Vascular segmentation based on variational approach

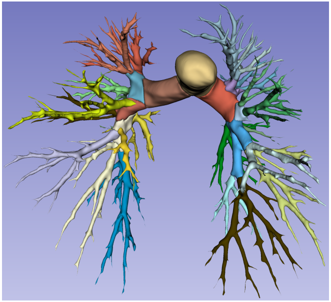
Odyssée Merveille

Workshop DIPOpt
27/11/2023

CREATIS

Introduction

- **Odyssée Merveille**
  Assistant professor at CREATIS Laboratory



Pulmonary vascular network

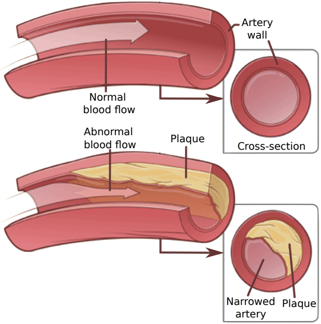
- **Research topic**
  Detection and modeling of vascular network in 3D images
  Deep learning and variational approaches

Why study the vascular networks ?

Cardiovascular diseases (CVDs) are the leading cause of death worldwide

- **CVDs include :**
  - Coronary artery diseases
  - Aneurysms
  - Strokes
  - Pulmonary embolism

- **Mostly caused by atherosclerosis**
  build up of a lipidic plaque in the vessel wall



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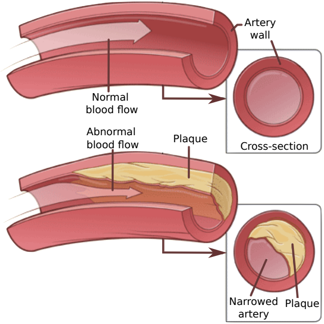

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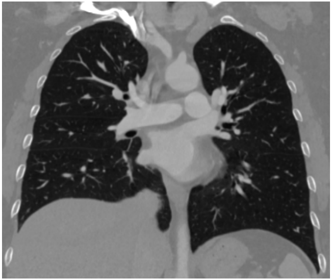
Diagnosis and treatment require the examination of the patients' vascular network.

Vascular imaging

- Several imaging modalities reveal blood vessels :
  - **Magnetic Resonance Angiography (MRA)**
  - **Computed Tomography Angiography (CTA)**
  - Cathether Angiography
  - Vascular Ultrasound

MIP of a brain MRA

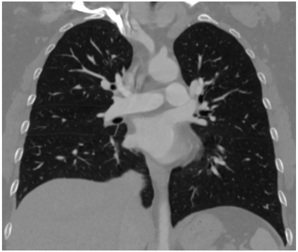


Slice of a pulmonary CTA

What can we do with image processing ?

- The vascular system is a **complex** network of **multi-scale** and **tortuous** blood vessels

- **Visual inspection of vascular images is :**
  - Time-consuming
  - Expert-dependent
  - Prone to fatigue-related error
  - Lacking quantitative data



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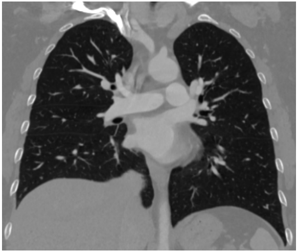

Slice of a pulmonary CTA

- **Image processing may provide automatic tools for :**
  - Computer-aided diagnosis
  - Computer-aided prognosis
  - Computer-aided decision support

PERSEVERE - Context

- **PERSEVERE project**
  Pulmonary Embolism Risk Stratification basEd on Vascular nEtwoRk modElling

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  - Upon diagnosis, doctors evaluate the patient prognosis based on established guidelines.
    - Low risk of death
    - Moderate risk of death
    - High risk of death

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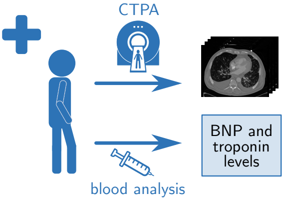
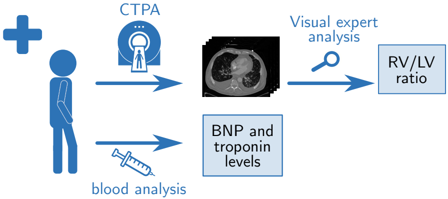
Patient management depends on this evaluation called **risk stratification**.

PERSEVERE - Current risk stratification



- The patient undergoes :
  - a pulmonary CT scan (CTPA)
  - a blood test to assess the levels of **functional biomarkers**

PERSEVERE - Current risk stratification



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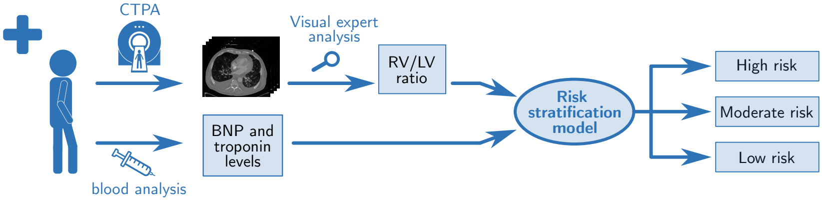
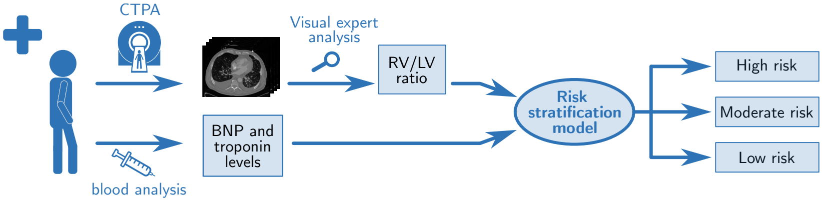
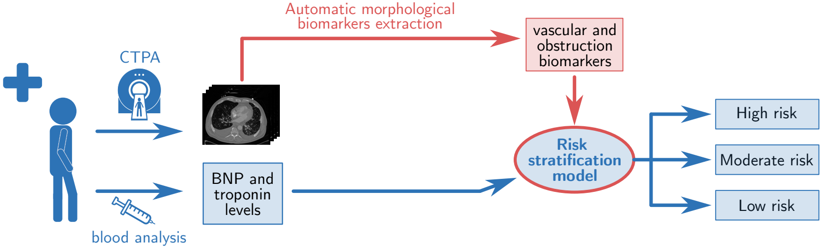


- The patient undergoes :
  - a pulmonary CT scan (CTPA)
  - a blood test to assess the levels of **functional biomarkers**
- A radiologist measures a **morphological biomarker** manually from the CTPA
- A prognosis is established based on these biomarkers



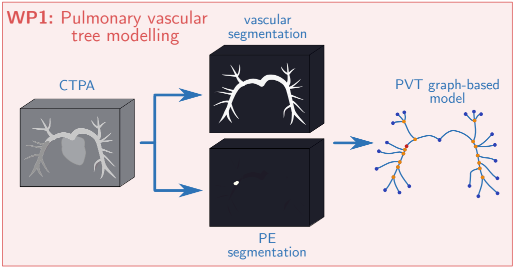
- **Limitations :**
  - No morphological biomarker directly related to the embolism
  - CTPA not synchronized to the heart rate $\rightarrow$ RV/LV ratio is unreliable

