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AIFNet: Automatic vascular function estimation for perfusion analysis using deep learning (2021)

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arxiv

pdf

CS가 적었다..! (오예)

AIFNET Replication: https://github.com/sebastianffx/aifnet_replication (원 저자 코드 아님, keras로 구현되어 있음)

pytorch version

Prerequisites

💡 **CTP**
= Computer Tomography Perfusion

💡 **Iodinated contrast agent**
= 조영제

💡 What is **Stroke?**

Acute neurologic dysfunction of vascular origin with sudden (within seconds) or at least rapid (within hours) occurrence of symptoms and signs corresponding to involvement of focal areas in the brain

💡 What is **ischemic stroke?**

There is a shortage in the blood supply to the brain tissue, cutting the provision of oxygen and glucose. During the ischemic event, brain tissue might become necrotic (i.e., cells are dead and the tissue is irreversibly damaged, known as core) or in a hypo-perfused but salvageable state (i.e., tissue is at risk but could return to a healthy condition, known as penumbra).

💡 **뇌졸중의 대표적 원인**

ref

1. 허혈성 (ischemic, 뇌경색): 혈관이 막혀 뇌로 혈액이 가지 않는 경우 ✅
2. 출혈성 (hemorrhagic, 뇌출혈): 혈관이 터져 뇌로 혈액이 가지 않는 경우

Core과 Penumbra가 뭔가요

2) Core 는 허혈 손상의 중심에 있는 지역으로 이 부분의 신경세포는 혈액공급이 빠른 시간 내에 재개되지 않으면 항상성을 유지할 수 없게 되고 세포사로 이어진다. 혈액 공급이 완전히 차단될 경우 수초 안에 신경세포의 전기적 활동이 중단되고 수분 내에 에너지 상태가 악화되며 이온펌프의 항상성이 깨지게 된다. 이러한 비가역적인 손상은 혈액공급이 중단된 후 5~10분내에 일어나게 된다.

3) Penumbra는 전통적으로 core 주변지역을 의미한다. 1970년대에 행하여진 뇌의 전기생리학적인 관찰을 통해 penumbra가 정의되었는데 시냅스에서 신경전달물질의 전달은 차단되지만(뇌혈류 50ml/100 g/min 이하) 이온의 항상성은 유지되는(뇌혈류 20mg/100 g/min 이상) 부분을 말한다. 시냅스의 활동에 따른 신경학적 장애는 발생하나 세포의 모양은 유지되고 있는 상태로 뇌혈류가 다시 공급된다면 가역적일 수 있고 임상증상 또한 호전될 수 있다

💡 **Manual AIF and VOF Selection**

A global **AIF** is usually selected from a given anatomic region, for example, the M1 or M2 branches of the middle cerebral artery (MCA) in MR studies, or from the anterior cerebral artery in CT studies where coverage on most current systems are limited.8,10 In clinical studies of stroke, the AIF is often selected in the hemisphere contralateral to the abnormality, which provides the most sensitive reference area to capture any hemodynamic abnormality, but this is inherently susceptible to potential bias from not capturing the delay and dispersion ipsilaterally. The manual AIF selection process varies widely with the software used, but it often involves an interactive interface where the user is able to explore concentration-time curves in an anatomic region visually and then select curves that exhibit the arterial characteristics listed previously.

The **VOF** can be selected in an analogous fashion, guided by the outlined curve shape properties. Here, the VOF is often chosen from the sagittal or transverse sinus, focusing on the curve with the highest area.

Perfusion CT in acuter ischemic stroke

[The process of evaluating brain tissue status]

1. **Obtain parameter maps from the CTP time series**

   Examples of parameter maps

   - cerebral blood flow (CBF)
   - cerebral blood volume (CBV)
   - time to peak (TTP)
   - time to the maximum of the residue function (Tmax)

   ⚠️ there is no gold standard for quantifying perfusion metrics. All methods found in literature provide merely non-exact solutions.

