As shown in Table SⅠ, CBN loss can improve the quality of quantitative maps. Especially, PSNR of NOE increases from 38.92dB to 39.08dB.

TABLE SI

RESULT OF 4-FOLD PROSPECTIVE HUMAN DATASET.

Data	Method	Raw images			LD NOE			LD APT			MTR_{asym}		
		PSNR	SSIM	TEN	PSNR	SSIM	TEN	PSNR	SSIM	TEN	PSNR	SSIM	TEN
Human	w/o L_{CBN}	**48.32**	0.9930	6.02e-2	38.92	0.9687	**2.11e-3**	39.38	0.9565	**1.30e-3**	40.78	0.9682	**4.24e-3**
	Ours	48.31	**0.9932**	**6.04e-2**	**39.08**	**0.9701**	2.04e-3	**39.48**	**0.9575**	**1.30e-3**	**40.84**	**0.9700**	4.21e-3

The comparation of model size and computational cost are shown in Table SⅡ. The Floating Point Operations (FLOPs) of COMET is significantly higher than other methods, which is a common problem for the unfolding network. Due to the share-parameter strategy, the number of parameters is not significantly more than other methods.

TABLE SⅡ

THE NUMBER OF PARAMETERS (PARAMS) AND FLOATING POINT OPERATIONS (FLOPS) OF DIFFERENT MODELS

Method	Params	FLOPs
T2Net	3.6M	246.58G
DPSR	3.32M	257.57G
RDN	8.09M	703.47G
EDSR	16.93M	757.82G
SRGAN	8.29M	330.38G
EPSRGAN	8.82M	290.79G
COMET	3.95M	1060.82G

To further validate the performance dependence on COMET to input data, we re-divided the training set and validation set for three times. As shown in Table SⅢ, there is no significant difference among three divided sets, which indicates stable training result can be obtained on the current rat dataset.

TABLE SⅢ

RESULT OF DIFFERENT METHODS IN DIFFERENT SETS

Data	Method	Set1			Set2			Set3		
		PSNR	SSIM	TEN	PSNR	SSIM	TEN	PSNR	SSIM	TEN
Rat	T2Net	41.27	0.9737	1.47e-2	41.30	0.9736	1.47e-2	41.19	0.9738	1.46e-3
	DPSR	41.30	0.9761	1.48e-1	41.25	0.9765	1.49e-2	41.37	0.9360	1.47e-3
	RDN	41.52	0.9705	**1.49e-1**	41.64	0.9710	1.48e-2	41.48	0.9767	1.48e-3
	EDSR	41.60	0.9778	**1.49e-1**	41.62	0.9777	**1.50e-2**	41.58	0.9780	**1.50e-3**
	SRGAN	41.89	**0.9793**	1.46e-1	41.80	**0.9793**	1.46e-2	41.96	**0.9796**	1.45e-2
	EPSRGAN	-	-	-	-	-	-	-	-	-
	COMET	**42.26**	0.9734	1.45e-1	**42.28**	0.9729	1.46e-2	**42.20**	0.9736	1.46e-3

The details of Net1, Net 2, Net 3, Net 4, Net 5 and the Down sampling operator in SFSM are shown in Table SⅣ. The input and output volume dimensions of each module is clarified in the first line and the last line. F, H, W represent the Frequency dimension, Height and Width, respectively. For Conv. and ConvTrans., c, k, s and p denote the channel dimension, kernel size, stride size and padding size, respectively.

TABLE SⅣ

THE DETAILS OF SUB-NETS IN THE PAPER

Net 1		Net 2		Net 3	
Layer	**Specification**	**Layer**	**Specification**	**Layer**	**Specification**
Input	F:3, H:256, W:256	**Input**	F:31, H:256, W:256	**Input**	F:31, H:64, W:64
Nonlocal Block	c:3, num_block:8	Nonlocal Block	c:31, num_block:8	Conv 3d	c:1, k:(3,1,1), s:1, p:(1,0,0)
Conv 2d	c:3,k:5,s:1,p:1	Conv 2d	c:31,k:3,s:1,p:1	Batch norm3d	Eps:1e-5,momentum:0.1
Batch norm2d	Eps:1e-5,momentum:0.1	Batch norm2d	Eps:1e-5,momentum:0.1	Leaky Relu	Negative slope:0.02
Conv 2d	c:3,k:4,s:2,p:1	Leaky Relu	Negative slope:0.02	ConvTrans 3d	c:1, k:(1,1,4), s:(1,2,2), p:(0,0,1)
Batch norm2d	Eps:1e-5,momentum:0.1	**Output**	F:3, H:256, W:256	Batch norm3d	Eps:1e-5,momentum:0.1
Leaky Relu	Negative slope:0.02			Leaky Relu	Negative slope:0.02
Conv 2d	c:6,k:3,s:1,p:1			ConvTrans 3d	c:2, k:(1,1,4), s:(1,2,2), p:(0,0,1)
Batch norm2d	Eps:1e-5,momentum:0.1			Batch norm3d	Eps:1e-5,momentum:0.1
Conv 2d	c:6,k:4,s:2,p:1			Leaky Relu	Negative slope:0.02
Batch norm2d	Eps:1e-5,momentum:0.1			Conv 3d	c:4, k:(3,1,1), s:1, p:(1,0,0)
Leaky Relu	Negative slope:0.02			Batch norm3d	Eps:1e-5,momentum:0.1
Conv 2d	c:12,k:3,s:1,p:1			Leaky Relu	Negative slope:0.02
Batch norm2d	Eps:1e-5,momentum:0.1			Conv 3d	c:2, k:(3,1,1), s:1, p:(1,0,0)
Leaky Relu	Negative slope:0.02			Batch norm3d	Eps:1e-5,momentum:0.1
Conv 2d	c:12,k:3,s:1,p:1			Leaky Relu	Negative slope:0.02
Batch norm2d	Eps:1e-5,momentum:0.1			**Output**	F:31, H:256, W:256
Leaky Relu	Negative slope:0.02				
Conv 2d	c:24,k:3,s:1,p:1				
Batch norm2d	Eps:1e-5,momentum:0.1				
Leaky Relu	Negative slope:0.02				
Conv 2d	c:24,k:3,s:1,p:1				
Batch norm2d	Eps:1e-5,momentum:0.1				
ConvTrans 2d	c:12,k:4,s:2,p:1				
Batch norm2d	Eps:1e-5,momentum:0.1				
Leaky Relu	Negative slope:0.02				
Conv 2d	c:18,k:3,s:1,p:1				
Batch norm2d	Eps:1e-5,momentum:0.1				
ConvTrans 2d	c:12,k:4,s:2,p:1				
Batch norm2d	Eps:1e-5,momentum:0.1				
Leaky Relu	Negative slope:0.02				
Conv 2d	c:9,k:3,s:1,p:1				
Batch norm2d	Eps:1e-5,momentum:0.1				
ConvTrans 2d	c:6,k:3,s:1,p:1				

Batch norm2d	Eps:1e-5,momentum:0.1				
Leaky Relu	Negative slope:0.02				
Output	F:31, H:256, W:256				

Net 4		Net 5		Down sampling operator in SFSM	
Layer	**Specification**	**Layer**	**Specification**	**Layer**	**Specification**
Input	F:34, H:256, W:256	**Input**	F:31, H:256, W:256	**Input**	F:31, H:256, W:256
Conv 2d	c:31,k:5,s:1,p:1	Conv 2d	c:34,k:5,s:1,p:1	Conv 3d	c:1, k:(3,1,1), s:1, p:(1,0,0)
Batch norm2d	Eps:1e-5,momentum:0.1	Batch norm2d	Eps:1e-5,momentum:0.1	Batch norm3d	Eps:1e-5,momentum:0.1
Conv 2d	c:31,k:4,s:2,p:1	Conv 2d	c:31,k:4,s:2,p:1	Leaky Relu	Negative slope:0.2
Batch norm2d	Eps:1e-5,momentum:0.1	Batch norm2d	Eps:1e-5,momentum:0.1	Conv 3d	c:1, k:(1,1,4), s:(1,2,2), p:(0,0,1)
Leaky Relu	Negative slope:0.02	Leaky Relu	Negative slope:0.02	Batch norm3d	Eps:1e-5,momentum:0.1
Conv 2d	c:62,k:3,s:1,p:1	Conv 2d	c:62,k:3,s:1,p:1	Leaky Relu	Negative slope:0.2
Batch norm2d	Eps:1e-5,momentum:0.1	Batch norm2d	Eps:1e-5,momentum:0.1	Conv 3d	c:2, k:(1,1,4), s:(1,2,2), p:(0,0,1)
Conv 2d	c:62,k:4,s:2,p:1	Conv 2d	c:62,k:4,s:2,p:1	Batch norm3d	Eps:1e-5,momentum:0.1
Batch norm2d	Eps:1e-5,momentum:0.1	Batch norm2d	Eps:1e-5,momentum:0.1	Leaky Relu	Negative slope:0.2
Leaky Relu	Negative slope:0.02	Leaky Relu	Negative slope:0.02	Conv 3d	c:4, k:(3,1,1), s:1, p:(1,0,0)
Conv 2d	c:124,k:3,s:1,p:1	Conv 2d	c:124,k:3,s:1,p:1	Batch norm3d	Eps:1e-5,momentum:0.1
Batch norm2d	Eps:1e-5,momentum:0.1	Batch norm2d	Eps:1e-5,momentum:0.1	Leaky Relu	Negative slope:0.2
Leaky Relu	Negative slope:0.02	Leaky Relu	Negative slope:0.02	Conv 3d	c:2, k:(3,1,1), s:1, p:(1,0,0)
Conv 2d	c:124,k:3,s:1,p:1	Conv 2d	c:124,k:3,s:1,p:1	Batch norm3d	Eps:1e-5,momentum:0.1
Batch norm2d	Eps:1e-5,momentum:0.1	Batch norm2d	Eps:1e-5,momentum:0.1	Leaky Relu	Negative slope:0.2
Leaky Relu	Negative slope:0.02	Leaky Relu	Negative slope:0.02	**Output**	C:1, F:31, H:64, W:64
Conv 2d	c:248,k:3,s:1,p:1	Conv 2d	c:248,k:3,s:1,p:1		
Batch norm2d	Eps:1e-5,momentum:0.1	Batch norm2d	Eps:1e-5,momentum:0.1		
Leaky Relu	Negative slope:0.02	Leaky Relu	Negative slope:0.02		
Conv 2d	c:24,k:3,s:1,p:1	Conv 2d	c:24,k:3,s:1,p:1		
Batch norm2d	Eps:1e-5,momentum:0.1	Batch norm2d	Eps:1e-5,momentum:0.1		
ConvTrans 2d	c:124,k:4,s:2,p:1	ConvTrans 2d	c:124,k:4,s:2,p:1		
Batch norm2d	Eps:1e-5,momentum:0.1	Batch norm2d	Eps:1e-5,momentum:0.1		
Leaky Relu	Negative slope:0.02	Leaky Relu	Negative slope:0.02		
Conv 2d	c:186,k:3,s:1,p:1	Conv 2d	c:186,k:3,s:1,p:1		
Batch norm2d	Eps:1e-5,momentum:0.1	Batch norm2d	Eps:1e-5,momentum:0.1		
ConvTrans 2d	c:124,k:4,s:2,p:1	ConvTrans 2d	c:124,k:4,s:2,p:1		
Batch norm2d	Eps:1e-5,momentum:0.1	Batch norm2d	Eps:1e-5,momentum:0.1		
Leaky Relu	Negative slope:0.02	Leaky Relu	Negative slope:0.02		
Conv 2d	c:93,k:3,s:1,p:1	Conv 2d	c:93,k:3,s:1,p:1		
Batch norm2d	Eps:1e-5,momentum:0.1	Batch norm2d	Eps:1e-5,momentum:0.1		
ConvTrans 2d	c:62,k:3,s:1,p:1	ConvTrans 2d	c:62,k:3,s:1,p:1		
Batch norm2d	Eps:1e-5,momentum:0.1	Batch norm2d	Eps:1e-5,momentum:0.1		
Leaky Relu	Negative slope:0.02	Leaky Relu	Negative slope:0.02		
Output	F:31, H:256, W:256	**Output**	F:31, H:256, W:256		

