# FastSurferVINN: Building resolution-independence into deep learning segmentation methods — A solution for HighRes brain MRI

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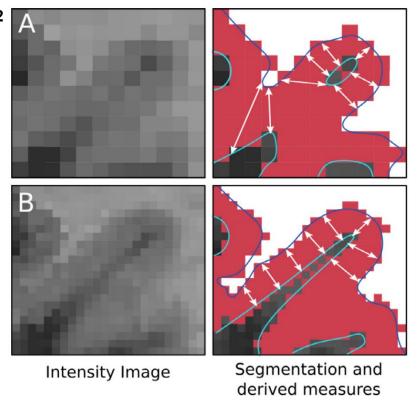
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# **Context: Partial volume effect VS segmentation**

Fig. 2



- 1.4 mm resolution (2x2 max pooling on image B)
- ⇒ Partial volume effect (PVE): signals accumulated across tissue boundaries into larger voxels

- 0.7 mm resolution (High resolution)
- ⇒ Precise region delineation or more details
- → improved shape (WM/GM in blue and GM/CSF in cyan) or thickness analysis (white arrows)

# **Context: Architectures of data-driven computational methods**

- Freesurfer: several hours per image at 1.0 mm
  - $\rightarrow$  Worse with HiRes:  $(1.0/0.7)^3$  = **2.915 times more voxels**
  - → VS Convolutional neural networks (CNNs): seconds on the GPU
- Recent works: 2.5D and 3D U-Net architecture
  - → With HiRes, GPU memories often surpassed
  - → Different view aggregation strategies mentioned

Other architectures mentioned (not always for segmentation):

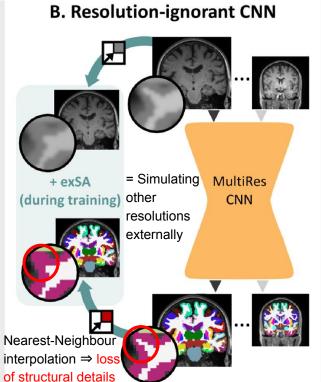
- Super-resolution networks based on post-sampling interpolation
- Multi-source domain adaptations (MSDAs) with intermediate domain generators
- Spatial transformers

# **Hypothesis**

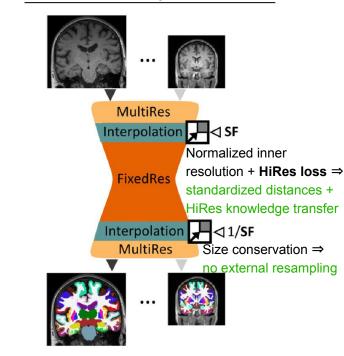
- Limited data in HiRes, especially in sub-groups:
   resolution, age-group, diseases, genetic variants, scanners
   → Unbalanced training data for data-driven computational methods
   → Introduction of biases into the model
- Manual reference labels for validation published exclusively for 1.0 mm
- **⇒** Data-driven computational methods require built-in resolution independence

# Deep learning network solutions for Multi-Resolution sMRI segmentation

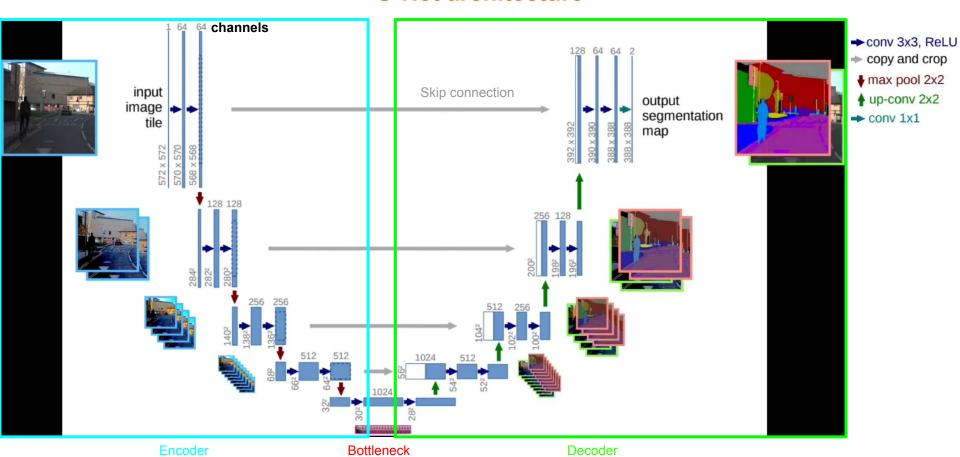
Fig. 1 A. Fixed-resolution CNNs **FixedRes FixedRes** CNN CNN ... (1.0 mm)(0.7 mm)



