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Supplemental information

**Fast and low-dose medical imaging
generation empowered by hybrid
deep-learning and iterative reconstruction**

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Supplemental Figures

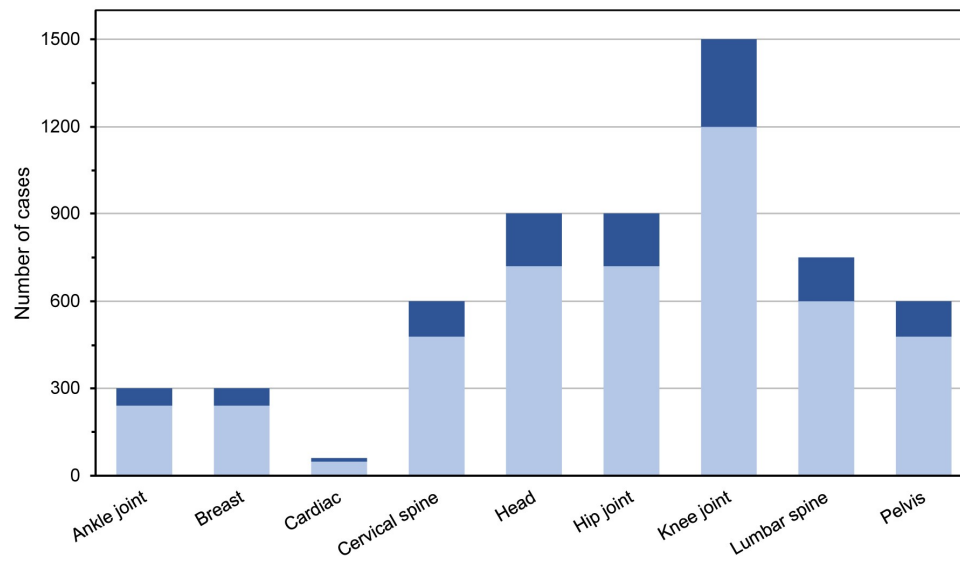


Figure S1. ACS is trained and tested on 5,910 cases for fast MRI scans of 9 organs. Related to Figure 2 and STAR Methods. In each column, the darker one represents the testing set, and the lighter one represents the training set.