PERSEVERE - Problems and objectives



- **Limitations :**
  - No morphological biomarker directly related to the embolism
  - CTPA not synchronized to the heart rate $\rightarrow$ RV/LV ratio is unreliable
- **Goals of the PERSEVERE project :**
  - Build risk stratification models based on **automatically extracted morphological biomarkers**

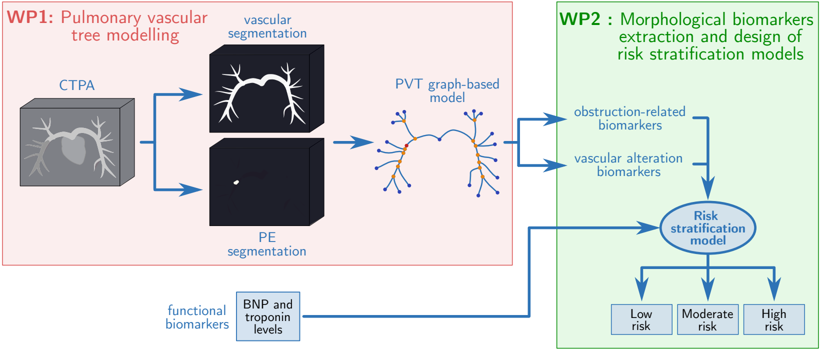
Methodology



Pulmonary vascular tree modelling

- Develop an accurate and topologically correct vascular segmentation approach
- Develop a precise pixel-wise thrombus segmentation approach
- Feature-enhanced graph of the pulmonary vascular tree

Methodology

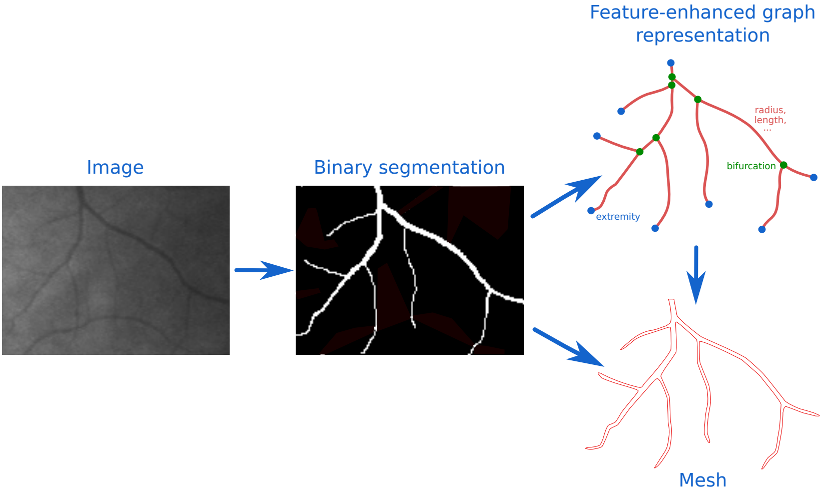


Risk stratification model

- Extract clinically relevant morphological biomarkers from the graph
- Develop a risk stratification model that can be used in a clinical context : robust, automated, interpretable

Analysis of vascular networks

- **Common first steps of the analysis of vascular network:**



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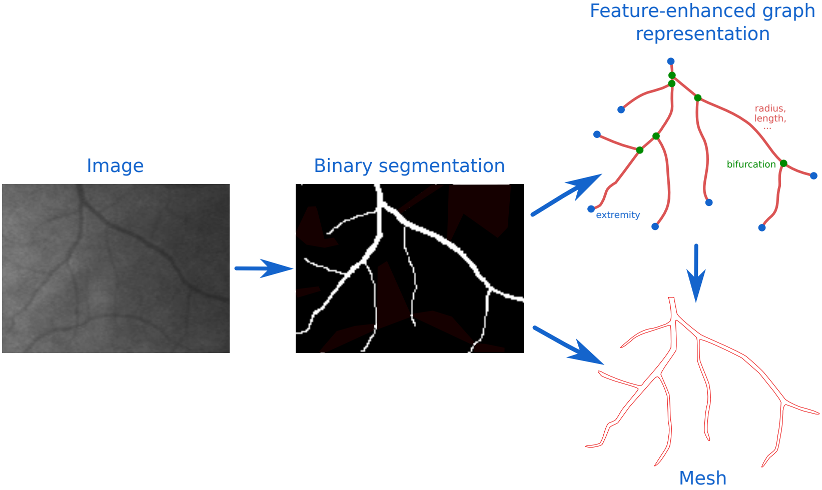

→ An accurate and connected segmentation is key

Vascular segmentation challenges

- **Geometrically complex**
  - thin, elongated, and tortuous structures
  - low-contrast at the extremities
  - multi-scale
  - organized in networks
  - scattered in the image
- **Extensive and accurate annotation extremely costly**
  - 2D annotation of intrinsically 3D structures
  - huge inter-expert variability
- **Complex qualitative and quantitative analysis**

Segmentation of vascular networks

More than 30 years of research [1-2]

- Vesselness-based
- Tracking
- Deformable models
- Machine learning
- Deep learning

[1] Lesage et al., MedIA 2009
[2] Moccia et al., CMPB, 2018

Segmentation of vascular networks

More than 30 years of research [1-2]

- Vesselness-based
- Tracking
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- **Focus of my research :**
  - Preserve the vascular network connectivity
  - Learn vascular segmentation with limited labels

[1] Lesage et al., MedIA 2009
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Outline of the presentation

1. Directional total variation
2. Learning a reconnecting regularization term
3. Deep learning-based vascular network segmentation

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Variational segmentation

The **Chan-Vese binary** segmentation model [1] is :

$$
\begin{aligned}
u^\star = \underset{u,C}{\operatorname{argmin}}\ & \mu.\text{Length}(C) + \nu.\text{Area}(\text{inside}(C)) \\
& + \lambda_1 \int_{\text{inside}(C)} |f(x) - c_1|^2 \mathrm{d}x \\
& + \lambda_2 \int_{\text{outside}(C)} |f(x) - c_2|^2 \mathrm{d}x.
\end{aligned}
$$

where,

- $f \in \mathbb{R}^{\mathbb{N}^2}$ is a 2D-grayscale image to be segmented
- C is the boundary of the segmentation
- c_1 and c_2 are the forward and background intensity of f.
- μ, ν, λ_1, $\lambda_2 \in \mathbb{R}$ parameters

Variational segmentation

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$\rightarrow$ **Non-convex problem**

[1] Chan et al., TIP 2001

Variational segmentation

Convexification of the Chan-Vese model [1] :

$$u^\star = \underset{u \in [0,1]^{\mathbb{N}^2}}{\text{argmin}} < c_f, u >_F + \lambda ||\nabla u||_{2,1},$$

with :