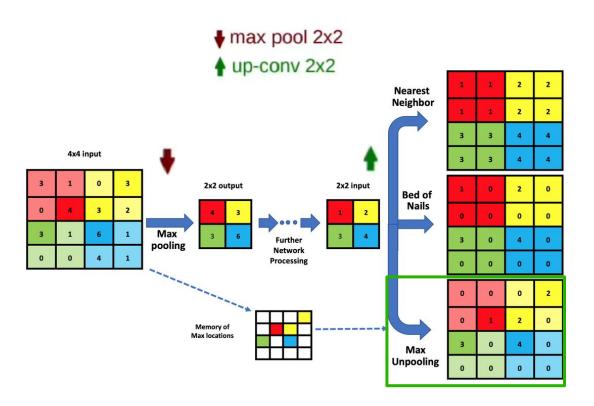
#### C. Resolution-independent VINN



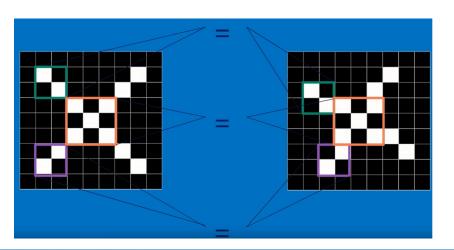
# **U-Net architecture**



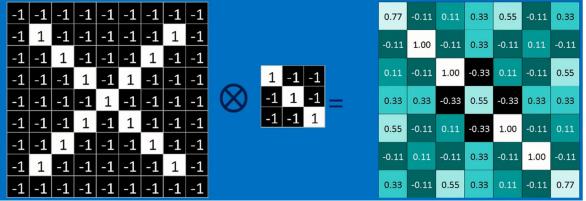
# Down-scaling and up-scaling



### **Concept of CNN**

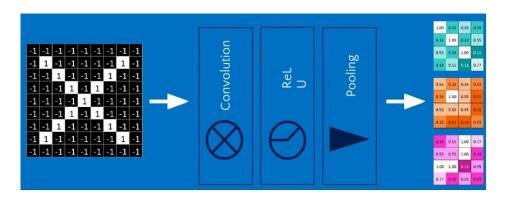


⇒ Compare similarity on lower scale features



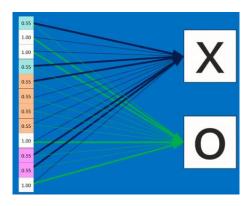
⇒ Convolution is producing a **probability map** of the similarity between input and a feature (trained kernel)

# **Concept of CNN**



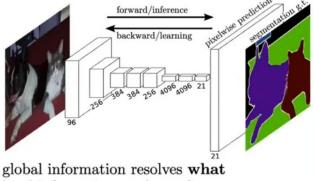
#### Encoder:

→ Downscale the analyzed features



Bottleneck and decoder:

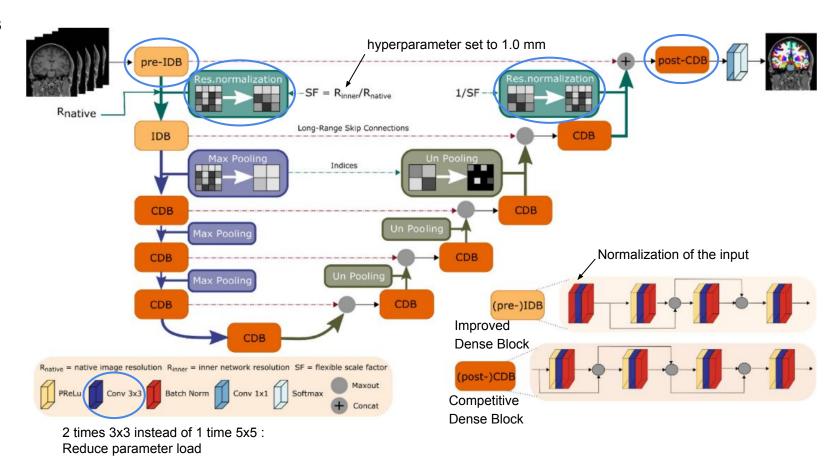
→ Learn how to use features to discern between different labels



