Requirements for Imaging

Max Seidensticker

Universitätsklinikum Magdeburg
Klinik für Radiologie & Nuklearmedizin
SORAMIC: Evaluation of Sorafenib and microtherapy guided by Gd-EOB-DTPA enhanced MRI in patients with inoperable hepatocellular carcinoma

Primary study objective No. 3:
“To confirm in a 2-step procedure that Primovist®-enhanced MRI is non-inferior (first step) or superior (second step) compared with contrast-enhanced multislice CT for stratification of patients to a palliative vs. curative treatment strategy.”

Secondary study objectives:
– “to compare the number of detected lesions and the diagnostic confidence in Primovist-enhanced MRI with contrast-enhanced CT”
– “to compare Primovist-enhanced MRI with contrast-enhanced CT regarding the detection of recurrence (patients in the curative study group only)”
Requirements for Imaging

Diagnostic substudy

Primary endpoint:
“correct assignment to curative or palliative strategy”

Secondary endpoint:
“lesion detection and detection of tumor recurrence in the curative treatment arm”
Imaging: Objectives
Ensure Standardization of Imaging data

- Defining same scanning parameters for imaging modalities across sites
- Consider conflicts with existing local protocols
Ensure Quality of Imaging data

- Qualified equipment – same equipment for screening & follow-up
- Consistent images over time for a patient (anatomy, modality, parameters)
- Complete data set
- Independent evaluation with minimal variability
Ensure Quality of Imaging data

• Quality assurance:
  
  – Validation of CT and MRI scans of the liver before study initiation
  
  – Imaging work-shop, Primovist training
  
  – Investigator meeting
  
  – Validation of CT and MRI quality during the study course

  – MRI: Phantom measurements
Ensure Quality of Imaging data

• Concerning MRI-scanners:
  - large variety of scanners in SORAMIC (manufacturers / models / age of device ...)
  - differences in image quality maybe expected

• Concerning MRI-scanner manufacturers:
  - large variety of SOPs concerning quality assurance (phantoms / sequences)
  - low procedure transparency

• comparable, transparent and independent quality evaluation has to be established
Ensure Quality of Imaging data

- MRI Phantom:
  - ACR MRI-Quality Phantom (will be provided)
  - Quality assurance for each MRI-Scanner throughout the SORAMIC study.
  - Confirmation of MRI validity in SORAMIC
Imaging: Screening & Follow-Up
• Screening phase:
  - Primovist-enhanced MRI and contrast-enhanced-CT
    • assessment of disease stage
    • decision on treatment strategy (curative vs. palliative)

IMAGE FOLLOW-UP EVERY 2 MONTHS!

IMAGE FOLLOW-UP NOT MANDATORY!
Follow-Up (curative treatment group):

- Primovist-enhanced MRI and contrast-enhanced-CT
  - every two months
  - assessment and reading by local investigator (endpoint: Time-To-Recurrence)
- only recurrence to be confirmed by truth panel
  - recurrence: endpoint is reached
  - no recurrence: continued imaging follow-up
• Follow-Up (palliative treatment group):
  
  – Diagnostic imaging is not required in the trial context
    (endpoint: Overall Survival)
  
  – Will be performed in investigator’s discretion
  
  – If diagnostic imaging is performed during follow-up, results
    must be reported on the CRF
HCC
Image Characteristics
• Arterial enhancement plus portal-venous washout plus hypointensity in hepatobiliary phase
  (typical HCC)

• Arterial enhancement plus portal-venous washout with iso-to hyperintensity in hepatobiliary phase
  (well-differentiated HCC)

• Arterial enhancement without portal-venous wash-out plus hypointensity in hepatobiliary phase
  (strong indication for HCC)
Contrast-enhanced CT

- Arterial enhancement plus portal-venous washout
- Mosaic pattern
- Pseudocapsule
- (Calcifications, necrosis, hemorrhage, intralesional fat)
Tumor Recurrence in both modalities

• Newly detected lesion:
  – longest diameter at least 10mm
  – typical vascular pattern of HCC (arterial enhancement plus portal-venous washout)