- $c_f(x) = ((c_1 - f(x))^2 - (c_2 - f(x))^2$
- $< u, v >_F$ the Frobenius product
- $||\nabla u||_{2,1}$ the total variation

[1] Chan et al, SIAP 2006

$$u^\star = \underset{u\in[0,1]^{\mathbb{N}^2}}{\operatorname{argmin}} \overbrace{< c_f, u >_F}^{g(u)} + \overbrace{\lambda||\nabla u||_{2,1}}^{h(u)},$$

with :

- $g(u)$ convex and differentiable
- $h(u)$ convex but non-differentiable

Solved by proximal splitting algorithm :

$u_{n+1} = \text{prox}_{\gamma h}(u_n - \gamma\nabla g(u_n)), \quad \gamma \in]0, +\infty[$a step-size parameter

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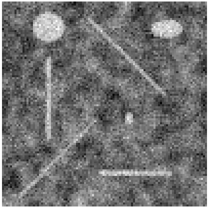
$\text{prox}_{\gamma h}$ is computed with the Fast Gradient Projection (FGP) algorithm [1]

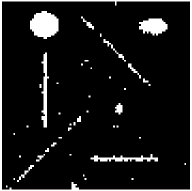
[1] Beck et al., TIP 2009

Problem for thin structures

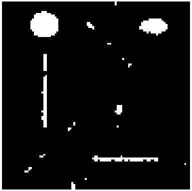
- **Results of the Chan et al. model :**



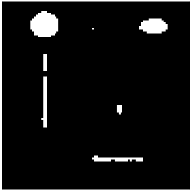
$\lambda = 0.1$



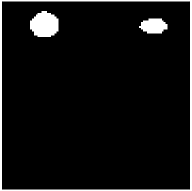
$\lambda = 0.3$



$\lambda = 0.6$



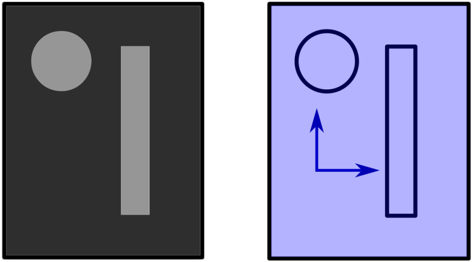
$\lambda = 1$



$\rightarrow$ **Thin structures vanish**

Directional total variation idea

$$TV(u) = \sum_i \sum_j |\sqrt{(u_{ij}^x)^2 + (u_{ij}^y)^2}|$$



image

Total variation (TV)

Directional total variation idea

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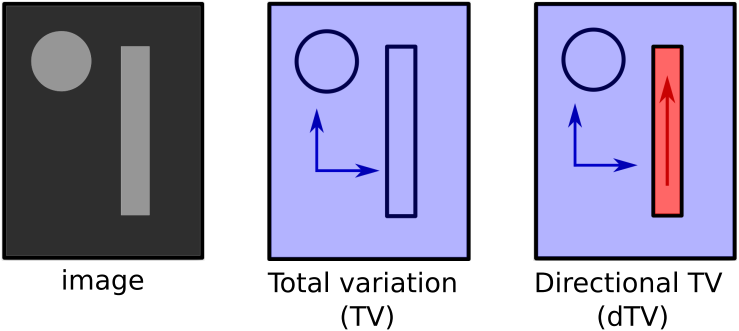


- **Direction TV goal** :
  - Only regularize in the direction of the thin structures
  - Denoise and tends to reconnect thin structures

Merveille et al TIP 2019

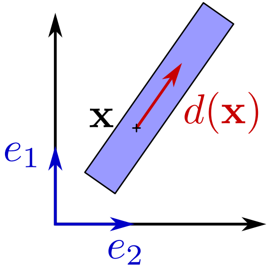
Mixed gradient

Classic gradient:

$$\nabla u(\mathbf{x}) = \big(u(\mathbf{x} + \mathbf{e}_i) - u(\mathbf{x})\big)_{i=1}^{n}$$

Directional gradient:

$$\nabla_{\mathbf{d}} u(\mathbf{x}) = \big(u(\mathbf{x} + \mathbf{d}(\mathbf{x})) - u(\mathbf{x})\big).\mathbf{d}(\mathbf{x})$$



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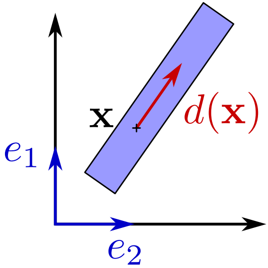
Mixed gradient:

$$\nabla_m u(\mathbf{x}) = \begin{cases} \nabla u(\mathbf{x}) & \text{if } x \notin \text{thin structure} \\ \nabla_{\mathbf{d}} u(\mathbf{x}) & \text{otherwise} \end{cases}$$



Merveille et al TIP 2019

Directional total variation

- **Total variation**

$$\mathrm{TV}(u) = ||\nabla u||_{2,1}$$

- **Directional total variation** [1]

$$\mathrm{dTV}(u) = ||\nabla_m u||_{2,1},$$

where $\nabla_m u(x)$ the a mixed gradient defined by:

$$\nabla_m u(x) = \begin{cases} \nabla_d u(x) & \text{if } x \in \text{curvilinear structure} \\ \nabla u(x) & \text{otherwise} \end{cases}$$

and

- $\nabla_m u(x) = (u(x + d(x)) - u(x)).d(x)$
- $d(x)$ the unit vector lying in the direction of the thin structure at x

[1] **Merveille et al., TIP 2019**

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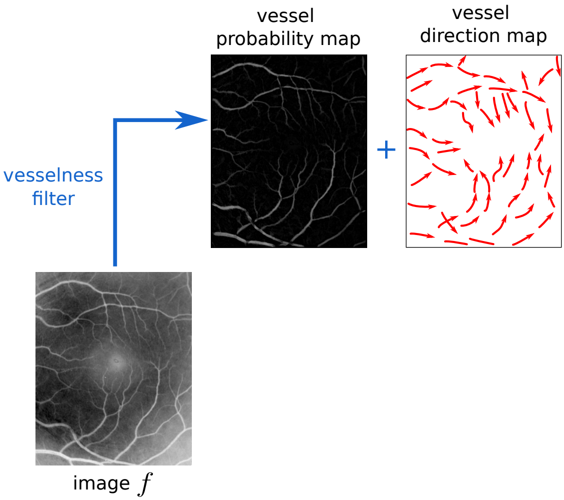
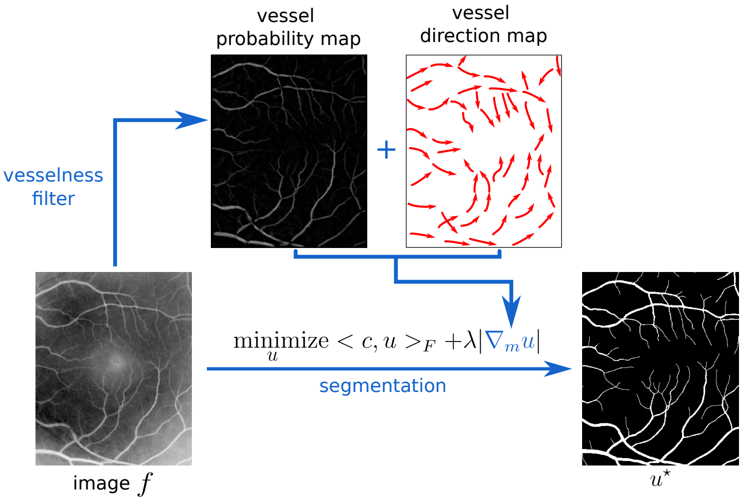


