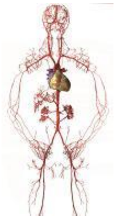


Использование синтетической базы пациентов для оценки гемодинамических индексов

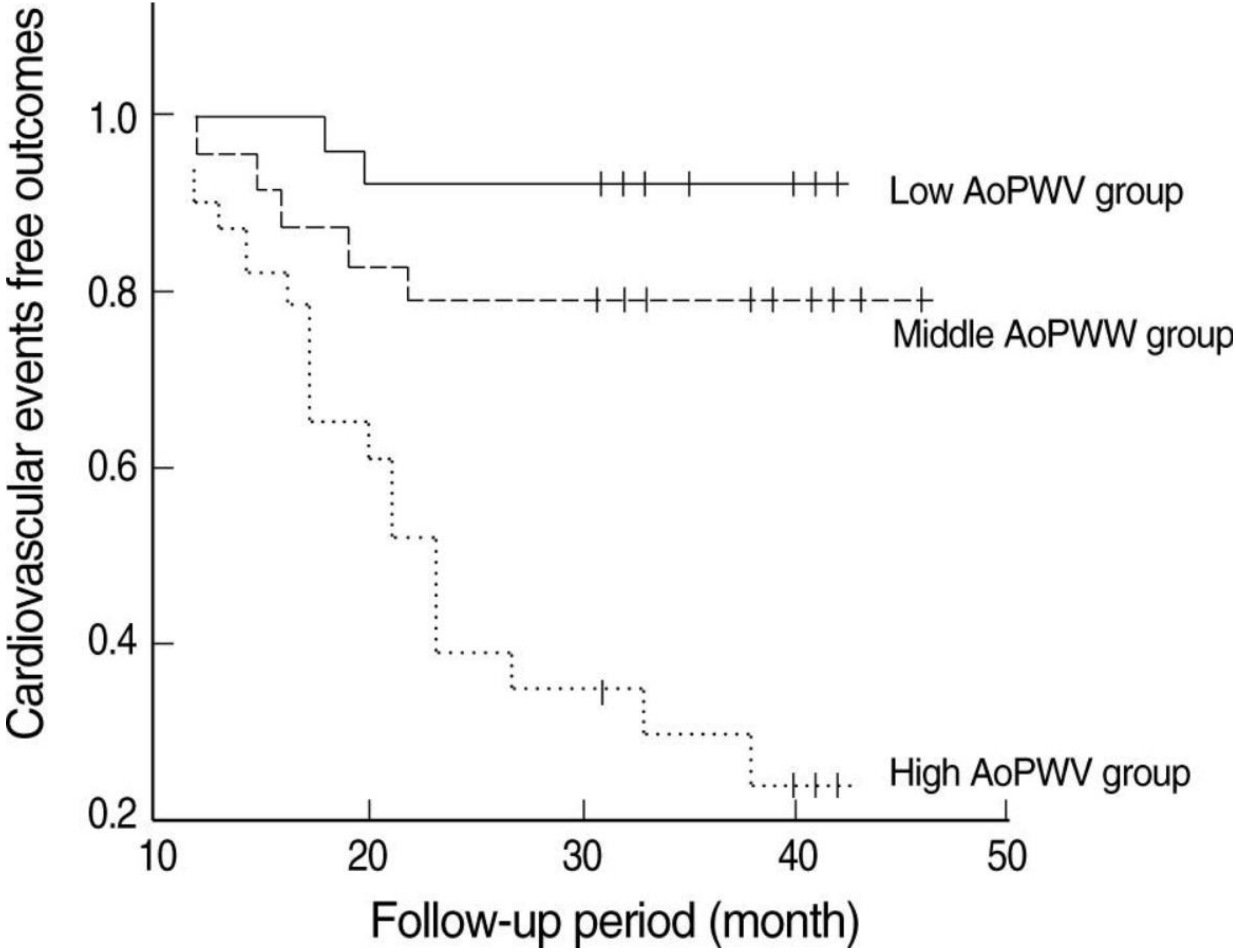
Тимур Гамилов[1-3] , Ниженко Илья [1] ,
Jordi Alastruey[1,4], Peter Charlton[4]

[1] Первый МГМУ им. И. М. Сеченова
[2] Московский физико-технический институт
[3] Институт Вычислительной Математики РАН
[4] King’s College, London

ИВМ РАН, 2-3.11.2020

gamilov@crec.mipt.ru

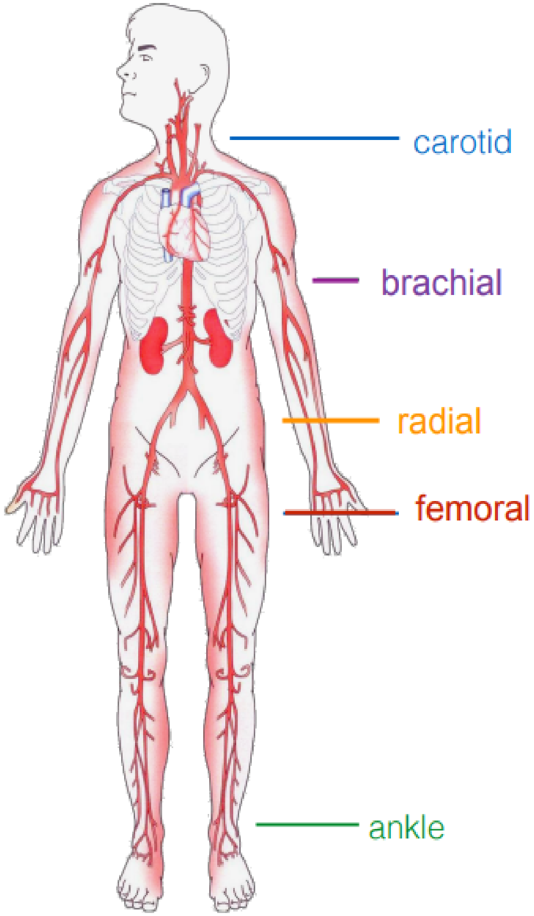
Скорость пульсовой волны в аорте



Shin SJ, Kim YK, Chung S, et al. The impact of the aortic pulse wave velocity on the cardiovascular outcomes of hemodialysis patients. *J Korean Med Sci*. 2009;24 Suppl(Suppl 1):S121-S128. doi:10.3346/jkms.2009.24.S1.S121

Скорость пульсовой волны в аорте

$$ePWV = 9.587 - 0.402 \times age + 4.560 \times 10^{-3} \times age^2 - 2.621 \times 10^{-5} \times age^2 \times MBP + 3.176 \times 10^{-3} \times age \times MBP - 1.832 \times 10^{-2} \times MBP$$


carotid
brachial
radial
femoral
ankle

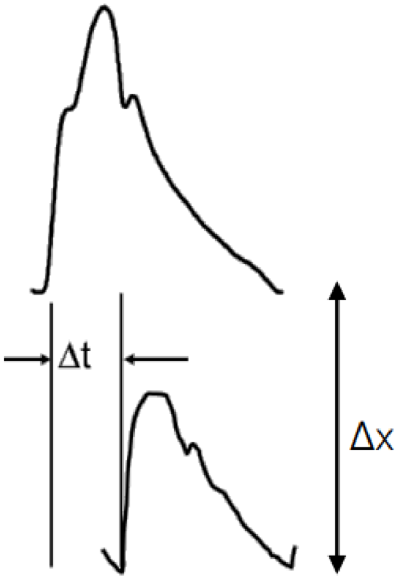
carotid-femoral PWV

brachial-ankle PWV

carotid-radial PWV

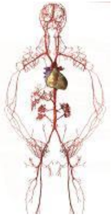
femoral-ankle PWV

foot-to-foot method



$$PWV_{ff} = \Delta x/\Delta t$$

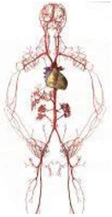
Синтетическая база данных пациентов



- Разработка и тестирование алгоритмов анализа пульсовых волн требует обширные базы данных

- Сбор информации для этих баз данных – это долго и дорого

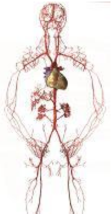
Синтетическая база данных пациентов



- Разработка и тестирование алгоритмов анализа пульсовых волн требует обширные базы данных

- Сбор информации для этих баз данных – это долго и дорого
- Альтернатива – генерирование синтетических баз данных

Основные уравнения



ЗСМ

$$\frac{\partial A}{\partial t}+\frac{\partial (AU)}{\partial x}=0,$$

ЗСИ

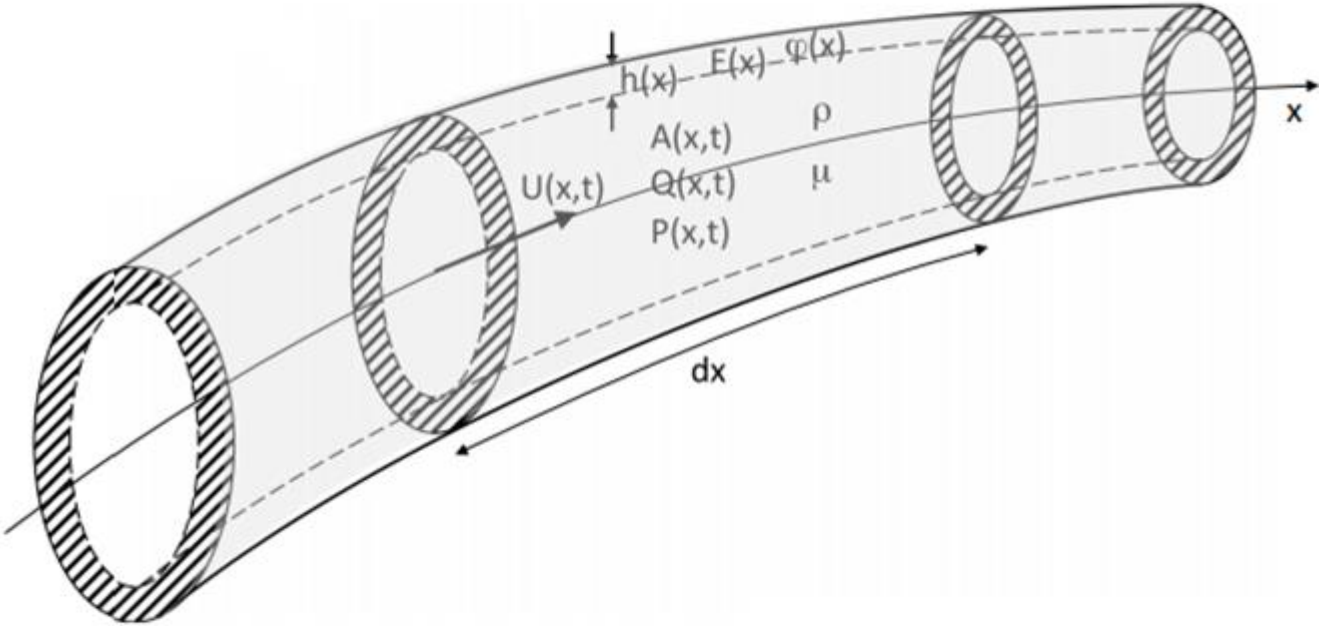
$$\frac{\partial U}{\partial t}+U\frac{\partial U}{\partial x}+\frac{1}{\rho}\frac{\partial P}{\partial x}=\frac{f}{\rho A},$$

$$P=P_0+\frac{\beta}{A_0}(\sqrt{A}-\sqrt{A_0})+\frac{\Gamma}{A_0\sqrt{A}}\frac{\partial A}{\partial t}$$

$$\beta(x)=\frac{4}{3}\sqrt{\pi}Eh$$

$$\Gamma(x)=\frac{2\sqrt{\pi}\varphi h}{3A_0^{3/2}}.$$

$$c_0=\sqrt{\frac{\beta}{2\rho}}A_0^{-1/4}=\sqrt{\frac{2Eh}{3\rho\mathcal{R}_0}}$$

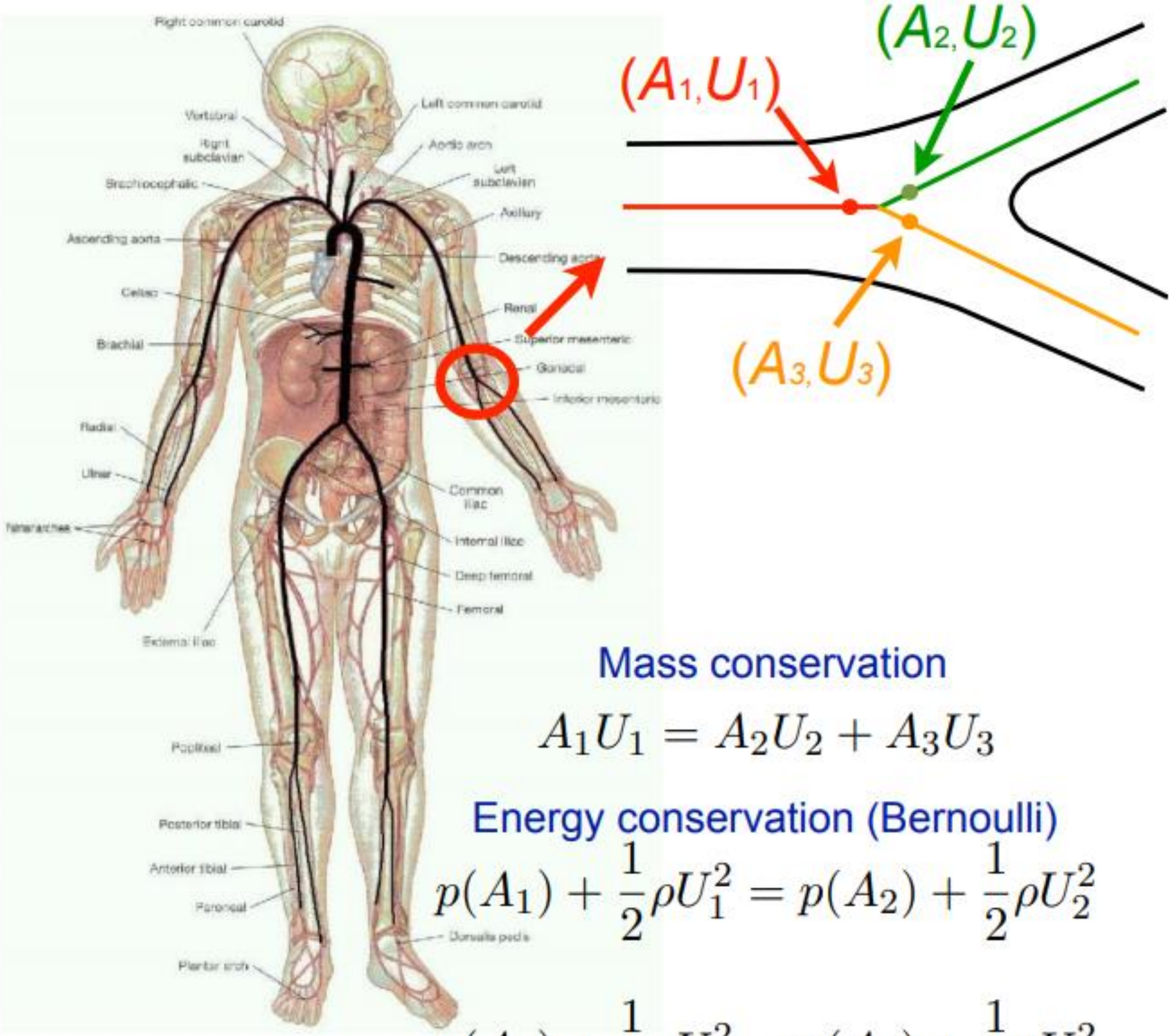


KING'S College LONDON

Alastruey, Parker, Sherwin. *In BHR Group's 11th Intern Conf* Ch 7, 401–42, 2012

Области бифуркаций

KING'S College LONDON


Right common carotid
Vertebral
Right subclavian
Brachiocephalic
Ascending aorta
Celiac
Brachial
Radial
Ulnar
Palmar arches
External iliac
Popliteal
Posterior tibial
Anterior tibial
Peroneal
Plantar arch
Left common carotid
Aortic arch
Left subclavian
Axillary
Descending aorta
Renal
Superior mesenteric
Gonadal
Inferior mesenteric
Common iliac
Internal iliac
Deep femoral
Femoral
Dorsalis pedis
(A_1, U_1)
(A_2, U_2)
(A_3, U_3)