OR

• Any lesion:
  – with at least 10mm interval growth in subsequent scans

• Continue follow up scans until verification of tumor recurrence by truth panel!
Examples
MRI - HCC in cirrhosis

2D T1-w GRE, noncontrast
3D T1-w GRE, FS noncontrast
3D T1-w GRE, FS arterial
3D T1-w GRE, FS portal
3D T1-w GRE, FS late dyn

2D T2-w TSE, FS

3D T1-w GRE, FS 20 min post Primovist
MRI - HCC in cirrhosis

3D T1-w GRE, FS noncontrast
3D T1-w GRE, FS arterial
3D T1-w GRE, FS portal
3D T1-w GRE, FS late dyn

2D T2-w TSE, FS
3D T1-w GRE, FS 20 min post Primovist
MRI - HCC in cirrhosis

3D T1-w GRE, FS noncontrast

3D T1-w GRE, FS arterial

3D T1-w GRE, FS portal

3D T1-w GRE, FS late dyn

2D T2-w TSE, FS

3D T1-w GRE, FS 20 min post Primovist
CT - HCC in cirrhosis

MSCT, noncontrast
arterial
portalvenous
Requirements: MRI
Technical Requirements

• High-field MRI (1.5 - 3T)

• Phased-array surface coil

• Arms should be positioned overhead, out of field of view (FOV)

• FOV large enough, just to enclose entire liver (consistent throughout the study)
Contrast Requirements

- **Contrast Media:**
  
  Primovist® (Gadolinium-EOB-DTPA)
  
  0.1 mL/kg (10 mL maximum) or
  
  0.025 mmol/kg
  
  via rapid hand or power injector (1.5mL/sec)

- + 30 ml saline flush (1.5mL/sec)

- Venous access (preferably 20G)
Primovist®
(Gadolinium-EOB-DTPA)

- Uptake by hepatocyte and excrete via biliary system

➤ Hepatocyte specific CM

➤ Combination of dynamic vascular phase and hepatocyte specific late phase imaging
  - Dynamic perfusion information comparable to ECCM
  - Hepatocyte specific phase: improved lesion detection
Primovist®
(Gadolinium-EOB-DTPA)

- Side effects (<1/100, >1/1000):
  - headache, dizziness, paraesthesia, parosmia, increased blood pressure, flushing, dyspnea, respiratory distress, vomiting, nausea, rash, pruritus, chest pain
  - Electrolyte changes, elevated LFTs
  - Transient QT prolongation
  - Anaphylactic reactions

- (Nephrogenic systemic fibrosis)

➢ All AEs have to be reported to the sponsor
Standard Protocol Recommendation MRI

Standard protocol recommendation

~ 2 ½ min

SCAN
1 2 3 4 5 6 7 8 9 10
Scanning Parameters: MRI
**General**

**Patient orientation:** supine

**Coil:** Phased-array coil

**Scan location / coverage:** ensure complete coverage of the liver.

**Scan FOV:** Large (consistent throughout the study), e.g. ±350x350mm

**Skip /gap (slice spacing):** As close to 0% as possible while avoiding cross talk

**Breath-hold:** not to exceed 20sec scan time.
MRI of the liver
Start

**Localizer**

Should be performed at least in coronal orientation (mandatory)

Other orientations are optional
**Scan 1 (Precontrast)**

**T1-w GRE, 2D**
- **Slice thickness:** \( \leq 6\text{mm} \)
- **Orientation:** Axial
- **Sequence:** 2D T1-w gradient echo, breath-hold sequence
  **with** fat-suppression
  (e.g. WATS, FLASH, SPGR, FFE)

Dual- (in- and opposed) phase imaging optional
Scan 1 (Precontrast)

2D T1-w gradient echo, breath-hold sequence

without fat-suppression
**T1-w GRE, 3D**

- **Slice thickness:** \( \leq 5\text{mm} \)
- **Orientation:** Axial
- **Sequence:** 3D T1-w gradient echo, breath-hold sequence **with** fat-suppression (e.g. VIBE, THRIVE, LAVA)
Scan 2 (Precontrast)