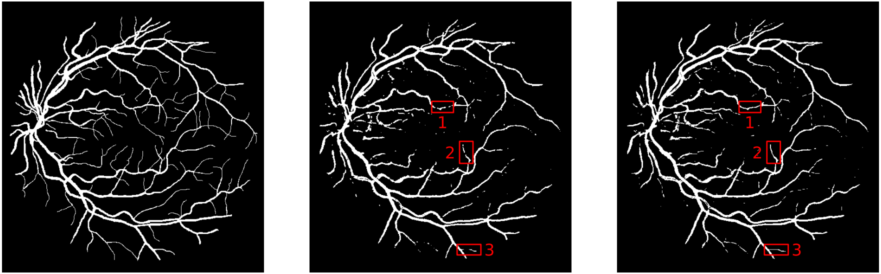
Lamy et al., TIP 2022

Directional total variation

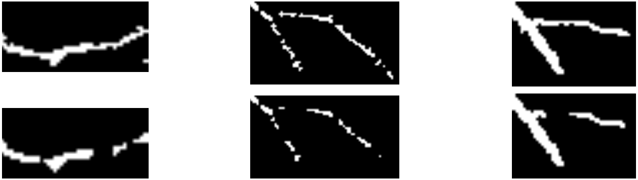


Lamy et al., TIP 2022

Directional total variation - Results



label TV directional TV



dTV

TV

box 1 box 2 box 3

Conclusion

- Regularization term adapted to thin structures like vessels
- Works in a unsupervised variational segmentation framework
- Improves the connectivity of segmentation results
- Reconnection power depends on vesselness results

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2. Learning a reconnecting regularization term
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Learning a reconnecting regularization

- Difficult to enforce connectivity with an explicit regularization term
  $\longrightarrow$ **What about learning it ?**

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  $\longrightarrow$ **Plug & Play**

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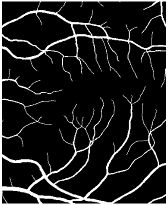
CNN learning connectivity

image f

$$\underset{u}{\text{minimize}} < c, u >_F + E_{\text{reg}}(u)$$

segmentation



$u^\star$

Learning a reconnecting regularization

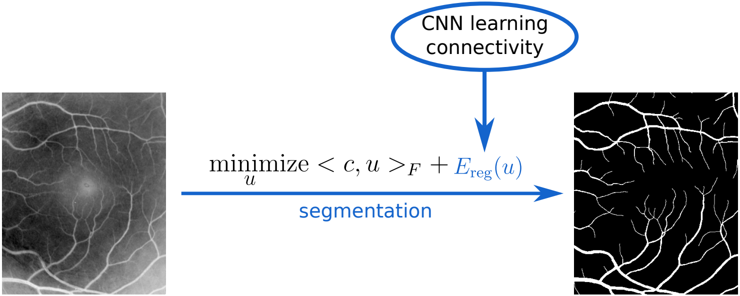
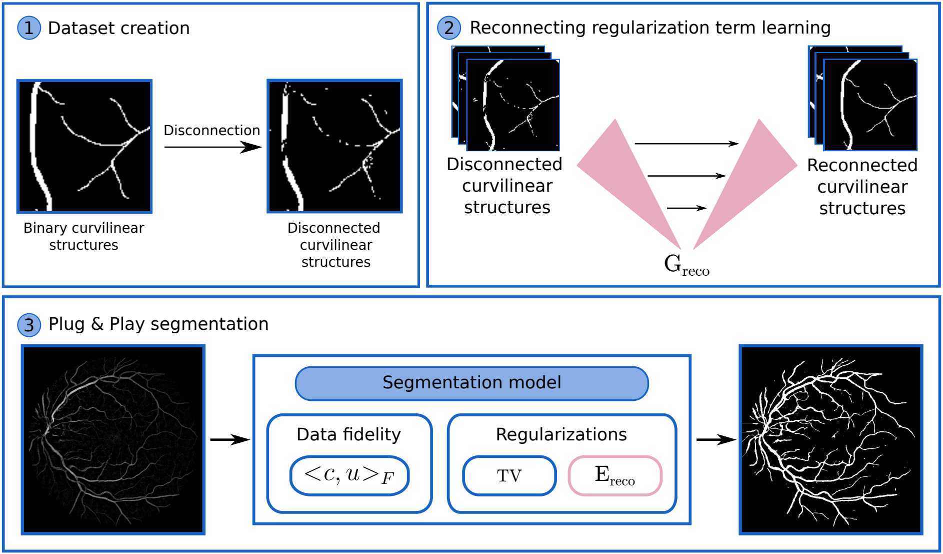


image f $\qquad$ $u^\star$

- **Connectivity** :
  - Geometric property $\longrightarrow$ may be learned based on synthetic data
  - Binary property $\longrightarrow$ easy to plug in a segmentation framework

Learning a reconnecting regularization



Carneiro et al Neurocomputing [under revision]

Dataset of disconnected vascular structures

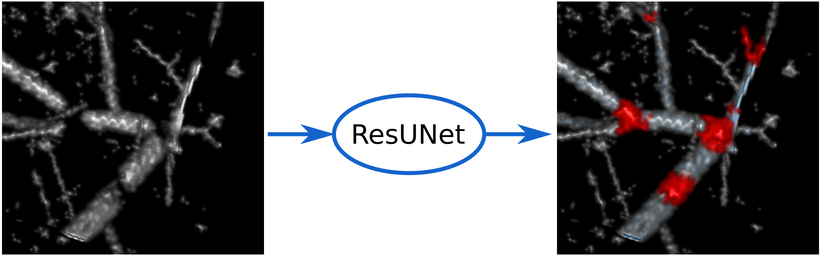
- **Synthetic images of vascular structures**
  - 2D : CCO algorithm [1]
  - 3D : VascuSynth [2]

Vascusynth

- **Realistic disconnection algorithm**
  - The thinner the vessel the longer the disconnection
  - Disconnection with random shapes
  - Addition of small non vessel structures

