

# Nanoparticle oxygen carriers and stroke – from diagnosis to treatment

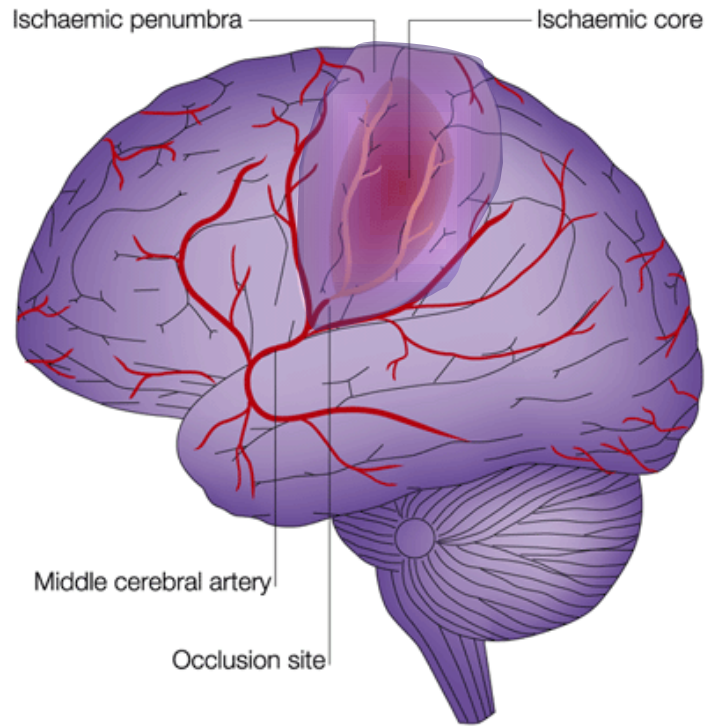
**I Mhairi Macrae**

***Institute of Neuroscience & Psychology  
College of Medicine, Veterinary and Life Sciences***



# The importance of Penumbra in stroke:

## Diagnostic & Therapeutic target



Nature Reviews | Neuroscience

The penumbra has a finite life span

Over a matter of hours,  
tissue will either  
become incorporated  
into the infarct

**OR**

if blood flow is restored  
may recover normal function

Stroke patients who show evidence of a penumbra are most likely to benefit from acute therapy (e.g. thrombolytic tPA or mechanical thrombectomy)

**Currently no practical & accurate diagnostic technique  
to identify viable tissue capable of recovery “Metabolic Penumbra”.**

**GOLD:** an i.v oxygen carrier (Oxycyte) combined with normobaric hyperoxia provides:



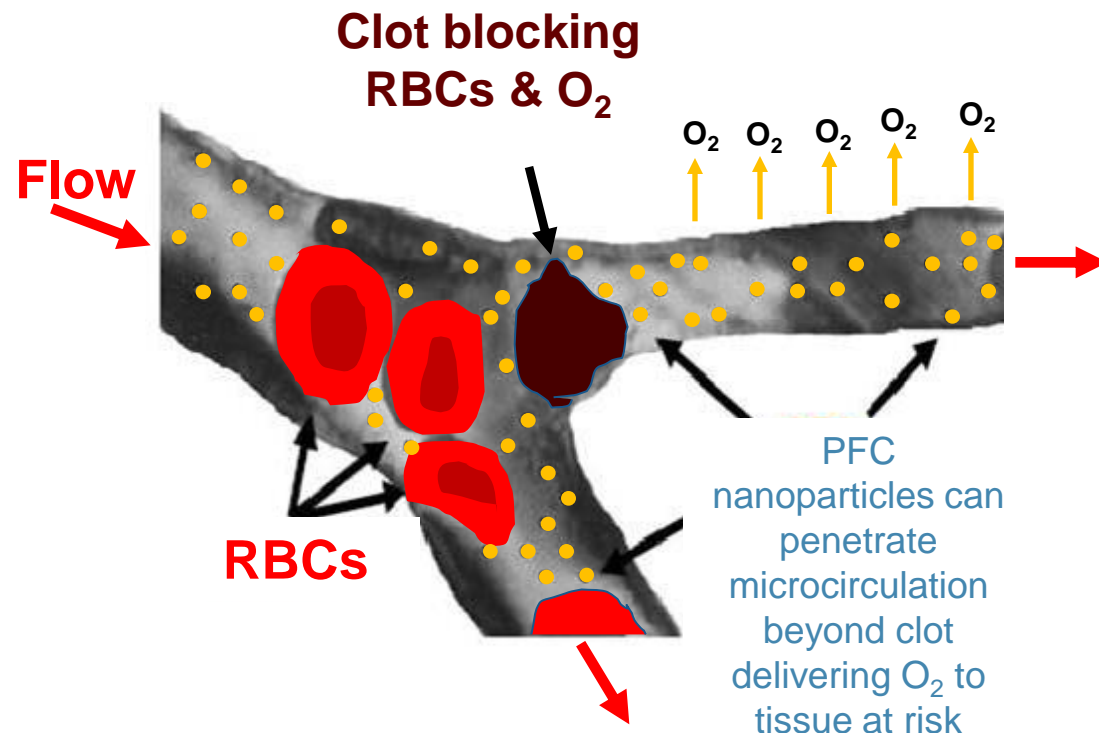
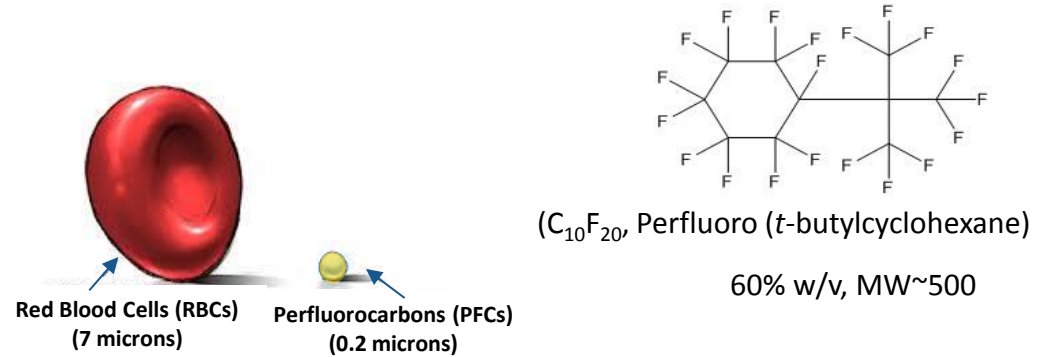
a) **DIAGNOSTIC:** MRI contrast for metabolic brain imaging  
to identify penumbra

