFF	OFF
	Base resolution	512	256
	Phase resolution [%]	100	100
	Slice resolution [%]	100	100
	Phase partial Fourier	Off	Off
	Slice partial Fourier	Off	Off

Sequence Settings and Parameters: Siemens 3T Scanners - 2

Interface card	Parameter name	Sagittal 3D T1-w FLASH WE/FS	Coronal 2D T1-w FSE
Contrast iPAT	PAT Mode	None	Default settings
Resolution	Imaging mode	3D	2D
	Filter	Norm	2D Distortion correction
	Interpolation	None	None
Geometry common	Multi-slice mode	NA	Interleave
Sequence Part 1	Bandwidth [Hz/px]	180 - 240	180 - 240
	Flow comp	On in frequency direction	None
Sequence Part 2	Turbo Factor	NA	3 - 5
	RF pulse type	Normal (Fast)	Normal (Fast)
	Gradient mode	Normal (Fast)	Normal (Fast)
	Asymmetric echo	On (if available)	OFF
	RF spoiling	Default setting	Default setting
	Scan time [min]	9 – 14	3-4

Sequence Settings and Parameters: GE 1.5T Scanners - 1

Interface card	Parameter name	Sagittal 3D T1-w GRE FS	Coronal 2D T1-w FSE
Patient position	Patient position	Supine	Supine
	Patient entry	Feet first	Feet first
	Coil	Multichan'l knee	Multichan'l knee
Imaging parameters	Plane	Sagittal (Oblique)	Coronal (Oblique)
	Mode	3D	2D
	Pulse seq	SPGR	FSE-XL
	Imaging options	fast, EDR, FC	fast, EDR, VBW
	Gradient mode	zoom if available	zoom if available
Scan timing	# of Echoes	1	NA
	TE [ms]	min	7 – 15
	TR [ms]	Default value	400 – 650
	TI [ms]	NA	NA
	Flip angle	15	NA
	Echo train length	NA	3 – 5
	Bandwidth [±kHz]	~24 for pre- 450 model scanners 24-48 for 450 and later release scanners	15.6 for pre- 450 model scanners 32-48 for 450 and later release scanners
Acquisition timing	Frequency	512	256
	Phase	512	256
	NEX	1	1
	Phase FOV	1	1
	Acquisitions before pause	NA	NA
	Frequency direction	SI	SI
	Flow comp direction	frequency	NA
	Shim	Auto	Auto
	Phase correct	NA	NA

Sequence Settings and Parameters: GE 1.5T Scanners - 2

Interface card	Parameter name	Sagittal 3D T1-w GRE FS	Coronal 2D T1-w FSE
Scanning range	FOV [cm]	16	16
	Slice thick. [mm]	1.5	3
	Spacing	NA	0.3
	# of slabs	1	NA
	Locs per slab	80	NA
	# of slices	NA	36
Additional Parameters Graphic Rx FAT	SAT band	no	no
	SAT	Fat	none
	Shim FOV	NA	NA
	Scan time [min]	10 – 16	2-3

Sequence Settings and Parameters: GE 3T Scanners - 1

Interface card	Parameter name	Sagittal 3D T1-w GRE FS	Coronal 2D T1-w FSE
Patient position	Patient position	Supine	Supine
	Patient entry	Feet first	Feet first
	Coil	Multichan'l knee	Multichan'l knee
Imaging parameters	Plane	Sagittal (Oblique)	Coronal (Oblique)
	Mode	3D	2D
	Pulse seq	SPGR	FSE-XL
	Imaging options	fast, EDR, FC	fast, EDR, VBW
	Gradient mode	zoom if available	zoom if available
Scan timing	# of Echoes	1	NA
	TE [ms]	min	7-15
	TR [ms]	Default value	500 - 800
	TI [ms]	NA	NA
	Flip angle	12	NA
	Echo train length	NA	3 – 5
	Bandwidth [±kHz]	~48 for pre- 450 model scanners 48-90 for 750 and later release scanners	24-32 for pre- 750 model scanners ~64-96 for 750 and later release scanners
Acquisition timing	Frequency	512	256
	Phase	512	256
	NEX	1	1
	Phase FOV	1	1
	Acquisitions before pause	NA	NA
	Frequency direction	SI	SI
	Flow comp direction	frequency	NA
	Shim	Auto	Auto
	Phase correct	NA	NA

Sequence Settings and Parameters: GE 3T Scanners - 2

Interface card	Parameter name	Sagittal 3D T1-w GRE FS	Coronal 2D T1-w FSE
Scanning range	FOV [cm]	16	16
	Slice thick. [mm]	1.5	3
	Spacing	NA	0.3
	# of slabs	1	NA
	Locs per slab	80	NA
	# of slices	NA	36
Additional Parameters Graphic Rx FAT	SAT band	no	no
	SAT	Fat	none
	Shim FOV	NA	NA
	Scan time [min]	10 – 16	2-3