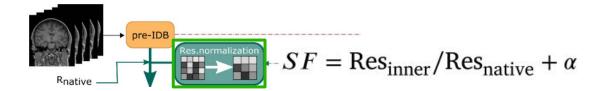
local information resolves where

#### **FastSurferVINN**

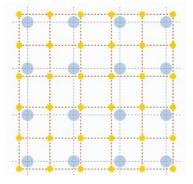
Fig. 3



# Inner scale augmentation (inSA) in resolution normalization



- α sampled from a Gaussian distribution with parameters sigma = 0.1 and mean = 0
  - → introduces small resolution variations within the grid sampling procedure
  - → internal scale augmentation randomly resizing the feature maps in the latent space



# HiRes specific adjustments to improve overall segmentation accuracy

- 1. Loss-function weighting scheme
- 2. Adaptive attention mechanism

#### **Loss function**

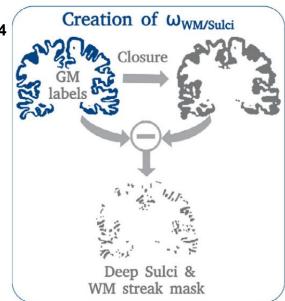
$$\mathcal{L} = -\sum_{l,i} \omega_i y_{l,i} \log p_{l,i}(x) - \sum_{l} \frac{2 \sum_{i} p_{l,i}(x) y_{l,i}}{\sum_{i} p_{l,i}(x) + \sum_{i} y_{l,i}}$$
Logistic loss
Soft Dice loss

with 
$$\omega_i = \omega_{\text{median freq.}} + \omega_{\text{gradient}} + \omega_{\text{GM}} + \omega_{\text{WM/Sulci}}$$
.

- $p_{l,i}(x)$  estimated probability of pixel i to belong to class I
- $\mathcal{Y}_{l,i}$  ground truth of pixel i to belong to class I
- $\omega_i$  localized weights factor
  - $\rightarrow \omega_{
    m median\ freq.}$  median frequency balancing
  - $^{
    ightharpoonup} \omega_{
    m gradient}$  boundary refinement through a 2D gradient vector

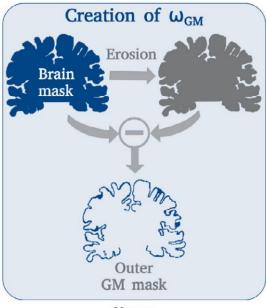
# **Loss function**

Fig. 4



 $\omega_{
m WM/Sulci}$ 

→ emphasizing thin WM strands and narrow sulci



 $\omega_{\mathrm{GM}}$ 

→ accentuating pixels at the boundary of the cortex

⇒ Adjust the underlying decision boundary to closely match the target segmentation in **PVE-affected locations** 

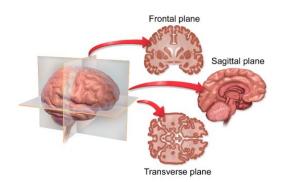
# **Adaptive attention module**

- Automatically select optimal scale or filter sizes for specific image regions
- Method proposed in Qin et al. (2018):
  - → convolution features in CDB dynamically weighted based on learned activation maps
  - → introducing non-linearity

# **View aggregation scheme (3D image)**

#### Same as FastSurferCNN:

- One Fully-CNN per anatomical plane
  - → resulting probability maps are weighted averaged (1/3÷2 for sagittal plane, because of missing lateralization)
  - $\hookrightarrow$  reduced number of class: 78  $\rightarrow$  50 (95 labels in FreeSurfer)