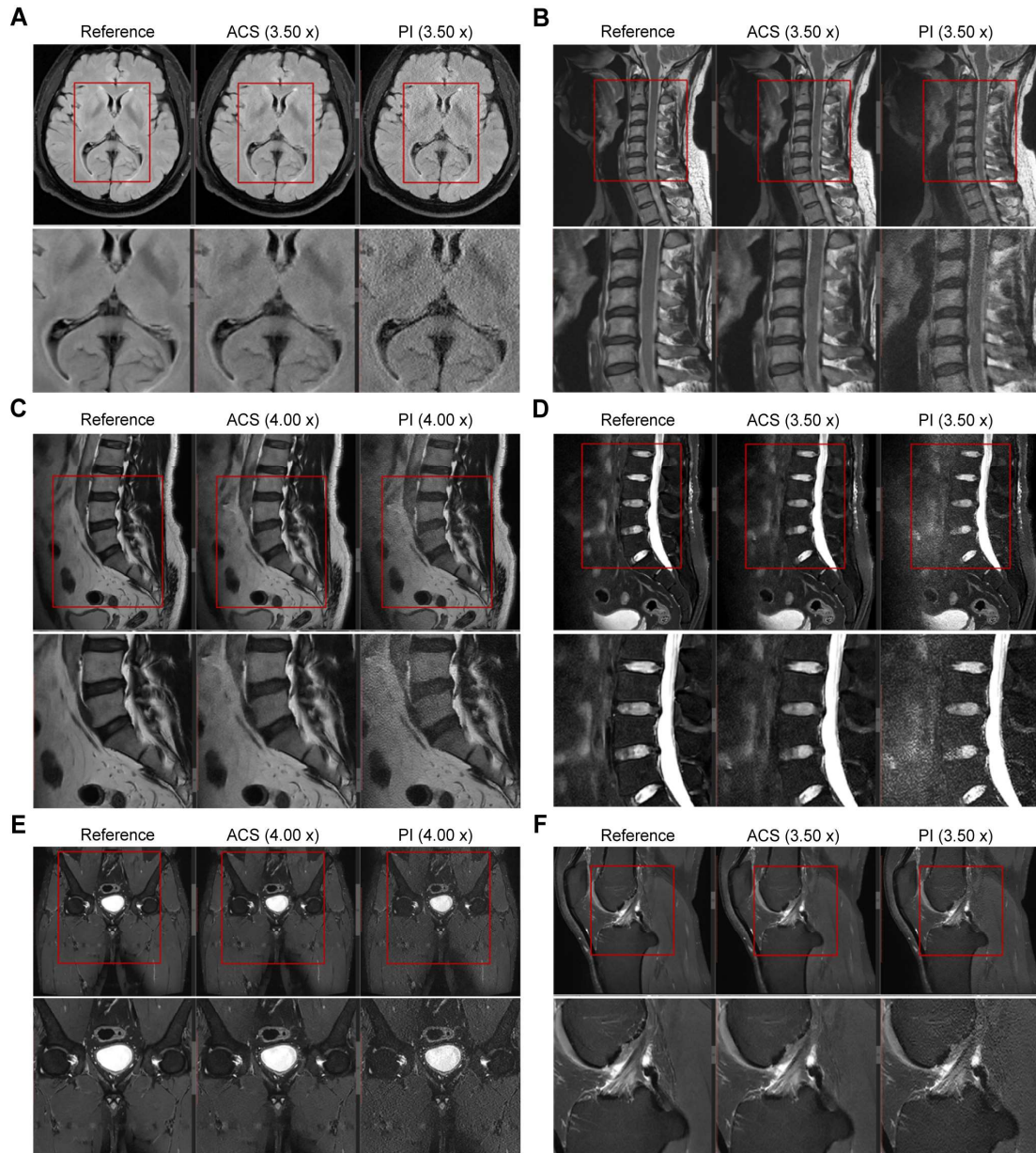


Figure S2. Comparison between ACS and PI reconstructions of down-sampled MRI data collected from various organs using multiple pulse sequences in the testing dataset. Related to Figure 2. (A) T2w FLAIR images of the head ($3.50 \times$ acceleration). (B) T2w images of the cervical spine ($3.50 \times$ acceleration). (C) T2w images of the lumbar spine ($4.00 \times$ acceleration). (D) T2w fat reduction images of the lumbar spine ($3.50 \times$ acceleration). (E) STIR images of the hip ($4.00 \times$ acceleration). (F) PDw fat reduction images of the knee ($3.50 \times$ acceleration).

