Cerebral Small Vessel Disease : *A HISTORY*

THE UNIVERSITY *of* EDINBURGH
Row Fogo Centre for Research into Ageing and the Brain

Small Vessel Diseases Research

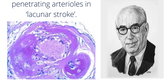
1800 | **1900** | **1980** | **1990** | **2000** | **2010** | **2015** | **2020** | **2025**

1843
Durand-Fardel
'état crible' –
"… disgruntled at the lack of focus on brain tissue at autopsy, especially the interior brain structures…trying to figure out the main features of état crible."

1838
Deschambres, Paris
'Cerebral softenings' and 'lacune'

1902
Ferrand
"Les Lacunes de Désintegration Cérébrale"

1950s - 1960s
C Miller Fisher, Boston, USA
"Segmental arteriolar disorganisation." Meticulous dissections of individual penetrating arterioles in 'lacunar stroke'.



c1970
Stroke Prone Spontaneously Hypertensive Rat (SHRSP) rat model bred

1972
Godfrey Hounsfield co-invents Computed Tomography (CT) with Dr. Allan Cormack

1973
Lauterbur
First MR image: two test tubes of water

1980
First clinical MRI scanners installed

1986
Hachinski et al
"LeAcoAraiosis"or white matter lesions of vascular origin on CT.

1987
Fazekas et al
Fazekas Score to quantify the amount of white matter T2 hypertensities on MRI.

1990s
Lacunes in imaging

1990s
Lammie, Poirier
Four subtypes of lacunar stroke pathology

1991
Bamford et al, Oxford
OCSP stroke subtype clinical classification
LACI, PACI
TACI, POCI

1993
Adams
TOAST; risk factor based stroke classification

1996
Microbleeds

2001
Wardlaw
Abnormal arteriole in lacunar stroke

2001
VasCog
Society forms

2003
Perivascular Spaces

2003
Wardlaw
Blood Brain Barrier hypothesis

c2005
Diffusion Tensor Imaging (DTI) reveals underlying white matter structure

2006
Hachinski
NINDS-CSN Vasc cognitive impairment tests

2007
Bailey
SHRSP models SVD

2007
International Stroke Genetics Consortium

2009
Potter et al
Visual PVS

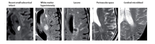
2010
BBB abnormal in SVD

2011
Genetics – large studies of WMH and lacunar stroke eg CHARGE consortium

2011 - 2013
SHRSP predisposition to SVD not just HT

2012
SPS3 (Secondary Prevention of Small Subcortical Strokes)Trial

2013
STRIVE-1 (STandards for Reporting Vascular changes on nEuroimaging)



c2014
CVR abnormal in SVD

2015
Staals et al
Total SVD Score

2016
Duering
PSMD

2016
METACOHORTS for the study of vascular disease and its contribution to cognitive decline and neurodegeneration

2017
STROKOG (Stroke and Cognition Consortium)

2017
SVDs@TARGET (Small vessel diseases in a mechanistic perspective: Targets for InterventionAffected pathways and mechanistic exploitation for prevention of stroke and dementia)

2017
INVESTIGATE@SVDs (Imaging NeuroVascular, Endothelial and STructural InteGrity in prepAration to TrEat Small Vessel Diseases)

2017
Rogers
SHRSP ATP11B gene defect

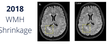
2018
Hachinski
"The commonest manifestation of cerebrovascular disease is cognitive impairment, not stroke"

2018
MARK-VCID (Biomarkers for Vascular Contributions to Cognitive Impairment and Dementia)

2018
Ballerini et al
PVS Computational Measures

2018
PRESERVE Trial (Randomized Trial of Intensive Versus Standard Blood Pressure Control in Small Vessel Disease)

2018
WMH Shrinkage



2019
SHRSP / defect identified

2019
MICON microbleeds consortium

2019
META-VCI Map

2019
HARNESS (HARmoNizing Brain Imaging MEthodS for VaScular Contributions to Neurodegeneration)

2019
LACI-1 (LACunar Intervention-1)

2019
SPRINT-MIND (Systolic Blood Pressure Intervention Trial Memory and Cognition in Decreased Hypertension)

2020
International PVS Collaboration

2020
Perivascular spaces in small-vessel disease

2021
ESO Guideline on covert cerebral small vessel disease Part 1

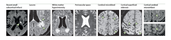
2021
ZOOM@SVDs (Zooming in on cerebral small vessel function in small vessel diseases with 7T MRI)

2021 - 2022
Quick ATP11B Knock Out Rat

2018 - 2024
R4VaD (Rates, Risks & Routes to Reduce Vascular Dementia)

2022
FINESSE (Framework for Clinical Trials in Cerebral Small Vessel Disease) SVD Trials Guidance

2023
STRIVE-2 (STandards for Reporting Vascular changes on nEuroimaging)



2023
LACI-2 (LACunar Intervention-2)

2023
TREAT@SVDs (The EffecTs of Amlodipine and other Blood PREssure Lowering Agents on Microvascular FunCTion in Small Vessel Diseases)

2024
ESO Guideline on covert cerebral small vessel disease Part 2

2025 - 2029
LACI-3 (LACunar Intervention-3)

Pink - Preclinical studies
Black – Pathology studies
Green – Clinical studies
Orange – Randomised trials
Blue – Imaging (CT or MRI) studies
Violet – Large scale consortia studies