Rural Health and Research Congress

#RHRC2019

Connecting researchers and biospecimens across NSW and beyond

Future of biobanking research today

Associate Professor Murray Killingsworth (NSW Health Pathology)
and
Dr Sonu Bhaskar (Neurology)

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What is Biobanking?

Wikipedia

A biobank is a type of biorepository that stores biological samples (usually human) for use in research. Since the late 1990s biobanks have become an important resource in medical research, supporting many types of contemporary research like genomics and personalized medicine.

- *Resource to enable translation of biomedical research*
- *Diseases: cancer, heart diseases, stroke, diabetes, arthritis, osteoporosis, eye disorders, depression and forms of dementia*
- *Biospecimen samples: tissue, blood, urine, etc.*

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Biobanking collections

- [1]*Generalised collection: pathology based*
- [1]*Targeted collection: organ specific e.g. brain, retina, blood*
- [1,2]*Research question-based collection: NSW Brain Clot Bank*

[1]Important for the study of **rare diseases**: e.g. CADASIL, some childhood cancers, cystic fibrosis

[2]Important for **translational research**

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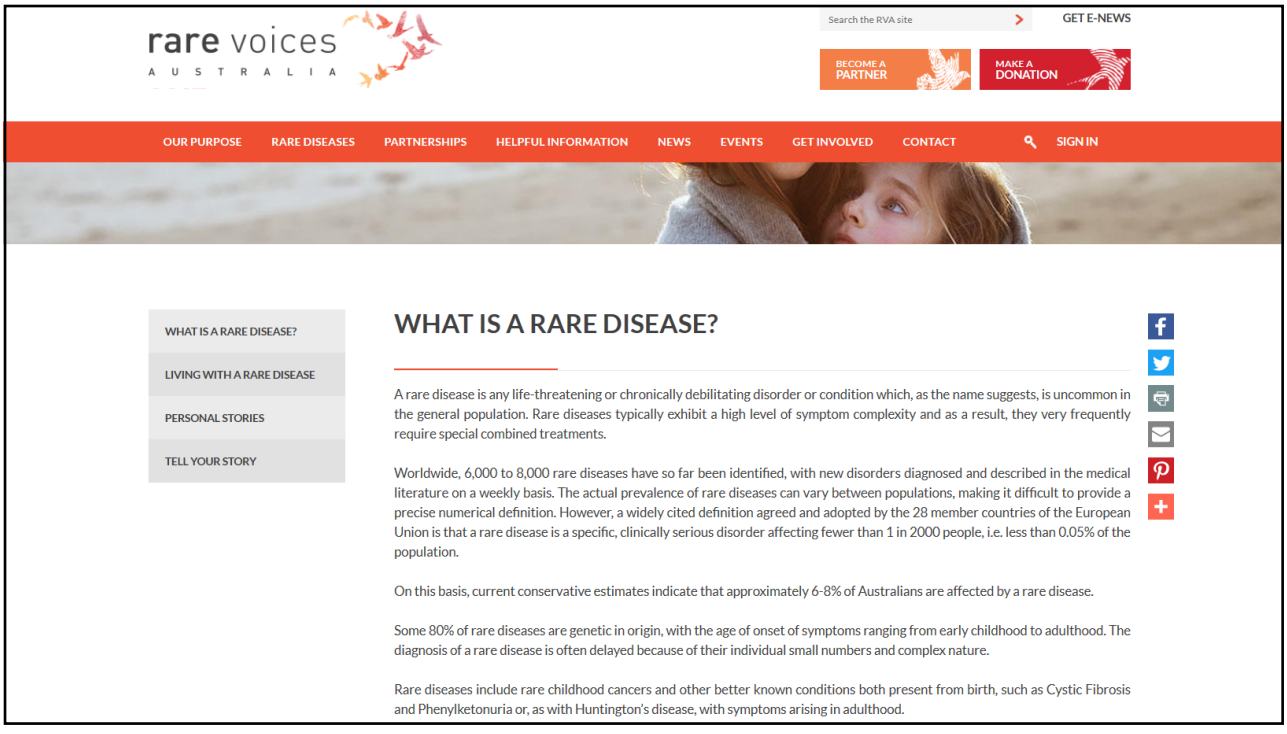

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Biobanking outcomes

- *Relevance - studies based on human samples rather than animal/cell models*
- *Study power*
- *Research impact:*
  - *Patient "quality of life" improvement*
  - *Policy change*
  - *Understanding of disease pathogenesis / "mechanisms"*
  - *Intellectual property*

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Is biobanking done elsewhere?