Mass conservation

$$A_1 U_1 = A_2 U_2 + A_3 U_3$$

Energy conservation (Bernoulli)

$$p(A_1) + \frac{1}{2}\rho U_1^2 = p(A_2) + \frac{1}{2}\rho U_2^2$$

$$p(A_1) + \frac{1}{2}\rho U_1^2 = p(A_3) + \frac{1}{2}\rho U_3^2$$

Propagation of characteristic variables

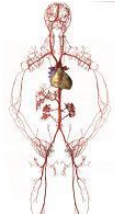
$$W_f(A_1, U_1)_t = W_f(A_1, U_1)_{t+\Delta t}$$

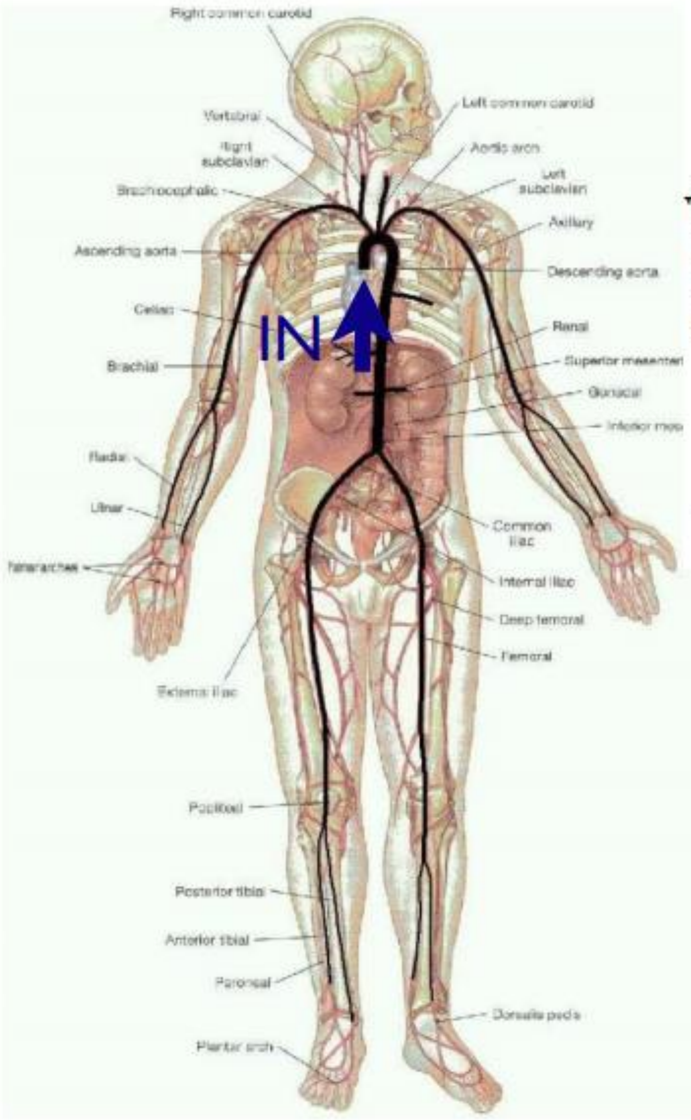
$$W_b(A_2, U_2)_t = W_b(A_2, U_2)_{t+\Delta t}$$

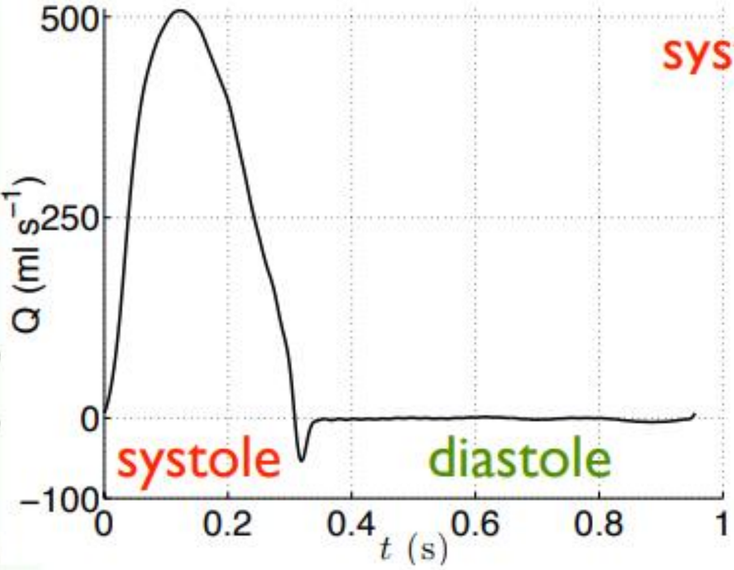
$$W_b(A_3, U_3)_t = W_b(A_3, U_3)_{t+\Delta t}$$

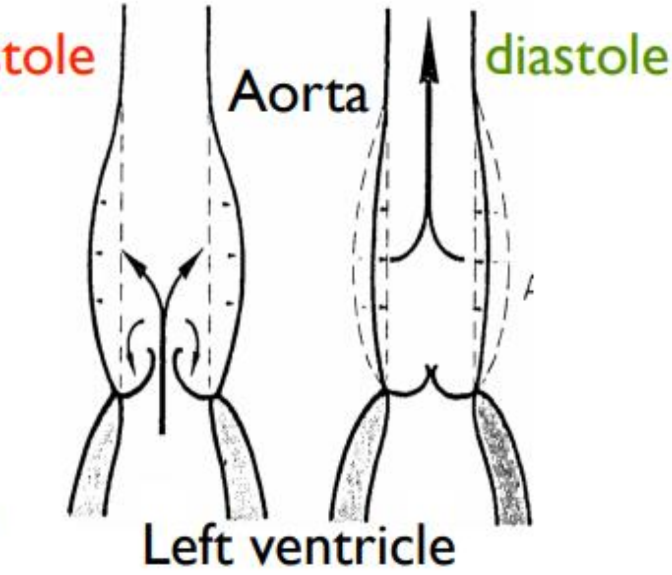
Alastruey, Parker, Sherwin. *In BHR Group's 11th Intern Conf* Ch 7, 401–42, 2012

Граничное условие на входе




Right common carotid
Vertebral
Right subclavian
Brachiocephalic
Ascending aorta
Celiac
Brachial
Radial
Ulnar
Palmar arches
External iliac
Popliteal
Posterior tibial
Anterior tibial
Peroneal
Plantar arch
Left common carotid
Aortic arch
Left subclavian
Axillary
Descending aorta
Renal
Superior mesenteric
Gonadal
Inferior mes
Common iliac
Internal iliac
Deep femoral
Femoral
Dorsalis pedis
IN

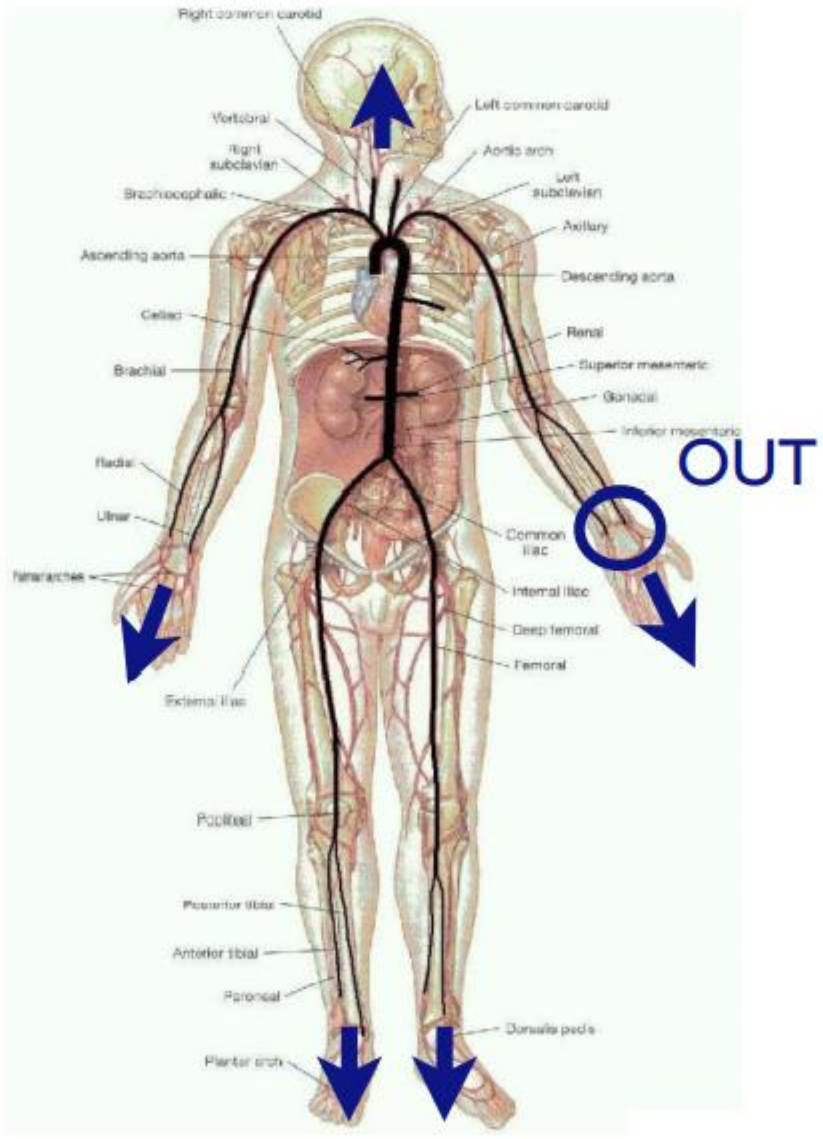


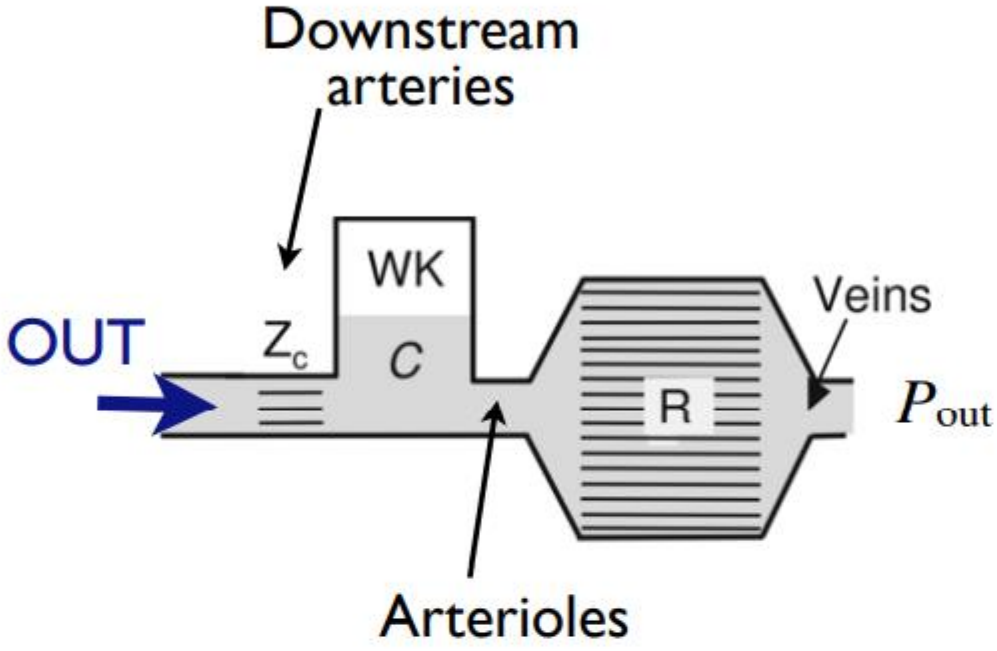

systole
Aorta
diastole
Left ventricle

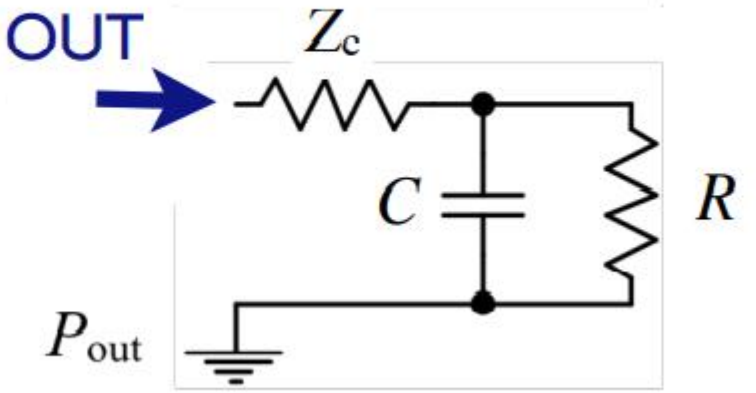
KING'S College LONDON

Alastruey, Parker, Sherwin. *In BHR Group's 11th Intern Conf* Ch 7, 401–42, 2012

Граничное условие на выходе


Right common carotid
Vertebral
Right subclavian
Brachiocephalic
Ascending aorta
Celiac
Brachial
Radial
Ulnar
Palmar arches
External iliac
Popliteal
Posterior tibial
Anterior tibial
Peroneal
Plantar arch
Left common carotid
Aortic arch
Left subclavian
Axillary
Descending aorta
Renal
Superior mesenteric
Gonadal
Inferior mesenteric
OUT
Common iliac
Internal iliac
Deep femoral
Femoral
Dorsalis pedis