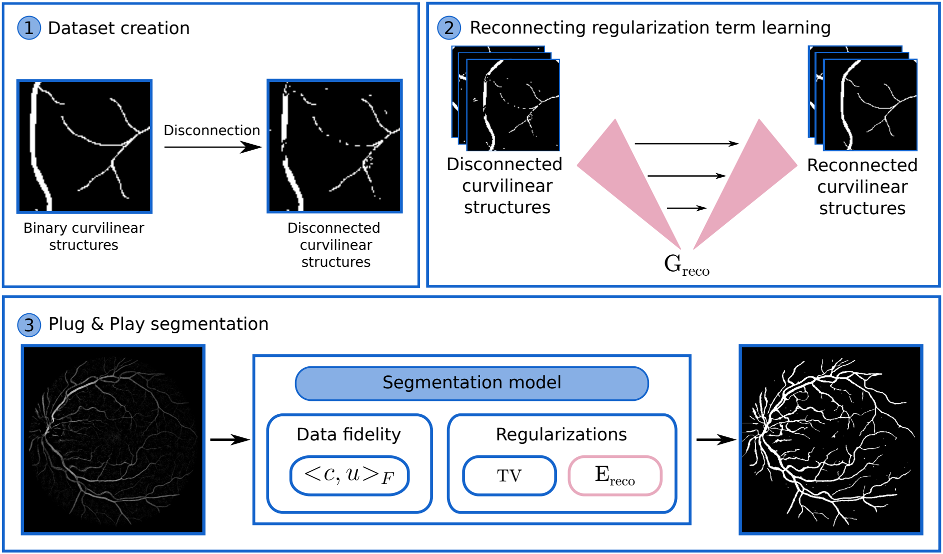
[1] Kerautret et al "OpenCCO [...]" IPOL 2023
[2] Hamarneh et al "VascuSynth[...]" CMIG 2010

- **2D or 3D Residual UNet**
  - 96^n patch, 4-layer deep
  - Dice + Weighted Dice loss around the disconnections
  - On-the fly data augmentation with rotation and flip



3D reconnection example, added fragments in red

Learning a reconnecting regularization



Carneiro et al Neurocomputing [under revision]

Plug & Play segmentation

- **Segmentation model**

$$u^\star = \underset{u}{\operatorname{argmin}} < c_f, u >_F + \lambda ||\nabla u||_{2,1} + \mathrm{E}_{\mathrm{reco}}(u)$$

- **Forward-Backward Primal Dual reformulation** [1]

$$u^\star = \underset{u}{\operatorname{argmin}}\, h(u, f) + g(Lu) + k(u)$$

with h, g, k lower-semicontinuous and g non-differentiable s.t:

$$\begin{aligned}
h(u, f) &=< u, c_f >_F \\
g(u) &= \lambda ||u||_{2,1} \\
L &= \nabla \\
k(u) &= \begin{cases} \mathrm{E}_{\mathrm{reco}}(u) & \text{if } u \text{ almost binary} \\ \iota_{u \in [0,1]^N}(u) & \text{otherwise} \end{cases}
\end{aligned}$$

[1] Komodakis et al., SPM, 2015

Forward-Backward Primal Dual algorithm

Set $u_0 \in \mathbb{R}^N$ and $v_0 \in \mathbb{R}^K$
Set $(\tau, \sigma) \in]0, +\infty\left[^2\right.$
For $i = 0, 1, \ldots.$

$$
\left\lfloor
\begin{array}{l}
p_i = \operatorname{prox}_{\tau k}\left(u_i - \tau\left(\nabla h\left(u_i\right) + L^\top v_i\right)\right) \\[2ex]
q_i = \operatorname{prox}_{\sigma g^*}\left(v_i + \sigma L\left(2p_i - u_i\right)\right) \\[2ex]
\text{Set } \ \lambda_i \in]\, 0, +\infty[\\[2ex]
\left(u_{i+1}, v_{i+1}\right) = \left(u_i, v_i\right) + \lambda_i\left(\left(p_i, q_i\right) - \left(u_i, v_i\right)\right)
\end{array}
\right.
$$

Plug & Play segmentation

Forward-Backward Primal Dual algorithm

$$p_i = \mathrm{prox}_{\tau k}\left(u_i - \tau\left(\nabla h\left(u_i\right) + L^\top v_i\right)\right)$$

$$q_i = \mathrm{prox}_{\sigma g^*}\left(v_i + \sigma L\left(2p_i - u_i\right)\right)$$

with :

$$h(u,f) = < u, c_f >_F$$

$$g(u) = \lambda|u|$$

$$L = \nabla$$

$$k(u) = \begin{cases} \mathrm{E_{reco}}(u) & \text{if } u \text{ almost binary} \\ \iota_{u\in[0,1]^N}(u) & \text{otherwise} \end{cases}$$

Plug & Play segmentation

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then :

$$\mathrm{prox}_{\sigma g^*}(u) = \frac{\lambda \sigma^{-1}}{\max(||\frac{u}{\sigma}||_2, \lambda\sigma^{-1})}$$

Plug & Play segmentation

- **Forward-Backward Primal Dual algorithm**

$$p_i = \text{prox}_{\tau k}\left(u_i - \tau\left(\nabla h\left(u_i\right) + L^\top v_i\right)\right)$$

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then :

$$\text{prox}_{\sigma g^*}(u) = \frac{\lambda\sigma^{-1}}{\max(||\frac{u}{\sigma}||_2, \lambda\sigma^{-1})}$$

$$\text{prox}_{\tau k}(u) = \begin{cases} G_{\text{reco}} & \text{if u almost binary} \\ \mathcal{P}(u) & \text{otherwise} \end{cases}$$

$$\mathcal{P}(u) = \begin{cases} u & \text{if } u \in [0,1] \\ 0 & \text{if } u < 0 \\ 1 & \text{if } u > 0 \end{cases}$$

Plug & Play Segmentation

Algorithm 1: Plug-and-play segmentation with the learned reconnecting operator

Data: $\alpha \in \mathbb{N}^{+*}$,
$u_0 \in \mathbb{R}^{\mathbb{N}^2}, v_0 \in \mathbb{R}^{2\mathbb{N}^2}, (\tau, \sigma) \in]0, +\infty[^2, \lambda_n \in]0, +\infty[$

for $i \geq 1$ **do**

$\quad p_i = (u_i - \tau\big(\nabla h(u_i) + L^T v_i\big)$

$\quad$ **if** $i < \alpha$ **then**

$\quad\quad p_i = \mathrm{prox}_{\sigma \iota_{[0,1]^{\mathrm{N}}}}(p_i)$

$\quad$ **else**

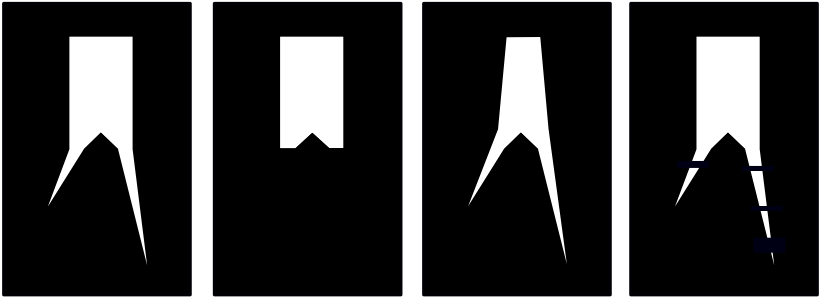
$\quad\quad p_i = \mathrm{G}_{\mathrm{reco}}\big(\mathrm{proj}(p_i)\big)$

