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Title: Magnetic Resonance Imaging of Multiple Sclerosis at 7.0 Tesla

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Author Questionnaire

1. Microscopy: Does your protocol demonstrate the use of a dissecting or stereomicroscope for performing a complex dissection, microinjection technique, or similar? **N**

2. Software: Does the part of your protocol being filmed demonstrate software usage? **Y**

3. Interview statements: Considering the Covid-19-imposed mask-wearing and social distancing recommendations, which interview statement filming option is the most appropriate for your group? **Please select one**.

☒ Interviewees wear masks until the videographer steps away (≥6 ft/2 m) and begins filming. The interviewee then removes the mask for line delivery only. When the shot is acquired, the interviewee puts the mask back on. Statements can be filmed outside if weather permits.

3. Filming location: Will the filming need to take place in multiple locations (greater than walking distance)? **N**

Protocol Length
Number of Shots: **12**

Introduction

1. Introductory Interview Statements

REQUIRED:

1.1. **Thoralf Niendorf**: This technical approach can be employed to study cerebral white and grey matter lesions in MS patients with greater detail at 7.0 T **[1]**.

1.1.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera

REQUIRED:

1.2. **Thoralf Niendorf**: The main advantage is that we can study brain changes in greater detail at 7.0 T compared to lower magnetic field strengths. The enhanced spatial resolution is made possible by the increased signal-to-noise ratio at 7.0 T **[1]**.

1.2.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera

OPTIONAL:

1.3. **Sonia Waiczies**: Disseminating these methods will be significant, as they will serve as a foundation for other groups that are starting new MS studies at 7.0 T and as the overall goal is to gain further insight into the MS pathology **[1]**.

1.3.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera

Introduction of Demonstrator on Camera

1.4. **Thoralf Niendorf**: Demonstrating the procedure will be Antje Els, a Radiographer and Study Nurse from my laboratory **[1][2]**.

1.4.1. INTERVIEW: Author saying the above
1.4.2. The named demonstrator(s) looks up from workbench or desk or microscope and acknowledges the camera

Ethics Title Card

1.5. Procedures involving human subjects have been approved by the ethics committee at Charité – Universitätsmedizin Berlin.

Protocol

2. Subject Preparation

2.1. When the Subject is ready, accompany them to the T7 MR (T-seven M-R) scanner room **[1-TXT]** and ask the Subject to lie on the scanning table, using pillows, leg cushions, and blankets to make the Subject as comfortable as possible **[2]**. NOTE: Videographer unfortunately forgot the clapperboard

2.1.1. WIDE: Talent accompanying Subject into room **TEXT: See text for full subject preparation details**

2.1.2. Subject lying down while Talent provides pillows/blankets/cushions/etc NOTE: Both 2.1.2 and 2.1.3 are in one shot. Clips 1 to 5

2.2. Connect an MRI-safe pulse oximeter to the Subject **[1]** and provide ear plugs and a handheld squeeze ball to be used during the examination in the case of an emergency **[2]**.

2.2.1. Talent connecting oximeter

2.2.2. Talent providing earplugs and/or ball NOTE: Both 2.2.1 and 2.2.2 are in one shot. Clips 6 and 7

2.3. Ask the Subject to move closer to the radio frequency head coil **[1]** and have the Subject close their eyes while the table is moved very slowly until the laser positioning is in full alignment with the marker cross on top of the coil **[2]**.

2.3.1. Talent indicating/Subject moving

2.3.2. Talent moving table NOTE: Both 2.3.1 and 2.3.2 are in one shot with 2.4.1 included. Clips 8 to 10

2.4. After saving this position, move the Subject table very slowly to the isocenter of the MR scanner **[1]** while explaining to the Subject that any side effects should resolve as soon as the table comes to a halt **[2]**.

2.4.1. Talent moving table into scanner

2.4.2. Talent communicating to Subject NOTE: Clip 11

2.5. After leaving the scanner room, use the intercom to confirm audible communication with the Subject within the scanner **[1-TXT]**.

2.5.1. Talent at intercom, checking Subject communication **TEXT: Ensure subject comfort before leaving scanner room** NOTE: Clip 12

3. Data Acquisition

3.1. Before acquiring the scanning data, enter the required Subject details, including the subject ID, date of birth, sex, age, and weight **[1]** as well as the study details, such as the study name, institution, and individual performing the MR investigation **[2]**.