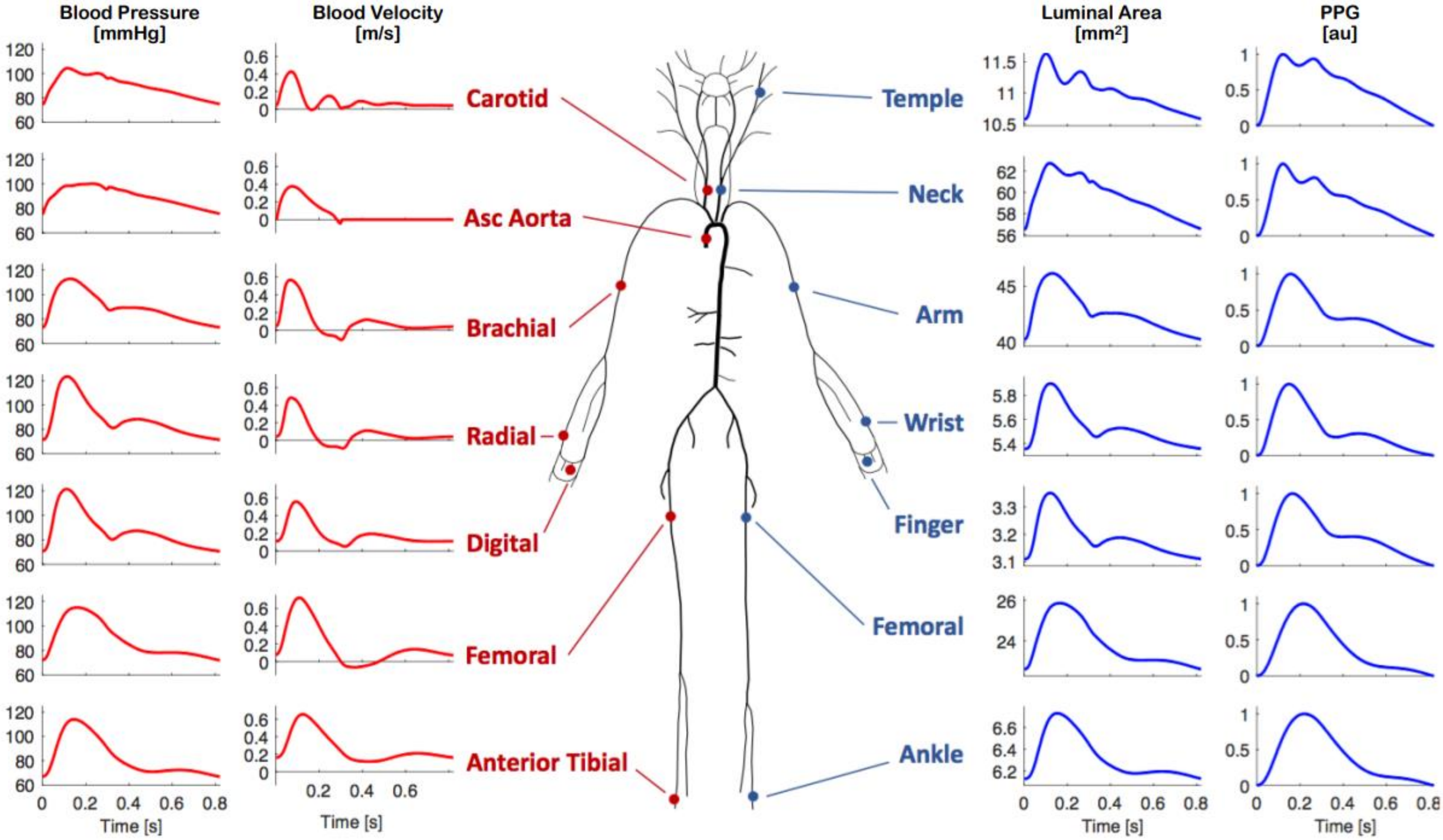

Downstream arteries
OUT
Z_c
WK
C
R
Veins
P_{out}
Arterioles


OUT
Z_c
C
R
P_{out}

KING'S College LONDON

Alastruey, Parker, Sherwin. *In BHR Group's 11th Intern Conf* Ch 7, 401–42, 2012

Базовая модель



Charlton, Mariscal-Harana, Vennin, Li, Chowienczyk, Alastruey. *Am J Physiol Heart Circ Physiol* 317:H1062-85, 2019

Литературный обзор: параметры, меняющиеся с возрастом

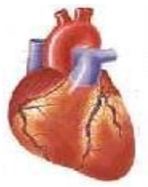
Changed with age

- ↑ Luminal diameter of larger arteries (24)
- ↑ Length of proximal aorta (4)
- ↑ Pulse wave velocity (25)
- ↓ Stroke volume (10)
- ↷ Heart rate (21)
- ↷ Mean blood pressure

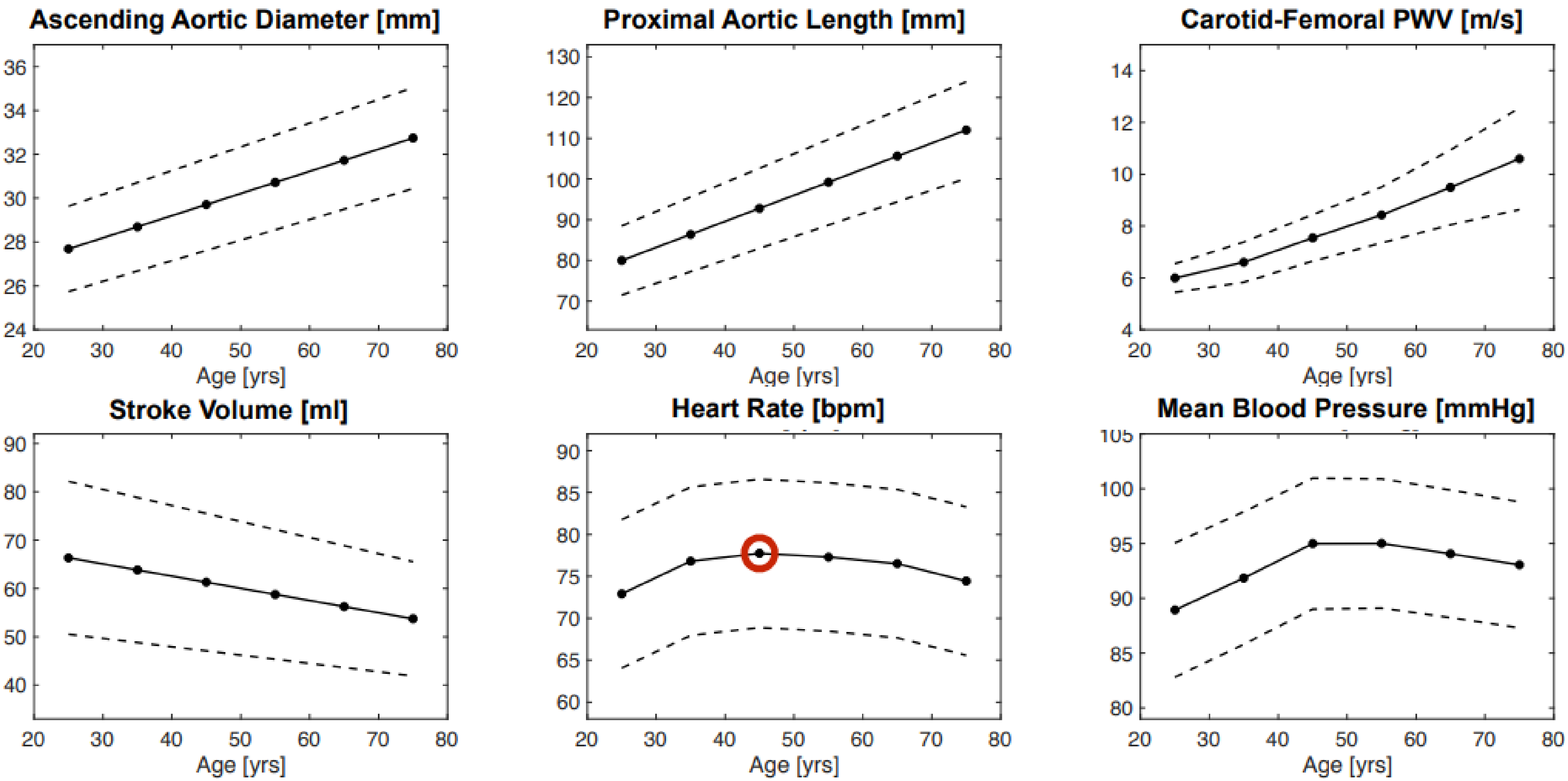
No change with age

- Luminal diameter of remaining arteries (4)
- Length of remaining arteries (3)
- Left ventricular ejection time (9)
- Time to peak aortic flow (3)
- Aortic reverse flow volume (1)

Charlton, Mariscal-Harana, Vennin, Li, Chowienczyk, Alastruey. *Am J Physiol Heart Circ Physiol* 317:H1062-85, 2019



Базовая модель для возрастной группы



Ascending Aortic Diameter [mm]

Proximal Aortic Length [mm]

Carotid-Femoral PWV [m/s]

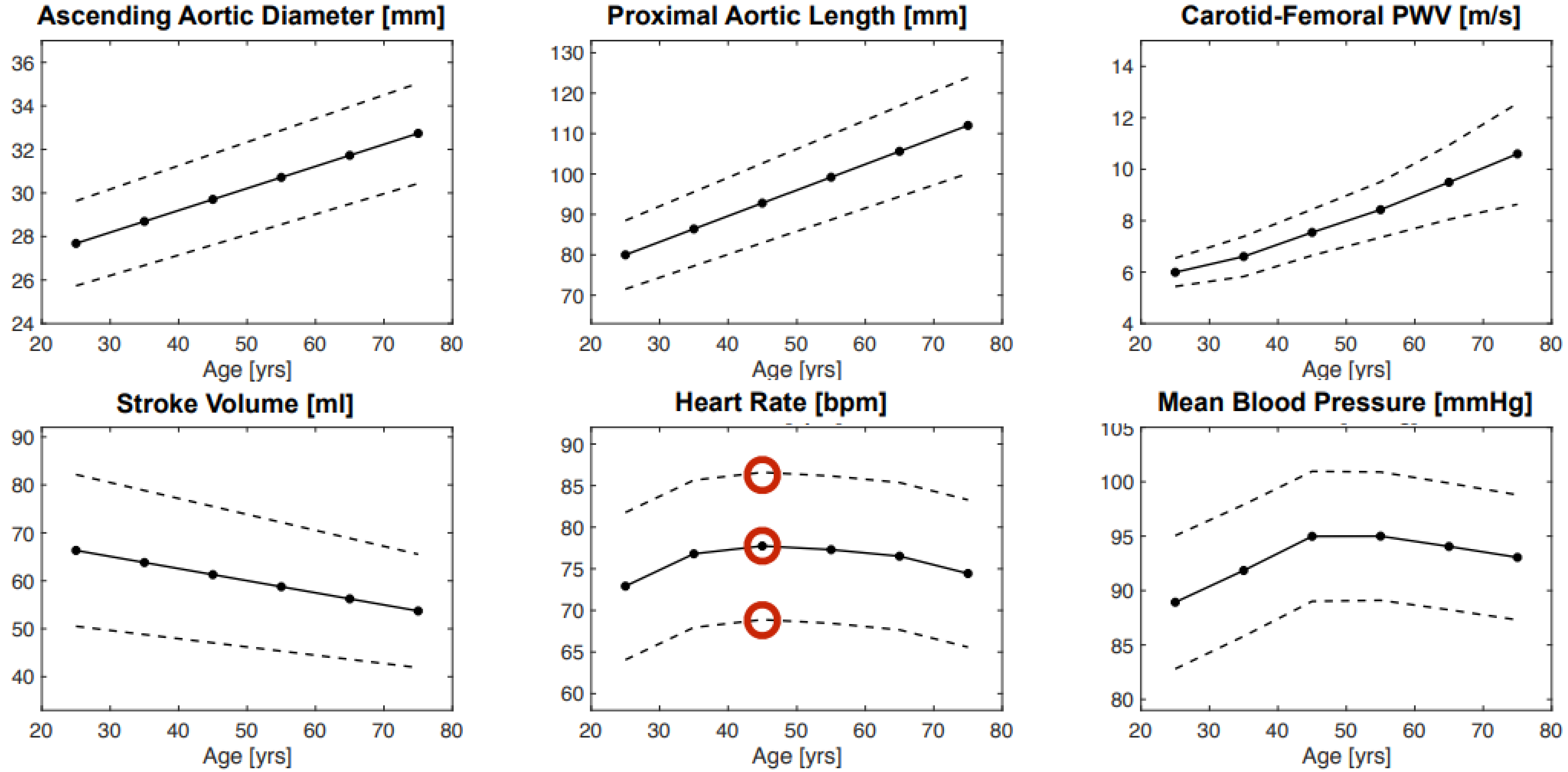
Stroke Volume [ml]

Heart Rate [bpm]

Mean Blood Pressure [mmHg]

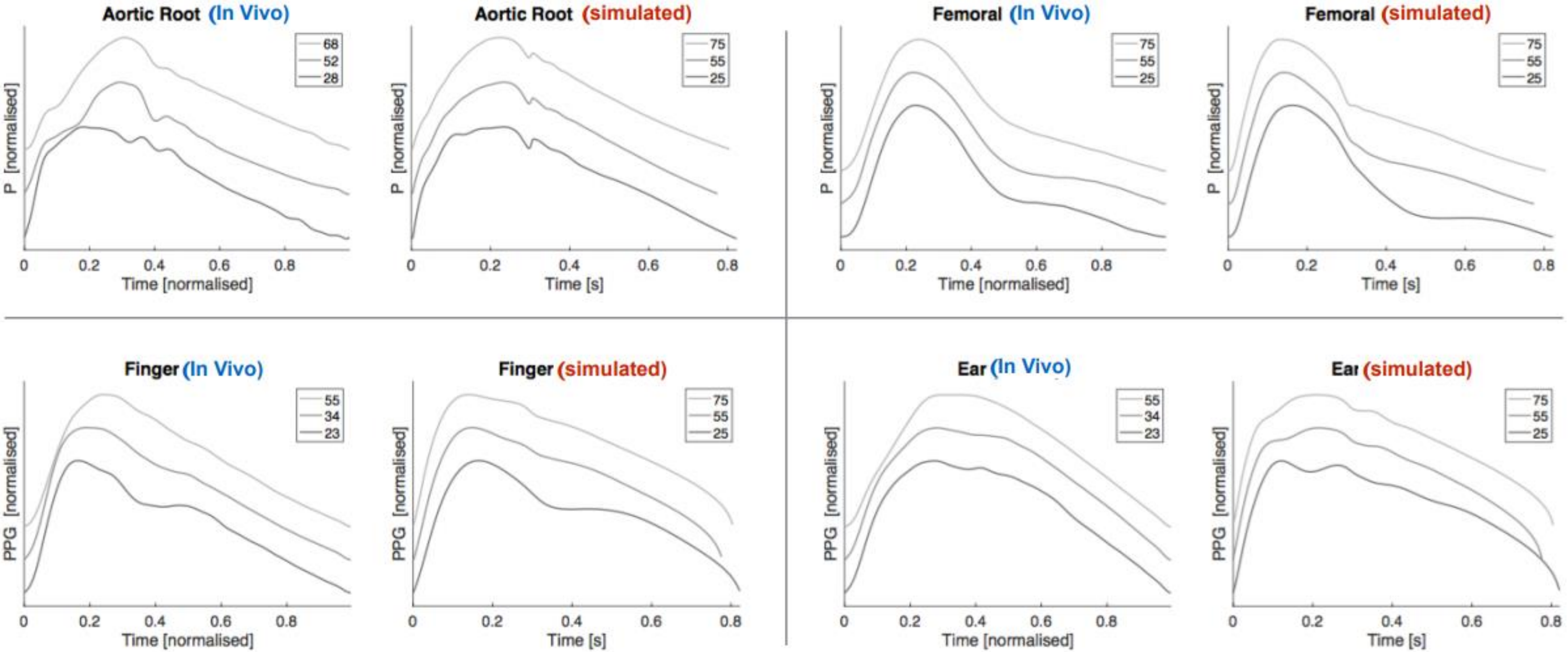
- базовая модель для возрастной группы использует средние значения параметров