$\quad q_i = \mathrm{prox}_{\sigma g^\star}\left(v_i + \sigma L(2p_i - u_i)\right)$

$\quad \big(u_{i+1}, v_{i+1}\big) = (u_i, v_i) + \lambda_i\big((p_i, q_i) - (u_i, v_i)\big)$

Metrics for vascular segmentation

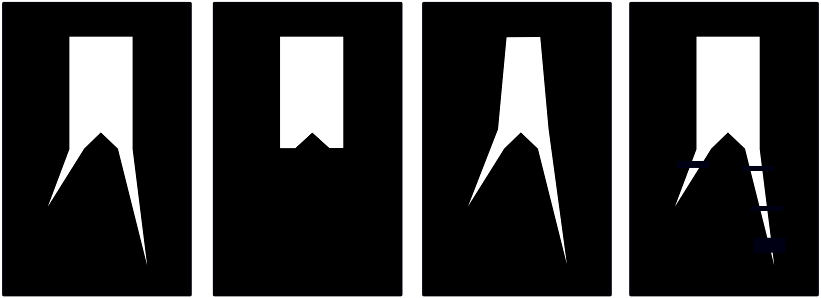
- How to evaluate vascular segmentation quantitatively ?



label result 1 result 2 result 3

Metrics for vascular segmentation

- How to evaluate vascular segmentation quantitatively ?



label | result 1 | result 2 | result 3

segmentation-based overlap metric : $\text{Dice}_1 \simeq \text{Dice}_2 < \text{Dice}_3$

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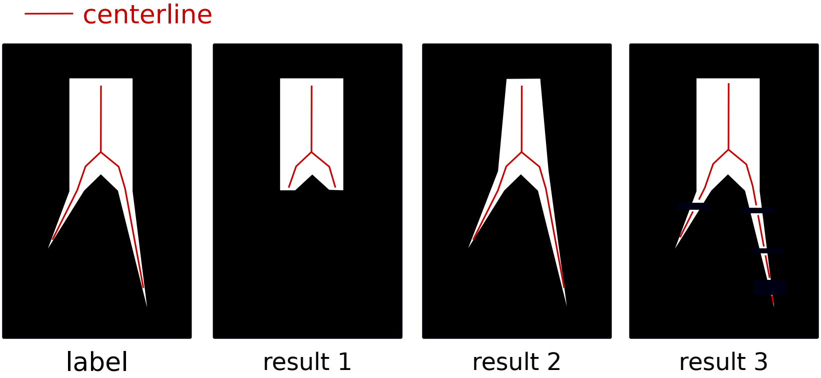

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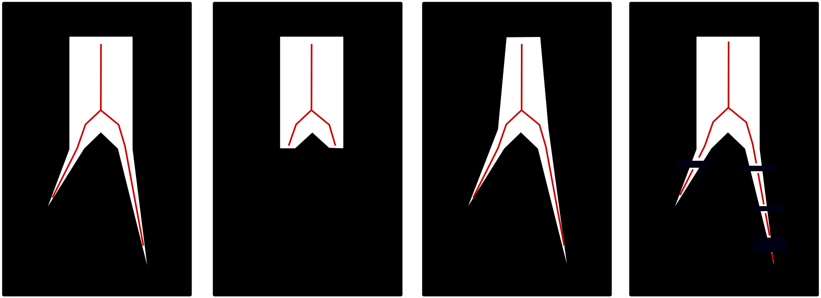
centerline-based overlap metric : $\mathrm{ClDice}_1 < \mathrm{ClDice}_3 \lesssim \mathrm{ClDice}_2$

Metrics for vascular segmentation

- How to evaluate vascular segmentation quantitatively ?

—— centerline



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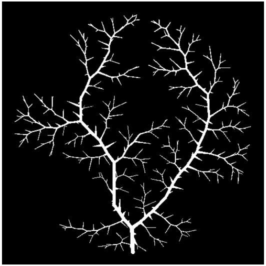
segmentation-based overlap metric : $\text{Dice}_1 \simeq \text{Dice}_2 < \text{Dice}_3$

centerline-based overlap metric : $\text{ClDice}_1 < \text{ClDice}_3 \lesssim \text{ClDice}_2$

error number of connected components: $\epsilon_{\beta_0 1} = \epsilon_{\beta_0 2} < \epsilon_{\beta_0 3}$

2D Dataset

- **Training dataset**
  - 20 Synthetic images
  - CCO algorithm [1]

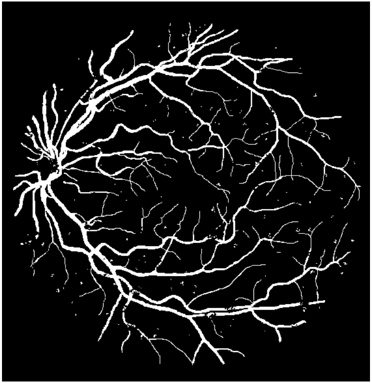


- **Test dataset**
  - 40 retinal images
  - Drive dataset [2]

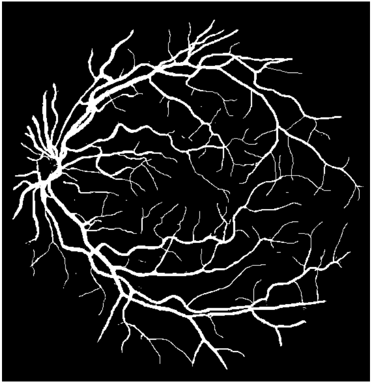
[1] Kerautret et al, IPOL, 2023
[2] Niemeijer et al, SPIE Medical Imaging, 2004

Reconnecting model (G_{reco}) results

	Before reconnection	After reconnection
Dice	0.974 $\pm$0.004	0.983 $\pm$0.003
ϵ_{β_0}	107.4 $\pm$71.88	17.30 $\pm$12.69



