

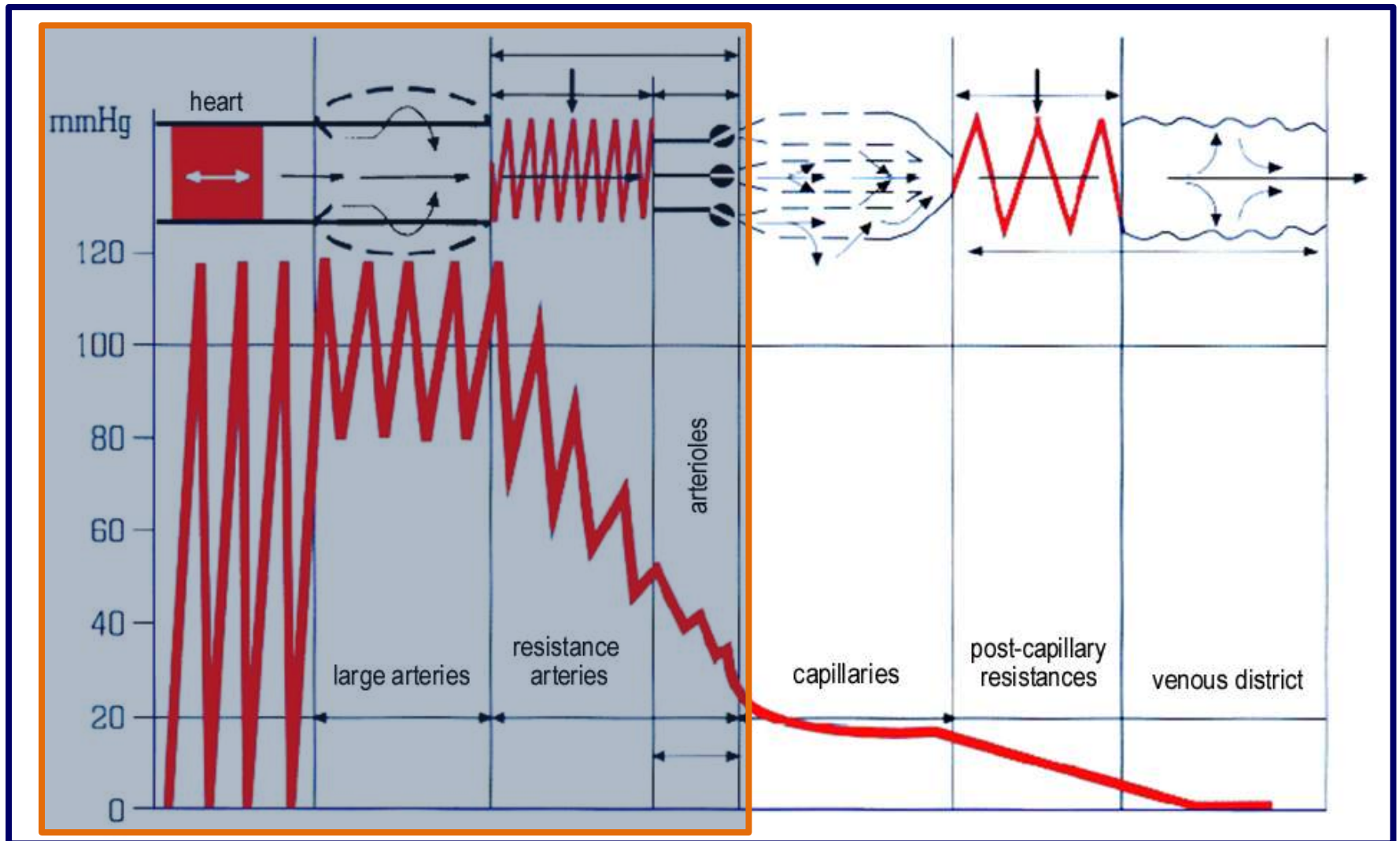
Alterazioni vascolari: nuove metodologie di studio e nuovi farmaci