3D T1-w gradient echo, breath-hold sequence

with fat-suppression
**Scan 3 (Post-Contrast, Arterial Phase)**

**T1-w GRE, 3D**

- **Slice thickness:** ≤ 5mm
- **Orientation:** Axial
- **Sequence:** 3D T1-w gradient echo, breath-hold sequence
  
  *with* fat-suppression
  
  *(e.g. VIBE, THRIVE, LAVA)*

- **Scan Delay** Via bolus tracking to ensure arterial phase of the liver (approximately 20 sec. p.i.)
Scan 3 (Post-Contrast, Arterial Phase)
3D T1-w gradient echo, breath-hold technique

with fat-suppression
Scan 4 (Post-Contrast, Portal Venous Phase)

**T1-w GRE, 3D**
- Slice thickness: \( \leq 5\text{mm} \)
- Orientation: Axial
- Sequence: 3D T1-w gradient echo, breath-hold sequence with fat-suppression (e.g. VIBE, THRIVE, LAVA)
- Scan Delay: Approximately 60-70 sec. post injection of CM to ensure portal phase of the liver
Scan 4 (Post-Contrast, Portal Venous Phase)

3D T1-w gradient echo, breath-hold technique

with fat-suppression
Scan 5 (Post-Contrast, Late Dynamic Phase)

**T1-w GRE, 3D**
- **Slice thickness:** \( \leq 5\text{mm} \)
- **Orientation:** Axial
- **Sequence:** 3D T1-w gradient echo, breath-hold sequence *with* fat-suppression (e.g. VIBE, THRIVE, LAVA)
- **Scan Delay** Approximately 120 sec. post injection of CM to ensure equilibrium phase of the liver
Scan 5 (Post-Contrast, Late Dynamic Phase)

3D T1-w gradient echo, breath-hold technique

with fat-suppression
**T2-w TSE, 2D**

- **Slice thickness:** \(\leq 8\text{mm}\)
- **Orientation:** Axial
- **Sequence:** 2D T2-w turbo/fast spin echo (TSE, FSE, RARE) 
  respiratory triggered or navigator gated

*With and without* fat suppression
Scan 6+7 (Post-Contrast)

2D T2-w turbo/fast spin echo (TSE), respiratory triggered

with fat-suppression

without fat-suppression
Scan 8  
(Hepatobiliary Phase)

**T1-w GRE, 3D**
- Slice thickness: \( \leq 6\text{mm} \)
- Scan delay: at least 20 min post injection
- Orientation: Coronal
- Sequence: 3D T1-w gradient echo breath-hold sequence

*With* fat suppression
(e.g. VIBE, THRIVE, LAVA)
Scan 8

(Hepatobiliary Phase)

3D T1-w gradient echo, breath-hold sequence

with fat-suppression
Scan 9 (Hepatobiliary Phase)

**T1-w GRE, 3D**
- Slice thickness: $\leq 5\text{mm}$
- Scan delay: at least 20 min post injection
- Orientation: Axial
- Sequence: 3D T1-w gradient echo breath-hold sequence

*With* fat suppression
(e.g. VIBE, THRIVE, LAVA)
Scan 9
(Hepatobiliary Phase)
3D T1-w gradient echo, breath-hold sequence
with fat-suppression
Scan 10
(Hepatobiliary Phase)

**T1-w GRE, 2D**
- Slice thickness: \( \leq 6\text{mm} \)
- Orientation: Axial
- Sequence: 2D T1-w gradient echo, breath-hold sequence
  
  with fat-suppression

(e.g. WATS, FLASH, SPGR, FFE)
Scan 10
(Hepatobiliary Phase)
2D T1-w gradient echo, breath-hold sequence
with fat-suppression
Tips and Tricks: MRI
Enhancement