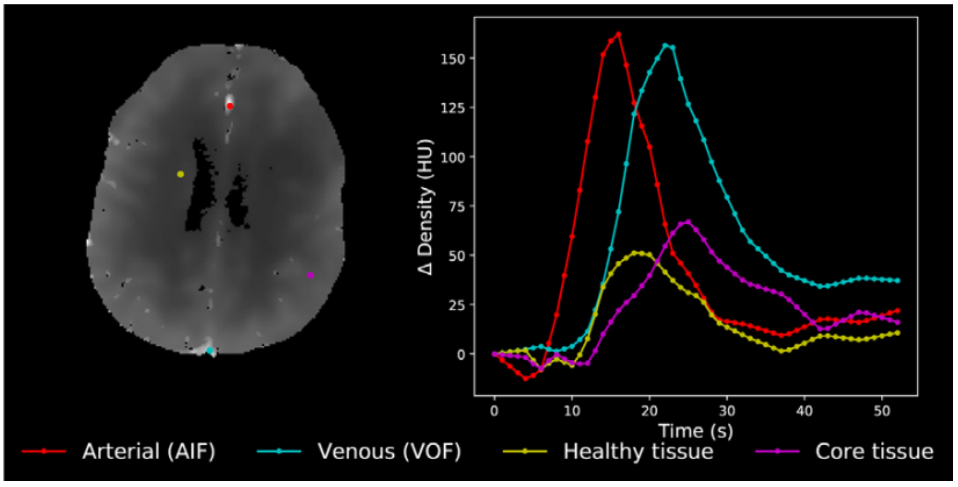
💡 **Deconvolution**
The most widely used methods for CTP parameter map estimation

$$c_{tissue}(t) = c_{art}(t) \circledast h(t)$$

[Notations]
- $c_{tissue}(t)$: the CTP contrast enhancement in a voxel of tissue
- $c_{art}(t)$: contrast enhancement in the arteries (=AIF)
- $h(t)$: the flow-scaled residue function
- $\circledast$: convolution operator

2. **Apply a tissue discrimination rule (mainly, thresholding)**

[Status quo/challenge]



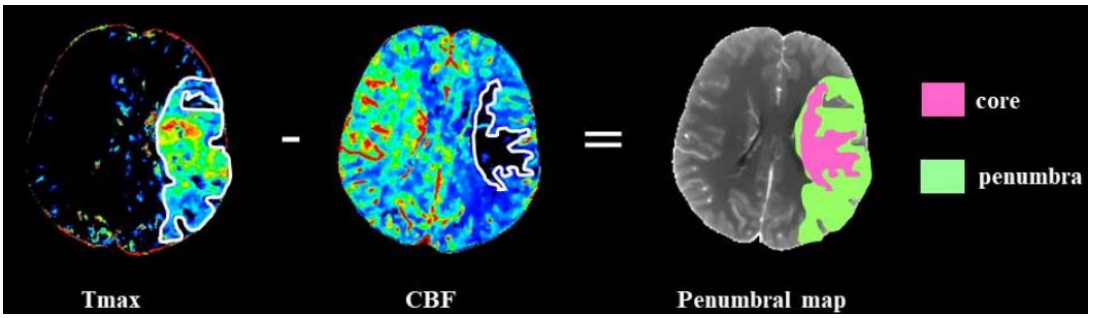
Left: a perfusion CT example from ISLES18

In clinical practice the AIF and VOF are generally selected by a radiologist, **a time demanding and highly variable** process that implies selecting in the CTP series the optimal candidate voxels. Frequently, a single voxel per vascular function is selected, which leads to low SNR curves. Voxel selection is, moreover, **subject** to the professionals' training and experience, which not only **introduces human bias** but it may also affect CBF maps depending which side of the brain the AIF is chosen from. The AIF is **so critical for generating accurate maps** that very small changes in its

shape and/or location may produce a profound effect over the generated maps. Besides, given the acute context of the disease, **a fast voxel selection has to be performed.** It has been shown that for every 30-minute delay in reperfusion, the probability of good outcome decreases by 20%.

> = Given these limitations, automatic, fast and reproducible core and penumbra quantification are highly desired.

Automatic core and penumbra segmentation



ref: https://www.senr.org/wp-content/uploads/2019/11/3_2-Fainardi.pdf

In this work we aim to automatize, instead, the well validated deconvolution process by the automatic selection of vascular functions. we avoid approximating parameters that can be directly estimated through a physical model while also preserving explainability and quality control in clinical settings.