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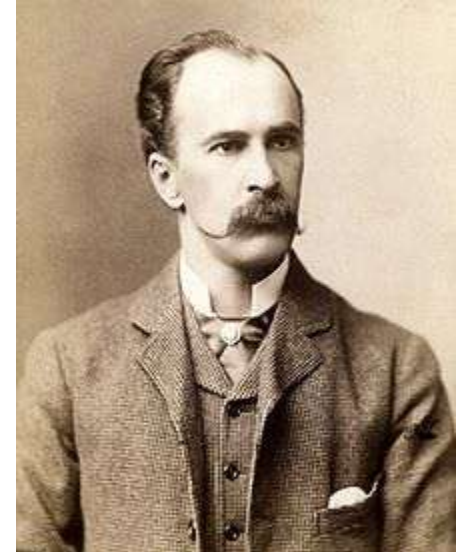
The Cardiovascular System



Laboratorio per lo studio del macrocircolo

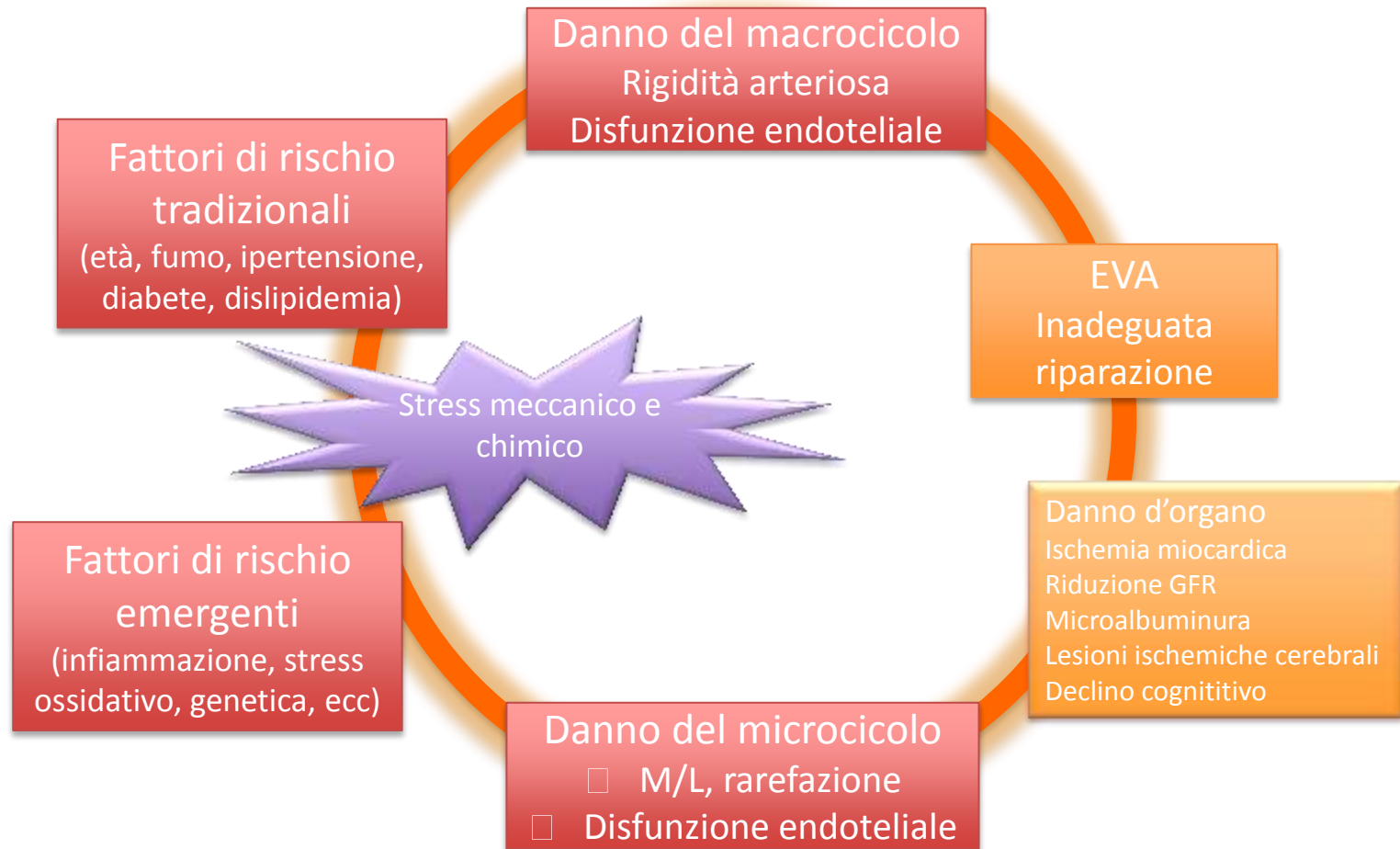
Responsabile: Dr.Lorenzo Ghiadoni

“A man is as old as his arteries”



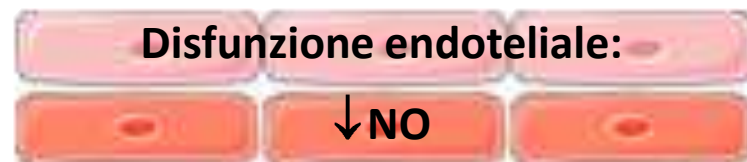
William Osler
The Principles and Practice of Medicine. 3rd edition.
New York, NY: Appleton, 1898.

Early Vascular Aging (EVA)



Possibile uso dei biomarcatori vascolari basati su “imaging”

- Stratificazione del rischio cardiovascolare
- End-points surrogati in trials clinici
- Valutazione il rischio di patologie non cardiovascolari e di fattori emergenti
- Studi di fisiopatologia



Limiti delle metodiche attualmente in uso

- Operatore-dipendente
- Risultati non sempre affidabili
- Scarsa riproducibilità

Carotid stiffness and intima – media thickness by echotracking



European Heart Journal
