## Clinical application of intrathecal gadobutrol for assessment of cerebrospinal fluid tracer clearance to blood

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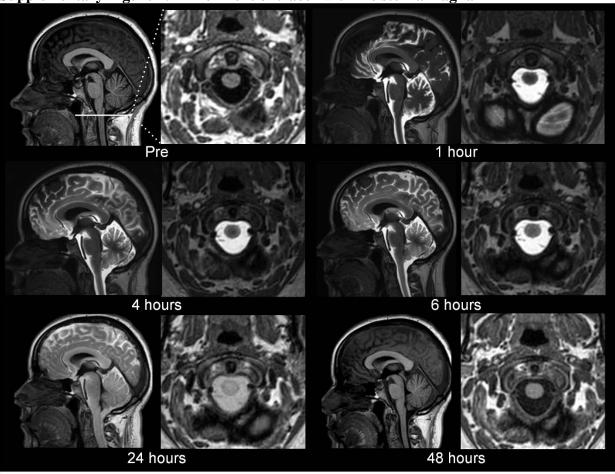
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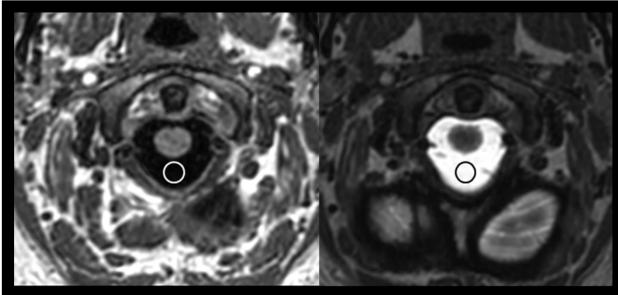
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Supplementary Figure 1. Enrichment of tracer within cisterna magna



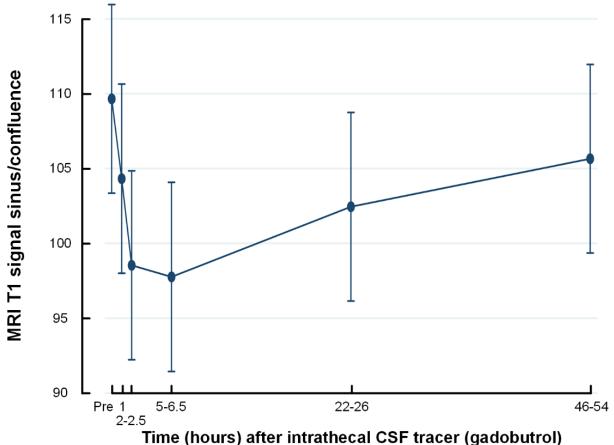
The change in MRI T1 signal within the cisterna magna is shown before (Pre) and 1, 4, 6, 24 and 48 hours after injection of intrathecal gadobutrol in one REF subject

**Supplementary Figure 2. Placement of region of interest within cisterna magna** 



The placement of region of interest (open circle) within the cisterna magna is shown before (left) and 1 after (right) injection of intrathecal gadobutrol.

## Supplementary Figure 3. Change in MRI T1 within sagittal sinus/confluence over time



The change in mean MRI T1 signal within the sagittal sinus/confluence before (Pre) and 1, 2-2.5, 5-6.5, 22-26 and 46-54 after injection of intrathecal gadobutrol. Bars represented by standard error. Provided gadobutrol enriched blood, a T1 signal increase would be expected, which is not seen. The trend plot does not indicate enrichment of tracer within the sagittal sinus/confluence.

Suppl Table 1. Age-adjusted differences in CSF tracer enrichment between REF patients and patients with CSF disturbances