Before reconnection



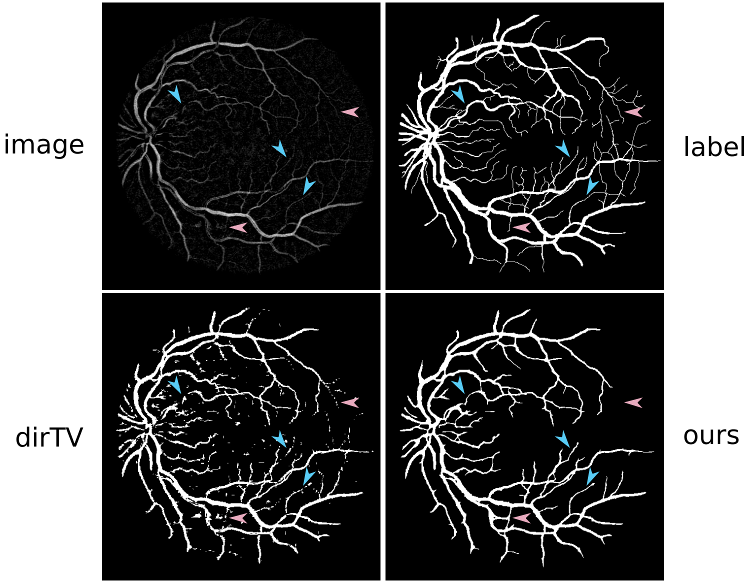
After reconnection

2D segmentation results

- **Results on the drive dataset**

	Dice	**ClDice**	ϵ_{β_0}
TV	0.747 ±0.036	0.730 ±0.044	24.22 ±15.89
dirTV	0.748 ±0.041	0.728 ±0.049	25.83 ±22.35
ours	**0.759** ±0.036	**0.744** ±0.045	**2.685** ±2.77

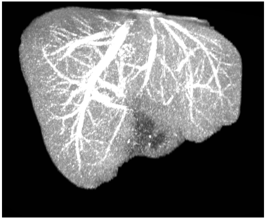
2D segmentation results



3D datasets

- **Training dataset**
  - 315 Synthetic images
  - VascuSynth [1]

- **Test dataset**
  - 19 liver CT-scans
  - IRCAD dataset [2]



[1] Hamarneh et al "VascuSynth[...]" CMIG 2010
[2] https://www.ircad.fr/research/data-sets/liver-segmentation-3d-ircadb-01/

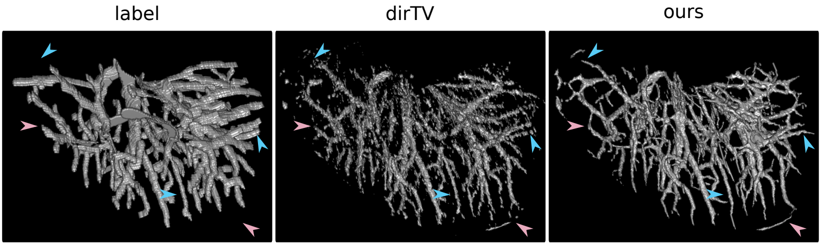
3D segmentation results

Results on the IRCAD dataset

	Dice	**ClDice**	ϵ_{β_0}
TV	0.450 ±0.129	0.533 ±0.166	2.25 ±3.30
dirTV	0.462 ±0.105	0.562 ±0.106	1.68 ±2.26
ours	**0.507** ±0.102	**0.585** ±0.079	**0.75** ±0.43

3D segmentation results

- **Results on the IRCAD dataset**



Conclusion and limitations

- **Contributions**
  - Successfully learn a regularization term enforcing connectivity
  - Plug this learned regularization inside a variational segmentation framework
  - Competitive unsupervised vascular segmentation results
  - Significantly improves the segmentation connectivity
- **Limitations**
  - Huge gap w.r.t. supervised learning
    - 2D Dice : 0.759 *v.s* 0.99 / 3D Dice : 0.5 *v.s.* 0.9
  - Data fidelity term
  - Purely geometrical reconnecting prior

Outline of the presentation

1. Directional total variation
2. Learning a reconnecting regularization term
3. Deep learning-based vascular network segmentation

Deep Learning-based vascular segmentation

- Most research focus on fully supervised approaches

Deep Learning-based vascular segmentation

- Most research focus on fully supervised approaches
- Labeling of vascular networks is extremely time-consuming
- Volume-segmented labeled datasets are rare and small

cerebral arterial vascular network labeling

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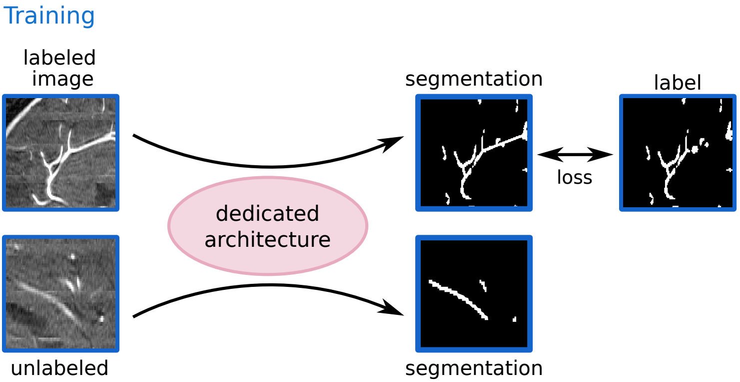
cerebral arterial vascular network labeling

- **How to use deep learning-based vascular segmentation with few labels ?**

$\longrightarrow$ **Semi-supervised learning**

$\longrightarrow$ **Domain adaptation**

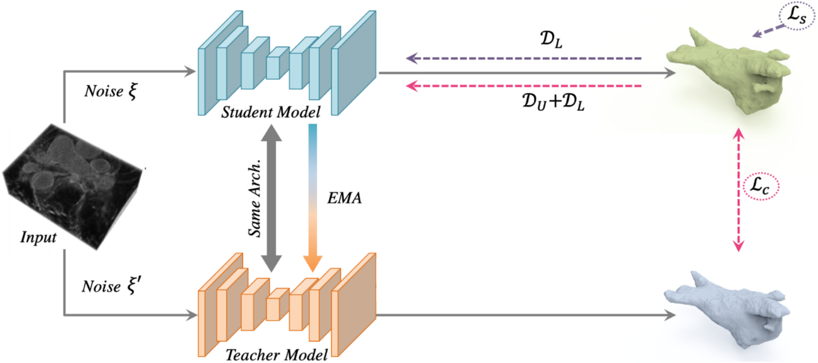
Semi-supervised learning



- **Training dataset** : a few labeled samples + many unlabeled samples
- Most architectures based on consistency losses

Example of semi-supervised learning

- **Mean Teacher (MT)** [1] (figure from [2])



- Supervision
  - Labeled data : $\mathcal{L}_s + \mathcal{L}_c$
  - Unlabeled data : $\mathcal{L}_c$

[1] A Tarvainen et al., NeurIPS, 2017
[2] Yu et al., MICCAI 2019

Semi-supervised benchmark for cerebral vascular segmentation

- Training and test dataset : Bullitt
  - Total in the dataset : 109 unlabeled and 34 labeled

Dice results for different semi-supervised segmentation strategies

num. labeled data	1 (1%)	2	3	5	9	18 (20%)
U-Net supervised	0.55	0.66	0.66	0.69	0.69	0.71