Sequence Settings and Parameters: Philips 1.5T Scanners - 1

Interface card	Parameter name	Sagittal 3D T1-w GRE WE	Coronal 2D T1-w TSE
Geometry	Coil selection	SENSE-Knee-multichannel	SENSE-Knee-multichannel
	Dual coil	no	no
	Homogeneity correction	none	none
	CLEAR	yes	yes
	body tuned	no	no
	FOV FH [mm]	160	160
	AP [mm]	160	119
	RL [mm]	114	160
	Voxel size FH [mm]	0.312	0.625
	AP [mm]	0.312	NA
	RL [mm]	1.5	0.625
	Slice thickness [mm]	NA	3
	Recon voxel size [mm]	0.312	0.625
	Fold-over suppression	no	no
	Reconstruction matrix	512	256
	SENSE	no	no
	Over-contiguous slices	no	NA
	Stacks	1	1
	type	NA	Parallel
	slices	76	36
	slice gap	NA	user defined
	gap [mm]	NA	0.3
	slice orientation	sagittal	coronal
	foldover direction	AP	RL
	fat shift direction	F	P
	Chunks	1	NA
	Minimum number of packages	NA	1
	Slice scan order	NA	interleaved
	Large table movement	no	no
	PlanAlign	no	no
	REST slabs	0	0
	type	NA	NA
	orientation	NA	NA
	thickness [mm]	NA	NA
	power	NA	NA

Images should be submitted in:

- Uncompressed dicom format. Compressed dicom is not accepted.
- These dicom attributes (tags) should be present in mages submitted to Bioclinica. Be sure to not delete, anonymize or otherwise alter the values associated with these tags.

0028,1052: Rescale Intercept
0028,1053: Rescale Slope
2005,100d: Scale Intercept
2005,100e: Scale Slope

Sequence Settings and Parameters: Philips 1.5T Scanners - 2

Interface card	Parameter name	Sagittal 3D T1-w GRE WE	Coronal 2D T1-w TSE
Contrast	Patient position	feet first	feet first
	orientation	supine	supine
	Scan mode	3D WATSC	MS
	technique	FFE	SE
	Modified SE	NA	no
	Contrast enhancement	T1	NA
	Acquisition mode	cartesian	cartesian
	Fast imaging mode	none	TSE
	shot mode	NA	multishot
	TSE factor	NA	3 - 5
	TE spacing	NA	shortest
	[ms]	NA	NA
	startup echoes	NA	0
	profile order	NA	asymmetric
	DRIVE	NA	no
	ultrashort	NA	yes
	Echoes	1	1
	partial echo	yes	no
	shifted echo	no	NA
	TE	shortest	shortest
	[ms]	NA	NA
	Flip angle [degree]	15	90
	Refocusing control	NA	yes
	angle [degree]	NA	Default
	TR	shortest	shortest
	User defined	NA	NA
	Half scan	no	no
	Water-fat shift	User defined	max
	[px]	1.0 – 1.8	NA
	Shim	auto	auto
	Fat suppression	Proset	no
	pulse type	121	NA
	Inver. delay [ms]	NA	NA
	frequency offset	NA	NA
	Water suppression	no	no
	BB pulse	NA	no
	Gradient mode	default	default
	SoftTone mode	no	no

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Sequence Settings and Parameters: Philips 1.5T Scanners - 3

Interface card	Parameter name	Sagittal 3D T1-w GRE WE	Coronal 2D T1-w TSE
Motion	Cardiac synchronization	no	no
	Respiratory compensation	no	no
	Navigator respiratory comp	no	no
	Flow compensation	ON in Frequency direction	yes
	Motion smoothing	NA	yes
	fMRI echo stabilization	no	NA
	NSA	1	1
Dyn/angio	Angio/Contrast enh.	no	NA
	Quantitative flow	no	NA
	Manual start	no	no
	Dynamic study	no	no
Post proc	Preparation phases	auto	auto
	Manual Offset Freq	no	no
	Reference tissue	Skeletal muscle	Skeletal muscle
	Preset window contrast	soft	soft
	Reconstruction mode	immediate	immediate
	Ringing filtering	default	default
	Geometry correction	default	default
	Elliptical k-space shutter	default	default
	Scan time [min]	10 - 15	3-4

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2005,100e: Scale Slope

Sequence Settings and Parameters: Philips 3T Scanners - 1

Interface card	Parameter name	Sagittal 3D T1-w GRE WE	Coronal 2D T1-w TSE
Geometry	Coil selection	SENSE-Knee-multichannel	SENSE-Knee-multichannel
	Dual coil	no	no
	Homogeneity correction	none	none
	CLEAR	yes	yes
	body tuned	no	no
	FOV FH [mm]	160	160
	AP [mm]	160	119
	RL [mm]	114	160
	Voxel size FH [mm]	0.312	0.625
	AP [mm]	0.312	NA
	RL [mm]	1.5	0.625
	Slice thickness [mm]	NA	3
	Recon voxel size [mm]	0.312	0.625
	Fold-over suppression	no	no
	Reconstruction matrix	512	256
	SENSE	no	no
	Over-contiguous slices	no	NA
	Stacks	1	1
	type	NA	Parallel
	slices	76	38
	slice gap	NA	user defined
	gap [mm]	NA	0.3
	slice orientation	sagittal	coronal
	foldover direction	AP	RL
	fat shift direction	F	P
	Chunks	1	NA
	Minimum number of packages	NA	1
	Slice scan order	NA	interleaved
	Large table movement	no	no
	PlanAlign	no	no
	REST slabs	0	0
	type	NA	NA
	orientation	NA	NA
	thickness [mm]	NA	NA
	power	NA	NA