#### All used datasets

#### Table 3

Dataset	Scanner	1.5T/3T	Groups	Age	Res
НСР	Siemens	3T	Normal	22–35	0.7 mm
HCPL	Siemens	3T	Normal	25-75	0.8 mm
RS	Siemens	3T	Normal	30-95	0.8 mm
ABIDE-II ETHZ1	Philips	3T	ASD/Normal	20-31	0.9 mm
ABIDE-I	Philips/GE/Siemens	3T	ASD/Normal	18-64	1.0 mm
ADNI	Philips/GE/Siemens	1.5T/3T	AD/MCI/Normal	55-93	1.0 mm
IXI	Philips/GE	1.5T/3T	Normal	19–87	1.0 mm
LA5C	Siemens	3T	Neuropsych/Normal	21-50	1.0 mm
MBB	Siemens	3T	Normal	20-77	1.0 mm
MIRIAD	GE	1.5T	AD/Normal	55-86	1.0 mm
OASIS1	Siemens	1.5T/3T	Normal	18-90	1.0 mm
OASIS2	Siemens	1.5T/3T	AD/Normal	60–96	1.0 mm

- ASD = autism spectrum disorder
- AD = adjustments disorder
- MID = Mild cognitive impairment (memory or thinking problems relative to age)
- Neuropsychiatric disorder = broad range of medical conditions that involve both neurology and psychiatry

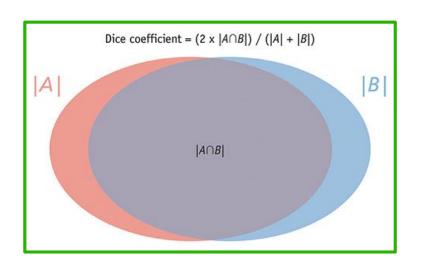
#### **Produced sets**

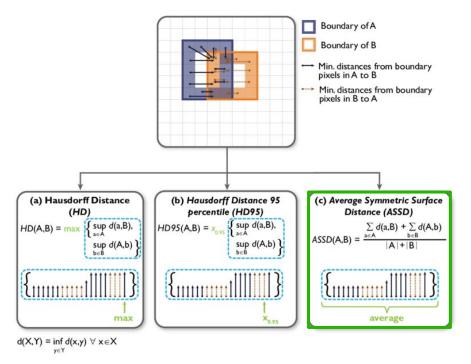
Table 4
Composition of training, validation and testing set used throughout the paper. The asterisk (\*) indicates submillimeter datasets are resampled to 1.0 mm.

Usage		Datasets (subjects)	n
	Mix	HCP (30), RS (30), ADNI (15), LA5C (16), MIRIAD (7), OASIS1 (14), OASIS2 (8)	120
	No 0.8 mm	HCP (60), ADNI (15), LA5C (16), MIRIAD (7), OASIS1 (14), OASIS2 (8)	120
	No 0.7 mm	RS (60), ADNI (15), LA5C (16), MIRIAD (7), OASIS1 (14), OASIS2 (8)	120
	Only 0.8 mm	RS (small=60, big=120)	60/120
	Only 1.0 mm	HCP* (30), RS* (30), ADNI (15), LA5C (16), MIRIAD (7), OASIS1 (14), OASIS2 (8)	120
Training	Mix (Big)	HCP (30), RS (30), ABIDE-I (68), ADNI (215), IXI (400), LA5C (203), MBB (195), MIRIAD (30), OASIS1 (79), OASIS2 (65)	1315
	Mix (Big), No 0.8 mm, No 0.7 mm	HCP (20), RS (20), ADNI (8), LA5C (9), MIRIAD (7), OASIS1 (11), OASIS2 (5)	80
	Only 0.8 mm	RS (20)	20
Validation	Only 1.0 mm	HCP* (20), RS* (20), ADNI (8), LA5C (9), MIRIAD (7),	
	5	OASIS1 (11), OASIS2 (5)	80
	Mix	HCP (80), RS (80), ABIDE-II (25), ABIDE-I (20), ADNI (40),	
		IXI (43), LA5C (15), OASIS1 (30), OASIS2 (17)	350
	No 0.7 mm,		
	No 0.8 mm	HCP (80), RS (80), ABIDE-II (25)	185
	Manual Labels	RS (6), Mindboggle (78)	84
	Only 0.8 mm,	RS (102), HCPL (10), ABIDE-I (20), ADNI (40), IXI (43)	
	Only 1.0 mm	LA5C (15), OASIS1 (36), OASIS2 (17)	259
Testing	Mix (Big)	HCP (80), RS (80), ABIDE-II (25), ABIDE-I (20), ADNI (40),	
		IXI (43), LA5C (15), OASIS1 (35), OASIS2 (17)	355

- Balancing sets for gender and age
- No common image in training and validation datasets to avoid data-leakage and overfitting
- Empty slices filtered out ⇒ 155 single view planes per subject in average

#### **Evaluation metrics**





- Silver truth: Freesurfer 7.1.1
- Golden truth: manual label
- Improvements in segmentation performance evaluated by statistical testing:
   Wilcoxon signed-rank test (Wilcoxon, 1945) after Benjamini-Hochberg correction (Benjamini and Hochberg, 1995) for multiple testing (corrected p < 0.05)</li>

#### Results

- 1. Ablative architecture improvements
- 2. Comparison of performances between FastSurferVINN and FastSurferCNN in different settings

# **Ablative architecture improvements**

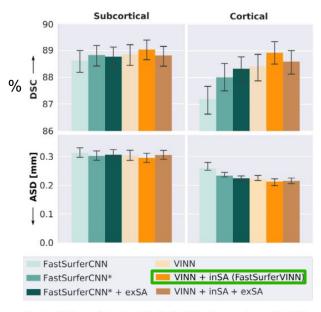
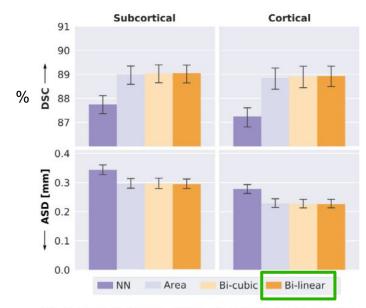
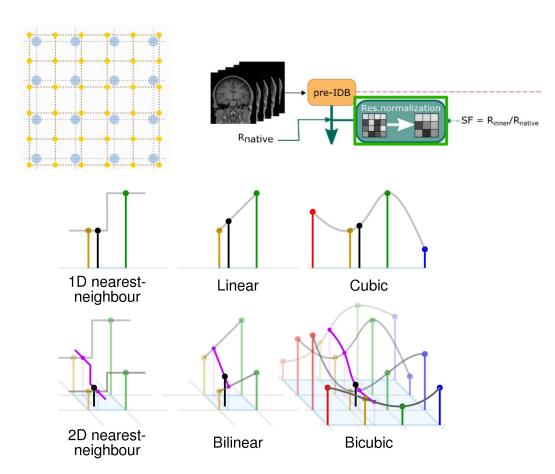


Fig. 5. Ablative optimization of FastSurferCNN and comparison to FastSurfer-VINN. FastSurferCNN (light green) is optimized through a switch to  $3\times3$  kernels (FastSurferCNN\*, green). Addition of data augmentation (external scaling augmentation, FastSurferCNN\* + exSA, dark green) improves performance further. VINN equipped with internal scaling augmentation (inSA) (FastSurferVINN, orange) outperforms all other models on both subcortical (left) and cortical (right) structures with respect to Dice Similarity Coefficient (DSC, top) and average surface distance (ASD, bottom). Further addition of external scaling augmentation negatively affects performance (VINN + inSA + exSA). Segmentation results with FastSurferVINN are significantly better compared to all other models (corrected  $p < 10^{-7}$ ).

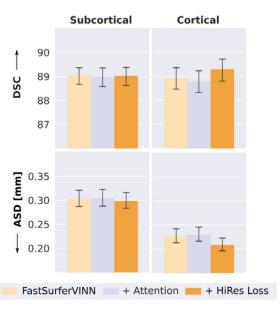
# **Ablative architecture improvements**



**Fig. 6.** Effect of sampling kernels on network-integrated resolution-normalization. Comparison of nearest-neighbour (NN, purple), area (light violet), bi-cubic (light yellow), and bi-linear (orange) sampling kernels with respect to the Dice Similarity Coefficient (DSC, top) and the average surface distance (ASD, bottom) for subcortical (left) and cortical (right) structures. Segmentation performance with NN is significantly worse than all other interpolation strategies (corrected  $p < 10^{-13}$ ). Area, bi-cubic and bi-linear give equivalent results.