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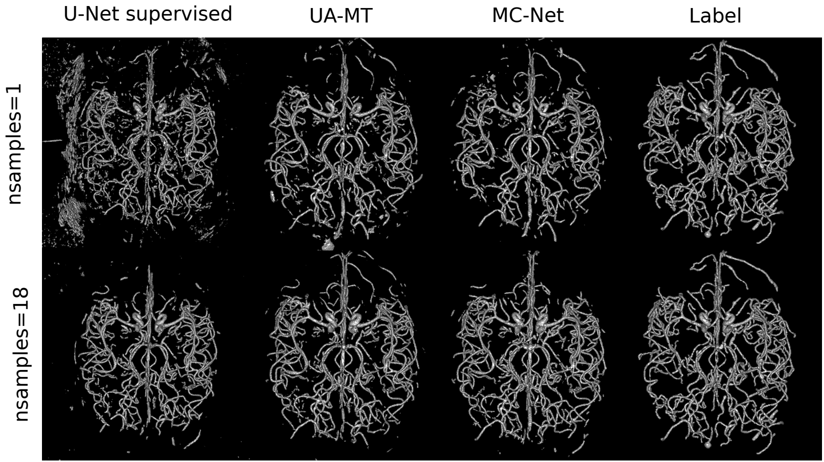
Dice results for different semi-supervised segmentation strategies

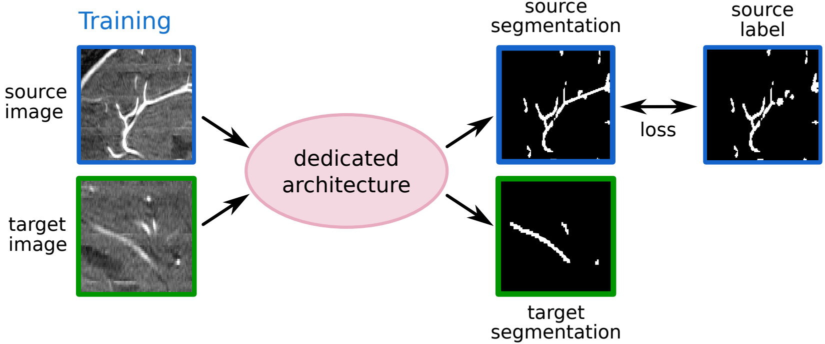
num. labeled data	1 (1%)	2	3	5	9	18 (20%)
U-Net supervised	0.55	0.66	0.66	0.69	0.69	0.71
MT [1]	0.63	0.69	0.70	0.72	0.71	0.72
UA-MT [2]	0.63	0.69	0.70	0.71	0.71	0.72
SASSnet [3]	0.63	0.68	0.70	0.71	0.72	0.72
DTC [4]	0.62	0.68	0.69	0.71	0.72	0.72
MC-NET [5]	0.64	0.66	0.70	0.70	0.71	0.72

[1] Tarvainen et al., NeurIPS, 2017
[2] Yu et al., MICCAI, 2019
[3] Zhang et al, MICCAI 2020
[4] Luo et. al, AAAI, 2021
[5] Wu et. al, MedIA, 2022

Semi-supervised benchmark for cerebral vascular segmentation



Unsupervised Domain Adaptation (UDA)



- **Training dataset** : labeled target samples + unlabeled source samples
- Goal : reduce domain-shift

Domain-shit

What is domain-shift ?

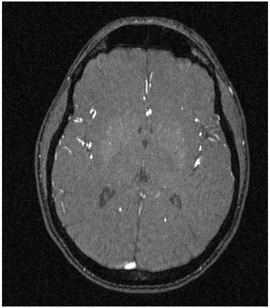
The distribution of the source data differs from the distribution of the target data

Origin

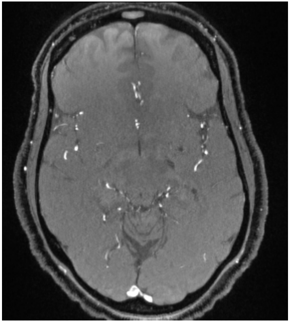
- Image modality
- Acquisition parameters / Manufacturer
- Subject / Patient population
- Label quality
- ...

Domain-shift in cerebral vascular imaging

- **Same organ / same modality**



Bullitt [1]



Brava [2]

$\longrightarrow$ **Is domain adaptation dedicated architecture required for same modality / same organ ?**

[1] Aylward et al., TMI, 2002
[2] Wright et. al, NeuroImage, 2013

Semi-supervised for cerebral vascular segmentation

- Training dataset : Brava
- Test dataset : Bullitt

	Naive	Fully supervised	UA-MT[1]	DTC[2]	MC-Net[3]
Dice	0.384	0.750	0.428	0.457	0.408

[1] Yu et al., MICCAI, 2019
[2] Luo et. al, AAAI, 2021
[3] Wu et. al, MedIA, 2022

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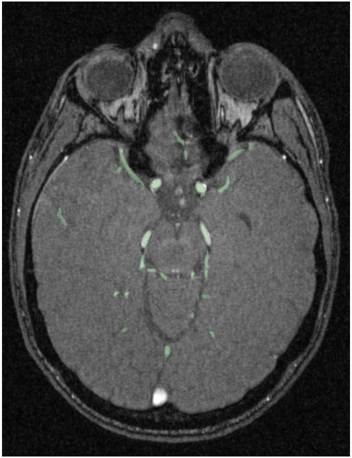
$\longrightarrow$ **Domain-shift more important than we thought**

[1] Yu et al., MICCAI, 2019
[2] Luo et. al, AAAI, 2021
[3] Wu et. al, MedIA, 2022

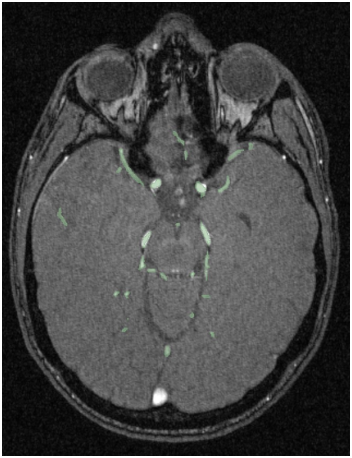
Semi-supervised for cerebral vascular segmentation



Bullitt

Brava

Semi-supervised for cerebral vascular segmentation



Bullitt

Brava

⟶ **Probably high label-shift**

Conclusion - Perspectives

- **Proposed several vascular segmentation strategies to :**
  - Enforce the segmentation connectivity
  - Work with limited labeled data

- **Variational segmentation**
  - Unsupervised
  - Limited performances due to data fidelity term

- **Deep learning-based segmentation**
  - Semi-supervised learning yield encouraging results

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- **Proposed several vascular segmentation strategies to :**
  - Enforce the segmentation connectivity
  - Work with limited labeled data
- **Variational segmentation**
  - Unsupervised
  - Limited performances due to data fidelity term
- **Deep learning-based segmentation**
  - Semi-supervised learning yield encouraging results
- **Perspectives**
  - Post-processing reconnecting network
  - Include topological constraints [1] in semi-supervised learning
  - Study semi-supervised domain adaptation strategies (SSDA)
  - Semi-automatic plugin for vascular network labeling [2]

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[1] **Rougé et al., arXiV, 2023**
[2] Lamy et al., JOSS, 2022

Any questions ?