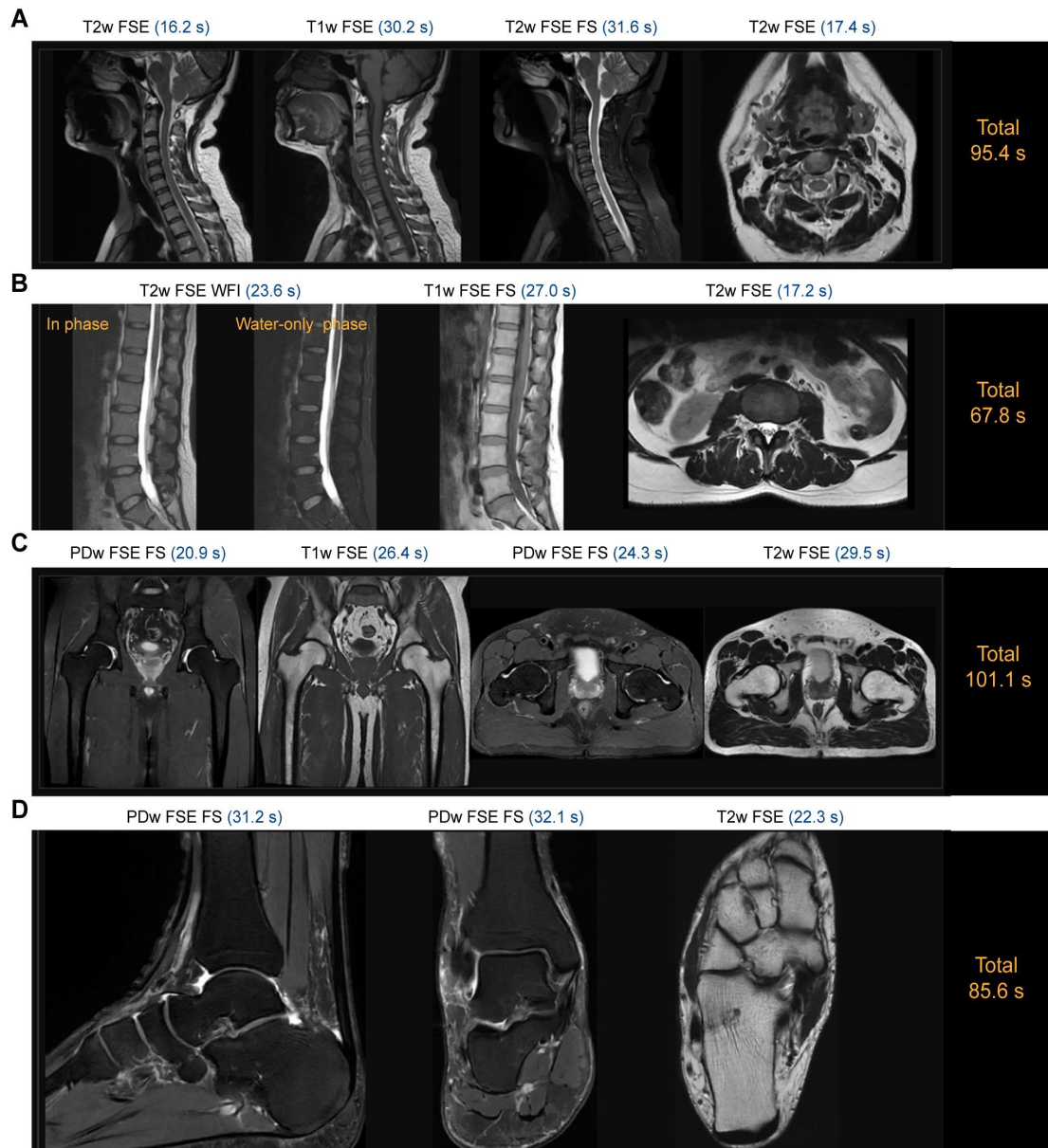


Figure S3. ACS reconstruction of 100-s level fast MRI scans for multiple organs. Related to Figure 4. ACS achieves 100 s-level fast MRI scans for cervical spine (A), lumbar spine (B), hip joint (C), and ankle joint (D). Reasonable reconstruction can be achieved for 3 to 4 fast MRI scans performed in ~100 s using different pulse sequences.

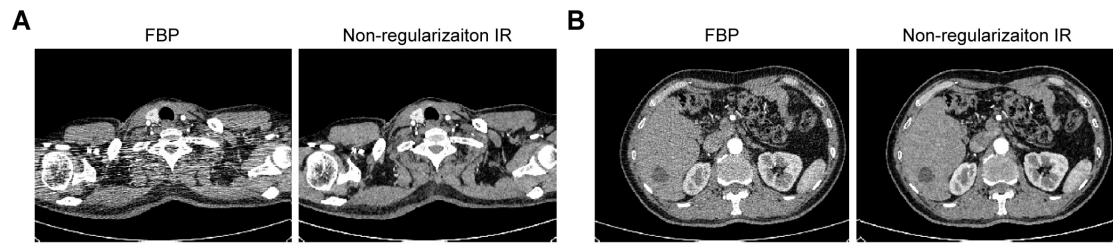


Figure S4. CT images of the shoulder (A) and the abdomen (B) reconstructed by FBP and non-regularization IR. Related to STAR Methods.

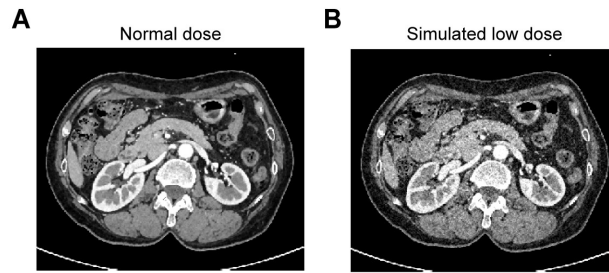


Figure S5. CT images reconstructed by non-regularization IR at a normal dose (A) and a simulated low dose (B). Related to STAR Methods.