# **HiRes specific adjustments**



**Fig. 7.** Adaptation of the original loss function through addition of HiRes weights focusing on areas strongly effected by PVEs (HiRes Loss, right bar) significantly improves segmentation performance on the cortical structures (compared to FastSurfer/INN with original loss, left bar). Addition of attention (middle bar) does not lead to a significant improvement compared to the baseline. Dice Similarity Coefficient (DSC, top) and average surface distance (ASD, bottom) are shown for subcortical (left) and cortical (right) structures. Cortical structures are significantly better segmented with the HiRes Loss (corrected  $p < 10^{-5}$ ). No significant change was detected on the subcortical structures.

#### FastSurferCNN\*+exSA VS FastSurferVINN on different datasets

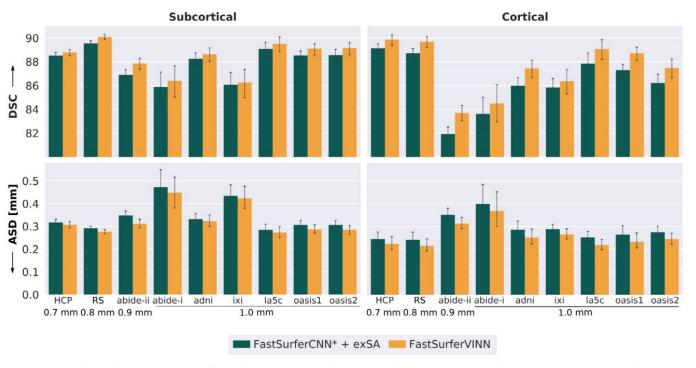


Fig. 8. Improved generalization performance of FastSurferVINN across nine datasets. FastSurferVINN (orange) outperforms FastSurferCNN\* + external scale augmentation (+exSA, dark green) across subcortical (left) and cortical structures (right) with respect to Dice Similarity Coefficient (DSC, top) and average surface distance (ASD, bottom). Results are consistently better for all datasets (HCP, RS, ABIDE-II, ABIDE-I, ADNI, IXI, LA5C, OASIS1 and OASIS2).

# FastSurferVINN performances across different resolutions

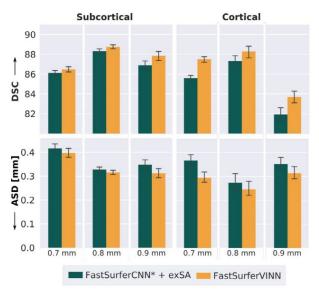
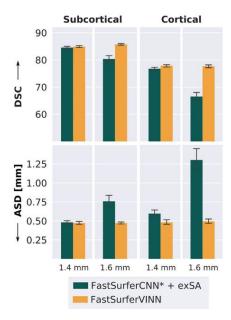
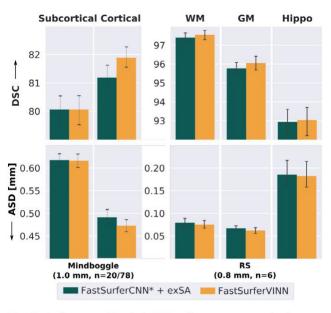


Fig. 9. Improved generalization performance of FastSurferVINN to resolutions not encountered during network training (here training datasets are customized, see Sections 4.3.2 and A.3). FastSurferVINN (orange) outperforms FastSurferCNN\* equipped with external scale augmentation (+ exSA, dark green) with respect to Dice Similarity Coefficient (DSC, top) and average surface distance (ASD, bottom) across subcortical (left) and cortical structures (right). Results are significantly better across all resolutions (0.7 mm, 0.8 mm, and 0.9 mm, corrected  $p < 10^{-4}$ ).



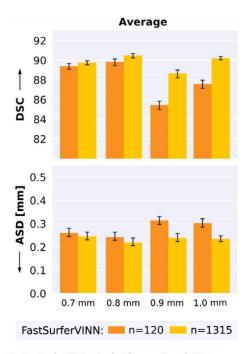
**Fig. 10.** Superior generalization performance of FastSurferVINN to resolutions vastly outside the training domain (1.4 mm, 1.6 mm). FastSurferVINN (orange) outperforms scale-augmentation (FastSurferCNN\* + exSA, green) highlighting its extrapolation capabilities. Results are significantly better with respect to Dice Similarity Coefficient (DSC, top) and average surface distance (ASD, bottom) across subcortical (left) and cortical structures (right) (corrected p < 0.001 for 1.4 mm and  $p < 10^{-13}$  for 1.6 mm).