3.1.1. WIDE: Talent entering subject information, with monitor visible in frame NOTE: Clips 13-14

3.1.2. SCREEN: 3.1: 00:20-00:37 *Video Editor: please speed up*

3.2. Select **Localizer** and mark the sequence **[1]**.

3.2.1. SCREEN: 3.2

3.3. Select **Options** and **Adjustments** and select **Go** under the **Frequency** tab. Under the **Transmitter** tab, set the voltage as appropriate for the radio frequency coil and amplifier being used and click **Apply [1]**.

3.3.1. SCREEN: 3.3 *Video Editor: can speed up*

3.4. Under **3D Shim**, select **Measure [1]**. When the B-zero Map is generated, select **Calculate** to acquire the shim values **[2-TXT]**. When the shim values are consistent with the previous value, make sure that the basic frequency is recentered and select **Apply** and **Close [3]**.

3.4.1. SCREEN: 3.4: 00:00-00:04

3.4.2. SCREEN: 3.4: 00:13-00:18 **Repeat Frequency and 3D adjustments at ≥2x**

3.4.3. SCREEN: 3.4: 00:33-00:47

3.5. Then, using at least 3 slices per orientation, make sure that all of the channels have been selected and press **Apply** to run the Localizer sequence in the sagittal, transversal, and coronal orientations **[1]**.

3.5.1. SCREEN: 3.5 *Video Editor: can speed up*

3.6. To acquire a 3D MPRAGE (M-P-rage) sequence, use the zoom and panning tool to zoom in and move the field of view on the localizer images and the adjustment volume **[1-TXT]**.

3.6.1. SCREEN: 4.1: 00:00-00:20 *Video Editor: please speed up* **TEXT: MPRAGE: Magnetization Prepared - RApid Acquisition Gradient Echo**

3.7. Make sure that all of the channels are selected and click **Apply** to acquire the sequence in the sagittal orientation in alignment with the interhemispheric fissure **[1]**.

3.7.1. SCREEN: 4.1: 00:20-00:55 *Video Editor: please speed up*

3.8. To run a FLAIR sequence, copy the geometry of the field of view in the same sagittal orientation and adjustment volume as for the MPRAGE scan, taking care that the phase encoding is in the anterior-to-posterior direction and that all of the channels are selected **[1]**. Then press **Apply** to start the scan **[2-TXT]**.

3.8.1. SCREEN: 4.2: 00:00-00:23 *Video Editor: please speed up* **TEXT: FLAIR: FLuid-Attenuated Inversion Recovery**

3.8.2. SCREEN: 4.2: 00:25-00:40 *Video Editor: please speed up*

3.9. To run a FLASH-ME (flash-M-E), adjust the field of view according to the anatomy of the Subject using the 3D MPRAGE and localizer images to plan the geometry and using the zoom and panning tool to manually adjust the field of view such that the entire head is in the middle **[1-TXT]**.

3.9.1. SCREEN: 4.3: 00:00-00:19 *Video Editor: please speed up* **TEXT: FLASH-ME: multi-echo fast low-angle shot sequence**

3.10. Tilt the head such that the lower boundary of the field of view is in line with the lower corpus callosum line before adjusting the uppermost layer end with the skull calotte **[1]**.

3.10.1. SCREEN: 4.3: 00:20-00:29

3.11. Modify the adjustment volume if it is no longer aligned with the geometry volume and rerun the manual 3D shimming and frequency adjustments **[1]** before clicking **Apply** to run the sequence **[2]**.

3.11.1. SCREEN: 4.3: 00:30-00:47

3.11.2. SCREEN: 4.3: 00:48-01:09 *Video Editor: please speed up*

3.12. For susceptibility weighted imaging, rearrange the field of view such that the slice slab is shifted in the cranial direction and the uppermost border is aligned with the skull calotte. Displace the slab in the ventral or dorsal direction so that the brain is completely in the middle of field of view **[1]**.

3.12.1. SCREEN: 5.1: 00:00-00:25 *Video Editor: please speed up*

3.13. Modify the adjustment volume if it is no longer aligned with the geometry volume and rerun the manual 3D shimming and frequency adjustments **[1]** before clicking **Apply** to start the scan **[2]**.

3.13.1. SCREEN: 5.1: 00:26-00:44 *Video Editor: please speed up*

3.13.2. SCREEN: 5.1: 00:45-01:02 *Video Editor: please speed up*

NOTE: Numbering changed to 6.2 starting here (from 3.14) in authors' postshoot notes, which may have caused issues with slating.

3.14. For quantitative susceptibility mapping, move the slice stack cranially so that the top layer is aligned with the skull calotte **[1-TXT]** and rerun the manual 3D shimming and frequency adjustments to make sure that all of the channels are selected **[2]**.