	A	B	C	D	E	F
OSEM_120 s/bp (A)		< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
DPR_120 s/bp (B)	***		1.000	0.735	1.000	1.000
DPR_90 s/bp (C)	***	no		1.000	1.000	1.000
DPR_60 s/bp (D)	***	no	no		0.773	1.000
DPR_40 s/bp (E)	***	no	no	no		1.000
DPR_30 s/bp (F)	***	no	no	no	no	

Significant difference test

	A	B	C	D	E	F
OSEM_120 s/bp (A)		< 0.001	< 0.001	< 0.001	0.759	0.001
DPR_120 s/bp (B)	***		< 0.001	< 0.001	< 0.001	< 0.001
DPR_90 s/bp (C)	***	***		< 0.001	< 0.001	< 0.001
DPR_60 s/bp (D)	***	**	***		< 0.001	< 0.001
DPR_40 s/bp (E)	no	***	***	***		< 0.001
DPR_30 s/bp (F)	**	***	***	***	***	

Significant difference test

Figure S6. Statistical difference tests for SUV_{max} of identified lesions (the left) and SNR in the liver (the right). Related to Figure 6. Statistical analyses on SUV_{max} are performed using repeated measures one-way ANOVA followed by Turkey's multiple comparisons tests ($n = 78$). Statistical analyses on SNR are performed using Friedman tests followed by Dunnett's multiple comparisons tests ($n = 51$). Asterisk represents two-tailed adjusted P value, with * indicating $P < 0.05$, ** indicating $P < 0.01$, and *** indicating $P < 0.001$.

Supplemental Tables

Table S1. Imaging protocols for 5,910 cases of MRI data from the training and testing datasets. Related to Figure 2.

Organ	MR pulse sequence	Case
Ankle joint	(1) pd_fse_fs; (2) t1_fse_cor	150 × 2
Breast	(1) t1_fse; (2) stir_fse; (3) t2_fse	100 × 3
Cardiac	(1) t1_fse; (2) t2_fse; (3) t2_fse_fs; (4) t2_fse_spair	15 × 4
Cervical spine	(1) stir_fse_sag; (2) t1_fse_sag; (3) t2_fse_sag; (4) t2_fse_wfi_sag	150 × 4
Head	(1) t1_fse_flair; (2) t2_fse_flair_fs; (3) t2_fse	300 × 3
Hip joint	(1) pd_fse_fs; (2) stir_fse_cor; (3) t1_fse_cor	300 × 3
Knee joint	(1) pd_fse_fs; (2) t1_fse; (3) t2_fse; (4) t2_fse_fs	375 × 4
Lumbar spine	(1) t1_fse_cor_fs; (2) t1_fse_sag; (3) t2_fse; (4) t2_fse_sag_fs; (5) t2_fse_wfi_sag	150 × 5
Pelvis	(1) t1_fse; (2) t2_fse	300 × 2

List of abbreviations: cor, coronal; flair, flow attenuated inversion recovery; fs, fat suppression; fse, fast spin echo; pd, proton density; sag, sagittal; spair, spectral attenuated inversion recovery; stir, short TI inversion recovery; wfi, water-fat imaging.

Table S2. Quantitative metrics of ACS, PI, AI, and PI + AI methods for reconstructing down-sampled MRI data from the testing dataset under different acceleration factors. Related to Figure 2. MSE and NMSE values with asymmetrical distributions are represented as median (25th, 75th percentiles). NRMSE, SNR, PSNR, and SSIM values fit normal distribution and are represented as mean \pm standard deviation. Lower error-related metrics (i.e., MSE, NMSE, and NRMSE) and higher consistency-related metrics (i.e., SNR, PSNR, and SSIM) stand for lower noise and better reconstruction performance. Statistical analyses are performed using two-way ANOVA followed by Sidak's multiple comparisons tests (n = 14).