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2005,100e: Scale Slope

Sequence Settings and Parameters: Philips 3T Scanners - 2

Interface card	Parameter name	Sagittal 3D T1-w GRE WE	Coronal 2D T1-w TSE
Contrast	Patient position	feet first	feet first
	orientation	supine	supine
	Scan mode	3D WATSC	MS
	technique	FFE	SE
	Modified SE	NA	no
	Contrast enhancement	T1	NA
	Acquisition mode	cartesian	cartesian
	Fast imaging mode	none	TSE
	shot mode	NA	multishot
	TSE factor	NA	3 - 5
	TE spacing	NA	shortest
	[ms]	NA	NA
	startup echoes	NA	0
	profile order	NA	asymmetric
	DRIVE	NA	no
	ultrashort	NA	yes
	Echoes	1	1
	partial echo	yes	no
	shifted echo	no	NA
	TE	shortest	shortest
	[ms]	NA	NA
	Flip angle [degree]	12	90
	Refocusing control	NA	yes
	angle [degree]	NA	Default
	TR	shortest	shortest
	User defined	NA	NA
	Half scan	no	no
	Water-fat shift	User defined	max
	[px]	1.0 – 1.8	NA
	Shim	auto	auto
	Fat suppression	Proset	no
	pulse type	121	NA
	Inver. delay [ms]	NA	NA
	frequency offset	NA	NA
	Water suppression	no	no
	BB pulse	NA	no
	Gradient mode	default	default
	SoftTone mode	no	no

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2005,100e: Scale Slope

Sequence Settings and Parameters: Philips 3T Scanners - 3

Interface card	Parameter name	Sagittal 3D T1-w GRE WE	Coronal 2D T1-w TSE
Motion	Cardiac synchronization	no	no
	Respiratory compensation	no	no
	Navigator respiratory comp	no	no
	Flow compensation	ON in Frequency direction	yes
	Motion smoothing	NA	yes
	fMRI echo stabilization	no	NA
	NSA	1	1
Dyn/angio	Angio/Contrast enh	no	NA
	Quantitative flow	no	NA
	Manual start	no	no
	Dynamic study	no	no
Post proc	Preparation phases	auto	auto
	Manual Offset Freq	no	no
	Reference tissue	Skeletal muscle	Skeletal muscle
	Preset window contrast	soft	soft
	Reconstruction mode	immediate	immediate
	Ringing filtering	default	default
	Geometry correction	default	default
	Elliptical k-space shutter	default	default
	Scan time [min]	10 - 15	3-4

Images should be submitted in:

- Uncompressed dicom format. Compressed dicom is not accepted.
- These dicom attributes (tags) should be present in mages submitted to Bioclinica. Be sure to not delete, anonymize or otherwise alter the values associated with these tags.

0028,1052: Rescale Intercept
0028,1053: Rescale Slope
2005,100d: Scale Intercept
2005,100e: Scale Slope

Post Image Acquisition

- Archive exams locally
- Complete the Transmittal Form*
- Forward to Site Coordinator and/or Bioclinica

These steps to be established between the study coordinator and the MRI facility

Overview

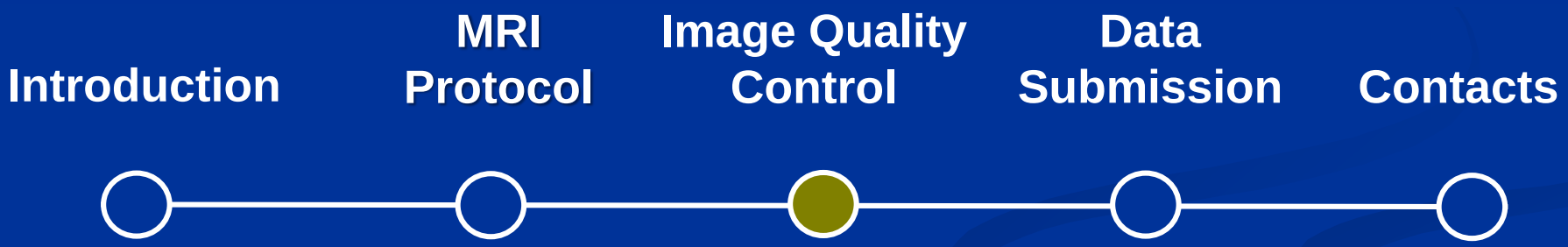
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Image Quality in a Clinical Trial

Consistency is very important! Please always ensure same scanner and coil is used when scanning a Subject

- Before Imaging - at the stage of patient preparation
- During imaging
  - Sequences and parameters should not be altered
  - Image acquisition technique by an operator
- Post image acquisition - preparing and submitting the data

Image Quality of 3D T1-w GRE WE/FS Images

- Sagittal 3D-w T1-w GRE WE/FS is the most important sequence in the protocol.
  - It is intended for cartilage segmentation and quantification.
- It‘s the operator’s responsibility to obtain adequate-quality sagittal 3D-w T1-w GRE WE/FS images.
  - Review images right after the scan and before acquiring other sequence(s).
  - If image quality is sub-standard or otherwise compromised, repeated the sequence immediately after initial failed acquisition.