Country	Biobank	Participants	Human samples	Initiative	Est.
Austria	Biobank Graz	?	20,000,000	University/ government	30 yr
China	Shanghai Zhangjiang Biobank	?	10,000,000 (Target)	Commercial	
USA	"All of Us"	1,000,000	?	?	?
UK	UK Biobank	500,000		Registered Charity	
Australia	NSW Statewide Biobank + multiple smaller biobanks	?	3,000,000	NSW Government/ University/ Hospital	1 yr 40 yr

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Statewide Biobank

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Robotic sample storage and re-location

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NSW Health Statewide Biobank (NSWHSB)

The potential of the NSWHSB :

- *utilisation of statewide services*
- *access to world-class infrastructure*
- *guidance on informed participant consent*
- *enrich biospecimens with linked data (CHeReL)*
- *standardised agreements to accelerate research*
- *best practice access and incidental findings policy*
- *Biobank Information Management System (BIMS)*
- *expertise and collaboration*
- *framework to enable future research*

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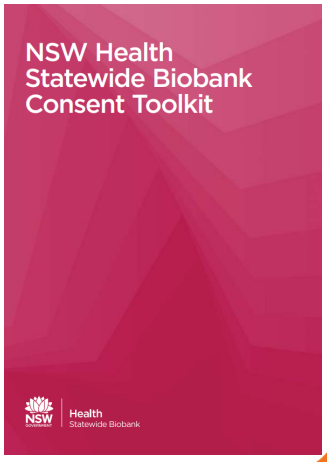
Participant Consent for Biobanking

> **"The Consent Toolkit is a vital and ground-breaking approach to standardised and ethical consent that aims to improve sample and associated data availability and help us find the answers that matter."**



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Relevance to rural clinicians and researchers

- *Cost-effective sample storage*
- *Standardized material transfer agreements (MTA) and consent toolkit*
- *Digital platforms for data sharing (regional NSW and beyond)*
- *Accreditation*
- *Open access framework*

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Relevance to rural clinicians and researchers

What does an open access framework mean?

- *Allows wider collaboration*
- *All data collected is accessible to collaborating researchers*
- *Results generated by project collaborators are accessible*
- *Important for participants from* **regional NSW and beyond**

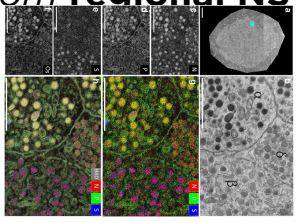

Image: Giepmans et al. 2018

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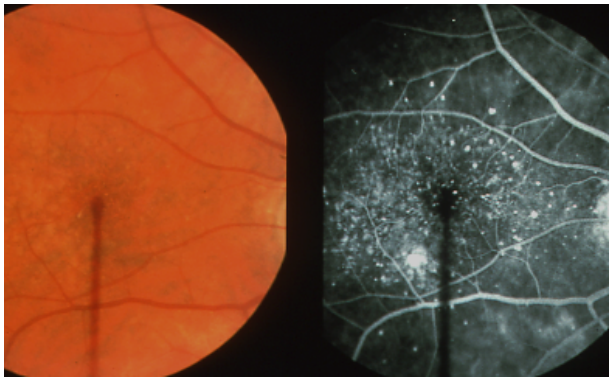
The power of biobanking research in practice

Targeted collection – Sarks Retinal Research Group



Age-related macular degeneration

Dr Shirley Sarks

Dr John Sarks

Dr Svetlana Cherepanoff

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Specimen: Sarks tissue bank collection

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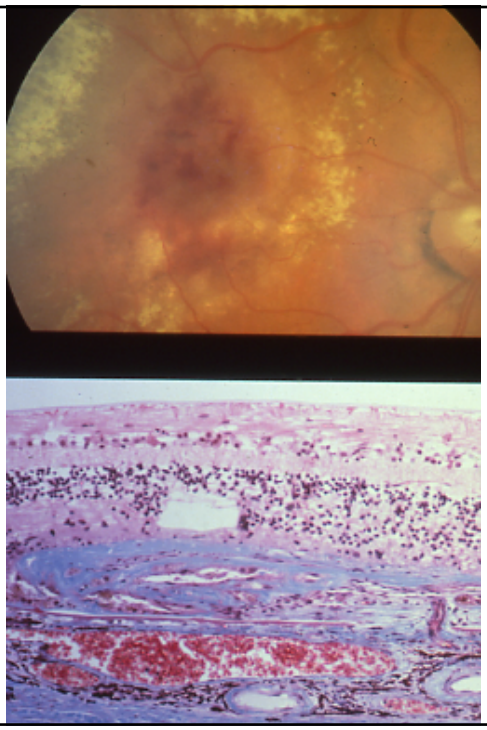
Age-related macular degeneration (AMD)



Sarks retinal tissue biobank:

- 1976 - 2019 >
- 350 clinically documented cases
- Clinical documentation up to 30 years
- Eyes obtained at post-mortem
- Analysis by state-of-the-art pathology