# Golden truth: manual references (1.0 mm and 0.8 mm in-house set)



**Fig. 11.** Performance of FastSurferVINN with respect to manual references. Based on the 1.0 mm scans in Mindboggle101 (left plot) FastSurferVINN (orange) outperforms external scale augmentation (+exSA, dark green) on the cortical structures (right, N=78) with respect to Dice Similarity Coefficient (DSC, top) and average surface distance (ASD, bottom). Results on the subcortical structures (left side, N=20) are equivalent for both approaches. Similarly, segmentation results are better for the 0.8 mm scans of the RS (right plot, N=6) for white matter (WM), gray matter (GM), and hippocampus (Hippo).

# Impact of training set size



**Fig. 13.** Big- FastSurferVINN trained with approximately 20 times more 1.0 mm scans (n=1315, yellow) than the original version (n=120, orange) raises segmentation performance across resolutions. Dice Similarity Coefficient (DSC, top) and average surface distance (ASD, bottom) improve on the submillimeter (0.7 mm–0.9 mm) as well as 1.0 mm scans.

#### **Discussion**

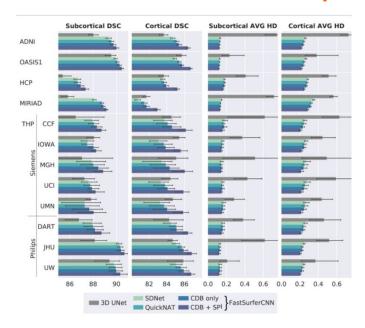
- LowRes and HiRes datasets have both an advantage on the other one:
  - → LowRes datasets are bigger and cover more sub-categories
  - → HiRes datasets offer more detailed structures
- FastSurferVINN outperforms LowRes fixed-resolution networks:
  - → predominantly motivated by the structural details provided by the submillimeter scans
- Performance dominated by the training corpus size and not significantly influenced by its heterogeneous resolution
- Imbalance between 1.0 mm and submillimeter training data distribution does not introduce a resolution bias
  - → improve generalization performance to future HiRes datasets without retraining

Link to the datasets in Annex A3

**Source Code**: https://github.com/Deep-MI/FastSurfer

# Thank you for your attention

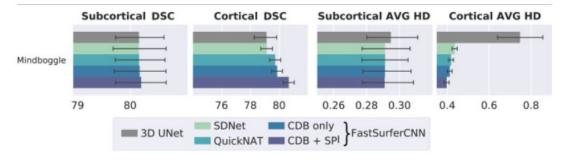
# Bonus:FastSurferCNN performances compared to other architectures



Download : Download high-res image (633KB)

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Fig. 4. Dice similarity coefficient (DSC, left, larger=better) and average Hausdorff distance (AVG HD, right, smaller=better) comparison of baselines and the proposed FastSurferCNN on four different datasets (mean  $\pm$  standard deviation). Network modifications (i) competitive dense blocks (CDB) and (ii) spatial information aggregation (SPI) are incrementally tested. The final FastSurferCNN (dark blue, CDB+SPI) outperforms all other models on both, subcortical and cortical structures.



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Fig. 5. Dice similarity coefficient (DSC, left, larger=better) and average Hausdorff distance (AVG HD, right, smaller=better) comparison across networks with respect to a manual reference (Mindboggle-101). FastSurferCNN outperforms all other models on both subcortical and cortical structures.

Source: Henchel et al., 2020 <a href="https://doi.org/10.1016/j.neuroimage.2020.117012">https://doi.org/10.1016/j.neuroimage.2020.117012</a>

# **Bonus: a fiew points on FastSurferVINN**

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# Bonus: a fiew points on FastSurferVINN

- Trained network not-dependent of skull-stripping or bias-field removal (FreeSurfer HiRes stream)
- Label related hemisphere found by nearest WM centroid of left and right hemisphere

# Bonus: labels in FastSurferCNN (78) VS in FreeSurfer (95)

Table 5
FastSurfer (FastS) internal segmentation IDs and mapping to FreeSurfer (FreeS).