3.14.1. SCREEN: 5.2: 00:00-00:25 **TEXT: Copy MPRAGE FOV and adjustment volume**

3.14.2. SCREEN: 5.2.: 00:26-00:42

3.15. Then click **Apply** to run the sequence **[1]**.

3.15.1. SCREEN: 5.2: 00:43-00:55 *Video Editor: can speed up*

3.16. For diffusion-weighted imaging, select a 2D echo planar imaging sequence and use the Localizer images to plan the geometry in the transversal orientation without introducing any angulation. Move the field of view such that the upper line of the layer block is aligned with the skull calotte **[1]**.

3.16.1. SCREEN: 5.3: 00:02-00:20 *Video Editor: can speed up*

3.17. With the brain is exactly in the middle of the field of view, make sure that the phase encoding is in the anterior-to-posterior direction, that 64 different diffusion encoding directions are selected, and that the b-values are set to 0 and 1000 seconds/square-millimeter **[1]** before clicking **Apply** to run the sequence **[2]**.

3.17.1. SCREEN: 5.3: 00:21-00:25 *Video Editor: please emphasize 64 Diff. directions and b-values when mentioned*

3.17.2. SCREEN: 5.3: 00:26-00:48 *Video Editor: please speed up*

3.18. To cancel any distortion artefacts, acquire the same echo planar imaging sequence but using the reversed polarity of the phase-encoding direction using the version of the echo planar imaging sequence with the phase encoding in the posterior-to-anterior direction **[1]**.

3.18.1. SCREEN: 5.4: 00:00-00:14 *Video Editor: can speed up*

3.19. Set the direction to 180 degrees, if necessary, and confirm that 64 different diffusion encoding directions are selected but only one b-value at 0 seconds/square-millimeter, which will significantly reduce the scan time but will be sufficient to correct any distortion artefacts during post processing **[1]**.

3.19.1. SCREEN: 5.4: 00:15-00:26 *Video Editor: please emphasize 64 Diff directions and b-values when mentioned*

3.20. Then click **Apply** to run the sequence. As soon as the last sequence has finished and been reconstructed, the MRI examination will be ready **[1]**.

3.20.1. SCREEN: 5.4: 00:27-00:48 *Video Editor: please speed up*

3.21. When all of the images have been acquired complete, move the Subject table slowly away from the isocenter of the scanner **[1]** and check in with the Subject regarding any side effects from during or after the measurements **[2]**. NOTE: Both 6.9.1 and 6.9.2 are in one shot. Clip 15

3.21.1. Talent moving bed out of scanner
3.21.2. Talent checking with Subject

Results

4. Results: Representative High-Resolution MS MRI at 7.0 T

4.1. In this analysis, a 26-year-old woman diagnosed with relapsing remitting MS was examined at 7 Tesla as demonstrated **[1]**.

4.1.1. LAB MEDIA: Figure 11

4.2. Some distortions in the B-one-plus profile can be observed in the MR images, which is anticipated when moving to higher resonance frequencies, as shorter wavelengths increase the destructive and constructive interferences **[1]**.

4.2.1. LAB MEDIA: Figure 11 *Video Editor: please emphasize darkened area in center of Figure 11e*

4.3. As observed, sagittal **[1]** and transversal views provide different contrasts in the brain images **[2]**.

4.3.1. LAB MEDIA: Figure 11 *Video Editor: please emphasize sagittal images*
4.3.2. LAB MEDIA: Figure 11 *Video Editor: please emphasize transversal images*

4.4. Although the MS diagnosis was subsequently challenged due to an increase in T-two lesions and multiple clinical relapses with incomplete remission **[1]**, 7T MRI supported the MS diagnosis by revealing the central vein sign in the majority of periventricular and juxtacortical lesions **[2]**.

4.4.1. LAB MEDIA: Figure 12
4.4.2. LAB MEDIA: Figure 12 *Video Editor: please emphasize red arrows in Figure 12a and 12b*

4.5. The MS diagnosis was further corroborated by cortical pathology **[1]** and hypointense rim structures surrounding a subset of T_2 hyperintense lesions **[2]**.

4.5.1. LAB MEDIA: Figures 13 and 14 *Video Editor: please emphasize red arrowheads in Figure 13a*
4.5.2. LAB MEDIA: Figures 13 and 14 *Video Editor: please emphasize arrowheads in Figures 13b and 14b*

Conclusion

5. Conclusion Interview Statements

8.1. **Thoralf Niendorf**: These techniques are derived from strong collaborations between MR Physics and Neurology/Neuroradiology experts and provide new MS-specific neuroimaging markers, such as the central vein sign and hypointense rim structures on T_2^*-weighted images **[1]**.

8.1.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera