Annotation-Efficient Selection and Collaborative Datasets for Clinical Translation in Brain Vessel Segmentation

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Abstract. Brain vessel segmentation is fundamental for understanding cerebrovascular diseases and planning neurosurgical treatments. Yet, current deep learning segmentation approaches face critical challenges, including extensive annotation requirements and inconsistent quality across datasets. These barriers create a significant gap between research and clinical translation in real-world medical environments.
This thesis proposes a set of contributions to advance the field of neurovascular imaging. First, to address the problem of expert vessel annotation requiring multiple hours per 3D volume and demanding specialized neuroanatomical knowledge, V-DiSNet introduces a one-shot active learning framework that uses dictionary learning to identify recurring vessel patterns, reducing annotation requirements by 70% while maintaining segmentation accuracy. Second, to tackle the dataset fragmentation caused by different annotation protocols across institutions, VesselVerse provides the largest public vessel annotation dataset comprising 950 3D images with a collaborative framework that supports version control, multi-expert annotation, and automated consensus generation.
Third, building on these contributions and leveraging a cross-modality adaptation vessel segmentation framework, three studies bridge the clinical translation gap by demonstrating practical utility in real-world clinical research. These studies include automated stroke diagnosis using 902 clinical TOF-MRA images, genetic analysis using automated vessel quantification in 230 twin pairs to identify heritable vascular traits and their clinical implications, and a multi-institutional federated learning vessel segmentation deployment across diverse hospitals.
This thesis aims to advance neurovascular image analysis through the development of annotation-efficient methodologies and collaborative infrastructure, thereby enabling the clinical translation of research algorithms into practical healthcare solutions.
Keywords: Brain vessel segmentation, Data-efficient learning, Collaborative datasets, Clinical translation, Neurovascular image analysis.

1 Research Problem and Motivation

Brain vessel segmentation is a crucial step for diagnosing cerebrovascular diseases, planning neurosurgical treatments, and understanding neurological disorders [4]. Despite significant advances in deep learning for medical image analysis [2,8,25,29], vessel segmentation faces unique challenges that create a fundamental gap between research achievements and clinical deployment. Current supervised learning approaches require hundreds or thousands of labeled examples to achieve reliable performance, creating a bottleneck where the need for vessel segmentation tools exceeds the capacity to generate the required training data. Expert vessel annotation is time-consuming, often requiring multiple hours per 3D volume, and demands specialized knowledge [3]. This data scarcity problem is coupled with quality inconsistencies, as applying these models to new datasets requires complete re-annotation due to variations in imaging protocols, scanner specifications, and annotation preferences. Different annotation protocols across institutions lead to dataset fragmentation, while subjective interpretations of vessel boundaries introduce inter-rater variability [23], undermining model reliability. The result is a substantial disconnect between research on curated datasets and performance in real-world clinical environments. This gap prevents promising research results from translating into practical clinical tools, limiting the benefits of AI advancements for patients.

This doctoral research addresses a fundamental challenge in medical imaging: developing robust, data-efficient methods for brain vessel segmentation, which is essential for understanding cerebrovascular diseases and planning neurosurgical treatments. The methodology presented addresses the extensive annotation requirements of advanced learning-based approaches and the inconsistent quality across datasets, two critical limitations that create a gap between research and clinical translation in real-world medical environments. To this end, this research advances the state-of-the-art through three contributions that bridge vessel segmentation research and clinical practice: 1) a data-efficient selection method for vessel annotation; 2) an *imperfect* dataset of brain vessel annotations and a collaborative infrastructure to improve it; and 3) a vascular analysis pipeline for clinical translation across multiple real-world research applications. This research directly addresses MICCAI's mission of advancing medical image computing and computer-assisted intervention by tackling these limitations.

2 Background

Vessel segmentation research has achieved significant algorithmic advances over the last decade. Early approaches, such as the Frangi filter (FF) [7], employed hand-crafted features for vessel detection. Deep learning improved vessel segmentation through the U-Net [18,24] and related architectures [14]. Recent methods [2,8,25,29] show high accuracy on benchmark datasets.

Despite these advances, current methods require extensive labeled datasets that are expensive to annotate. Transfer learning approaches [10,26,11] reduce data requirements but still need substantial domain-specific fine-tuning. Weakly supervised methods [3] trade accuracy for reduced annotation burden, while traditional active learning [13] requires iterative cycles that are impractical in clinical settings with limited expert availability. One-shot active learning (OSAL) addresses these practical constraints through a single-iteration selection. Current frameworks employ self-supervised learning [13], variational autoencoders [30], and contrastive learning [15,16]. However, these methods treat vessel regions uniformly and fail to exploit the tree-like structures inherent in brain vasculature, without considering vessel structure in sample selection.

A second critical gap emerges in dataset development. Public datasets exhibit fragmentation in size, protocols, and quality standards. Even large collections like COSTA (354 images) [20] and CAS (100 images) remain insufficient for robust training, while inconsistent annotation styles prevent unified applications across different research groups. Moreover, current datasets lack version control mechanisms that would enable systematic evolution and error correction over time. Existing collaborative platforms, such as EXACT [19], provide version control for image annotation but lack the 3D visualization and consensus generation capabilities needed for vessel annotation. Crowdsourcing approaches [21] show potential for scale but face quality limitations due to a lack of medical validation expertise [22].

As a result of these limitations, the most critical gap currently lies in clinical translation. While methods achieve strong performance on research datasets, few undergo evaluation in clinical environments where real-world conditions differ significantly from controlled research settings. Recent studies have explored stroke diagnosis [1], genetic analysis [28], and federated learning [9], but systematic clinical translation remains limited.

3 Scientific Approach

This doctoral research work is structured around the three limitations of brain vascular analysis that have been identified: the cost of data annotation, the lack of large datasets and the mechanisms to develop them, and the limited clinical translation of research tools. It presents three contributions addressing each of them, which are discussed in the following.

3.1 Mitigating the Costs of Data Annotation

The first contribution addresses the annotation bottleneck by building on the observation that the brain vessel tree exhibits recurring branching patterns. Thus, if the set of basis vessel patterns can be identified and extracted, it should be possible to cover the full spectrum of vascular structures present in a dataset. As a result, the annotation of the *basis set* would account for the annotation of a complete vascular structure. We implement this idea within a one-shot active learning framework [5] that leverages the similarity of vessel patterns after they have been identified through dictionary learning, as detailed in Section 4.1.

3.2 VesselVerse: Improving Imperfect Datasets

The second contribution tackles the limited availability of annotated brain vessel datasets and the variability across annotation protocols and annotation quality.

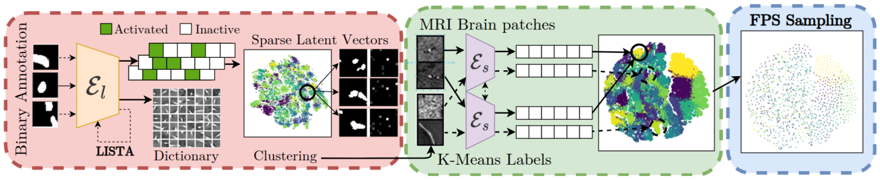

Fig. 1. V-DiSNet framework: One-shot active learning pipeline leveraging dictionary learning to capture vessel patterns and construct an informative latent space for efficient sample selection.

The working idea here is that datasets, particularly neurovascular imaging ones, are imperfect: brain vessel segmentation labels often contain errors and subjective inconsistencies (e.g., the extent of annotations, whether arteries or major veins are included). By acknowledging the inherent imperfection of medical annotations, this work focuses on the release of the largest public vessel annotation dataset, a dataset of imperfect annotations, along with a collaborative framework aimed at iteratively improving the annotations through collaborative refinement. This dynamic approach transforms static datasets into living resources enhanced through community contributions, with potential applications extending beyond vessel annotations to other medical imaging tasks.

3.3 Towards Clinical Translation in Real-World Settings

The last set of contributions addresses the clinical translation gap by focusing on the development of a robust brain vascular analysis pipeline that can be easily deployed across different clinical research applications. As such, the pipeline should allow for statistical analysis, cross-institutional training, and seamless integration with clinical workflows to ensure practical use. Our approach builds on MultiVesSeg [11], a cross-modality adaptation architecture for brain vessel segmentation that leverages feature disentanglement through StyleGAN2-based generators and label-preserving translation mechanisms to enable robust performance across different imaging modalities and clinical environments without requiring domain-specific preprocessing.

4 Proposed Solution

4.1 V-DiSNet: Pattern-Aware Active Learning

The proposed one-shot active learning solution (Fig. 1) builds on sparse representation theory where vessel patches are modeled as $\mathbf{Y} = \mathcal{B}\mathbf{z}$, with $\mathcal{B}$ representing an over-complete dictionary of vessel patterns and $\mathbf{z} \in \mathbb{R}^K$ being a sparse coefficient vector [17] that encodes the contribution of each dictionary element to the patch reconstruction. We rely on Dictionary Learning using LISTA [12] to extract recurring vessel patterns, followed by k-means clustering of the learned

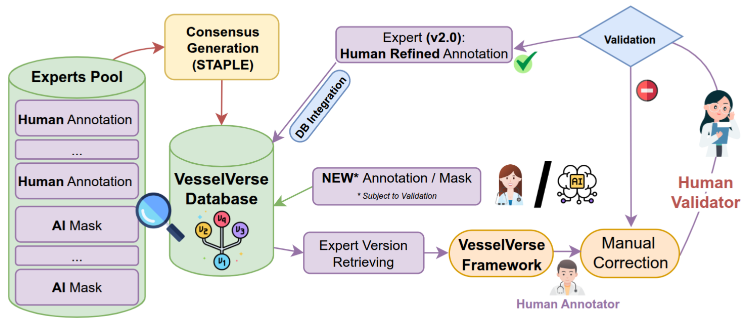

Fig. 2. VesselVerse framework: Collaborative dataset infrastructure supporting multi-expert annotation, consensus generation, and version control for continuous quality improvement.

Table 1. Summary of the VesselVerse dataset and annotation coverage.

Dataset	#Images	#Annotations	Method Coverage	Modality
IXI	600	4,822	9/9 methods	TOF-MRA
TubeTK	100	800	8/9 methods	T1-MRA
TopCoW MRA	125	1,000	8/9 methods	MRA
TopCoW CTA	125	635	6/9 methods	CTA
Total VesselVerse	**950**	**7,257**	—	

sparse representations to identify distinct pattern groups. These clusters enable Siamese encoder training to generate discriminative latent representations based on pattern similarity, where morphologically similar vessel structures cluster together. Finally, stratified Farthest Point Sampling leverages this learned latent space to select diverse patches that maximize coverage across different vessel pattern types in a single iteration, with the selected patches subsequently annotated and used to train a segmentation model.

4.2 VesselVerse: A Collaborative Dataset Infrastructure

VesselVerse [6] represents the largest public release of brain vessel annotations comprising 950 images across four datasets with over 7,000 annotations from up to 9 different sources per image, spanning multiple imaging modalities and including both expert annotators and state-of-the-art brain vessel segmentation models (Table 1). The accompanying collaborative framework (Fig. 2) implements version control mechanisms that enable complete annotation history tracking, collaborative refinement, and rollback mechanisms. A custom 3D Slicer extension also enables continuous dataset improvement with full traceability. Additionally, VesselVerse employs STAPLE-based consensus generation [27] to harmonize among different annotation protocols. The generic nature of the collaborative framework has potential applications beyond brain vessel annotation and could be used to improve annotations across other medical imaging tasks.

Table 2. V-DiSNet performance comparison across different annotation budgets on CAS dataset (15 test patients).

Annotation	V-DiSNet		Random		RA [30]		CA [16]		AET [15]	
Budget (%)	Dice	clDice	Dice	clDice	Dice	clDice	Dice	clDice	Dice	clDice
0.1	**59.3±8.2**	**50.8±9.2**	50.4±5.3	41.9±6.6	57.6±5.1	49.3±5.8	55.1±4.8	47.5±6.7	56.3±4.9	48.4±6.3
5	**77.4±1.4**	73.6±1.6	75.3±1.7	71.9±2.2	75.8±1.6	72.9±1.7	77.1±1.8	**74.0±1.7**	76.4±1.7	73.4±1.7
30	**81.5±0.7**	**77.9±1.1**	80.1±0.6	77.1±0.8	80.4±0.9	76.8±0.8	81.0±1.0	76.9±1.5	80.7±0.9	76.8±1.1
50	**82.0±0.6**	**78.0±0.9**	80.8±0.8	77.4±1.0	81.0±0.7	77.4±0.7	81.8±0.8	77.8±0.7	81.5±0.7	77.8±0.7
75	**82.0±0.7**	**78.3±0.7**	81.9±1.1	77.9±1.1	81.4±1.0	78.0±0.9	**82.0±0.7**	78.1±1.1	81.7±0.8	78.1±1.0

4.3 Clinical Translation through Cross-Modality Adaptation

Our clinical translation framework, MultiVesSeg, employs a two-phase training strategy with adversarial learning and cycle-consistency losses to selectively translate domain-specific features while preserving spatial vessel geometry across imaging modalities. The framework's cross-modal adaptation eliminates the need for model retraining when transitioning between different hospital environments and imaging protocols. Training leverages a subset of the VesselVerse [6] dataset to ensure robust cross-modal performance, enabling direct deployment in three distinct clinical research applications: automated stroke diagnosis using TOF-MRA imaging, genetic vascular analysis in twin populations, and federated multi-institutional vessel segmentation. Results from these clinical translation studies are discussed in Section 5.3.

5 Results and Contribution

5.1 V-DiSNet: Multi-Dataset Evaluation and Pattern Discovery.

V-DiSNet was evaluated across three public 3D Time-of-Flight MRA datasets (**CAS**, **OASIS-3**, **SMILE-UHURA**) for vessel segmentation, demonstrating it achieves near full supervision performance using only 30% of labeled data (Table 2). The method outperforms random sampling and state-of-the-art one-shot active learning methods (RA [30], CA [16], AET [15]) across evaluation scenarios, with notable improvements at low annotation rates (0.1-10% labeled data). The interpretability analysis reveals that learned dictionary elements capture semantically meaningful vessel features: deactivating specific elements affects vessel shape, size, or orientation in predictable ways, confirming that the sparse representation captures anatomical understanding rather than just statistical correlation. The optimal clustering analysis identified 50 distinct vessel pattern groups, with cluster centroids revealing consistent morphological structures across different datasets, validating the universality of the learned patterns.

5.2 VesselVerse: Inter-Rater Agreement Analysis and Quality Analysis

We conducted validation experiments to assess the framework's ability to maintain annotation quality across different protocols and datasets, and evaluate

Table 3. VesselVerse validation results showing inter-rater agreement and consensus quality across datasets.

Dataset	Quality Score (Mean/5)	Kendall's W (Agreement)	Kendall's τ (vs. Consensus)	Top Method Performance
IXI-MRA	3.71	0.714 ± 0.147	0.561 ± 0.224	nnUNet (4.39)
TopCoW-MR	3.56	0.511 ± 0.074	0.450 ± 0.068	STAPLE (3.69)
TopCoW-CT	3.33	0.552 ± 0.331	-0.407 ± 0.419	JoB-VS (4.03)
TubeTK	3.22	0.585 ± 0.105	0.311 ± 0.319	nnUNet (4.33)

STAPLE's effectiveness. Inter-rater agreement analysis across four expert evaluators from different institutions demonstrates strong concordance, with Kendall's W coefficients (0-1 scale) exceeding 0.5 for all datasets (Table 3). The STAPLE consensus mechanism shows positive correlation with expert rankings (Kendall's τ ranging from 0.31 to 0.56 on a -1 to 1 scale), validating its effectiveness in capturing collective expert judgment. Cross-institutional validation across France, Italy, and the UK confirms the framework's robustness across different annotation cultures and clinical practices.

5.3 Clinical Translation: Real-World Application Results

We discuss the three use cases described where our framework is applied.

Automated Stroke Diagnosis (AVA-Stroke study). This work presents a large-scale clinical study evaluating automated vessel analysis for stroke diagnosis using 902 TOF-MRA images from patients with suspected vascular occlusions spanning 2018-2023, encompassing diverse clinical cases including transient ischemic attacks, various stroke types, and hemorrhages. The MultiVesSeg vessel labeling combines with arterial territory atlas registration for anatomical localization and random forest classification for Large Vessel Occlusion (LVO) detection, achieving 89.6% recall and 96.0% ROC AUC with F1 score of 89.5%. Vessel-specific performance demonstrates excellent results for ICA occlusions (AUC=0.995) and MCA M1 occlusions (AUC=0.955), while asymmetry analysis proves robust for detecting vessel collapse. Qualitative assessment revealed mean segmentation accuracy of 3.56 ± 0.75 for anterior circulation and 3.31 ± 0.96 for posterior circulation on a 5-point scale, representing the first large-scale study on real-world clinical TOF-MRA data with statistical significance ($p < 10^{-4}$) for ICA, MCA, and PCA P1 occlusion detection.