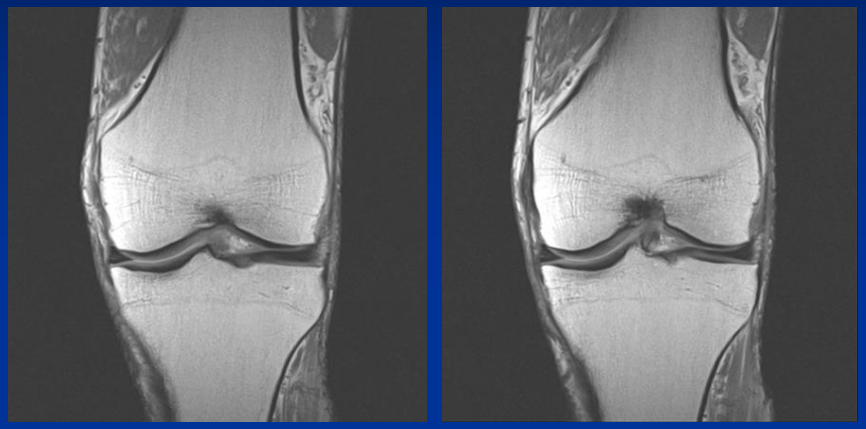
High-Quality Images - 1

3D FLASH WE – Siemens | 3D WATSC WE – Philips | 3D FSPGR Fat Sat – GE

Sagittal 3D T1-w GRE WE/FS

- Images are clear of artifacts obscuring knee anatomy
- FOV is well centered
- Bone signal is homogenous, and the bone/cartilage contrast-to-noise is of high quality which is critical for quantification of the articular cartilage.
- Images are clear of motion and aliasing artifacts obscuring the cartilage-bone interface.

High-Quality Images - 2



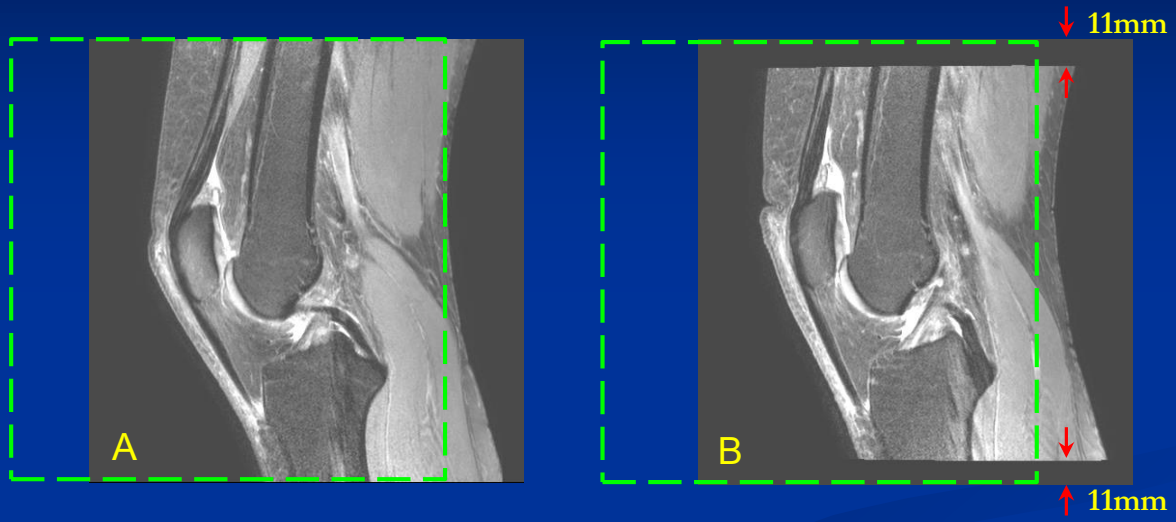
Coronal 2D T1-w FSE

- Images are clear of artifacts obscuring knee anatomy
- FOV is well centered
- Good contrast-to-noise allowing for clear delineation of the body of menisci and the synovial space.

Substandard Image Quality

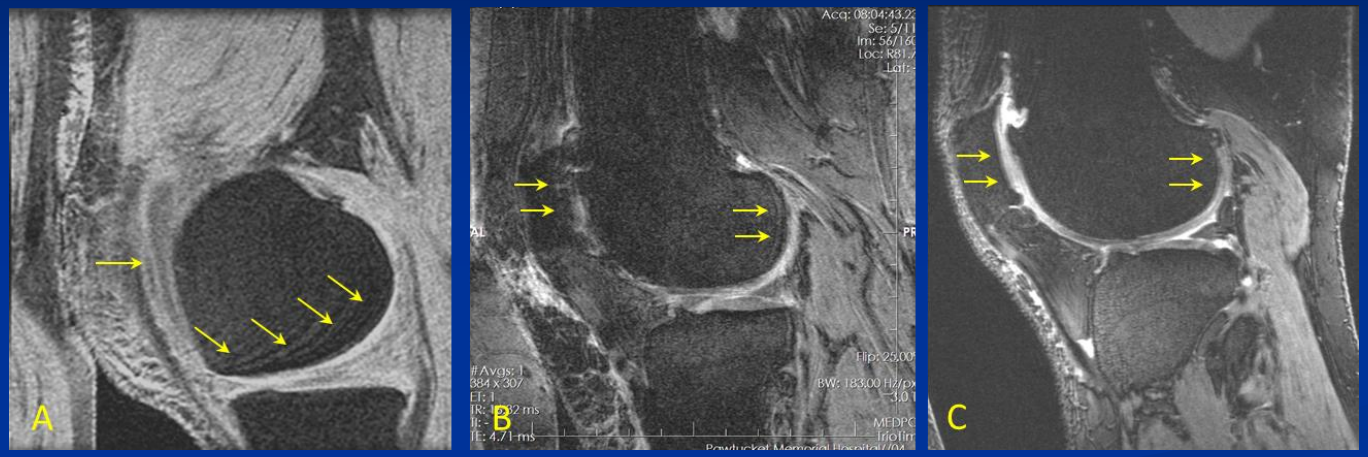
- Anatomical coverage
- Subject motion
- Pulsatile (flow-related) motion
- Aliasing (wraparound artifact)
- Other artifacts