Acceleration factor	ACS	PI	AI	PI + AI	$P_{(ACS \text{ vs. } PI)}$	$P_{(ACS \text{ vs. } AI)}$	$P_{(ACS \text{ vs. } PI + AI)}$
MSE (* 10⁸)							
2.00	0.74 (0.38, 1.68)	2.84 (1.36, 6.76)	3.40 (1.11, 5.19)	1.72 (0.73, 3.19)	0.028	0.015	0.025
2.25	0.98 (0.48, 2.15)	3.28 (1.51, 7.87)	4.05 (1.27, 5.73)	1.97 (0.87, 3.69)	0.028	0.015	0.026
2.50	1.16 (0.56, 2.55)	3.62 (1.62, 8.50)	4.45 (1.39, 6.14)	2.16 (0.96, 4.10)	0.030	0.015	0.027
2.75	1.32 (0.64, 2.99)	3.95 (1.75, 9.06)	4.80 (1.59, 7.52)	2.34 (1.06, 4.54)	0.034	0.019	0.025
3.00	1.48 (0.72, 3.30)	4.59 (1.85, 9.93)	5.09 (1.68, 8.05)	2.50 (1.14, 4.83)	0.051	0.023	0.025
NMSE (%)							
2.00	0.51 (0.30, 0.93)	1.72 (1.40, 2.28)	1.70 (1.11, 2.16)	0.90 (0.63, 1.38)	< 0.001	< 0.001	< 0.001
2.25	0.65 (0.38, 1.19)	2.00 (1.51, 2.76)	2.01 (1.22, 2.56)	1.05 (0.72, 1.74)	< 0.001	< 0.001	< 0.001
2.50	0.77 (0.45, 1.40)	2.24 (1.59, 3.04)	2.24 (1.30, 2.86)	1.19 (0.80, 1.98)	< 0.001	< 0.001	< 0.001
2.75	0.92 (0.52, 1.61)	2.46 (1.66, 3.37)	2.54 (1.40, 3.18)	1.34 (0.88, 2.19)	< 0.001	0.004	< 0.001
3.00	1.02 (0.57, 1.77)	2.94 (1.75, 4.06)	2.87 (1.52, 3.38)	1.47 (0.93, 2.38)	< 0.001	0.009	< 0.001
NRMSE (%)							
2.00	7.87 \pm 2.91	13.82 \pm 2.36	13.08 \pm 2.84	10.30 \pm 2.80	< 0.001	< 0.001	< 0.001
2.25	8.99 \pm 3.43	14.78 \pm 2.83	14.11 \pm 3.36	11.29 \pm 3.33	< 0.001	< 0.001	< 0.001
2.50	9.75 \pm 3.72	15.39 \pm 3.10	14.76 \pm 3.63	11.95 \pm 3.63	< 0.001	< 0.001	< 0.001
2.75	10.48 \pm 3.95	16.00 \pm 3.36	15.69 \pm 4.31	12.61 \pm 3.86	< 0.001	< 0.001	< 0.001
3.00	11.03 \pm 4.16	16.97 \pm 3.76	16.39 \pm 4.62	13.11 \pm 4.08	< 0.001	< 0.001	< 0.001
SNR							
2.00	22.28 \pm 3.25	16.62 \pm 1.58	17.20 \pm 2.00	19.49 \pm 2.41	< 0.001	< 0.001	< 0.001
2.25	21.09 \pm 3.39	16.04 \pm 1.79	16.53 \pm 2.22	18.69 \pm 2.64	< 0.001	< 0.001	< 0.001
2.50	20.35 \pm 3.41	15.68 \pm 1.89	16.11 \pm 2.31	18.17 \pm 2.73	< 0.001	< 0.001	< 0.001
2.75	19.67 \pm 3.40	15.35 \pm 1.98	15.61 \pm 2.55	17.68 \pm 2.79	< 0.001	< 0.001	< 0.001
3.00	19.20 \pm 3.42	14.88 \pm 2.11	15.22 \pm 2.61	17.33 \pm 2.84	< 0.001	< 0.001	< 0.001
PSNR							

2.00	41.69 ± 3.95	36.39 ± 3.34	36.94 ± 3.54	39.10 ± 3.57	< 0.001	< 0.001	< 0.001
2.25	40.57 ± 4.13	35.83 ± 3.46	36.32 ± 3.67	38.36 ± 3.74	< 0.001	< 0.001	< 0.001
2.50	39.86 ± 4.14	35.49 ± 3.49	35.95 ± 3.70	37.88 ± 3.78	< 0.001	< 0.001	< 0.001
2.75	39.22 ± 4.13	35.17 ± 3.54	35.47 ± 3.85	37.43 ± 3.79	< 0.001	< 0.001	< 0.001
3.00	38.78 ± 4.13	34.69 ± 3.71	35.11 ± 3.83	37.10 ± 3.81	< 0.001	< 0.001	< 0.001
SSIM							
2.00	0.95 ± 0.02	0.93 ± 0.02	0.94 ± 0.02	0.94 ± 0.02	< 0.001	< 0.001	< 0.001
2.25	0.94 ± 0.02	0.91 ± 0.04	0.92 ± 0.03	0.93 ± 0.03	< 0.001	< 0.001	< 0.001
2.50	0.93 ± 0.03	0.90 ± 0.04	0.91 ± 0.03	0.92 ± 0.03	< 0.001	< 0.001	< 0.001
2.75	0.92 ± 0.03	0.88 ± 0.05	0.90 ± 0.03	0.91 ± 0.03	0.003	< 0.001	< 0.001
3.00	0.91 ± 0.03	0.86 ± 0.07	0.89 ± 0.04	0.90 ± 0.03	0.021	< 0.001	< 0.001