- Use bolus detection techniques for proper and individual timing
- Need trigger delay for best enhancement of lesion, to be defined individually due to individual differences (circulation time, cardiac output) affecting time of bolus arrival and peak enhancement duration
Dynamic Enhancement

arterial

portal-venous

venous

Arterial perfusion

Portal venous

Venous

Liver parenchyma
MRI-Artifacts

• To avoid artifacts, arms should be positioned overhead, out of field of view (FOV)
MRI-Artifacts

- Minimize breathing artifacts
  - Relax and train patient to breath in and breath out
  - Perform exam at breath out
  - Delay between breath out order and start of acquisition
Requirements: CT
Technical Requirements

• Helical multislice CT (at least 4 rows)
• Arms should be positioned overhead, out of field of view (FOV)
• Scan FOV large
• Display FOV unique to patient size
Contrast Requirements

- Contrast Media:
  Non-ionic agent (250-400mg/ml Iodide, 300mg/ml recommended)
- 100 – 150 mL
- + 30 ml saline flush
- via rapid hand or power injector (at least 3mL/sec)
- Venous access (preferably 20G)
- Automatic bolus tracking
Contrast media

• **Side effects** *(AE: 3.13%, SAE: 0.004-0.04% (non-ionic CM))*

Katayama H, 1990, Radiology

  – Anaphylactic reaction (pruritus, urticaria, exanthema, erythema, angioedema, flush, dyspnea, hypotension, cardiovascular shock, respiratory arrest)
  – Vasovagal reaction (bradycardia, hypotension, nausea, vomiting)
  – Contrast induced nephropathy
  – Lactic acidosis
  – Extravasation

➤ **All AEs have to be reported to the sponsor**
General

**Patient orientation:** Supine

**Scan FOV:** Large, complete body diameter (consistent throughout the study)

**Breathing instructions:** One breath-hold

**Time per tube rotation:** 1 second or less

**Acquired slice thickness:** ≤5mm

**Reconstructed and submitted slice thickness:** 5mm

**Gap (slice spacing):** None (i.e. contiguous)

**Tube voltage (kV):** 120

**Tube current (mA):** 200-300 (anatomically adapted tube current modulation is preferred)

**Kernel:** Use standard abdominal soft tissue kernel
Standard protocol recommendation helical multislice CT

- **Liver**
  - Arterial Phase: Liver
  - Portal Venous Phase: Liver
  - Venous Phase: Abdomen & Pelvis

**Dynamic imaging**

- **CM**
- **t**
  - Scan 1
    - Bolustracking, start scan at 80-120 HU in aorta
  - Scan 2
    - Start scan 40 sec after CM-Injection
  - Scan 3
    - Start scan 80 sec after CM-Injection
  - Scan 4
Scanning Parameters: CT
Scan 1 (Precontrast)

- Scan coverage: right dome of diaphragma through kidneys (whole liver)
Scan 1 (Precontrast)
Scan 2 (Postcontrast Arterial Phase)

- **Scan coverage:** right dome of diaphragma through kidneys (whole liver)
- **Scan delay:** Via bolus tracking to ensure arterial phase of the liver (aortic enhancement between 80 – 120 HU)
- **Trigger delay:** none (scanning is initiated immediately, <5sec delay for breathing instruction)
Scan 2 (Postcontrast Arterial Phase)
Scan 3 (Postcontrast Portal Venous Phase)

- **Scan coverage:** right dome of diaphragma through kidneys (whole liver)
- **Scan delay:** Start 40 sec after starting injection of contrast media to ensure portal-venous phase of the liver
Scan 3 (Postcontrast Portal Venous Phase)
Scan 4 (Postcontrast Venous Phase)

- Scan coverage: right dome of diaphragma through kidneys (whole liver)
- Scan delay: Start 80 sec after starting injection of contrast media to ensure venous phase of the liver
Scan 4 (Postcontrast Venous Phase)
Frequent Imaging Issues
Axial CT images are required
Field of view should be large enough to view entire anatomy
• Compromise the unbiased nature of the external review

• External reviewer should be assessing each patient without any outside influence from site
Hardcopy films
Thank you for your attention!