Substandard Image Quality: Anatomical Coverage



- Both images are unacceptable due to compromised anatomical coverage.
- Image A - the FOV is prescribed incorrectly in AP direction.
- Image B – the FOV is prescribed incorrectly in AP direction and the calibration scan was performed incorrectly which reduced the actual image size in SI direction.

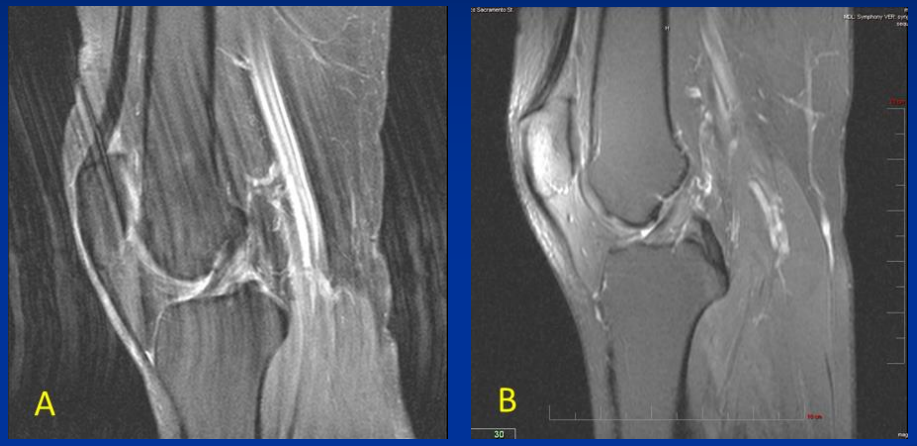
Substandard Image Quality: Motion



3D T1-w GRE fat sat/WE

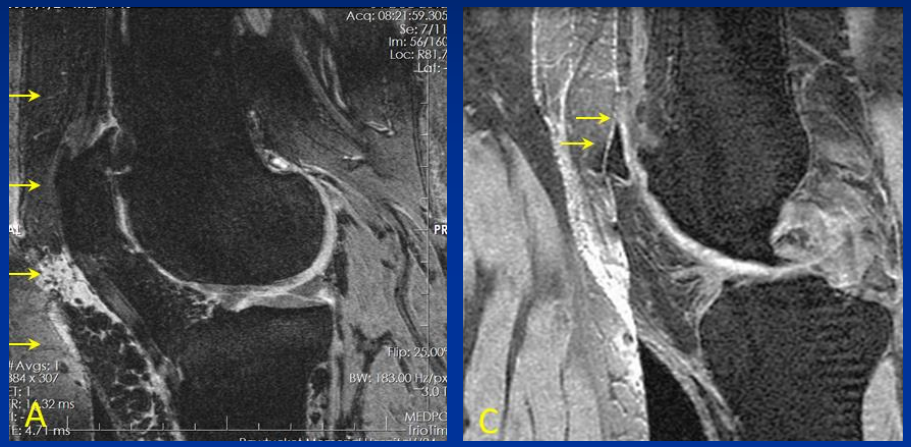
- A and B are the cases with severe motion artifacts; these datasets cannot be analyzed and are not acceptable
- C contains subtle motion artifacts and image quality is borderline acceptable.
- To minimize motion artifacts, position the patient comfortably using cushions and/or pads around the knee.

Substandard Image Quality: Pulsatile Motion (Flow) -1



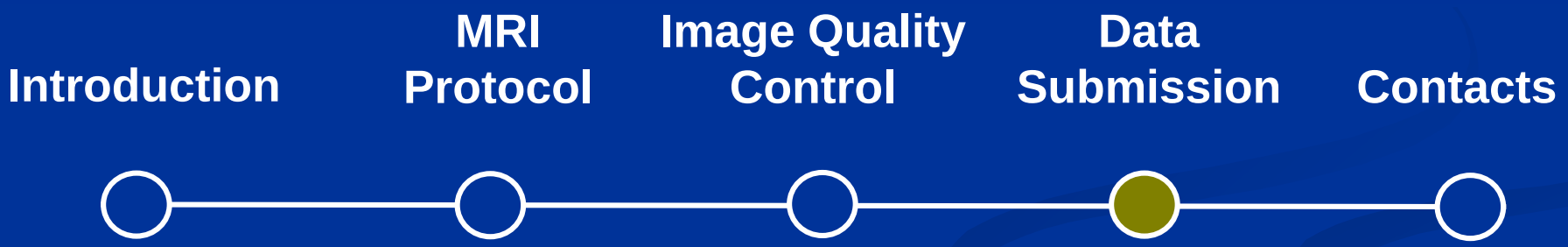
- In A, the pulsatile artifact projects into the knee and obscures anatomy. The image in A cannot be used for semi-quantitative scoring and is not acceptable.
- In B, the image is acceptable using phase oversample and superior saturation bands.

Substandard Image Quality: Aliasing



- In A the aliasing artifact does not obscure the anatomy of interest (the patellar cartilage and the knee joint), therefore these images can still be accepted and evaluated
- In image C the patellar cartilage is obscured by aliasing which renders the image unacceptable. In this case the FOV should be repositioned and the sequence reacquired.

Overview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Data Preparation

Before sending data to Bioclinica verify that

- All imaging sequences have been included (include all acquired localizers and additional sequences!)
- Incase scans or parameters were incorrect rescans were immediately acquired
- Demographic information is correct

Sending Data to Bioclinica

Electronic upload via SMART Portal (preferred)

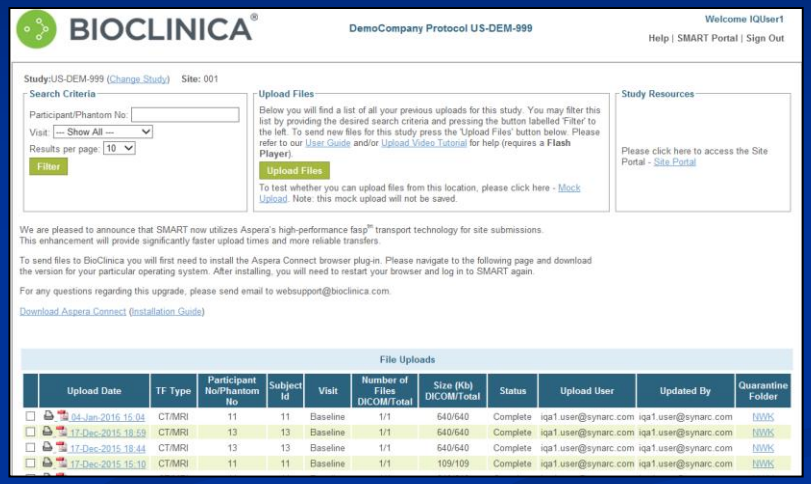
Go to https://smartsubmit.bioclinica.com/. Login information will be provided to you in a separate email

CD using courier postal service

- Paper TF must be filled out completely and should accompany the image dataset
- Keep the pink copy, send the white and yellow copies to Bioclinica
- Use UPS, FedEx or DHL airway bill

Data Submission: SMART Submit

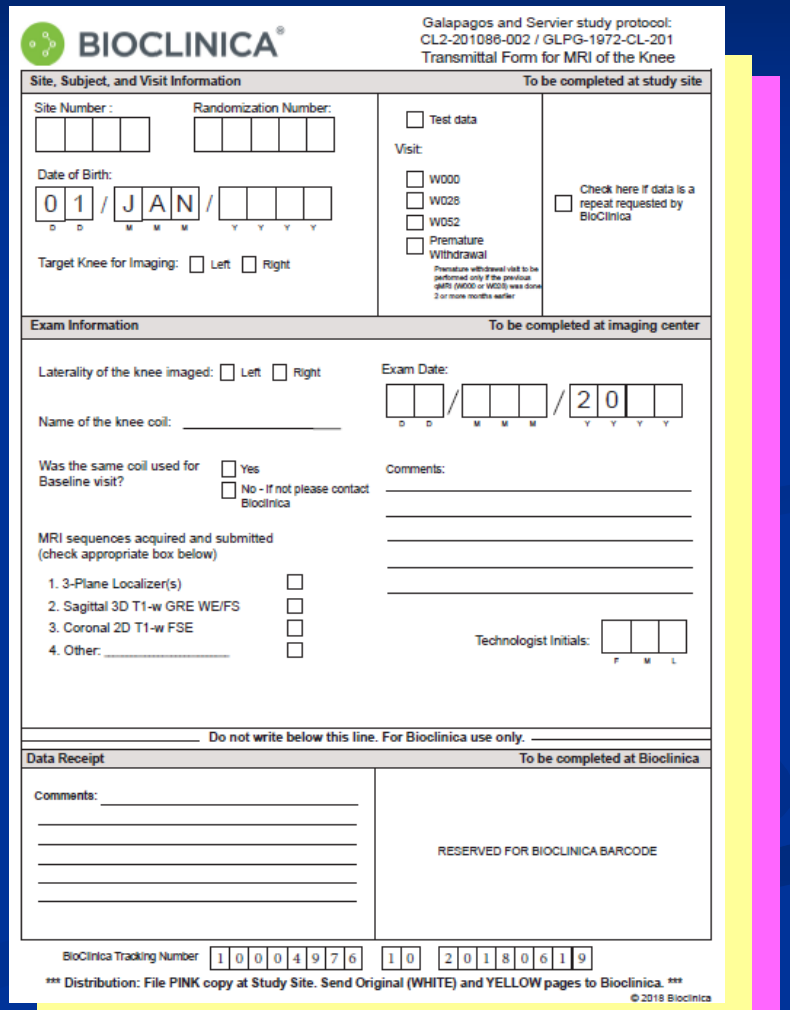
- Upload image data to Bioclinica within 24 hours of acquisition
- Enter information regarding current upload, such as visit name and participant information
- Submit visit info and upload data



Refer to the MRI Imaging Manual for additional instructions

Data Submission: MRI Transmittal Form for Standard Protocol

- Complete a single transmittal form (TF) per subject-visit
- Keep the pink copy at imaging center and send the white & yellow copies to Bioclinica
- Send the TF and image dataset to Bioclinica within 24 hours of acquisition



BIOCLINICA®

Galapagos and Servier study protocol:
CL2-201086-002 / GLPG-1972-CL-201
Transmittal Form for MRI of the Knee

Site, Subject, and Visit Information — To be completed at study site

Site Number : | Randomization Number:

Test data

Visit:
- W000
- W028
- W052
- Premature Withdrawal

Premature withdrawal visit to be performed only if the previous qMRI (W000 or W028) was done 2 or more months earlier

Check here if data is a repeat requested by BioClinica

Date of Birth: 0 1 / J A N / (D D / M M M / Y Y Y Y)

Target Knee for Imaging: Left Right

Exam Information — To be completed at imaging center

Laterality of the knee imaged: Left Right

Exam Date: (D D / M M M / 2 0 Y Y)

Name of the knee coil: _____

Was the same coil used for Baseline visit?
- Yes
- No - If not please contact Bioclinica

Comments: _____

MRI sequences acquired and submitted (check appropriate box below)
1. 3-Plane Localizer(s)
2. Sagittal 3D T1-w GRE WE/FS
3. Coronal 2D T1-w FSE
4. Other: _____

Technologist Initials: (F M L)

Do not write below this line. For Bioclinica use only.

Data Receipt — To be completed at Bioclinica

Comments: _____

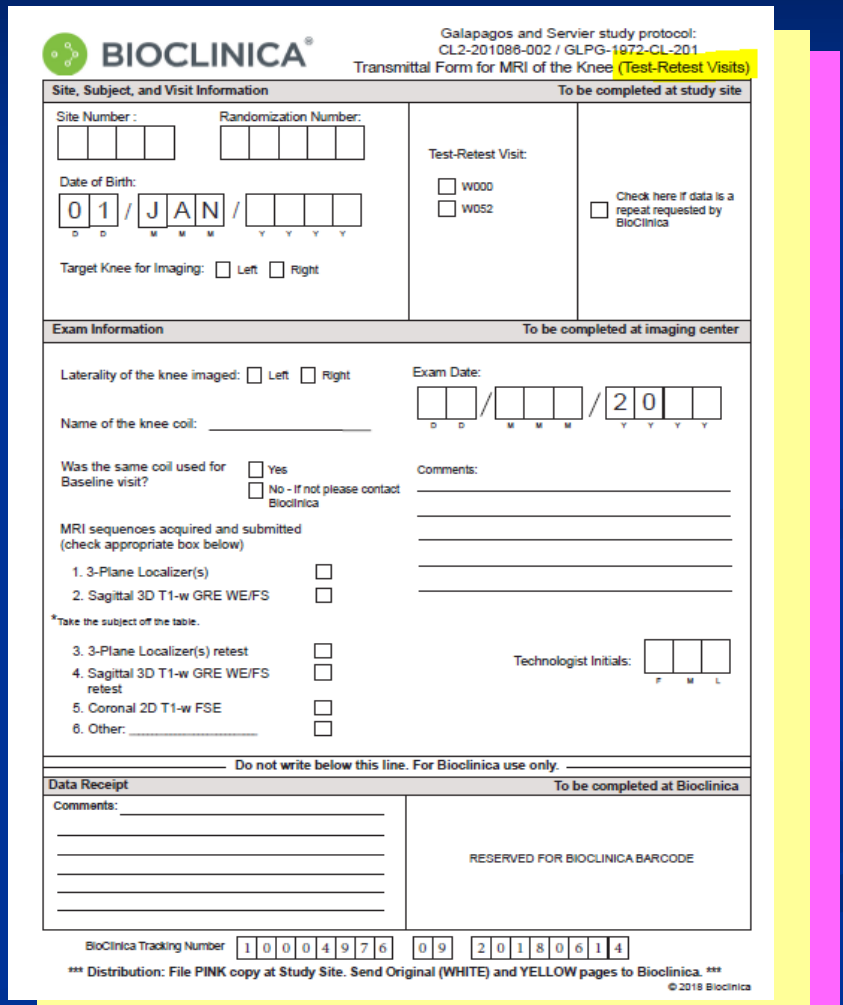
RESERVED FOR BIOCLINICA BARCODE

BioClinica Tracking Number: 1 0 0 0 4 9 7 6 | 1 0 | 2 0 1 8 0 6 1 9

*** Distribution: File PINK copy at Study Site. Send Original (WHITE) and YELLOW pages to Bioclinica. ***

Data Submission: MRI Transmittal Form for Test-Retest Protocol

- Complete a single transmittal form (TF) per subject-visit
- Keep the pink copy at imaging center and send the white & yellow copies to Bioclinica
- Send the TF and image dataset to Bioclinica within 24 hours of acquisition



BIOCLINICA®

Galapagos and Servier study protocol:
CL2-201086-002 / GLPG-1972-CL-201
Transmittal Form for MRI of the Knee (Test-Retest Visits)

Site, Subject, and Visit Information — To be completed at study site

Site Number : ☐☐☐☐ Randomization Number: ☐☐☐☐☐

Date of Birth: 0 1 / J A N / ☐☐☐☐ (D D / M M M / Y Y Y Y)

Target Knee for Imaging: ☐ Left ☐ Right

Test-Retest Visit: ☐ W000 ☐ W052

☐ Check here if data is a repeat requested by BioClinica

Exam Information — To be completed at imaging center

Laterality of the knee imaged: ☐ Left ☐ Right

Exam Date: ☐☐ / ☐☐☐ / 2 0 ☐☐ (D D / M M M / Y Y Y Y)

Name of the knee coil: _____

Was the same coil used for Baseline visit? ☐ Yes ☐ No - If not please contact Bioclinica

Comments: _____

MRI sequences acquired and submitted (check appropriate box below)

1. 3-Plane Localizer(s) ☐
2. Sagittal 3D T1-w GRE WE/FS ☐

*Take the subject off the table.