Набор из 729 моделей для каждой возрастной группы

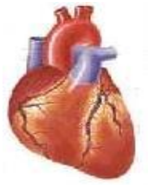


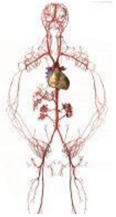
Charlton, Mariscal-Harana, Vennin, Li, Chowienczyk, Alastruey. *Am J Physiol Heart Circ Physiol* 317:H1062-85, 2019

Пульсовые волны для различных возрастных групп



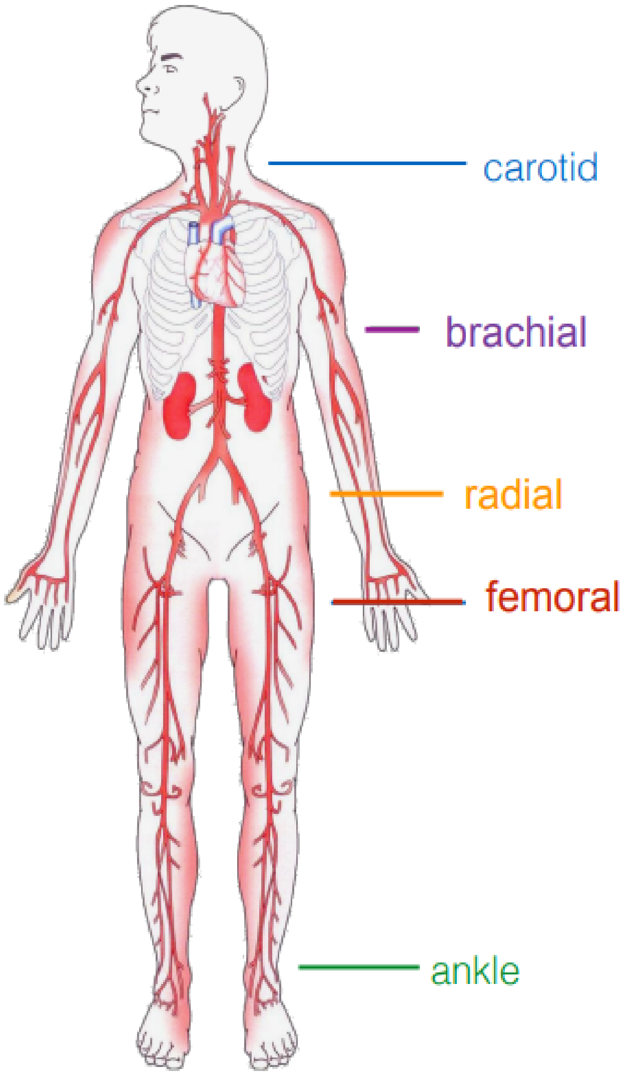
Charlton, Mariscal-Harana, Vennin, Li, Chowienczyk, Alastruey. *Am J Physiol Heart Circ Physiol* 317:H1062-85, 2019





Как использовать синтетическую базу данных ?

Методы оценки PWVa

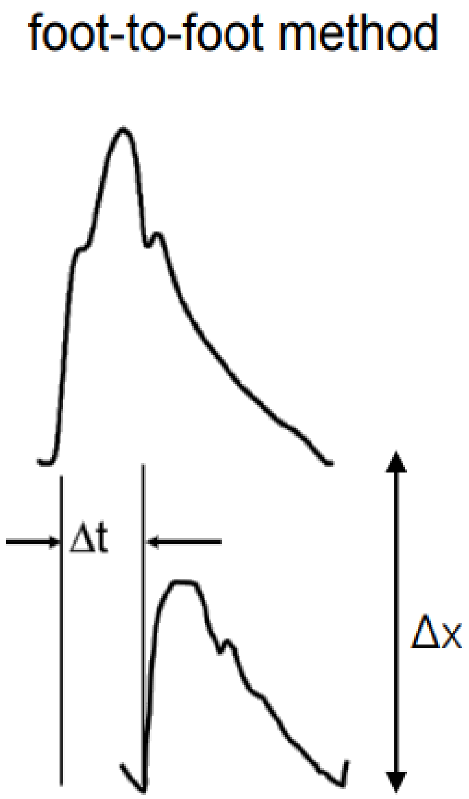

carotid
brachial
radial
femoral
ankle

carotid-femoral PWV

brachial-ankle PWV

carotid-radial PWV

femoral-ankle PWV

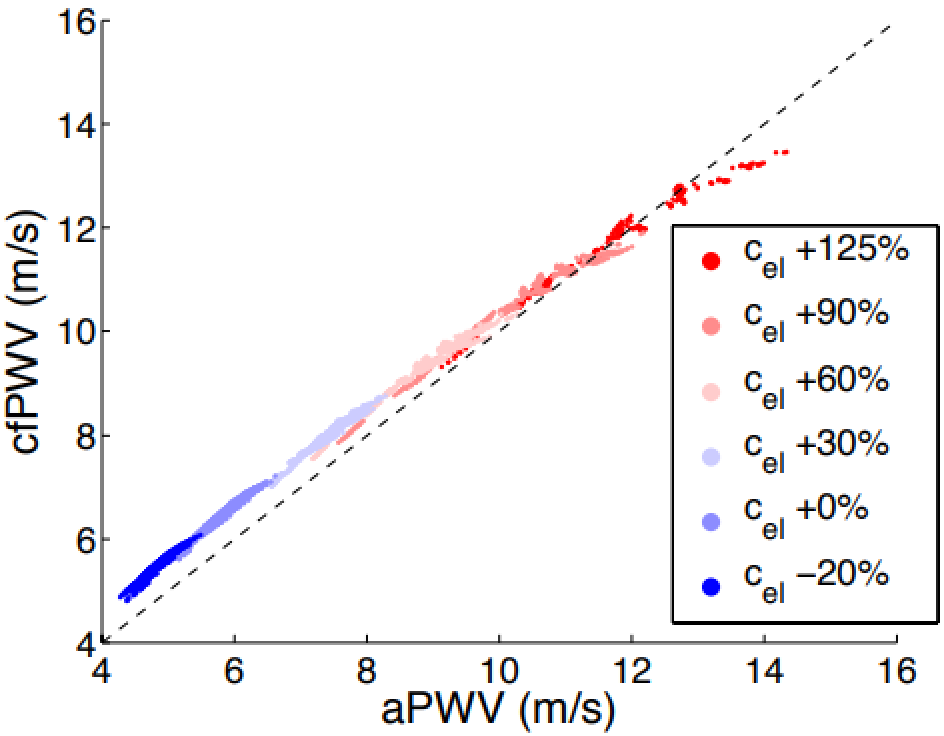

foot-to-foot method
Δt
Δx

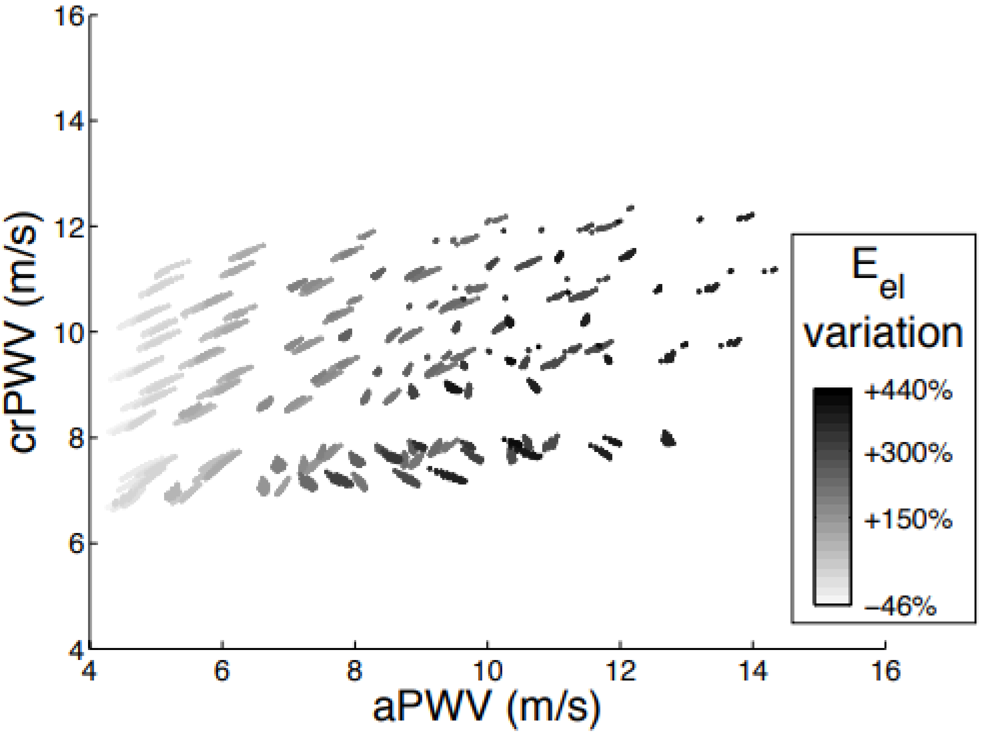
$$PWV_{ff} = \Delta x / \Delta t$$

Willemet, Chowienczyk, Alastruey, *Am J Physiol Heart Circ Physiol* 309:H663-75, 2015

Методы оценки PWVa

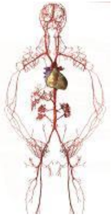
- PWVcf – «хороший» индекс эластичности аорты
- PWVcr – «плохой» индекс эластичности аорты

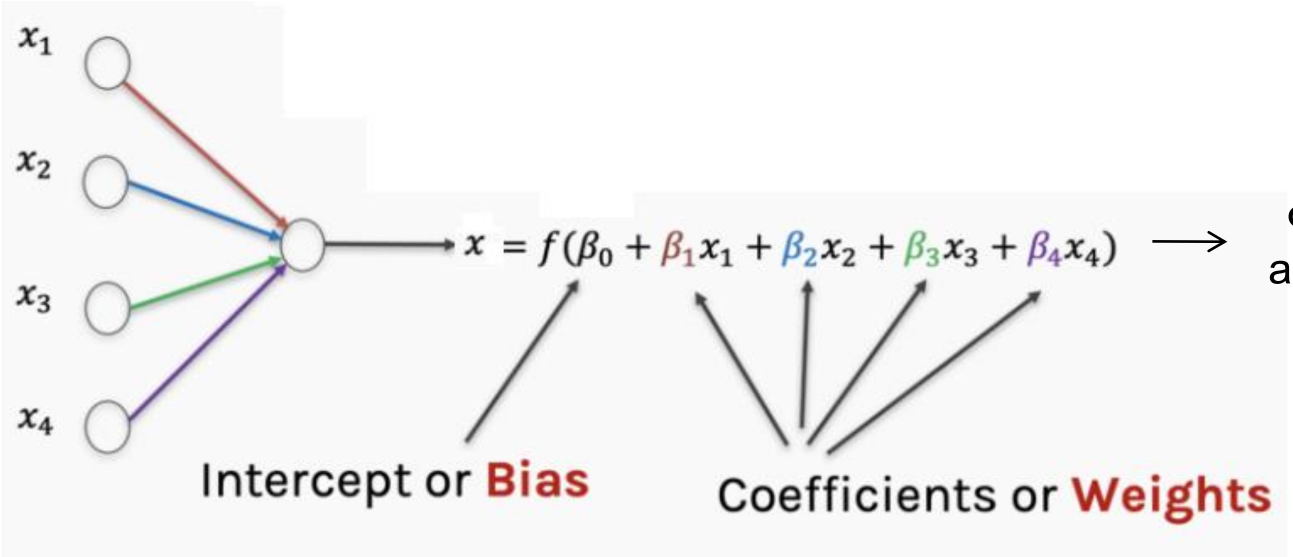




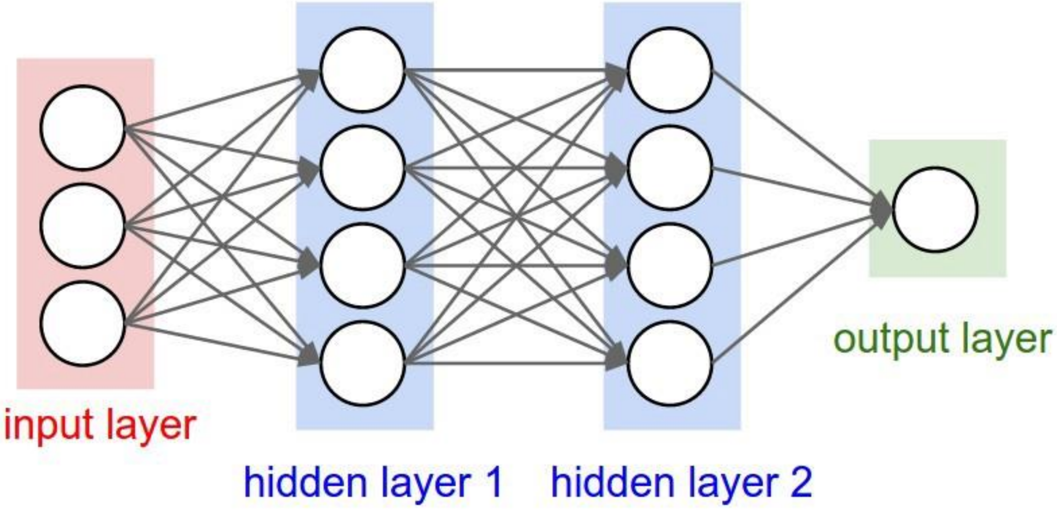
Willemet, Chowienczyk, Alastruey, *Am J Physiol Heart Circ Physiol* 309:H663-75, 2015

Нейронная сеть

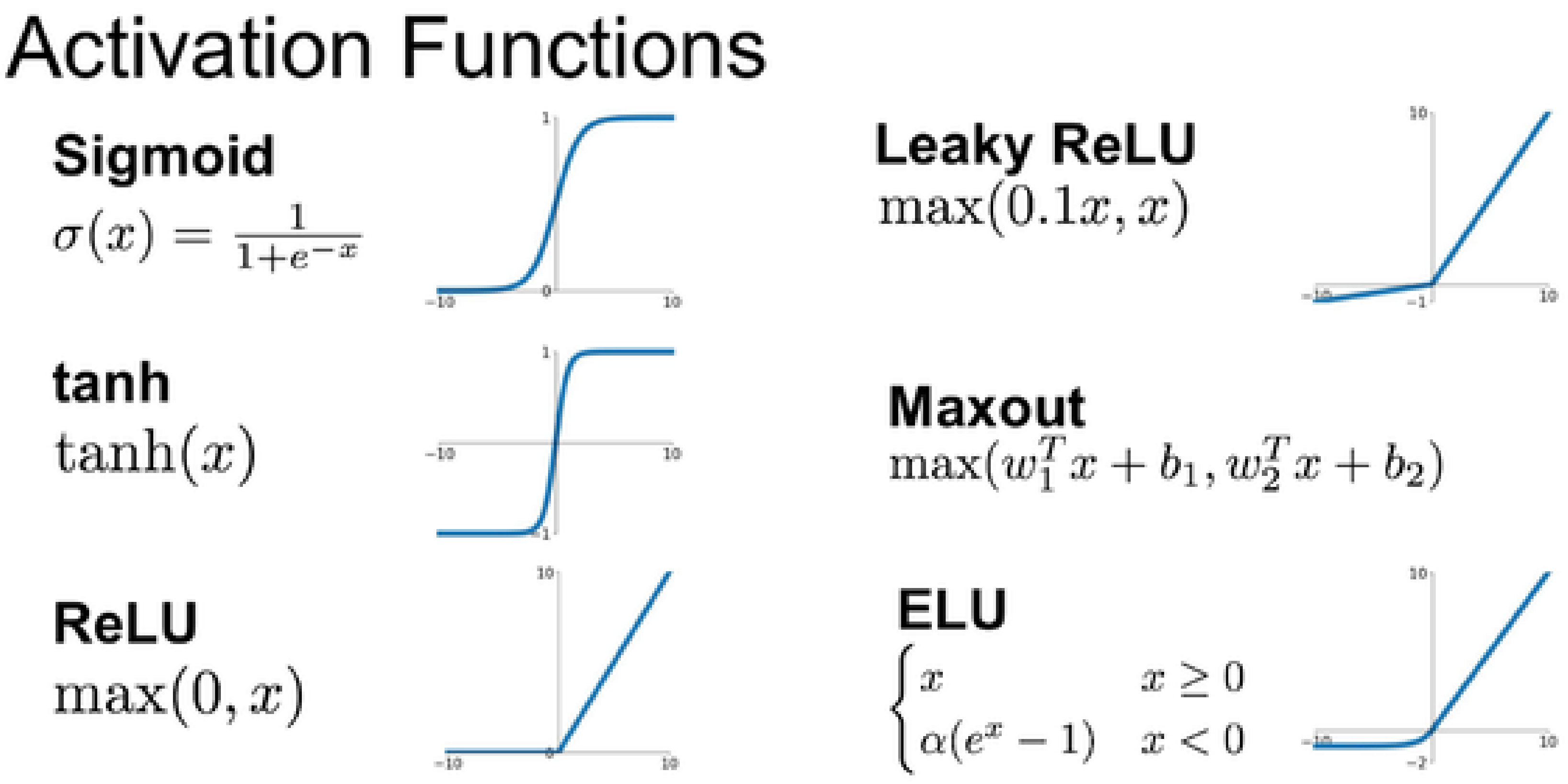



x_1
x_2
x_3
x_4
$x = f(\beta_0 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_4 x_4)$
Intercept or **Bias**
Coefficients or **Weights**

→ Функция активации


input layer
hidden layer 1
hidden layer 2
output layer

Функции активации



Activation Functions

Sigmoid

$\sigma(x) = \frac{1}{1+e^{-x}}$

tanh

$\tanh(x)$

ReLU

$\max(0, x)$

Leaky ReLU

$\max(0.1x, x)$

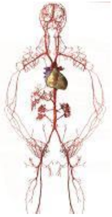
Maxout

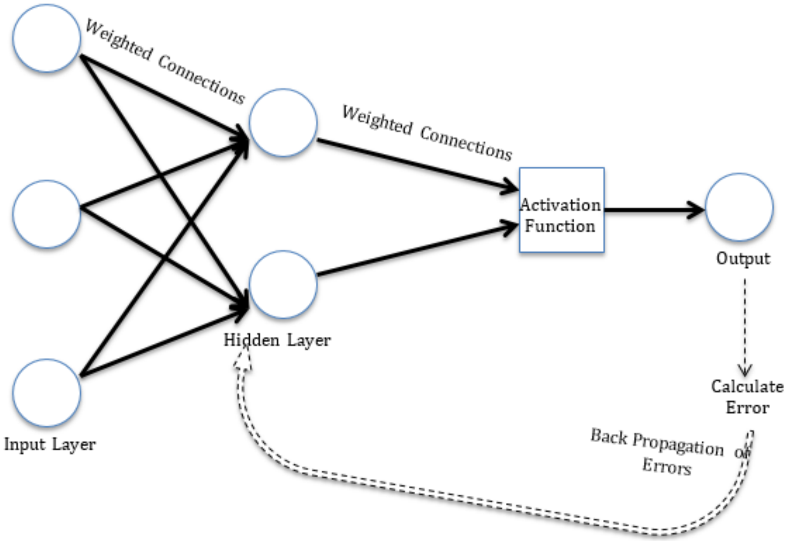
$\max(w_1^T x + b_1, w_2^T x + b_2)$

ELU

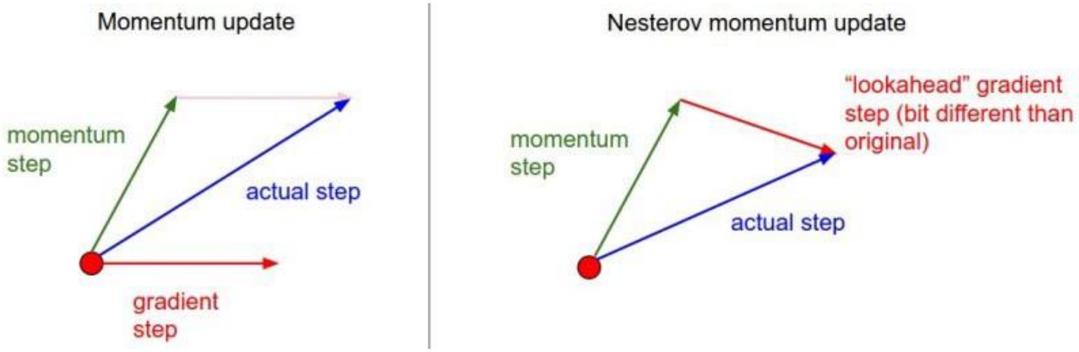
$\begin{cases} x & x \geq 0 \\ \alpha(e^x - 1) & x < 0 \end{cases}$

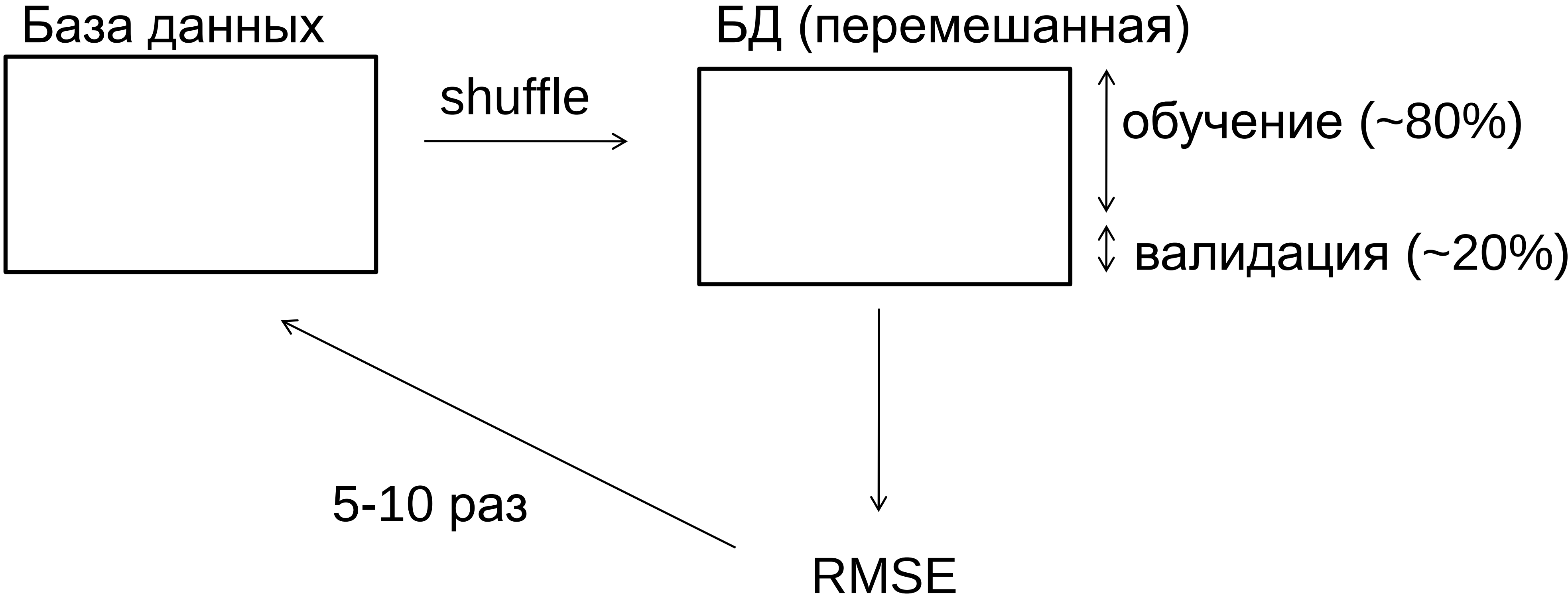
Оптимизация весов




Weighted Connections
Weighted Connections
Activation Function
Output
Hidden Layer
Input Layer
Calculate Error
Back Propagation of Errors

ADAM оптимизатор
https://arxiv.org/pdf/1412.6980.pdf


Momentum update
momentum step
actual step
gradient step
Nesterov momentum update
momentum step
"lookahead" gradient step (bit different than original)
actual step



База данных

shuffle

БД (перемешанная)

обучение (~80%)

валидация (~20%)

5-10 раз

RMSE

Input parameters:

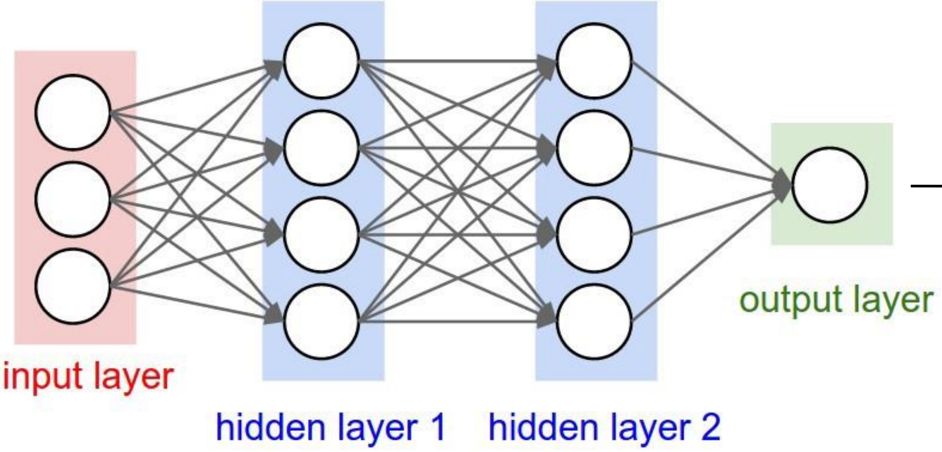
возраст

ЧСС

Ударный объём

MBP (сред. давл. плеч.)

DBP (диаст. давл. плеч.)


input layer
hidden layer 1
hidden layer 2
output layer

PWV
(аорта)

RMSE = 10%

Входные параметры:

возраст

ЧСС

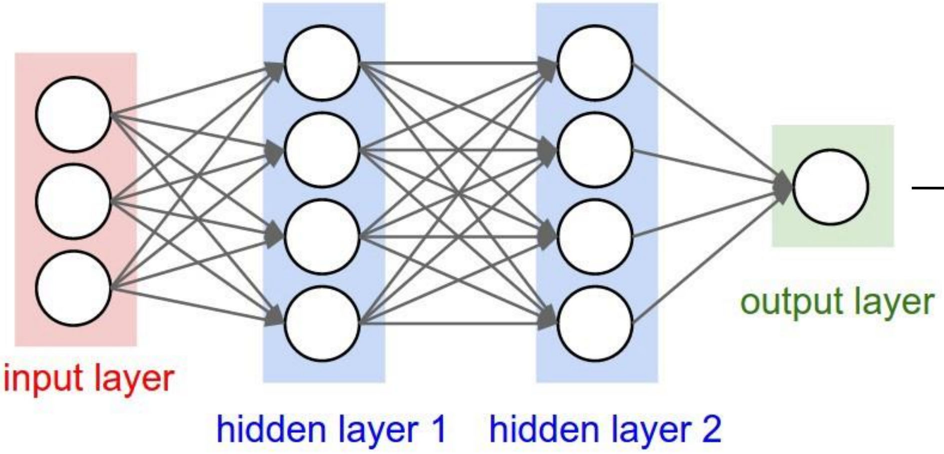
Ударный объём →

Время серд. выброса

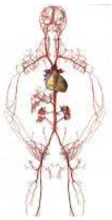
Сис. давл. (плеч.)

Диастол. давл. (плеч.)

PWV (плеч.)


input layer
hidden layer 1
hidden layer 2
output layer

→ Mean arterial pressure MAP (aortic)



Входные параметры:

age

HR

SV

LVET

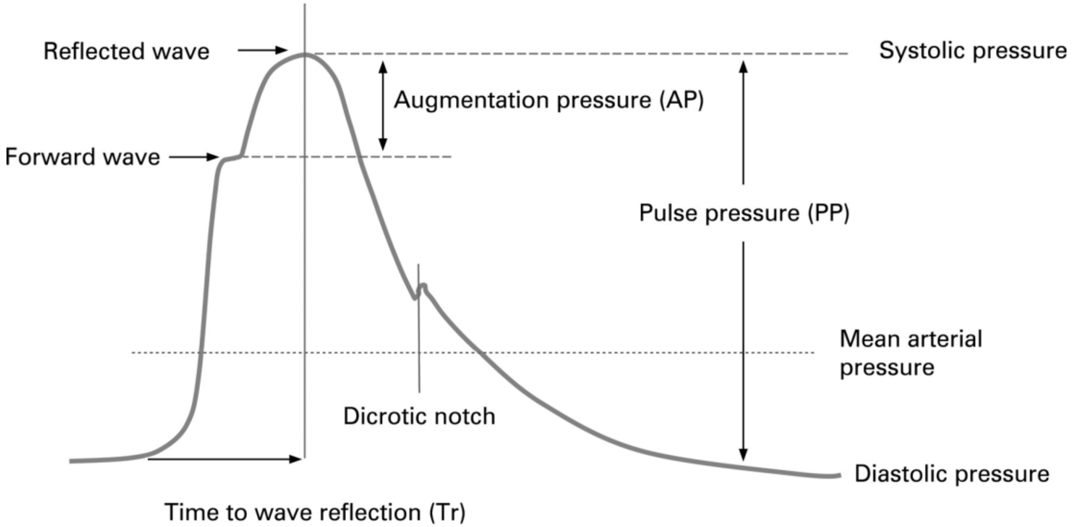
SBP_br

DBP_br

PWV_br

→

AP (aortic)
PP (aortic)


Reflected wave
Systolic pressure
Augmentation pressure (AP)
Forward wave
Pulse pressure (PP)
Mean arterial pressure
Dicrotic notch
Diastolic pressure
Time to wave reflection (Tr)

epochs	batches	layers	nodes in a layer	**RMSE_AP**	**RMSE_PP**
250	100	5	15	**0.2**	**0.8**

Input parameters:

age

HR

SV

LVET

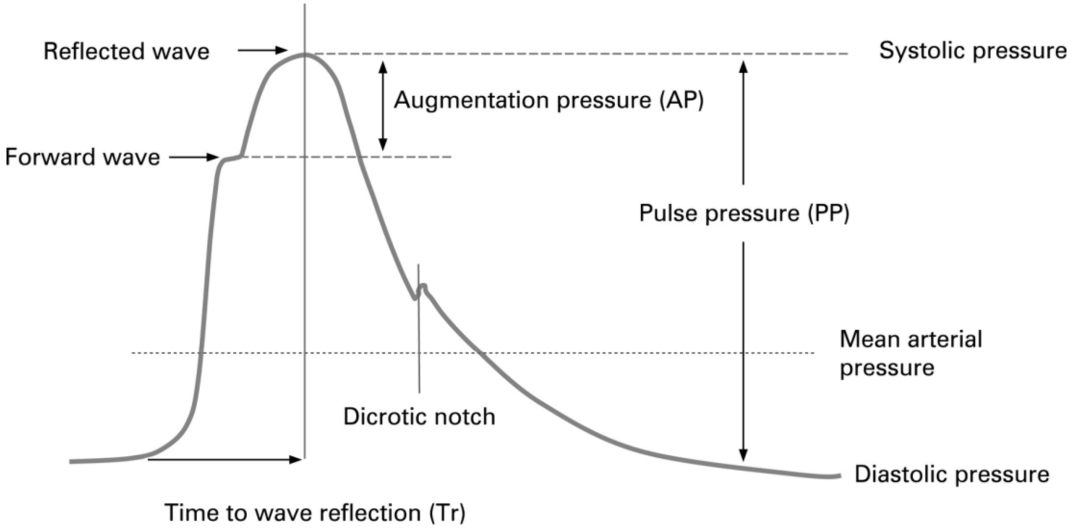
SBP_br

DBP_br

PWV_br

→

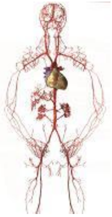
AP
(aortic)
PP
(aortic)

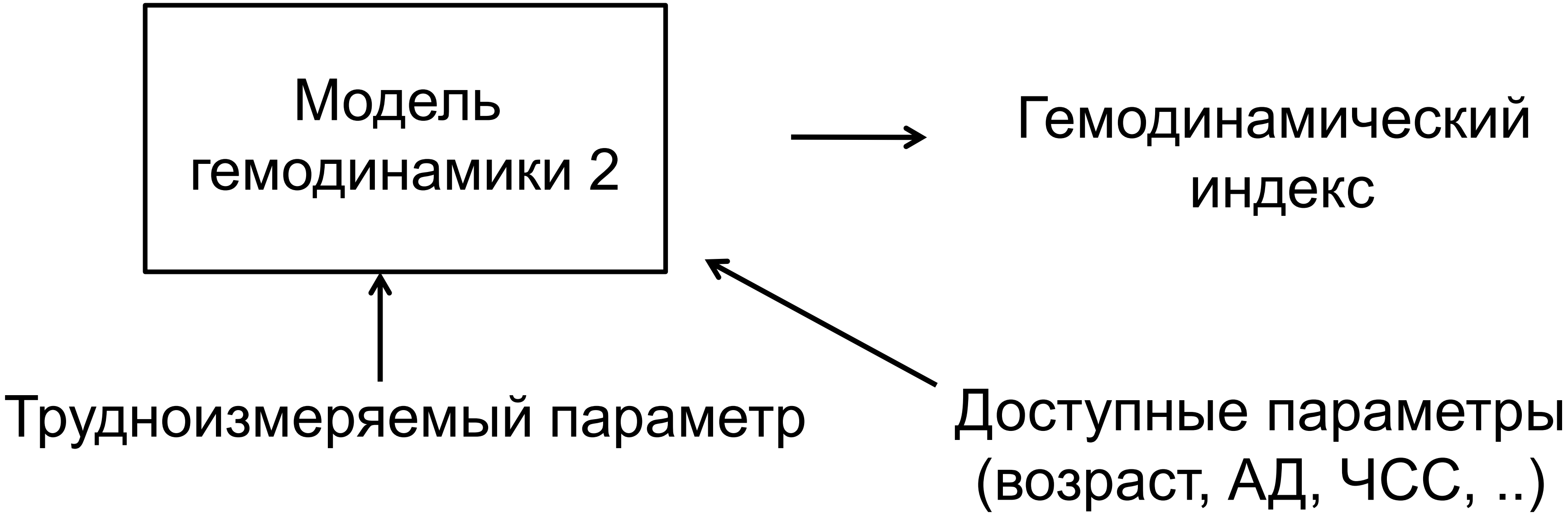

Reflected wave
Systolic pressure
Augmentation pressure (AP)
Forward wave
Pulse pressure (PP)
Mean arterial pressure
Dicrotic notch
Diastolic pressure
Time to wave reflection (Tr)

RMSE_AP	**RMSE_PP**
0.24	**1.7**

	RMSE_max, mm Hg	
Отсутствующий параметр	**AP**	**PP**
None	**0.3**	**0.8**
PWV_br	0.3	1.7
DBP_br	0.4	4
SBP_br	4.8	5.8
LVET	0.3	0.9
SV	0.3	0.9
HR	0.25	1.0
age	0.3	0.9
LVET, SV, HR, age	0.3	2.0
DBP_br, BP_br	6.0	7.0

Идентификация параметров





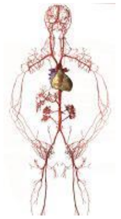
Модель
гемодинамики 2

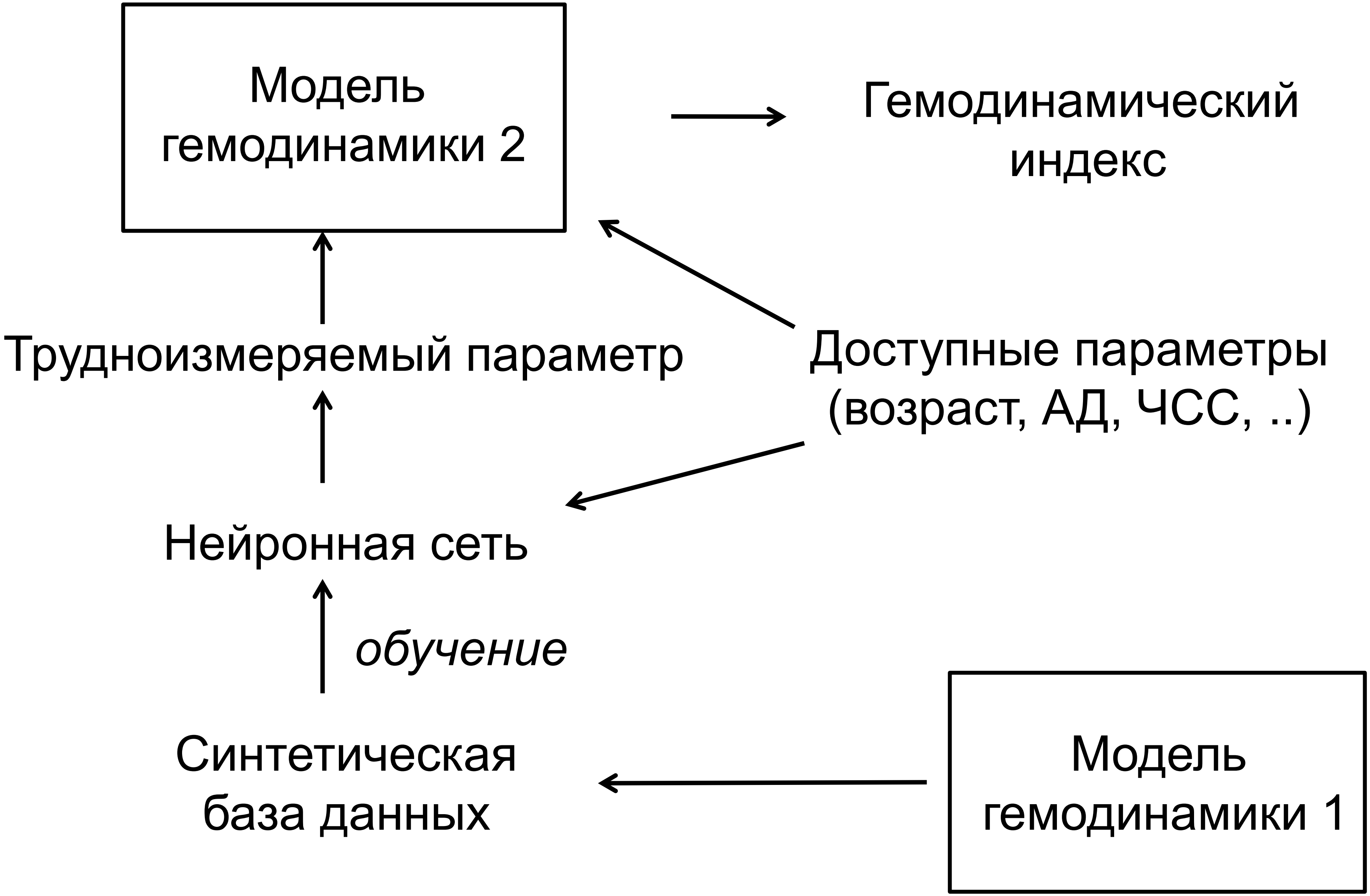
Гемодинамический
индекс

Трудноизмеряемый параметр

Доступные параметры
(возраст, АД, ЧСС, ..)

Идентификация параметров





Модель гемодинамики 2

Гемодинамический индекс

Трудноизмеряемый параметр

Доступные параметры (возраст, АД, ЧСС, ..)

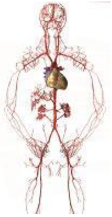
Нейронная сеть

обучение

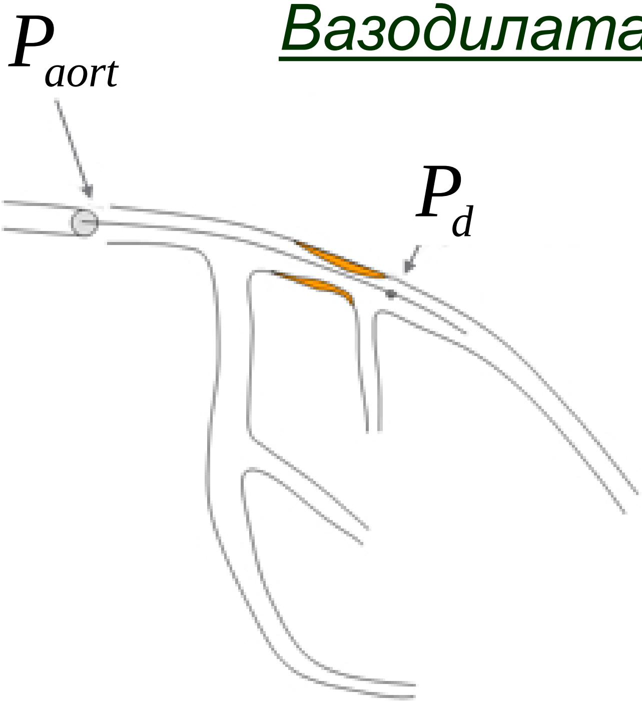
Синтетическая база данных

Модель гемодинамики 1

Фракционный резерв кровотока (FFR)



Вазодилатация



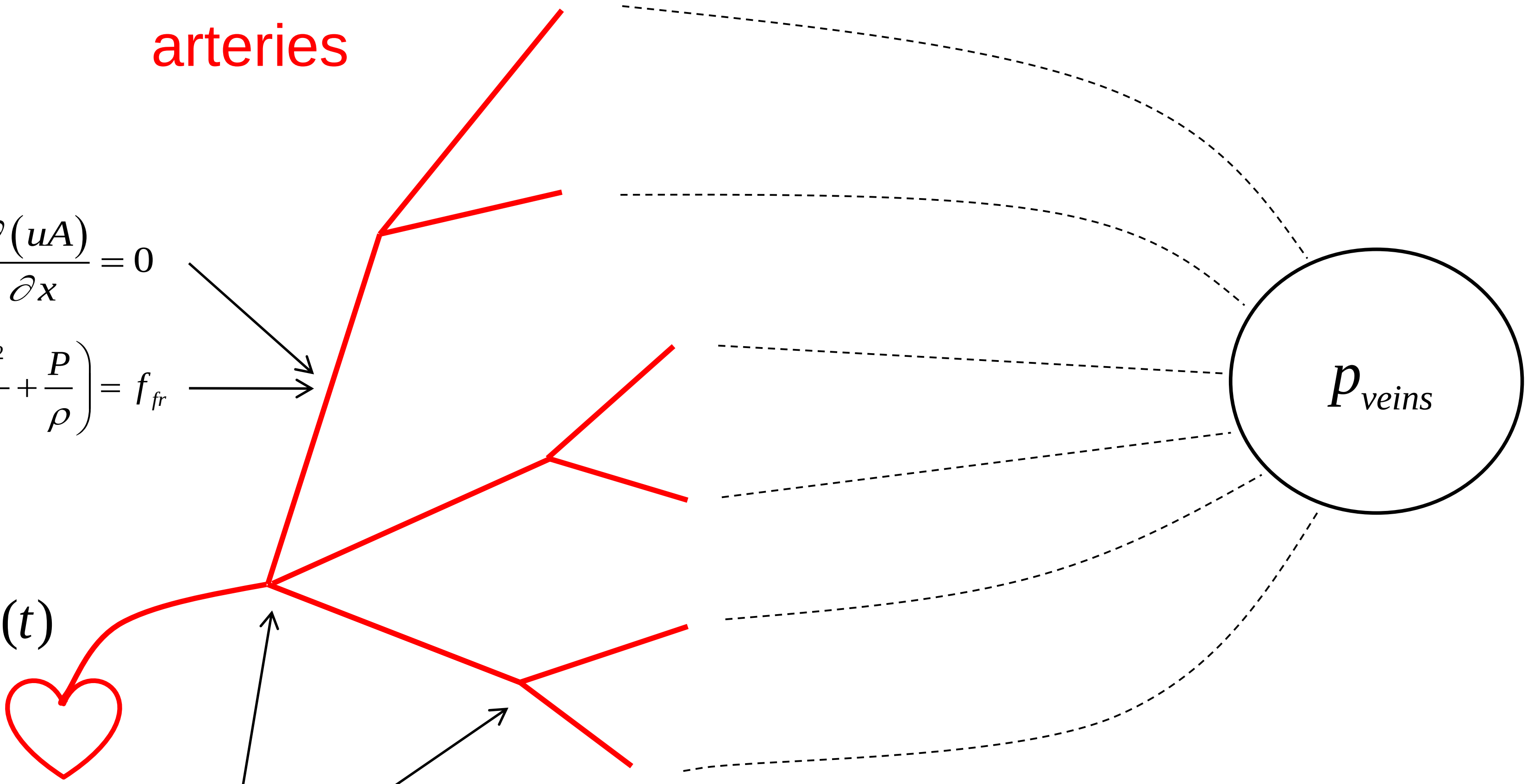
$$FFR = \frac{\text{pressure distal to the lesion } (\overline{P}_d)}{\text{aortic pressure } (\overline{P}_{aort})}$$

$FFR = 1$ ⟶ здоровый человек

$FFR \leq 0.75$ ⟶ необходимо стентирование

Модель коронарного кровообращения

$$p_k - p_{veins} = R_k Q_k$$

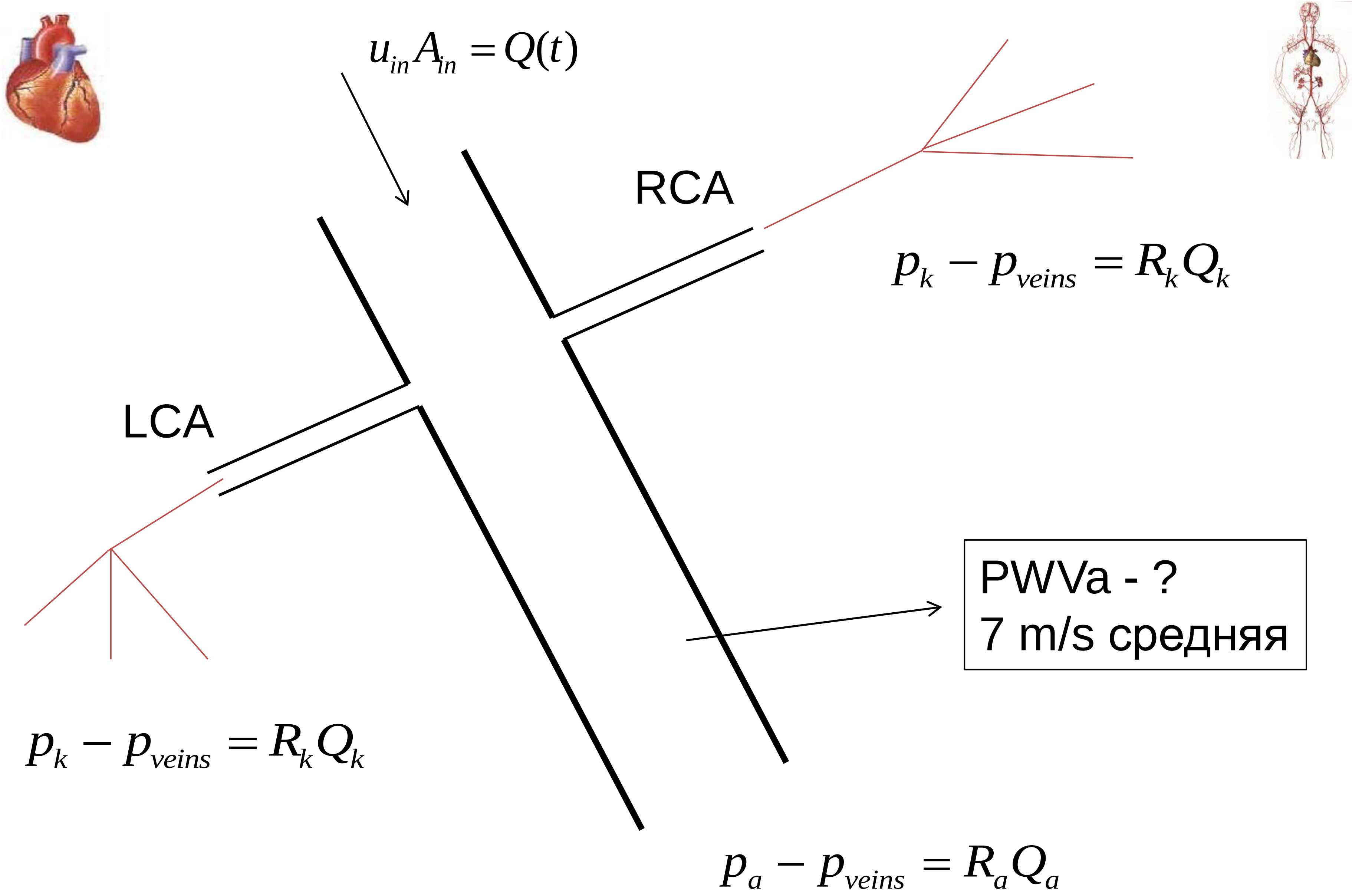


$$\frac{\partial A}{\partial t} + \frac{\partial (uA)}{\partial x} = 0$$

$$\frac{\partial u}{\partial t} + \frac{\partial}{\partial x}\left(\frac{u^2}{2} + \frac{P}{\rho}\right) = f_{fr}$$

$$u_{in} A_{in} = Q(t)$$

$$p_k + \frac{\rho u_k^2}{2} = p_j + \frac{\rho u_j^2}{2}, \quad \forall j, k$$



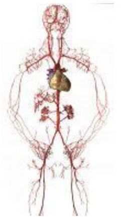
$$u_{in}A_{in}=Q(t)$$

$$p_k-p_{veins}=R_kQ_k$$

PWVa - ?
7 m/s средняя

$$p_k-p_{veins}=R_kQ_k$$

$$p_a-p_{veins}=R_aQ_a$$



Input parameters:

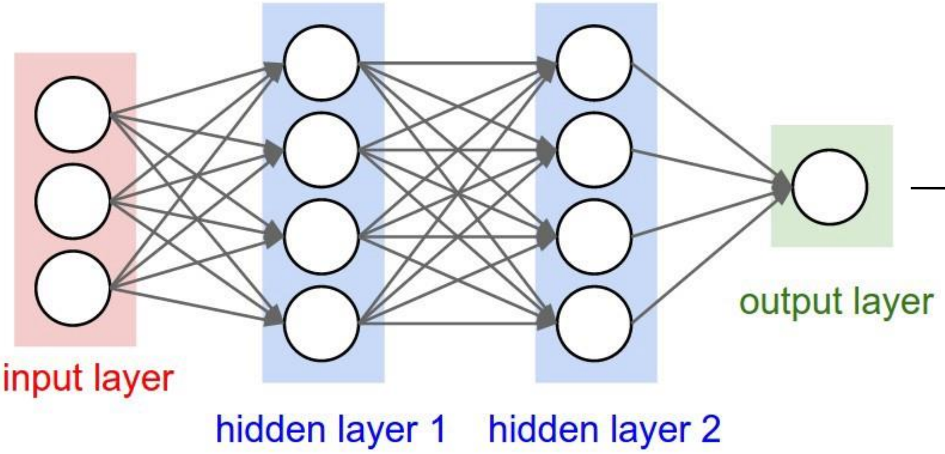
возраст

ЧСС

Ударный объём

MBP (сред. давл. плеч.)

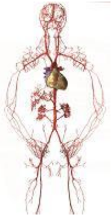
DBP (диаст. давл. плеч.)


input layer
hidden layer 1
hidden layer 2
output layer

PWV
(аорта)

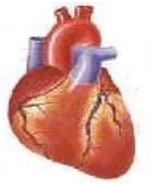
RMSE = 10%

Результаты

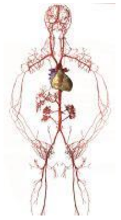


FFR_inv	FFR_ct (PWV = 700 cm/s)	PWV, cm/s	FFR_ct (PWV from NN)
0.89	0.870	970	0.887
0.86	0.863	636	0.858
0.88	0.842	1250	0.884
0.82	0.800	876	0.830
0.82	0.793	730	0.797
0.90	0.986	905	0.988
0.82	0.923	905	0.934
0.81	0.760	905	0.780
0.75	0.911	735	0.917
0.84	0.730	735	0.736
0.88	0.929	780	0.934
0.89	0.935	780	0.939
0.83	0.888	655	0.883
0.72	0.660	1320	0.760
	RMSE = 0.072	**RMSE = 50**	**RMSE = 0.071**