doi:10.1093/eurheartj/ehs380

CLINICAL RESEARCH

Reference intervals for common carotid intima-media thickness measured with echotracking: relation with risk factors

Lian Engelen^{1,2*}, Isabel Ferreira^{2,3}, Coen D. Stehouwer², Pierre Boutouyrie¹, and Stéphane Laurent^{1*}, on behalf of the Reference Values for Arterial Measurements Collaboration[†]

¹Department of Pharmacology, and INSERM UMR5163 Hospital European Georges Pompidou, Paris, France; ²Department of Internal Medicine and CAMH School for Cardiovascular Diseases, Maastricht University Medical Centre, Maastricht, The Netherlands; and ³Department of Clinical Epidemiology and Medical Technology Assessment, Maastricht University Medical Centre, Maastricht, The Netherlands

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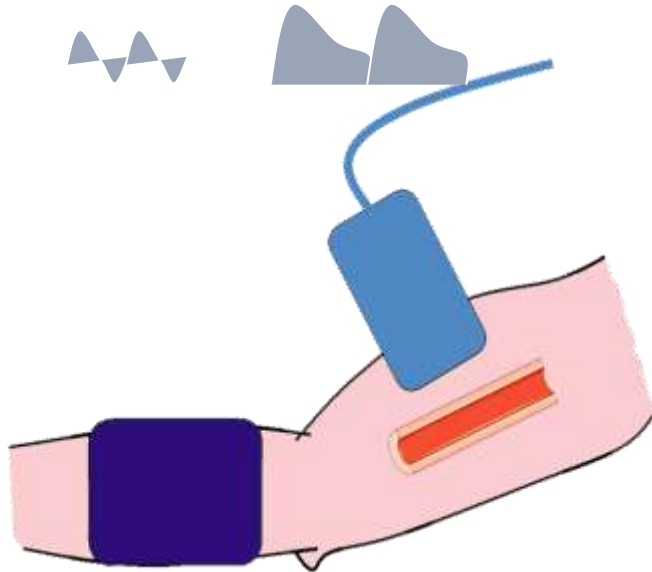
Automated analysis of B-mode ultrasound images
(*Carotid Studio*, CV suite)



