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Supplemental Information

Human cochlear diffusion

from the cerebrospinal fluid space with gadolinium

contrast

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Supplemental Methods

MRI Cisternogram:

Patients with suspected lateral skull base CSF leaks provided consent for off-label intrathecal gadolinium administration by a neuroradiologist. Fluoroscopic-guided lumbar puncture was performed and 10 mL of Isovue-M 300 and 0.5 mL of gadolinium were then administered intrathecally. Patients were subsequently imaged by neuroradiology. Initial imaging typically occurs around one hour after contrast administration. If a leak was identified on this scan, the patient was determined to have a CSF leak and no further imaging was performed. If no leak was identified on initial scan, the patient was re-imaged approximately 4-5 hours later. If a leak was identified at this time, the patient was determined to have a CSF leak. If no leak was identified the patient was not able to be diagnosed with a CSF leak. In addition, we were able to retrospectively assess these images for cochlear transduction of gadolinium contrast.

Cochlear Transduction Assessment:

3D-T1 SPACE fat-saturated (FS) MR imaging with coronal and axial 0.9 mm reformats were retrospectively reviewed to assess cochlear transduction. All imaging was performed on Siemens 3T MRI. Contrast intensity in the cochleae were compared to CSF. Maximal signal intensity was recorded using region of interest assessment of basal and middle turns. Axial reformats were standardized to medulla using freehand region of interest. 15 patients in total (both with and without CSF leak) were identified and included in this study.

Statistical Analysis:

Descriptive and demographic data were recorded as was presence or absence of CSF leak. Coronal images were assessed for presence or absence of contrast in the cochlea, vestibule, and semicircular canals was recorded for all patients at initial MRI and, where applicable, for delayed MRI. Peak contrast intensity in cochlea at initial and delayed MRIs were compared to peak contrast intensity in CSF and recorded as a ratio. Contrast intensity in axial images in cochlea and CSF were standardized to the medulla for inter-image consistency. Contrast intensities within the cochlea, CSF, and medulla were recorded at initial and delayed imaging. Difference in intensity was recorded. A student's t-test was performed to assess significance of change in CSF and cochlear intensity vs. medulla and cochlear intensity as compared to CSF.

Supplemental Table 1: Patient demographics, CSF leak results, and cochlea to CSF contrast ratios. BMI: body mass index, CSF: cerebrospinal fluid, M: Male, F: Female, N/A: data not available. Final row: For age, BMI, Ratios: Mean, SD: standard deviation.

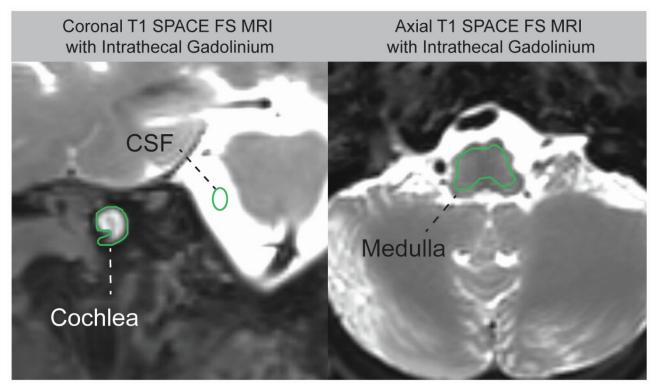
| Patient ID | Age (years) | Gender | Leak initial | Leak delayed | BMI | Initial Cochlea/CSF Ratio | Delayed Cochlea/CSF Ratio | Change in Cochlea/CSF Ratio |
|------------|-------------------|------------------|-------------------|-------------------|------------------|---------------------------------|---------------------------------|-----------------------------------|
| 3 | 69 | F | Yes | N/A | 39.9 | 0.3 | | |
| 11 | 73 | М | Yes | N/A | 30.5 | 0.27 | | |
| 13 | 48 | F | Yes | N/A | 37.8 | 0.25 | | |
| 15 | 37 | М | Yes | N/A | 49.2 | 0.37 | | |
| 1 | 44 | F | No | No | 45.5 | 0.29 | 0.43 | 1.45 |
| 2 | 31 | М | No | No | 34.8 | 0.35 | 0.69 | 1.95 |
| 4 | 73 | М | No | Yes | 28.7 | 0.14 | 0.21 | 1.52 |
| 5 | 37 | F | No | No | 25.4 | 0.33 | 0.5 | 1.51 |
| 6 | 64 | F | No | No | 27.9 | 0.33 | 0.46 | 1.39 |
| 7 | 25 | F | No | No | 23.2 | 0.19 | 0.67 | 3.45 |
| 8 | 50 | М | No | No | 41.6 | 0.145 | 0.27 | 1.8 |
| 9 | 22 | F | No | Yes | 28.7 | 0.15 | 0.73 | 5 |
| 10 | 73 | F | No | Yes | 24.2 | 0.19 | 0.32 | 1.73 |
| 12 | 39 | F | No | Yes | 49.3 | 0.19 | 0.29 | 1.52 |
| 14 | 28 | F | No | No | 26 | 0.2 | 0.46 | 2.33 |
| | 47.5 (SD 18.5) | F: 10 (66.7%) | Yes: 4 (26.7%) | Yes: 4 (26.7%) | 34.2 (SD 8.8) | 0.246 | 0.457 | 2.15 p=0.002 |