Table S3. Quantitative metrics of ACS, MoDL, and E2E-VarNet methods for reconstructing down-sampled MRI data from the testing dataset under different acceleration factors. Related to Figure 2. MSE and NMSE values with asymmetrical distributions are represented as median (25th, 75th percentiles). NRMSE, SNR, PSNR, and SSIM values fit normal distribution and are represented as mean \pm standard deviation. Lower error-related metrics (i.e., MSE, NMSE, and NRMSE) and higher consistency-related metrics (i.e., SNR, PSNR, and SSIM) stand for lower noise and better reconstruction performance. Statistical analyses are performed using two-way ANOVA followed by Sidak’s multiple comparisons tests (n = 14).

Acceleration factor	ACS	MoDL	E2E_VarNet	$P_{(ACS \text{ vs. MoDL})}$	$P_{(ACS \text{ vs. E2E_VarNet})}$
MSE (* 10⁸)					
2.00	0.74 (0.38, 1.68)	2.34 (1.00, 4.19)	11.77 (6.17, 34.15)	0.099	0.035
2.25	0.98 (0.48, 2.15)	2.51 (1.11, 4.46)	12.35 (6.35, 33.83)	0.054	0.033
2.50	1.16 (0.56, 2.55)	2.49 (1.09, 4.58)	12.65 (6.45, 34.18)	0.081	0.032
2.75	1.32 (0.64, 2.99)	2.44 (1.22, 4.45)	14.70 (6.69, 34.93)	0.115	0.028
3.00	1.48 (0.72, 3.30)	2.58 (1.25, 4.59)	15.40 (6.77, 35.53)	0.124	0.027
NMSE (%)					
2.00	0.51 (0.30, 0.93)	1.65 (0.89, 2.46)	7.93 (7.32, 8.46)	< 0.001	< 0.001
2.25	0.65 (0.38, 1.19)	1.78 (0.92, 2.51)	8.14 (7.42, 8.99)	< 0.001	< 0.001
2.50	0.77 (0.45, 1.40)	1.75 (0.95, 2.58)	8.32 (7.49, 9.33)	< 0.001	< 0.001
2.75	0.92 (0.52, 1.61)	1.67 (1.02, 2.62)	8.58 (7.70, 9.77)	< 0.001	< 0.001
3.00	1.02 (0.57, 1.77)	1.67 (1.00, 2.72)	8.93 (8.01, 9.98)	< 0.001	< 0.001
NRMSE (%)					
2.00	7.87 \pm 2.91	12.83 \pm 4.00	28.08 \pm 1.29	< 0.001	< 0.001
2.25	8.99 \pm 3.43	13.13 \pm 3.99	28.61 \pm 1.61	< 0.001	< 0.001
2.50	9.75 \pm 3.72	13.21 \pm 3.99	28.94 \pm 1.71	< 0.001	< 0.001
2.75	10.48 \pm 3.95	13.29 \pm 3.99	29.69 \pm 2.36	< 0.001	< 0.001
3.00	11.03 \pm 4.16	13.51 \pm 4.03	30.38 \pm 2.94	< 0.001	< 0.001
SNR					
2.00	22.28 \pm 3.25	17.94 \pm 3.03	9.94 \pm 0.55	< 0.001	< 0.001
2.25	21.09 \pm 3.39	17.76 \pm 2.98	9.75 \pm 0.64	< 0.001	< 0.001
2.50	20.35 \pm 3.41	17.70 \pm 2.95	9.62 \pm 0.69	< 0.001	< 0.001
2.75	19.67 \pm 3.40	17.64 \pm 2.93	9.39 \pm 0.80	< 0.001	< 0.001
3.00	19.20 \pm 3.42	17.49 \pm 2.90	9.18 \pm 0.90	< 0.001	< 0.001
PSNR					