Endothelial function: Flow-Mediated Dilation

Endothelium-dependent stimulus

↑ shear stress = post-ischemic flow
(Reactive Hyperemia) to 5 min. ischemia



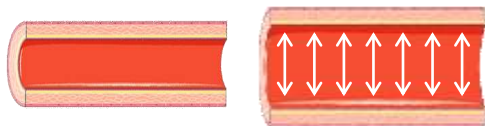
Automated analysis of B-mode ultrasound images
(*FMD Studio*, CV suite)

Ghiadoni L et al. *Curr Pharm Des* 2008



Endothelium-dependent response

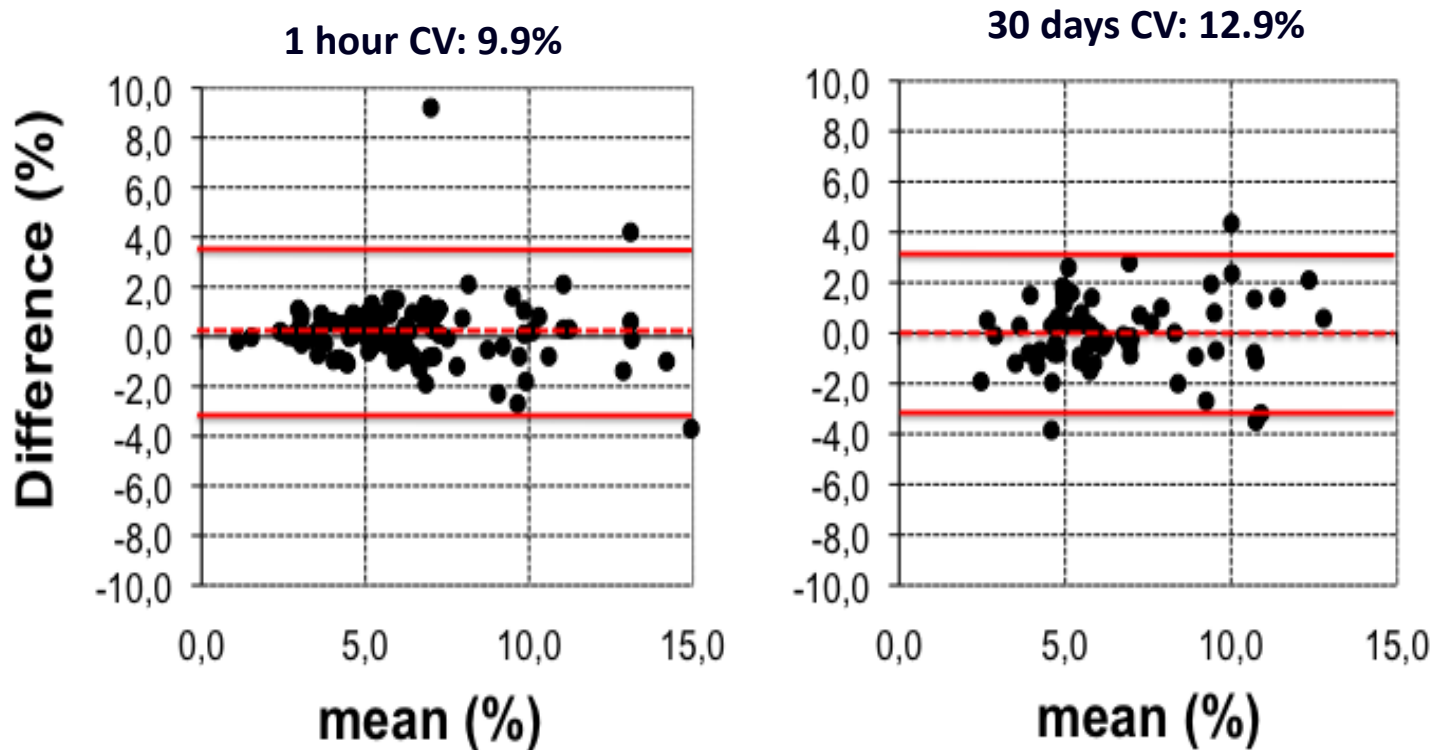
↑ Diameter following Reactive Hyperemia



Gemignani V et al. *Ultrasound Med & Biol* 2007

Assessment of flow-mediated dilation reproducibility: a nationwide multicenter study