Supplemental Table 2: Patient demographics and descriptive statistics

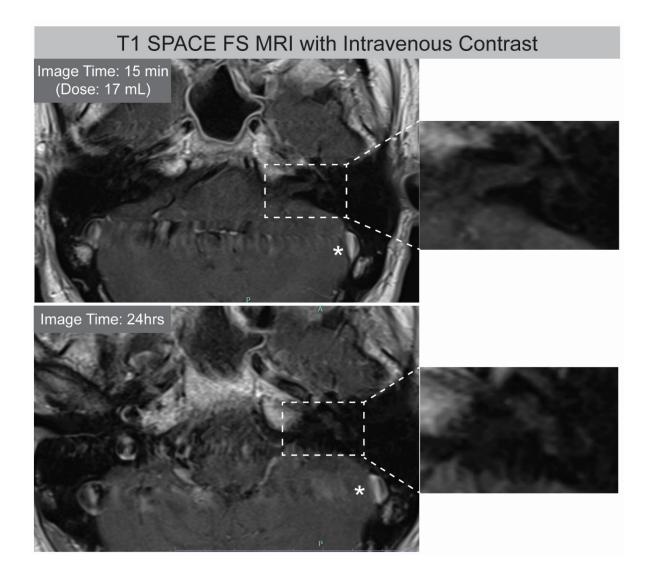
| | Mean | % (SD) |
|---------------------------|----------|--------|
| Age | 48 | (19) |
| Gender (F) | 10 | 67% |
| Race (W) | 13 | 93% |
| BMI | 34.16673 | (9) |
| Leak | 8 | 53% |
| | | |
| Subjective Hearing Change | 1 | 7% |
| Cochlear Uptake | 15 | 100% |
| Vestibular uptake | 7 | 47% |
| Minutes to First Scan | 74 | (51) |
| Minutes to Delayed Scan | 341 | (83) |

Supplemental Table 3: Descriptions of patients undergoing sequential magnetic resonance imaging (MRI) with contrast administered at least prior to initial MRI.

| Patient ID | Patient Age (Years) | Reason for Sequential MRI | Duration between MRIs (hours) | Dose IV contrast | Contrast Present in Cochlea either MRI? |
|---------------|---------------------------|---|----------------------------------|------------------|--|
| 1 | 55 | Movement initial MRI | 29:02 | 15 mL MultiHance | No |
| 2 | 6 | Pre-procedure planning, laser ablation of corpus callosum | 28:50 | 3.2 mL Dotarem | No |
| 3 | 61 | Pre-procedure planning, need for Stealth protocol after initial MRI | 23:05 | 17 mL MultiHance | No |



Supplemental Figure 1: Demonstration of intensity measurements in coronal (left) and axial (right) planes. Cochlear intensity and CSF intensity were compared directly in coronal plane and standardized to medulla for systematic comparisons in axial plane.



Supplemental Figure 2: Representative T1 MRI images from a patient that received intravenous (IV) gadolinium contrast (17 mL) for an intracranial infection. The next day (after 24 hours), the patient underwent repeat MRI imaging with another dose of IV gadolinium. There is no observed uptake of contrast in the cochlea (inset images) immediately or after 24 hours of intravenous contrast. * = sigmoid sinus with intralumenal contrast signal demonstrating the administration of contrast.