3. 3-Plane Localizer(s) retest ☐
4. Sagittal 3D T1-w GRE WE/FS retest ☐
5. Coronal 2D T1-w FSE ☐
6. Other: _____ ☐

Technologist Initials: ☐☐☐ (F M L)

Do not write below this line. For Bioclinica use only.

Data Receipt — To be completed at Bioclinica

Comments: _____

RESERVED FOR BIOCLINICA BARCODE

BioClinica Tracking Number 1 0 0 0 4 9 7 6 0 9 2 0 1 8 0 6 1 4

*** Distribution: File PINK copy at Study Site. Send Original (WHITE) and YELLOW pages to Bioclinica. ***

Data Submission: CD

- Use a blank CD for every subject-visit
- The following should be in DICOM headers and on a CD

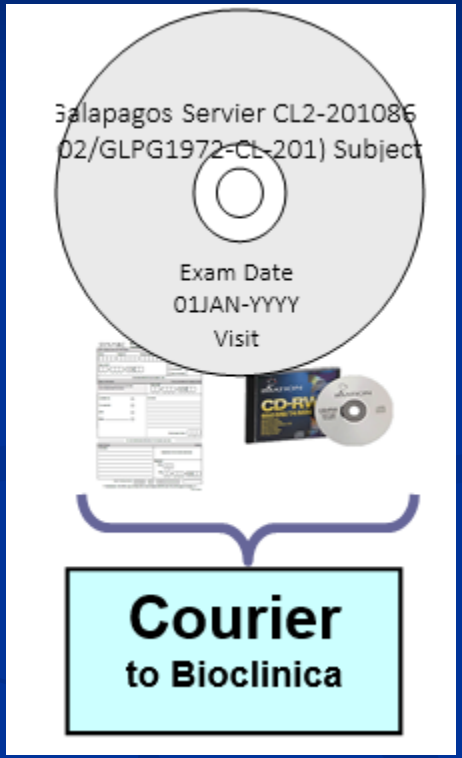
  Protocol: (Galapagos/Servier CL2-201086 002/GLPG1972-CL-201)

  4 digit site #

  5 digit Subject #

  Visit name and exam date

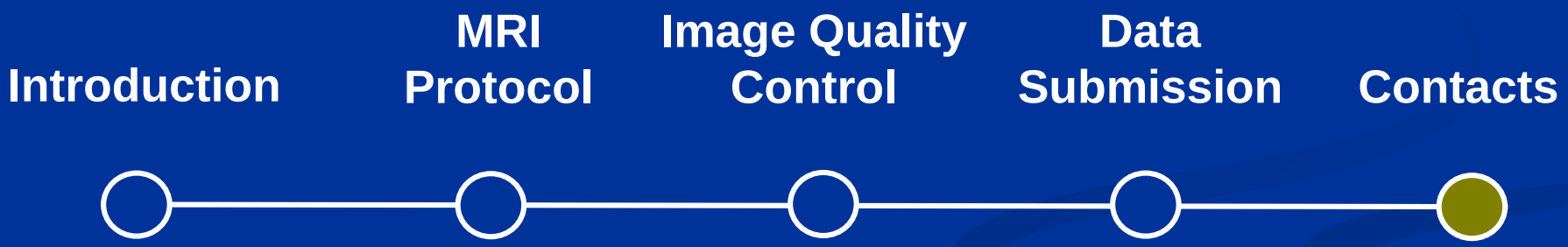
- Write information directly on the CD with an indelible pen. DO NOT AFFIX LABELS!



Bioclinica Forms

- Image Quality Assessment Report is sent out to the imaging center/site after QC is done at Bioclinica within 3 business days post data receipt
- Data Clarification Form (DCF) is for resolution of data discrepancies. It is sent out within 3 business days post data receipt to the study coordinator. The types of DCFs include:
  1. Discrepant Data relates to subject info
  2. Resubmission/Repeat Request is issued if image dataset fails QC.
  3. Incomplete Package asks for (re)submission of the missing data.
- Supply Order Form should be used to order additional supplies/forms

Overview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Contact Information

Newark Office:

7707 Gateway Blvd., Bldg. 3

Newark, CA 94560 USA

Phone: +1 415 817 8900

Fax: +1 415 817 8999

To reach the help desk call toll-free:

- from US/Canada 1-888-275-2462
- from other countries +1-484-928-6076

Email: helpdesk@Bioclinica.com

For a listing of all Toll Free numbers please click the link below
http://www.bioclinica.com/sites/default/files/u1/Bioclinica_Toll_Free_Numbers.pdf

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Questions