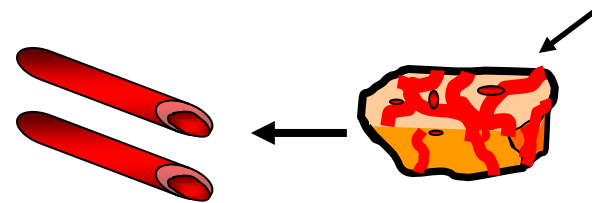
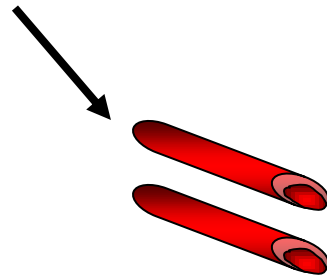
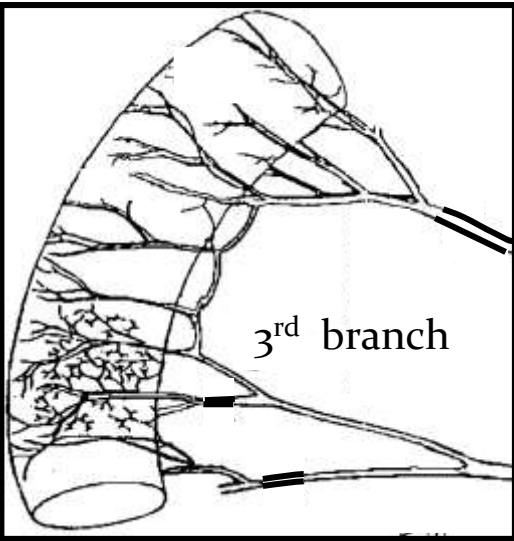
Lorenzo Ghiadoni^a, Francesco Faita^b, Massimo Salvetti^c, Carlo Cordiano^d, Almerina Biggi^e, Massimo Puato^f, Antonio Di Monaco^g, Luca De Siani^h, Massimo Volpe^{h,i}, Giuseppe Ambrosio^d, Vincenzo Gemignani^b, Maria L. Muiasan^c, Stefano Taddei^a, Gaetano A. Lanza^g, and Francesco Cosentino^h



Laboratorio per lo studio del microcircolo

Responsabile: Dr. Agostino Viridis

Studio dei piccoli vasi (micromiografo a pressione)