Сеченовский
Университет



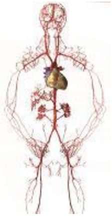
Факторы, влияющие на FFR

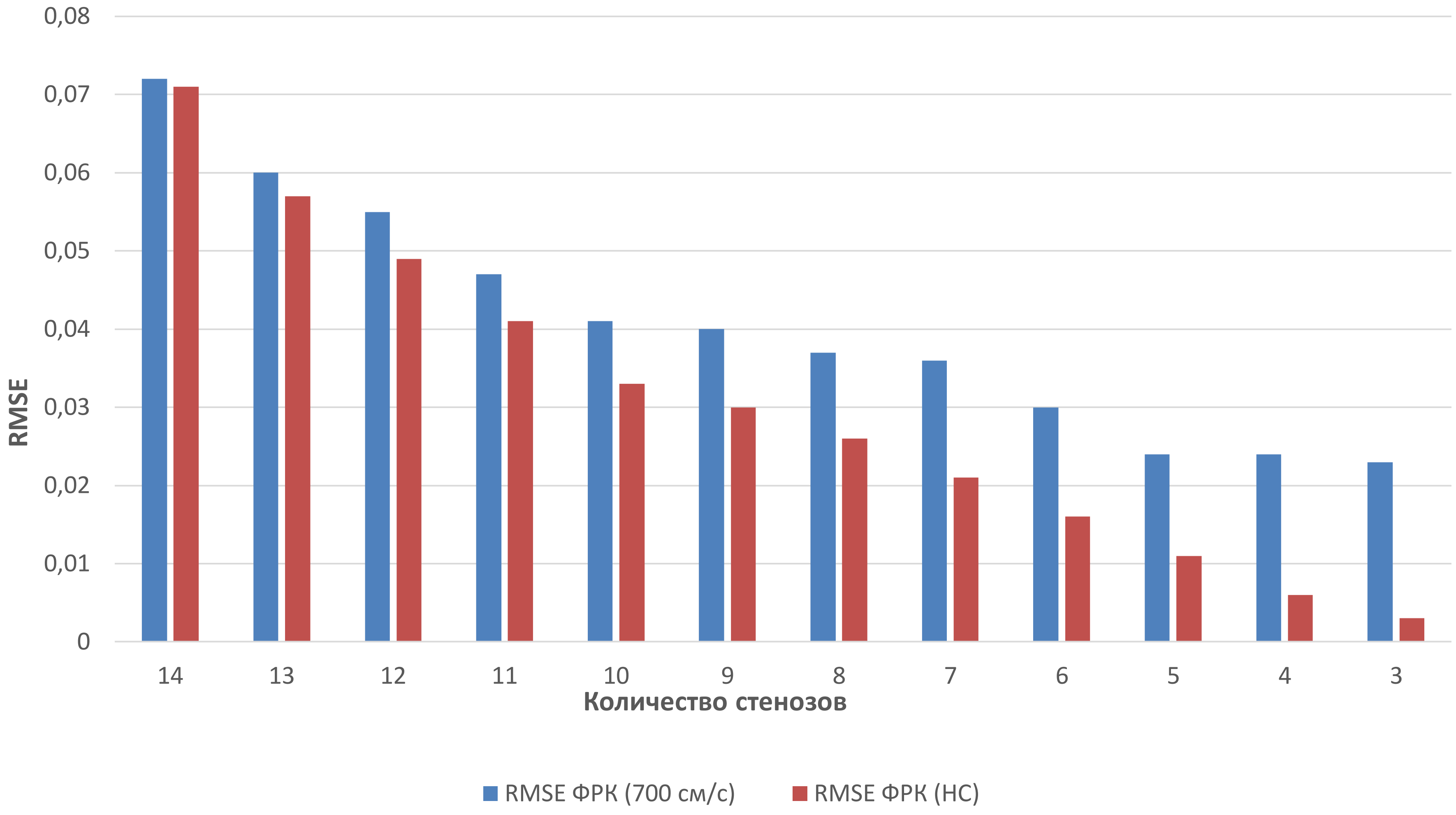


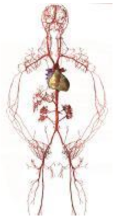
1. Геометрия, степень стеноза

2. Сердечный выброс, давление, PWV

Исключение случаев



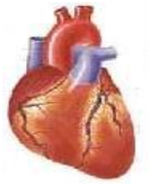




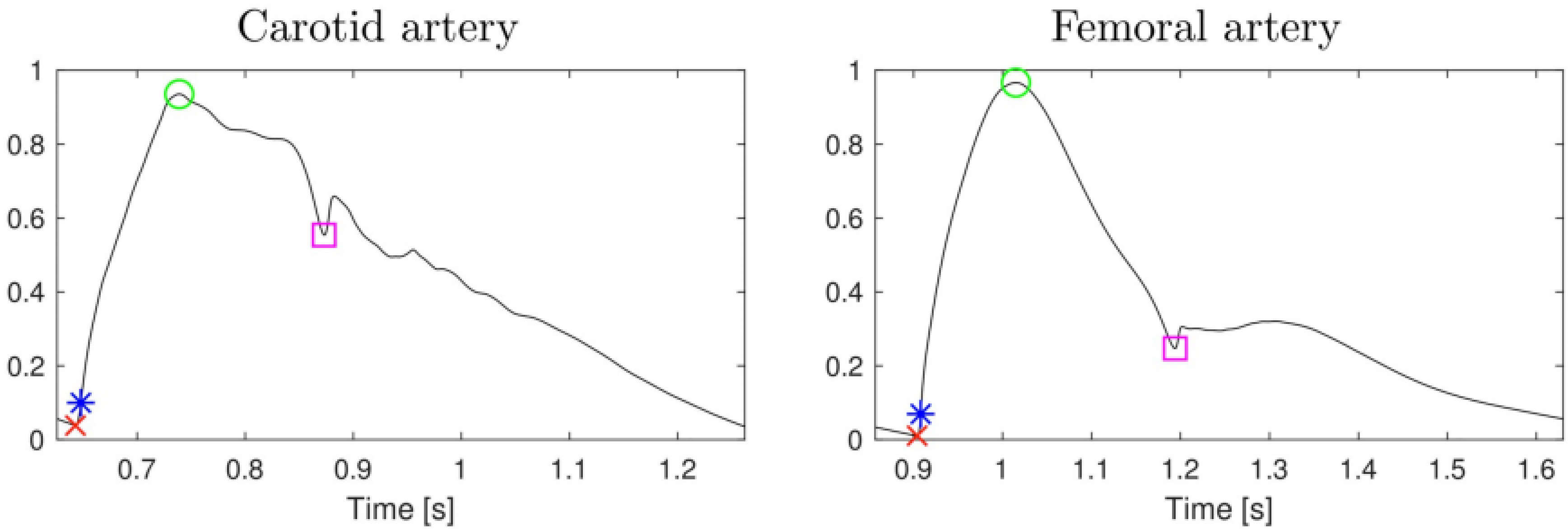
Спасибо за внимание

gamilov@crec.mipt.ru

Машинное обучение и синтетические базы данных в гемодинамике

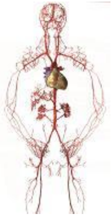


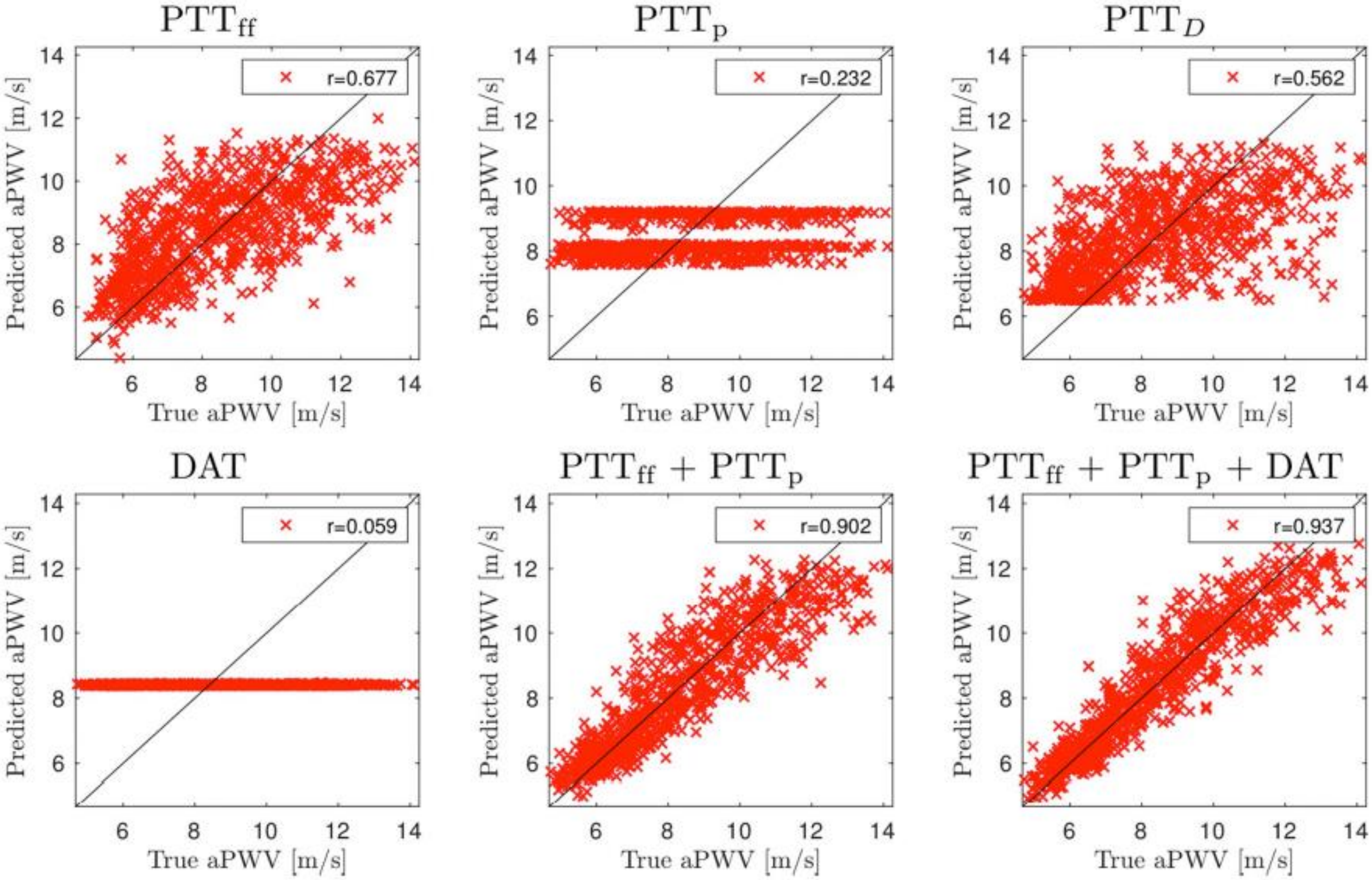
Обзор



Janne M. J. HuttunenI, Leo Karkkainen, Harri Lindholm. *Pulse transit time estimation of aortic pulse wave velocity and blood pressure using machine learning and simulated training data*, 2019

Обзор

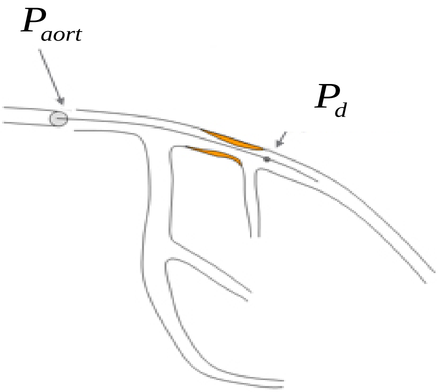




Janne M. J. HuttunenI, Leo Karkkainen, Harri Lindholm. *Pulse transit time estimation of aortic pulse wave velocity and blood pressure using machine learning and simulated training data*, 2019

Обзор

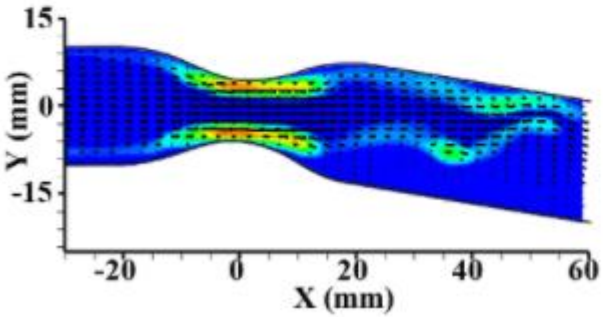
$$\mathrm{FFR} = \frac{\text{Pressure distal to stenosis}}{\text{Pressure proximal to stenosis}}$$



Стеноз:

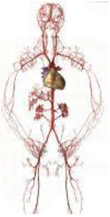
$$\Delta P_{\mathrm{3D}} = a_{\mathrm{3D}} Q + b_{\mathrm{3D}} Q^2 \,.$$

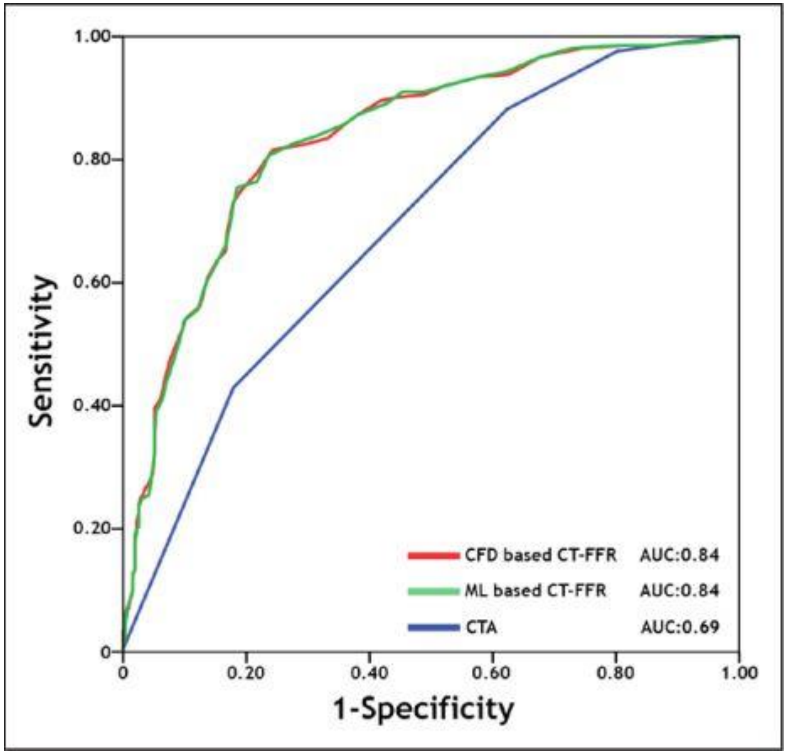
База данных 3D стенозов:
756 стенозов и 7532 перепада давления

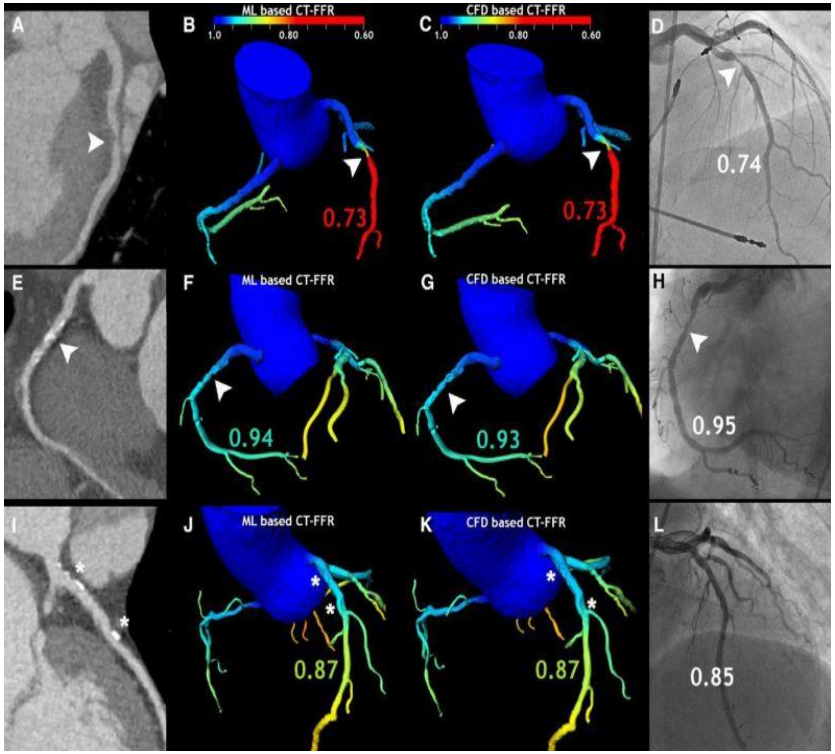


Источник: “Combining reduced-order models and deep learning for fast and accurate Fractional Flow Reserve prediction”, L.O. Muller

Обзор

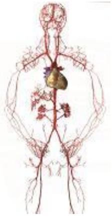


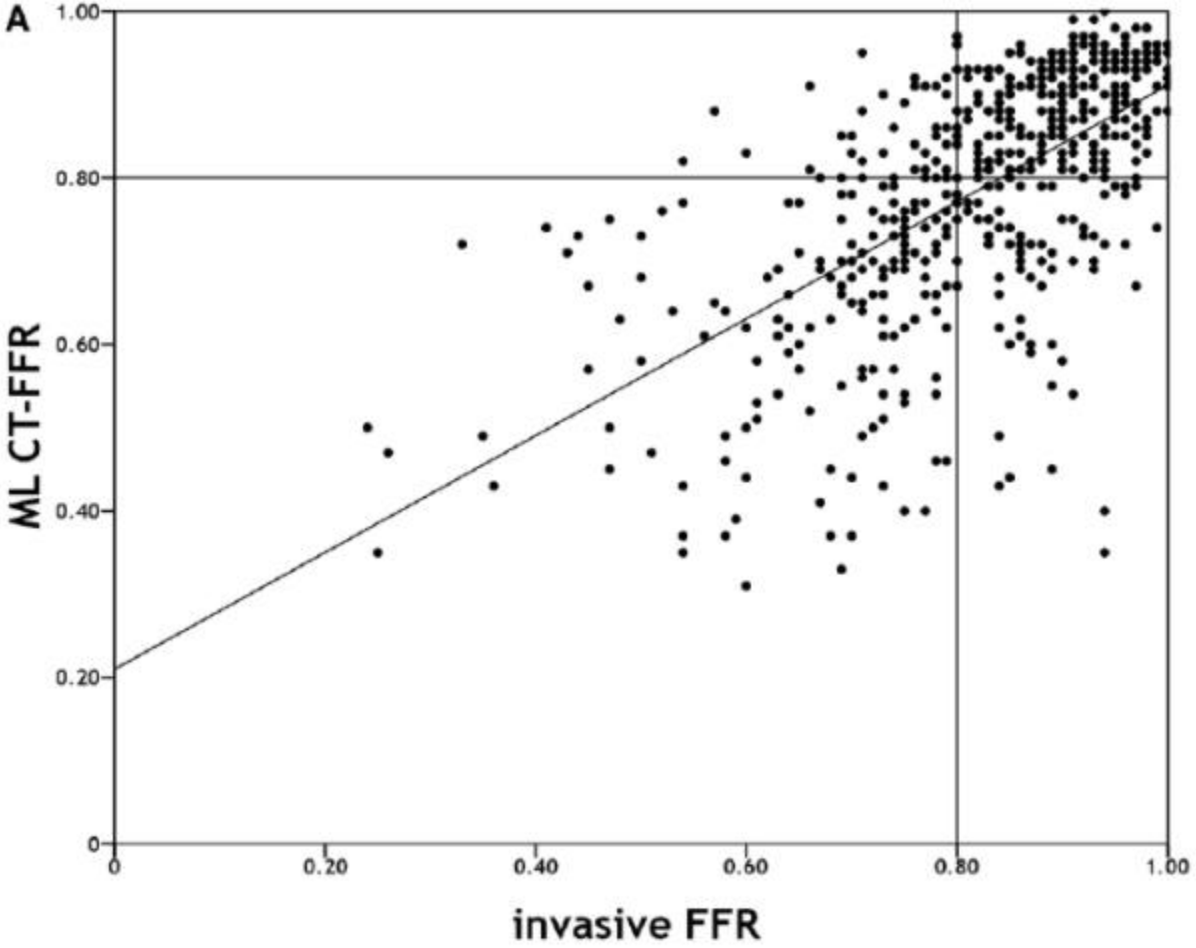



A
B
ML based CT-FFR
1.0
0.80
0.60
0.73
C
CFD based CT-FFR
1.0
0.80
0.60
0.73
D
0.74
E
F
ML based CT-FFR
0.94
G
CFD based CT-FFR
0.93
H
0.95
I
*
*
J
ML based CT-FFR
*
*
0.87
K
CFD based CT-FFR
*
*
0.87
L
0.85

Adriaan C, MD “Diagnostic Accuracy of a Machine-Learning Approach to Coronary Computed Tomographic Angiography-Based Fractional Flow Reserve”

Обзор





Adriaan C, MD “Diagnostic Accuracy of a Machine-Learning Approach to Coronary Computed Tomographic Angiography-Based Fractional Flow Reserve”