1. T2\*OC: BOLD based; different magnetic properties of oxy- & deoxyhaemoglobin
2. Lactate Change: Dynamically images changes in tissue Lactate levels in response to Oxycyte+hyperoxia

a) **THERAPEUTIC:** Enhanced oxygen delivery to penumbra  
promotes recovery

# Oxycyte: Improves Oxygen Delivery to Ischaemic Tissue Independent of RBCs

- Oxycyte carries **4x** more  $O_2$  than RBCs
- Nanoparticles, **35-45x** smaller than RBC
- Metabolically inert
- Oxycyte is well tolerated with no genotoxicity
- Oxycyte has gained regulatory approval for clinical trials
- Recent Phase 2 Traumatic Brain Injury study

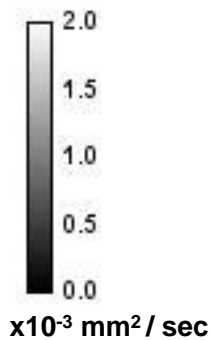
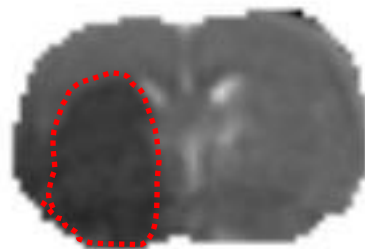


# Complementary Diagnostic Value: T2\*OC & Lactate Change simultaneously Identify Penumbra

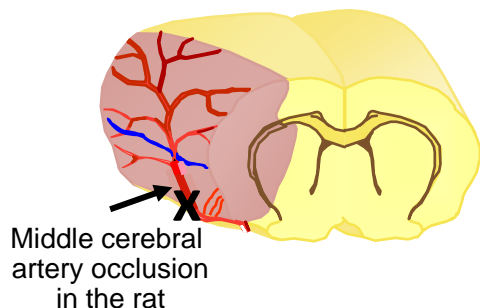
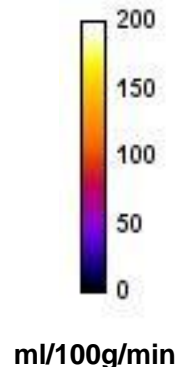
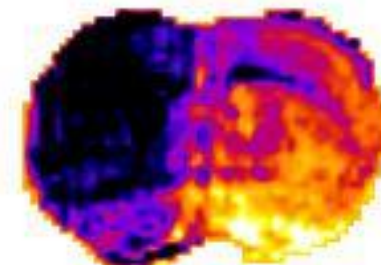
Scans from one rat following Oxycyte + hyperoxia