2.00	41.69 ± 3.95	37.33 ± 4.03	30.13 ± 3.40	< 0.001	< 0.001
2.25	40.57 ± 4.13	37.11 ± 3.98	29.97 ± 3.39	< 0.001	< 0.001
2.50	39.86 ± 4.14	37.05 ± 3.95	29.87 ± 3.38	< 0.001	< 0.001
2.75	39.22 ± 4.13	37.00 ± 3.90	29.66 ± 3.44	< 0.001	< 0.001
3.00	38.78 ± 4.13	36.85 ± 3.92	29.47 ± 3.41	< 0.001	< 0.001
SSIM					
2.00	0.95 ± 0.02	0.89 ± 0.05	0.89 ± 0.04	< 0.001	< 0.001
2.25	0.94 ± 0.02	0.89 ± 0.05	0.88 ± 0.04	< 0.001	< 0.001
2.50	0.93 ± 0.03	0.89 ± 0.05	0.88 ± 0.05	0.005	< 0.001
2.75	0.92 ± 0.03	0.88 ± 0.05	0.87 ± 0.05	0.047	< 0.001
3.00	0.91 ± 0.03	0.88 ± 0.06	0.86 ± 0.05	0.223	0.002

Table S4. NRMSE values of ACS and PI methods for reconstructing down-sampled MRI data from the external validation dataset under different acceleration factors. Related to Figure 3.

NRMSE value fits normal distribution and is represented as mean \pm standard deviation. Lower NRMSE stands for lower noise. Statistical analyses are performed using paired *t*-tests ($n = 78$).

Acceleration factor	ACS (%)	PI (%)	<i>P</i>
T1w FLAIR			
2.00	6.54 \pm 0.64	5.89 \pm 1.38	< 0.001
2.25	7.09 \pm 0.71	7.31 \pm 1.33	0.029
2.50	8.17 \pm 0.82	9.16 \pm 1.47	< 0.001
2.75	9.18 \pm 0.89	10.22 \pm 1.50	< 0.001
3.00	9.43 \pm 0.89	12.37 \pm 1.47	< 0.001
3.25	9.91 \pm 1.06	15.23 \pm 1.49	< 0.001
3.50	10.03 \pm 0.95	18.37 \pm 1.50	< 0.001
3.75	10.18 \pm 1.00	25.74 \pm 1.56	< 0.001
4.00	10.54 \pm 0.88	28.42 \pm 1.62	< 0.001
T2w FLAIR			
2.00	6.92 \pm 0.63	7.05 \pm 1.18	0.049
2.25	8.50 \pm 0.63	9.58 \pm 1.04	< 0.001
2.50	10.04 \pm 0.83	13.65 \pm 1.15	< 0.001
2.75	10.24 \pm 0.76	12.19 \pm 1.23	< 0.001
3.00	10.73 \pm 0.82	15.37 \pm 1.16	< 0.001
3.25	11.11 \pm 0.83	19.36 \pm 1.05	< 0.001
3.50	11.74 \pm 0.89	22.58 \pm 1.16	< 0.001
3.75	12.15 \pm 0.89	27.48 \pm 1.33	< 0.001
4.00	12.22 \pm 0.90	30.58 \pm 1.33	< 0.001

Table S5. Statistics for lesion SUV_{max} and liver SNR. Related to Figure 6. Lesion SUV_{max} does not fit the normal distribution and is thus represented as median (25th, 75th percentiles), while SNR fits normal distribution and is represented as mean \pm standard deviation.

Group	Lesion SUV _{max}	Liver SNR
OSEM_120 s/bp	9.42 (6.73, 13.07)	7.91 \pm 1.57
DPR_120 s/bp	11.42 (7.54, 15.28)	13.53 \pm 2.65
DRP_90 s/bp	11.14 (7.40, 14.73)	11.99 \pm 2.48
DPR_60 s/bp	11.17 (7.09, 15.11)	10.14 \pm 2.30
DPR_40 s/bp	11.25 (6.91, 16.44)	8.16 \pm 1.78
DPR_30 s/bp	10.99 (6.98, 16.23)	6.79 \pm 1.65