Automatic vascular function selection

Moreover, vascular function estimation using deep neural networks can be conducted through segmentation approaches aiming to detect arterial voxels candidates. [**An Automatic Estimation of Arterial Input Function Based on Multi-Stream 3D CNN**]

Contributions

- we propose AIFNet, an **end-to-end** supervised **convolutional neural network** devised for estimating vascular functions (i.e. **AIF and VOF**) in perfusion imaging.
- The model is easy to train and deploy given the minimal data annotation required, which can be as little as a single voxel per vascular function
- AIFNet receives **4D CTP** series as input and generates as output:

  i) the estimated AIF and VOF curves

  ii) a voxel-wise, interpretable probability map representing the voxelwise ontribution
  to the estimated vascular signal.
- is optimized at a vascular function level, which helps the network to better learn the time-curve profiles. The method preserves clinical **interpretability** and also **enables quality control** of the selected AIF/VOF brain vasculature, thus enhancing its clinical **transferability** potential.

Methods

1. Function Estimation with Deep Learning

It works by **estimating a 3D probabilistic volume that represents the voxelwise contribution to the ascular signal.**

Input: $x(t) = \{x_t; t = 1, 2, ..., T\}$, $x_t \in \mathbb{R}^{M \times N \times Q \times T}$ (native CTP series)
Output: $\hat{y} = AIF_{Net}(x(t))$, $\hat{y}(t) = \{\hat{y}_t; t = 1, 2, ..., T\}$

$\hat{y}_t$: A weighted average of all voxels of the volume x_t at that t time point

$$\hat{y}_t = \sum_{q=1}^{Q}\sum_{n=1}^{N}\sum_{m=1}^{M} x_t(m,n,q) * P_{vol}(m,n,q)$$

P_{vol}: the 3D probabilistic volume containing the **voxelwise contribution** to the vascular function and fulfilling (← 이걸 찾는 게 목적!)

$$\sum_{q=1}^{Q}\sum_{n=1}^{N}\sum_{m=1}^{M} P_{vol}(m,n,q) = 1$$

Loss: Pearson Correlation Loss

$$\mathcal{L}(y(t),\hat{y}(t)) = -\frac{\sum_{t=1}^{T}(y_t-\bar{y})(\hat{y}_t-\bar{\hat{y}})}{\sqrt{\sum_{t=1}^{T}(y_t-\bar{y})^2}\sqrt{\sum_{t=1}^{T}(\hat{y}_t-\bar{\hat{y}})^2}}$$

$$\bar{y} = \frac{1}{T}\sum_{t=1}^{T} y_t \text{ and } \bar{\hat{y}} = \frac{1}{T}\sum_{t=1}^{T} \hat{y}_t$$

2. Architecture

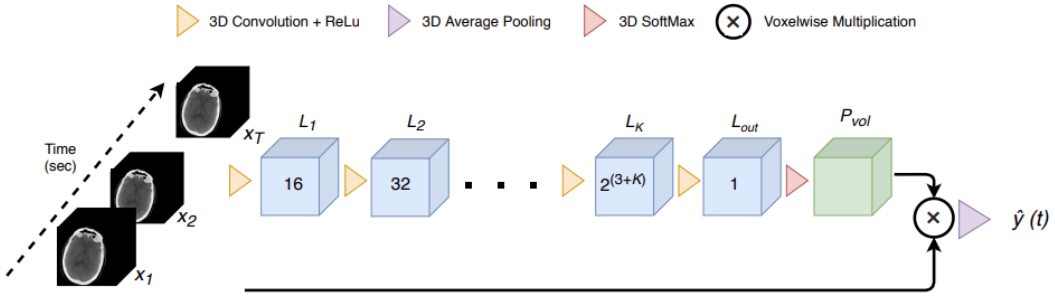


Figure 2: AIFNet architecture. The CTP time points x_t $(t = 1, 2, ..., T)$ are incorporated as channels in the network. All convolutional layers use 3x3x3 kernels except L_1, which uses 3x3x1. L_k is the $k-th$ convolutional layer (with $k = 1, 2, ..., K$). Inside each feature block the number of channels used is indicated. P_{vol} is the probabilistic volume. The 3D average pooling block averages the volumetric information along the x-y-z axes, such that the predicted vascular function $\hat{y}(t)$ is a 1D vector of length T.

3.1 Training Phase

3.2 Perfusion specific data augmentation

Two perfusion specific phenomena are modelled:

i) the variability of the contrast bolus arrival,
which depends on the injection protocol and the patient's cardiovascular system

ii) the variability of the curve's peak-to-baseline (PTB) values, which depends on the iodine concentration in the contrast agent.

4.1 Testing phase

4.2 VOF signal recalibration