	1 hr		2-2.5 hrs		4-5 hrs		5-6.5 hrs		22-26 hrs		46-54 hrs	
	Mean±SE	P-	Mean±SE	P-value								
		value										
Diff SIH - REF	$-16 \pm 651$	0.980	$250 \pm 1042$	0.810	$-640 \pm 707$	0.366	$-886 \pm 651$	0.174	$-433 \pm 650$	0.505	$-227 \pm 602$	0.706
Age-adjusted Diff SIH - REF	$-37 \pm 667$	0.956	$232 \pm 1050$	0.825	$-662 \pm 725$	0.362	$-906 \pm 668$	0.175	$-453 \pm 666$	0.496	$-248 \pm 619$	0.689
P-value of age		0.889		0.889		0.889		0.889		0.889		0.889
Diff iNPH - REF	$2005 \pm 600$	0.001	$1620 \pm 599$	0.007	$477 \pm 601$	0.428	$1294 \pm 617$	0.036	$1150 \pm 598$	0.055	$858 \pm 641$	0.181
Age-adjusted Diff iNPH - REF	$1906 \pm 827$	0.021	$1520 \pm 827$	0.066	$377 \pm 827$	0.649	$1193 \pm 842$	0.156	$1050 \pm 826$	0.204	$758 \pm 858$	0.377
P-value of age		0.861		0.861		0.861		0.861		0.861		0.861
Diff PC - REF	$1496 \pm 499$	0.003	$1201 \pm 498$	0.016	$600 \pm 530$	0.257	$390 \pm 512$	0.446	$-269 \pm 497$	0.589	$-99 \pm 514$	0.848
Age-adjusted Diff PC - REF	$1399 \pm 510$	0.006	$1105 \pm 509$	0.030	$505 \pm 540$	0.350	$294 \pm 523$	0.573	$-365 \pm 508$	0.472	$-195 \pm 526$	0.711
P-value of age		0.415		0.415		0.415		0.415		0.415		0.415
Diff IIH - REF *Age-adjusted	3346 ± 710	0.001	730 ± 801	0.362	454 ± 804	0.572	911 ± 802	0.256	57 ± 707	0.936	-149 ± 208	0.472
Diff IIH - REF P-value of age												

<sup>\*</sup>Age-adjusted differences between IIH and REF subjects could not be determined due to low number of observations.

Suppl Table 2. Age-adjusted differences in blood concentrations of CSF tracer between REF patients and patients with CSF disturbances

•	1 hr		2-2.5 hrs		4-5 hrs		5-6.5 hrs		22-26 hrs		46-54 hrs	
	Mean±SE	P-	Mean±SE	P-	Mean±SE	P-	Mean±SE	P-	Mean±SE	P-	Mean±SE	P-
		value		value		value		value		value		value
Diff SIH - REF	$1.51 \pm 0.42$	< 0.001	$1.48 \pm 0.48$	0.002	$1.91 \pm 0.57$	0.001	$1.45 \pm 0.58$	0.012	$0.23 \pm 0.42$	0.58	$-0.05 \pm 0.05$	0.37
Age-adjusted	$1.47 \pm 0.42$	< 0.001	$1.44 \pm 0.48$	0.003	$1.86 \pm 0.58$	0.001	$1.45 \pm 0.58$	0.013	$0.197 \pm$	0.64	$-0.08 \pm 0.05$	0.09
Diff SIH - REF									0.418			
P-value of age		0.008		0.008		0.008		0.008		0.008		0.008
Diff iNPH -	$-0.21 \pm 0.26$	0.416	$-0.43 \pm 0.28$	0.132	$-0.25 \pm 0.25$	0.306	$-0.29 \pm 0.32$	0.36	$0.31 \pm 0.24$	0.202	$0.18 \pm 0.06$	0.004
REF												
Age-adjusted	$-0.29 \pm 0.27$	0.27	$-0.50 \pm 0.29$	0.08	$-0.33 \pm 0.25$	0.191	$-0.37 \pm 0.32$	0.25	$0.23 \pm 0.25$	0.36	$0.10 \pm 0.07$	0.15
Diff iNPH -												
REF												
P-value of age		0.053		0.053		0.053		0.053		0.053		0.053
Diff PC - REF	$-0.11 \pm 0.29$	0.70	$-0.06 \pm 0.26$	0.80	$0.78 \pm 0.31$	0.012	$0.93 \pm 0.30$	0.002	$-0.03 \pm 0.25$	0.92	$-0.002 \pm 0.05$	0.97
Age-adjusted	$-0.09 \pm 0.29$	0.76	$-0.03 \pm 0.26$	0.90	$0.80 \pm 0.31$	0.010	$0.96 \pm 0.30$	0.001	$0.002\pm0.26$	0.93	$0.014 \pm 0.045$	0.76
Diff PC - REF												
P-value of age		0.009		0.009		0.009		0.009		0.009		0.009
Diff IIH - REF	$0.08 \pm 0.34$	0.80	$0.14 \pm 0.46$	0.77	$0.22 \pm 0.39$	0.572	$-0.30 \pm 0.65$	0.64	$0.19 \pm 0.46$	0.69	$0.29 \pm 0.10$	0.004
Age-adjusted	$0.12 \pm 0.34$	0.739	$0.16 \pm 0.47$	0.733	$0.25 \pm 0.39$	0.522	$-0.29 \pm 0.65$	0.656	$0.21 \pm 0.47$	0.656	$0.32 \pm 0.09$	< 0.001
Diff IIH - REF												
P-value of age		0.029		0.029		0.029		0.029		0.029		0.029