Specimen: Sarks tissue bank collection

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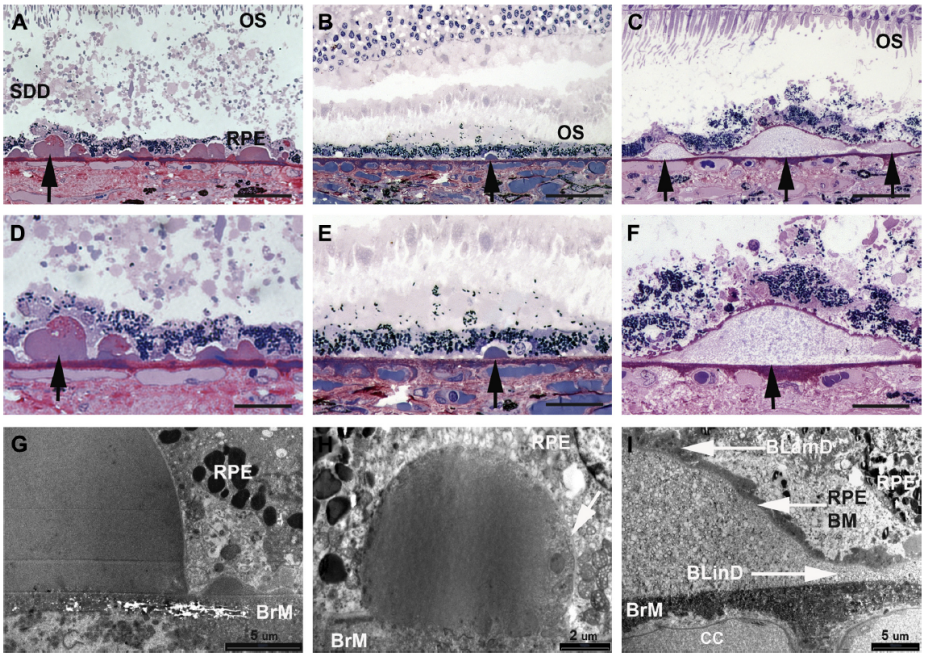

Figure 1. Comparative morphologic features of cuticular, small, hard and soft drusen as seen on (A–F) light microscopy and (G–I) transmission electron microscopy. Low-power light microscopy reveals that (A) cuticular drusen are found external to the retinal pigment epithelium (RPE), the same location that (B) small, hard drusen and (C) soft drusen are found. Cuticular drusen are small with steep sides and contain dense hyalinized contents that are

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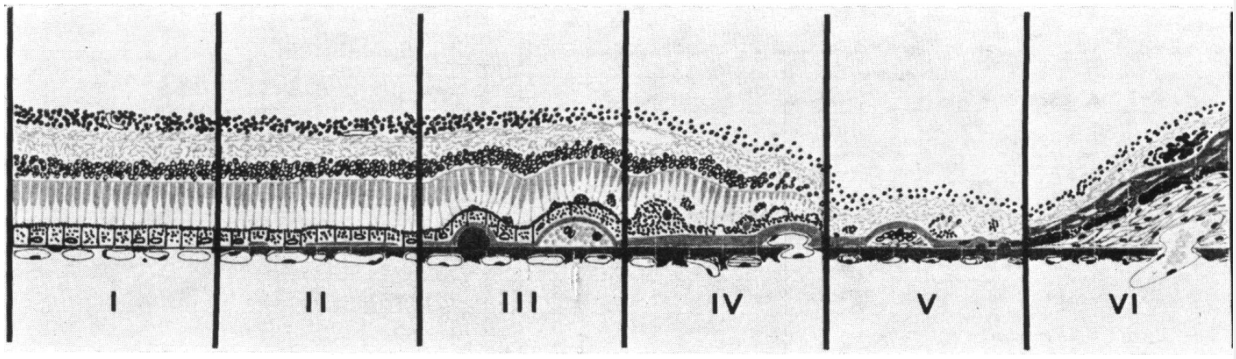

FIG. 4 *Diagram illustrating histological classification of 378 eyes acccrding to development of basal linear deposit under retinal pigment epithelium*

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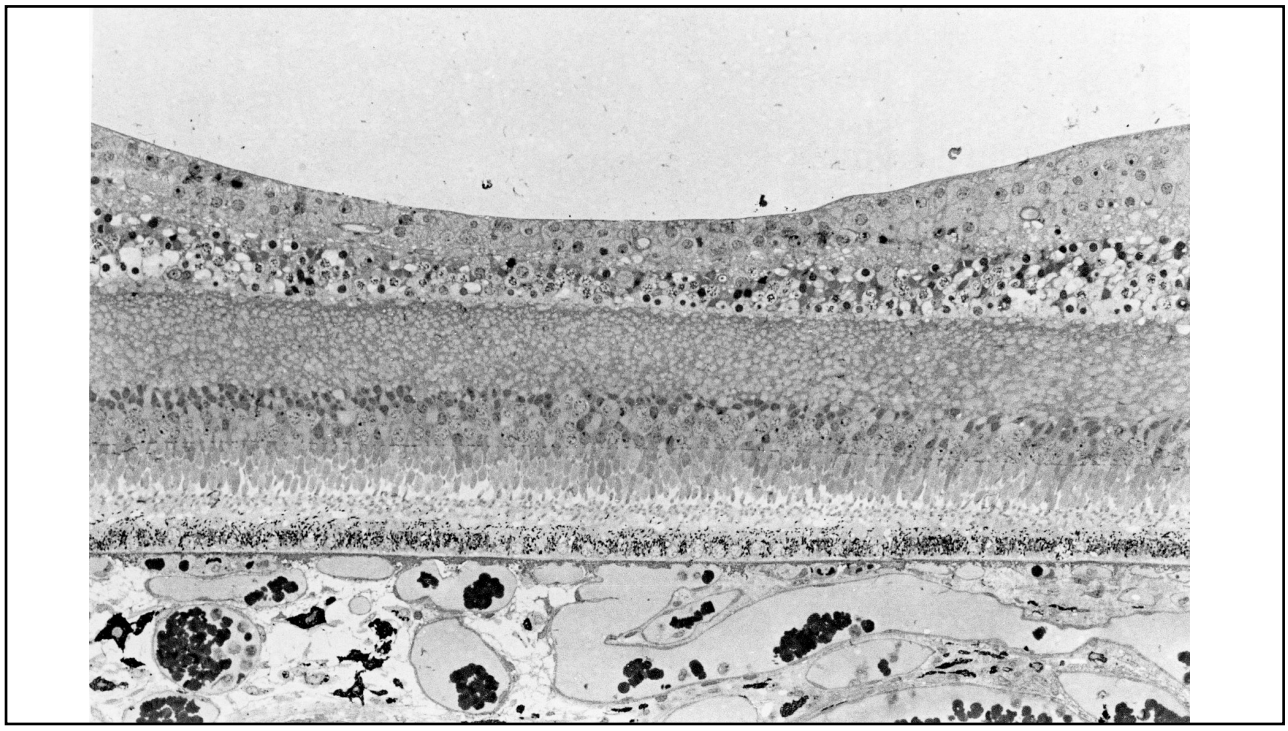

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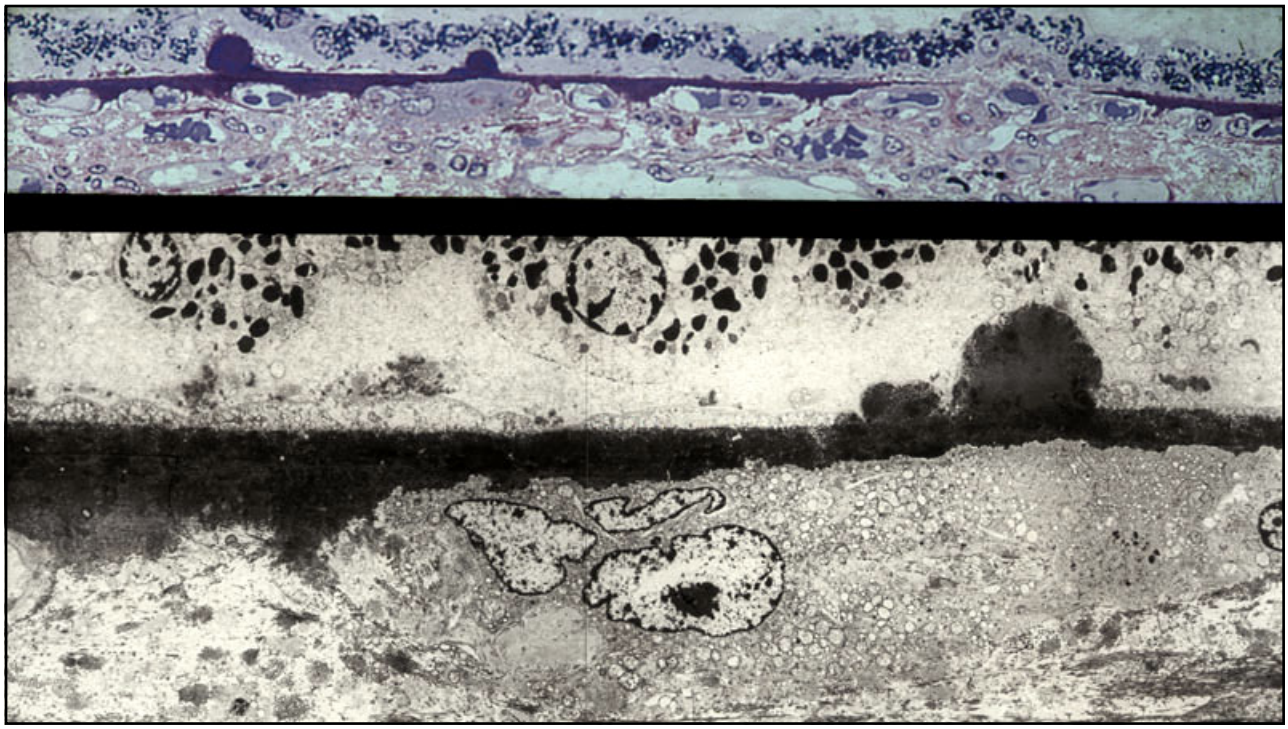

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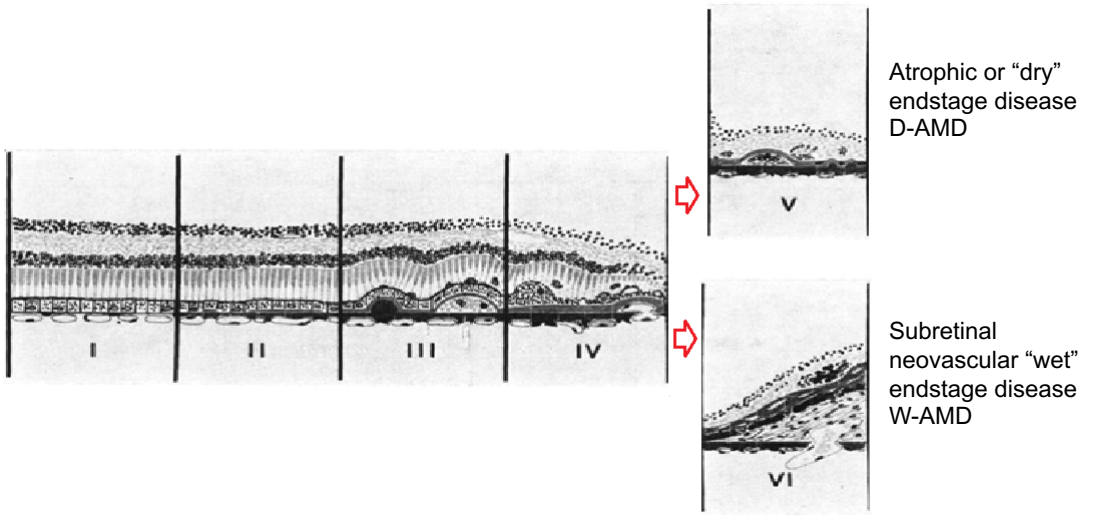
I
II
III
IV
V
VI
Atrophic or “dry” endstage disease D-AMD
Subretinal neovascular “wet” endstage disease W-AMD

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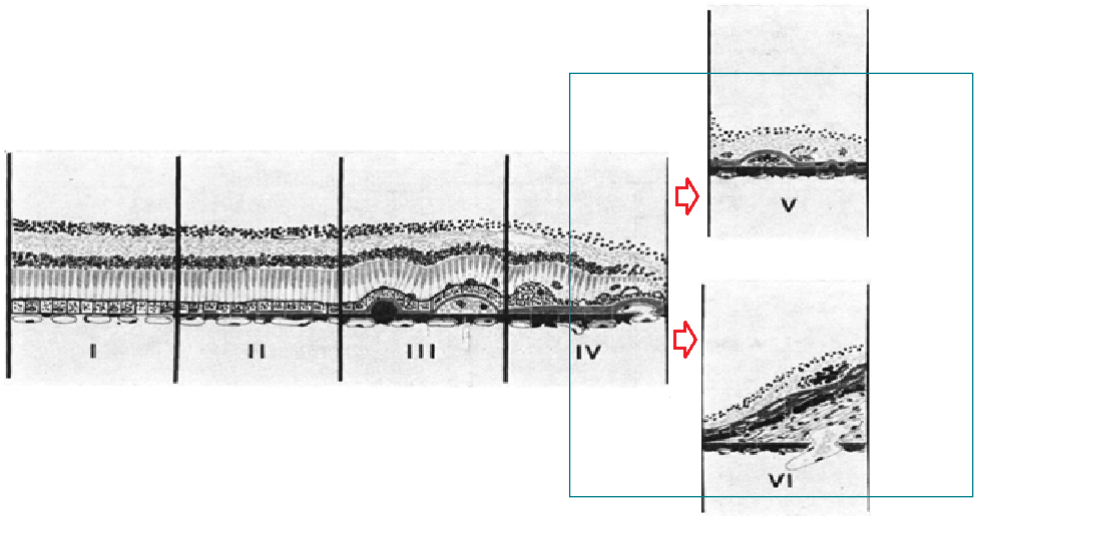
I
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III
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VI

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Translational outcomes

- *AMD recognised as a chronic inflammatory disease*
- *Injection into the globe to treat back of eye disease – new paradigm*
- *Injectable anti-inflammatory and anti-angiogenic drugs now used routinely*
- *Revolution in treatment of "wet" end-stage AMD*
- *Previously no drug intervention existed – only destructive laser photocoagulation*
- *Intellectual property - significant*

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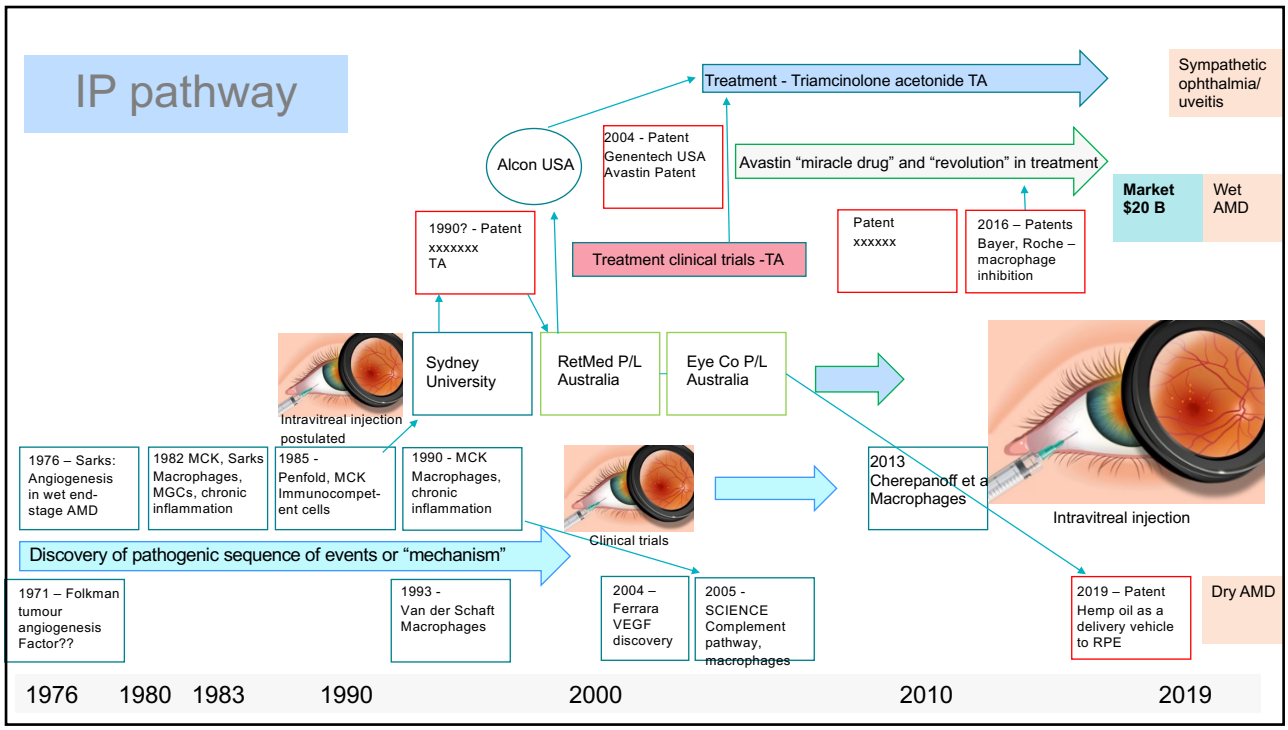

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The power of biobanking research in practice

NSW Brain Clot Bank:
a new model for collaborative research

BRAIN CLOT BANK

NSW BRAIN CLOT BANK

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NSW Brain Clot Bank

On the 1st of July 2019 the funding from NSW Health kicked off to start our 4-year Biospecimen Collection Grant with the NSW Health Statewide Biobank.

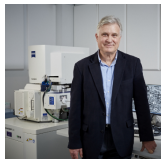
We have reached this milestone after two and a half years of exhausting work essentially starting with a "clean sheet of paper" and a "great idea" from Sonu.

The special research bond between Sonu and myself which started this project has now grown to be an exemplary collaboration between the disciplines of Neurology and Pathology of which we are very proud.

We now look forward to working hard to ensure the complex logistics of specimen collection are carried out to worlds-best practice. We can think of no better partners for this than the **NSW Health Statewide Biobank**.

This will be a **unique collection** that will not only benefit research groups in NSW, but potentially all stroke research groups in Australia and the World.

Dr Sonu Bhaskar



A/Prof Murray Killingsworth

Statement to the NSWBCB Board – inaugural meeting

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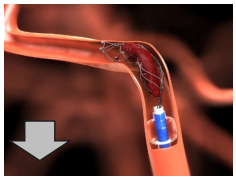
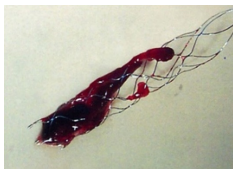
Retrieved clot analysis in ischaemic stroke

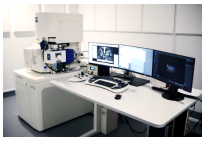
The procedure of endovascular thrombectomy (EVT) is a "treatment revolution" for ischaemic stroke



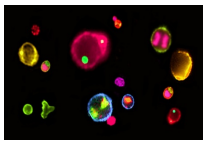


"The research discovery arm will identify mechanisms of pathogenesis using state-of-the-art characterisation tools available from NSWHP and the Ingham Institute"

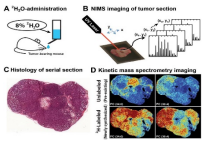
Histology and IHC



Correlative electron microscopy (CLEM)



Imaging flow cytometry



Imaging mass spectrometry

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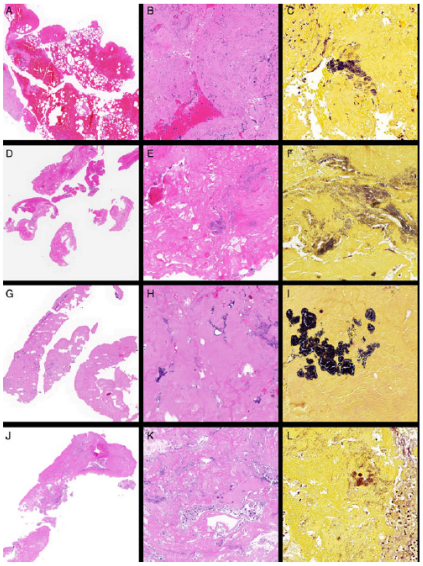

Figure 1: *Representative histopathological images of the clots retrieved after EVT from patients with IE. Case 1: (A) Low-power view of fibrin-rich thromboembolus (left) with attached blood-rich thrombus (right) (H&E stain, ×2), (B) high-power view of paucicellular fibrin-rich thromboembolus (H&E stain, ×20) and (C) Gram stain showing colonies of Gram-positive cocci (×40). Case 2: (D) Low-power view (H&E, ×2), (E) high-power view of paucicellular fibrin-rich thromboembolus showing suspected colonies of bacteria (H&E stain, ×20) and (F) Gram stain (×40). Case 3: (G) Low-power view of fibrin-rich thromboembolus (H&E, ×2), (H) high-power view of paucicellular fibrin-rich thromboembolus showing colonies of bacteria (H&E stain, ×20) and (I) Gram stain (×40). Case 4: (J) Low-power view of fibrin-rich thromboembolus (H&E, ×2), (K) high-power view (H&E stain, ×20) and (L) Gram stain (×40).*

ORIGINAL ARTICLE

Clot Histopathology in Ischemic Stroke with Infective Endocarditis

Sonu Bhaskar, Jawad Saab, Cecilia Cappelen-Smith, Murray Killingsworth, Xiao Juan Wu, Andrew Cheung, Nathan Manning, Patrick Aouad, Alan McDougall, Suzanne Hodgkinson, Dennis Cordato

ABSTRACT: ***Background:*** Endovascular thrombectomy (EVT) has shown efficacy in acute ischemic stroke (AIS) patients with infective endocarditis (IE). The possibility to undertake advanced histopathological clot analysis following EVT offers a new avenue to establish the etiological basis of the stroke – which is often labelled "cryptogenic." In this paper, we present our findings from four consecutive patients with IE who underwent EVT following an AIS at our tertiary referral comprehensive stroke centre. ***Methods:*** Comprehensive histopathological analysis of clot retrieved after EVT, including morphology, was undertaken. ***Results:*** The consistent observation was the presence of dense paucicellular fibrinoid material mixed/interspersed with clusters of bacterial cocci. This clot morphology may be specific to septic emboli due to IE unlike incidental bacteraemia and could possibly explain the refractoriness of such clots to systemic thrombolysis. ***Conclusion:*** Detailed morphological and histopathological analysis of EVT-retrieved clots including Gram staining can assist in etiological classification of the clot. Understanding the composition of the clot may be of clinical value in early diagnostics and mapping treatment planning in IE.

The presentation

#EPR222 Erythrocyte-rich clots are associated with cardioembolic aetiology, reduced number of manoeuvres, and improved clinical outcome in acute ischemic stroke patients.

presented by

Sonu Bhaskar
AUSTRALIA

at the 5th Congress of the European Academy of Neurology in Oslo, Norway, 29 June – 2 July 2019

is assigned the

Investigator Award 2019

consisting of a free registration to the 6th EAN Congress in Paris 2020.

Tony Marion
Programme Committee Chair

Marie Vidailhet
Scientific Committee Chair

ean

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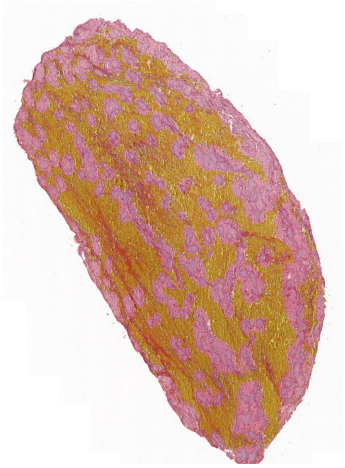
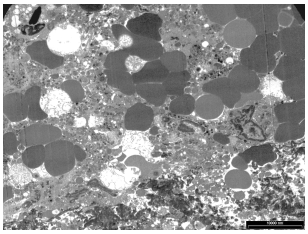
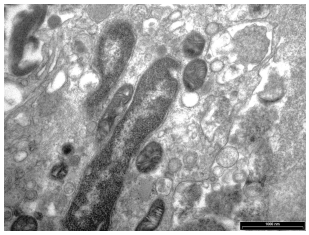


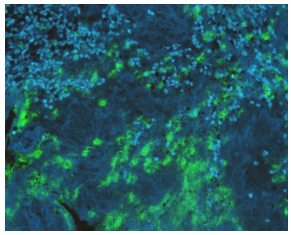
MSB histochemistry

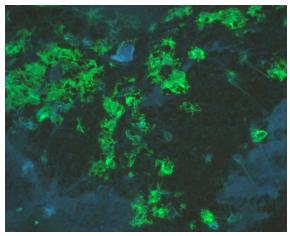
"We will identify key biomarkers and map their expression over the whole clot at single molecule resolution"