Subcortical structures	FastS	FreeS	Cortical structures	FastS	FreeS
Cerebral white matter (lh)	1	2	caudalanteriorcingulate (lh)	34	1002
Lateral Ventricle (lh)	2	4	caudalmiddlefrontal (lh, rh)	35	1003, 200
Inferior Lateral Ventricle (lh)	3	5	cuneus (lh)	36	1005
Cerebellar White Matter (lh)	4	7	entorhinal (lh, rh)	37	1006, 200
Cerebellar Cortex (lh)	5	8	fusiform (lh, rh)	38	1007, 200
Thalamus (lh)	6	10	inferiorparietal (lh, rh)	39	1008, 200
Caudate (lh)	7	11	inferiortemporal (lh, rh)	40	1009, 200
Putamen (lh)	8	12	isthmuscingulate (lh)	41	1010
Pallidum (lh)	9	13	lateraloccipital (lh, rh)	42	1011, 201
3rd-Ventricle	10	14	lateralorbitofrontal (lh)	43	1012
4th-Ventricle	11	15	lingual (lh)	44	1013
Brain Stem	12	16	medialorbitofrontal (lh)	45	1014
Hippocampus (lh)	13	17	middletemporal (lh, rh)	46	1015, 201
Amygdala (lh)	14	18	parahippocampal (lh)	47	1016
CSF	15	24	paracentral (lh)	48	1017
Accumbens (lh)	16	26	parsopercularis (lh, rh)	49	1018, 201
Ventral DC (lh)	17	28	parsorbitalis (lh, rh)	50	1019, 201
Choroid Plexus (lh)	18	31	parstriangularis (lh, rh)	51	1020, 202
Cerebral white matter (rh)	19	41	pericalcarine (lh)	52	1021
Lateral Ventricle (rh)	20	43	postcentral (lh)	53	1022
Inferior Lateral Ventricle (rh)	21	44	posteriorcingulate (lh)	54	1023
Cerebellar White Matter (rh)	22	46	precentral (lh)	55	1024
Cerebellar Cortex (rh)	23	47	precuneus (lh)	56	1025
Thalamus (rh)	24	49	rostralanteriorcingulate (lh, rh)	57	1026, 202
Caudate (rh)	25	50	rostralmiddlefrontal (lh, rh)	58	1027, 202
Putamen (rh)	26	51	superiorfrontal (lh)	59	1028
Pallidum (rh)	27	52	superiorparietal (lh, rh)	60	1029, 202
Hippocampus (rh)	28	53	superiortemporal (lh, rh)	61	1030, 203
Amygdala (rh)	29	54	supramarginal (lh, rh)	62	1031, 203
Accumbens (rh)	30	58	transversetemporal (lh, rh)	63	1034, 203
Ventral DC (rh)	31	60	insula (lh, rh)	64	1035, 203
Choroid Plexus (rh)	32	63	caudalanteriorcingulate (rh)	65	2002
WM-hypointensities	33	77	cuneus (rh)	66	2005
The hypometrical			isthmuscingulate (rh)	67	2010
			lateralorbitofrontal (rh)	68	2012
			lingual (rh)	69	2013
			medialorbitofrontal (rh)	70	2014
			parahippocampal (rh)	71	2016
			paracentral (rh)	72	2017
			pericalcarine (rh)	73	2021
			postcentral (rh)	74	2021
			posteriorcingulate (rh)	75	2022
			precentral (rh)	76	2023
			precuneus (rh)	77	2025
			superiorfrontal (rh)	78	2028
			superioritoritar (III)	70	2020

# Bonus: architectures of data-driven computational methods

other interesting but not case-solving architectures:

- Super-resolution networks based on post-sampling interpolation
- Multi-source domain adaptations (MSDAs) with intermediate domain generators (for semantic segmentation), pixel-level alignement learned by GAN (generative adversarial networks) -> limited to a single target distribution -> multi-target is a relatively unexplored area
- Spatial transformers: Our technique is different by directingly determine the sampling-grid based on input scale factors