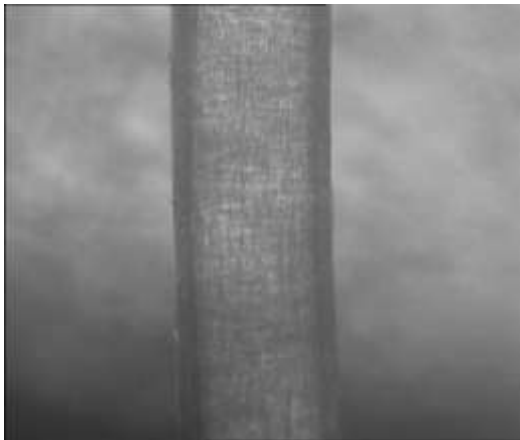
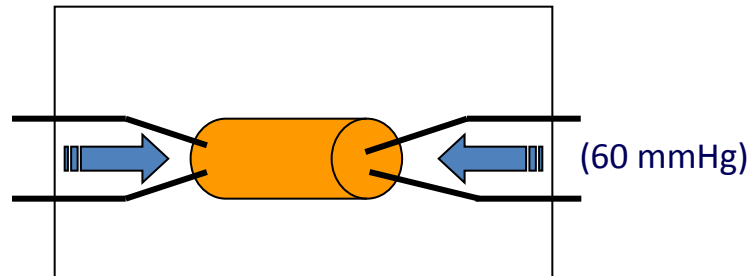


Gluteal subcutaneous biopsy

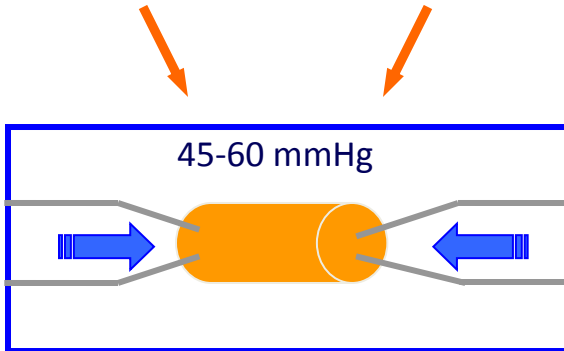
Mesenteric artery
(150 ~350 μm)

Peripheral resistance artery
(150 ~350 μm)

Isobaric (pressure myograph)



Miografo a pressione - Metodi



Peripheral resistance artery
(lumen \varnothing : 150-300 μm)

Studio della funzione endoteliale:

- Acetilcolina
- Nitroprussiato di Sodio

Studio dei meccanismi coinvolti:

COX-1 , COX-2 : SC-560, Dup 697 (COX-1 e COX-2 inibitori)

TP recettori: SQ 29548 (TP antagonista)

NO: L-NMMA (NOS inibitore)

ROS: Vitamin C, Tempol (antiossidanti)

Parametri strutturali:

misura delle dimensioni lume e tonaca media per calcolo del M/L e di MCSA

Proprietà meccaniche:

strain, stress, modulo elastico incrementale

Resistance arteries in patients at CV risk

Healthy condition

Disease

Hemodynamic:
pressure, flow, cyclic stress



Pathophysiologic
Remodeling

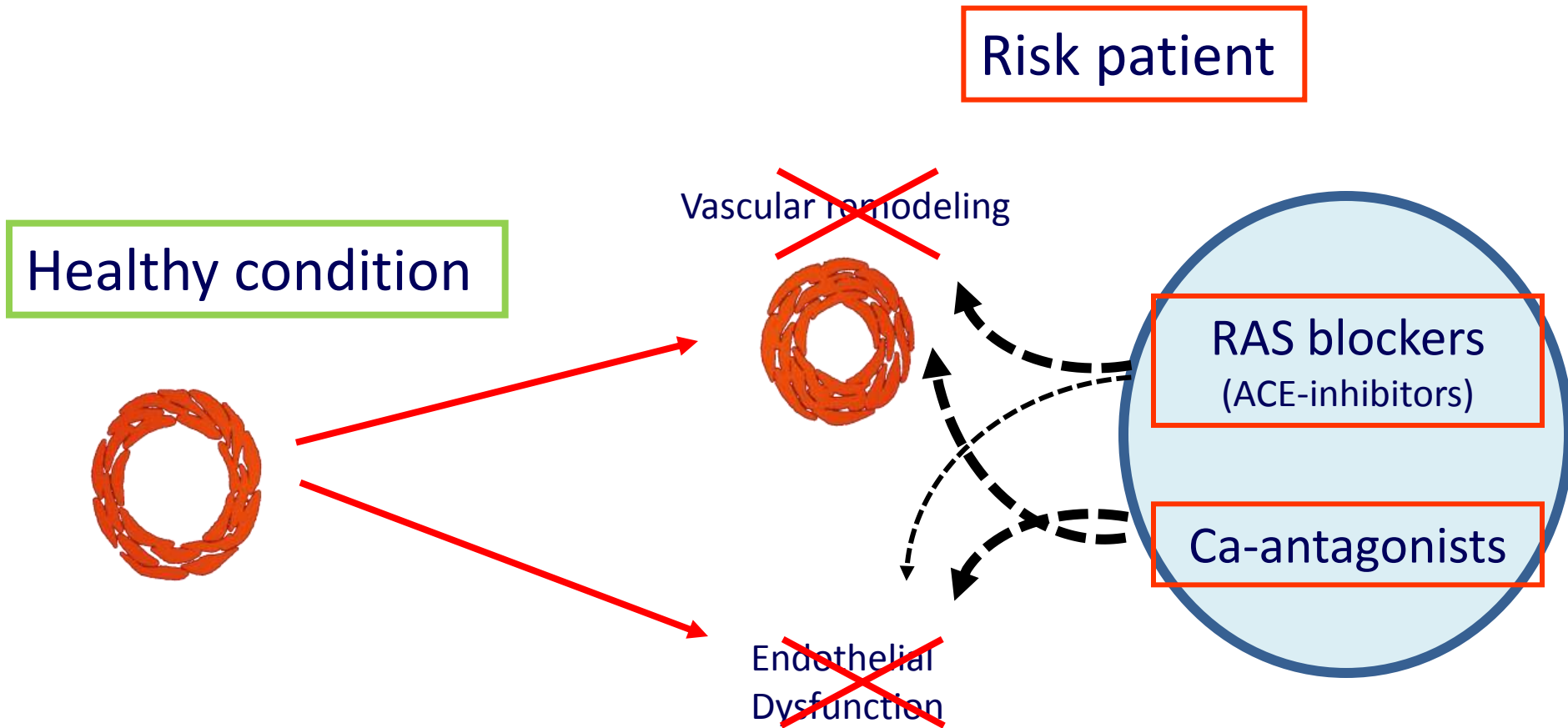
Structure



Extra/intra-cellular stimuli:
Ang II, ET, insulin, inflammation, O_2^-

Endothelial
Dysfunction

Microcirculation in CV risk patients



Lo studio della struttura e della funzione endoteliale può offrire informazioni aggiuntive sull'efficacia prognostica del nostro intervento terapeutico.

Future development of new compounds

Programma per la Ricerca Regionale in Materia di Salute 2009
Regional Health Research Program 2009

Pathophysiological role of H₂S in the cardiovascular system

evaluation of new pharmacotherapeutic targets
&
development of original drugs active on the
H₂S pathway

RESPONSABILE DEL PROGETTO E TITOLARE DEL FINANZIAMENTO

Dott. Vincenzo Calderone

Sezione di Farmacologia

Dipartimento di Psichiatria, Neurobiologia, Farmacologia e Biotecnologie

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OBIETTIVI DEL PROGETTO

- 1) Disegnare, sintetizzare e valutare le proprietà farmacologiche di nuovi farmaci in grado di agire sul sistema H₂S come:
 - a) donatori esogeni di H₂S
 - b) molecole ibride composte da un farmaco noto (es., sartano) e una frazione in grado di agire come donatrice esogena di H₂S

- 2) Saggiare gli effetti dei nuovi farmaci suddetti su modelli sperimentali di ipertensione, ischemia miocardica, trombosi