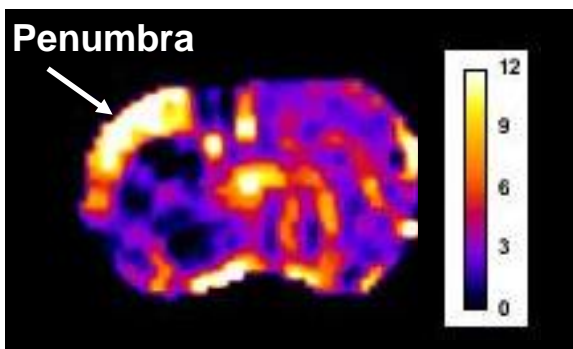
ADC map showing acute lesion



ASL map showing reduced CBF

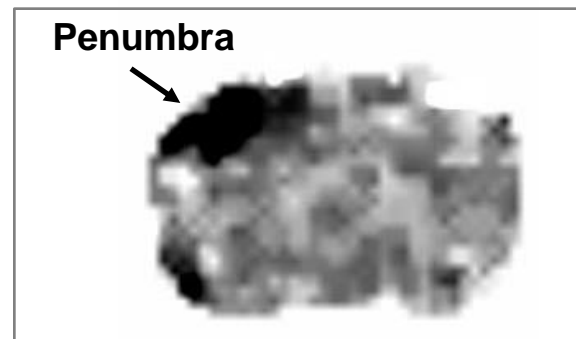


T2\*OC

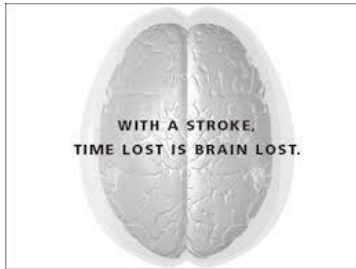


T2\* signal change (%) map identifying penumbra

Lactate Change



Aerobic Lactate Change map identifying penumbra



Brain damage associated with occlusive stroke occurs over ~ a 10 hour timeframe

If left untreated, a patient will lose:-

1.9 million neurones  
13.8 billion synapses and  
7 miles of axonal fibres } every  
minute

## Oxycyte + Hyperoxia slows acute lesion growth

Data removed as unpublished  
and could influence patent

from Saver, JL Time is brain - quantified,  
*Stroke* (2006) **37**, 263-266.

Diagnosis using GOLD reduces the penalty of time required for brain imaging  
by preventing further ischaemic brain damage.

- Intraluminal filament rat model of middle cerebral artery occlusion (60 mins MCAO)
- Treatment started 10mins prior to reperfusion: Hyperoxia (50% O<sub>2</sub>) maintained for 48hrs in ICU.
- Rats randomised to one of 4 groups. Infarct Size measure at 1 week using T2 MRI scan

**Reduced Infarct Volume &  
improved neurological score with Oxycyte. + hyperoxia**

Data removed as unpublished and could influence patent

- **GOLD offers unique benefits through its simultaneous diagnostic and therapeutic application in acute ischaemic stroke.**
- **Diagnostically providing clinicians with a single stratified measure of tissue viability irrespective of time from stroke onset.**
- **Therapeutically supporting survival of penumbra by improving oxygen delivery using the perfluorocarbon-based oxygen carrier Oxycyte plus hyperoxia.**

**Oxycyte + Hyperoxia could represent a safe, easily administered theranostic in the Acute Ischaemic Stroke setting.**



Stroke 

AMERICAN  
Heart  
Association

 frontiers  
in Neuroscience

REVIEW  
published: 29 April 2015  
doi: 10.3389/fnins.2015.00147

## Topical Review

### Functional Role of Regulatory Lymphocytes in Stroke Facts and Controversies

Arthur Liesz, MD; Xiaoming Hu, MD, PhD; Christoph Kleinschnitz, MD; Halina Offner, MD

### Rational modulation of the innate immune system for neuroprotection in ischemic stroke

Diana Amantea<sup>1\*</sup>, Giuseppe Micieli<sup>2</sup>, Cristina Tassorelli<sup>2,3</sup>, Maria I. Cuartero<sup>4</sup>,  
Iván Ballesteros<sup>4</sup>, Michelangelo Certo<sup>1</sup>, Maria A. Moro<sup>4</sup>, Ignacio Lizasoain<sup>4</sup> and  
Giacinto Bannetta<sup>1,5</sup>

Immunology  
The Journal of cells, molecules, systems and technologies

British Society for  
immunology 

IMMUNOLOGY REVIEW ARTICLE

### Inflammation in neurodegenerative diseases – an update



Journal of Cerebral Blood Flow & Metabolism (2015) 35, 888–901  
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[www.jcbfm.com](http://www.jcbfm.com)

#### REVIEW ARTICLE

### Targeting neutrophils in ischemic stroke: translational insights from experimental studies

Glen C Jickling, DaZhi Liu, Bradley P Ander, Boryana Stamova, Xinhua Zhan and Frank R Sharp

# Areas for potential collaboration

- Neuroimmunology: a significant research area in stroke acute inflammatory response (IL1-RA), involvement of neutrophils, T cells, B cells, microglia & macrophages cytokines, delayed response linked to cognitive decline (B cells) post-stroke immunodepression, etc.
- Good facilities for in vivo research at WSI
- Expertise in vivo rodent models, management & welfare
- Good physiological monitoring and maintenance of rodents under GA
- MRI
- Specific expertise in cerebral blood flow
- Specific expertise in perfluorocarbon oxygen carriers & oxygen-based therapy

- Dr Graeme Deuchar
- Dr Celestine Santosh
- Dr David Brennan
- Professor Keith Muir
- Dr Chris McCabe
- Dr William Holmes



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