The processes of tuning two hyper-parameters: weight of CEST-Based Normalization loss (CBN) and weight of Mutual learning loss (ML) are shown in Table S V and Table S VI. During the fine-tuning of hyperparameters, we adopt a sequential approach where we adjust one hyperparameter at a time while keeping other hyperparameters fixed. This allows us to isolate the effect of each individual hyperparameter. Once a parameter is optimized and reaches its optimal value, we then proceed to tune the remaining parameters. By adjusting the hyperparameters in a systematic manner, we can effectively optimize the overall performance of the model. Indeed, COMET has the limitation of too many hyper-parameters tuning, which is labor-consuming and hinder the adaption of COMET to new datasets. We will reduce the number of hyper-parameters and optimize this issue in the future work.

TABLE S V

RESULT OF DIFFERENT WEIGHT OF CEST-BASED NORMALIZATION LOSS (CBN) ON HUMAN AND RAT DATASETS.

Data	*CBN* (γ)	Raw image	
		PSNR	SSIM
Human	0.3	53.50	0.9968
	0.5	53.70	0.9966
	0.7	**53.92**	**0.9970**
	0.9	53.68	0.9966
Rat	0	41.98	**0.9742**
	0.5	**42.26**	0.9734
	1.0	42.15	0.9730

TABLE SVI

RESULT OF DIFFERENT WEIGHT OF MUTUAL LEARNING LOSS (ML) ON HUMAN AND RAT DATASETS..

Data	*ML* (β)	Raw image	
		PSNR	SSIM
Human	0	53.35	0.9965
	0.1	**53.70**	0.9966
	0.2	53.42	**0.9968**
Rat	0	41.92	**0.9737**
	0.5	**42.15**	0.9730
	1.0	41.96	0.9732

The DWI images used in this research were sourced from the Human Connectome Project (HCP) and were acquired using a 7T MR scanner. The acquisition parameters for these images are as follows: field of view (FOV) = 173×143mm², in-plane resolution = 1 mm, number of diffusion-encoding directions = 64, slice thickness = 1mm, and b-value = 1000 s/mm².Out of the total 640 images, 360 were utilized for training purposes, while 120 and 160 images were allocated to the validation set and test set, respectively. Regarding the results, it was observed that the COMET method outperformed all the compared methods in terms of Peak Signal-to-Noise Ratio (PSNR). This implies that COMET achieves higher fidelity and better reconstruction quality compared to the other methods.

TABLE SⅦ

THE PERFORMANCE OF ALL METHODS ON DWI

Data	Method	PSNR	SSIM	TEN
DWI	T2Net	37.00	0.9034	2.11e-2
	DPSR	36.69	**0.9080**	2.13e-1
	RDN	37.02	0.9027	2.10e-1
	EDSR	36.14	0.8890	**2.24e-1**
	SRGAN	36.60	0.9063	2.11e-1
	ESRGAN	36.53	0.9064	2.14e-1
	COMET	**37.25**	0.9034	2.11e-1