Genetic Vascular Analysis in TwinsUK. This genetic study analyzed brain vessel patterns in 230 twin pairs (460 participants, median age 67-69 years) comprising 174 dizygotic and 286 monozygotic twins from the TwinsUK imaging repository using automated vessel measurement with MultiVesSeg for vessel segmentation and vascular territory atlas mapping. The study develops a feature extraction tool capturing both basic morphometric measures (vessel length, volume, bifurcation features) and complex vascular characteristics (tortuosity, lacunarity, fractal dimensions), enabling systematic quantification of hereditary vascular traits through 3T MRI intracranial TOF angiography. Statistical comparison reveals significant genetic contributions ($p < 0.05$) to total vessel length, vessel volume, and largest segment size, with identical twins demonstrating consistently smaller absolute differences in vessel characteristics compared to fraternal twins, while no significant genetic influence was detected for vessel segment count or bifurcation number. This represents the first large-scale demonstration of hereditary components in brain blood vessel structure with implications for personalized cerebrovascular risk assessment and stroke prediction based on genetic vascular profiles. The outcome is currently under review[1].

Federated Multi-Centric Segmentation. The last application represents a collaborative project with INRIA, CHU Nice, and CHU Grenoble, implementing federated learning for brain vessel segmentation across multiple centers with non-uniformly distributed labeled datasets. The framework addresses heterogeneous data distributions across institutions, where clients exhibit data differences due to varying scanners and imaging modalities. This real-world federated learning deployment across three clinical institutions represents a step toward scalable clinical adoption, demonstrating the practical feasibility of collaborative AI model development without compromising patient data privacy. The implementation leverages MultiVesSeg through federated parameter exchange rather than raw data sharing [9], ensuring regulatory compliance while enabling institutions to benefit from collective expertise and diverse datasets, with results to be collected as the multi-center deployment progresses.

5.4 Scientific Contributions and Clinical Impact

This thesis contributes across multiple fronts, advancing sparse dictionary learning for recurring vessel pattern identification, collaborative dataset infrastructure with version control and consensus generation, and clinical translation through automated stroke diagnosis, genetic heritability analysis, and federated vessel segmentation multi-institutional deployment. The contributions address the two critical barriers of extensive annotation requirements and inconsistent dataset quality, consequently enabling clinical translation with proven impact on diagnostic accuracy across medical applications.

6 Open Challenges and Future Work

This research establishes robust frameworks for brain vessel segmentation, demonstrating clinical utility. Nonetheless, we identify several challenges for future investigation. On the methodological side, the current V-DiSNet framework operates on 2D patches, which may not fully capture complex 3D structural continuity in volumetric brain vessel data. Extending the dictionary learning framework to 3D patches could better preserve spatial relationships and vessel connectivity

[1] *Cleary JO, Canas LS, Zuluaga MA, **Falcetta D**, et al. "Initial Analysis of Intracranial MR Angiography from the TwinsUK Large Cohort Twin Imaging Study". Annual British Society of Neuroradiologists' Meeting (BSNR) 2025 (under review).*

across slices. On the operational side, a critical challenge lies in the sustainability of VesselVerse in the longer term. Reaching a *perfect* dataset involves securing community engagement by identifying the right incentives to promote contributions. Simultaneously, scaling to larger collections while maintaining annotation quality presents computational and organizational challenges that need to be addressed On the validation side, while the different clinical research studies conducted have demonstrated the versatility of the developed brain vessel analysis pipelines, further validation is definitely required. For instance, while MultiVesSeg is a cross-modality framework, it has been validated primarily on angiographic data, necessitating domain adaptation strategies for other vascular modalities. A study establishing its limitations when accounting for other image modalities is necessary. This could be achieved by expanding the scope of the clinical use cases considered, including broader clinical scenarios such as treatment planning, longitudinal monitoring, and multi-disease validation.

7 Long Term Goals

The research vision beyond this work extends vessel segmentation to establish principles for translating medical imaging research into clinical applications that benefit patients. Future work will focus on developing AI systems that bridge the gap between algorithmic innovation and real-world implementation, with emphasis on clinical translation and regulatory compliance. This "*from GPU to bedside*" transition represents the ultimate goal of contributing to medical imaging technologies that improve patient outcomes by addressing both technical algorithm development and practical clinical integration challenges.

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