Electron microscopy





Immunofluorescence

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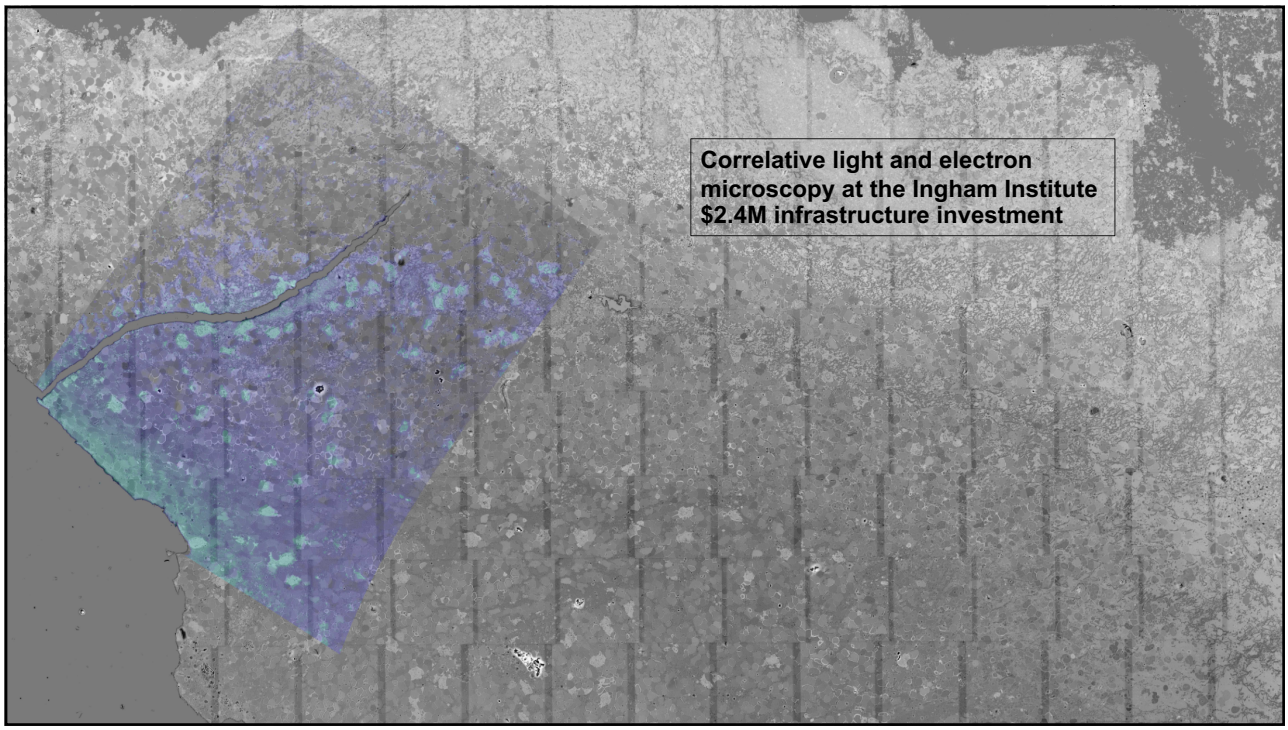

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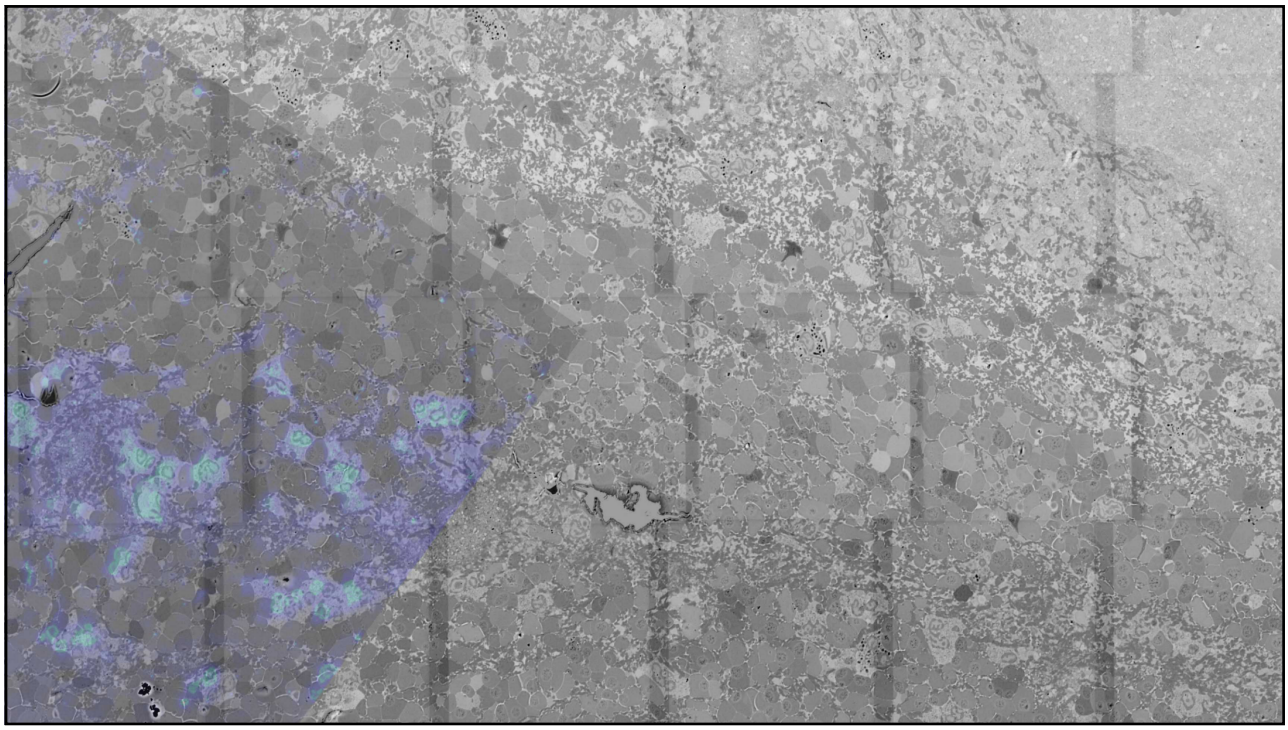

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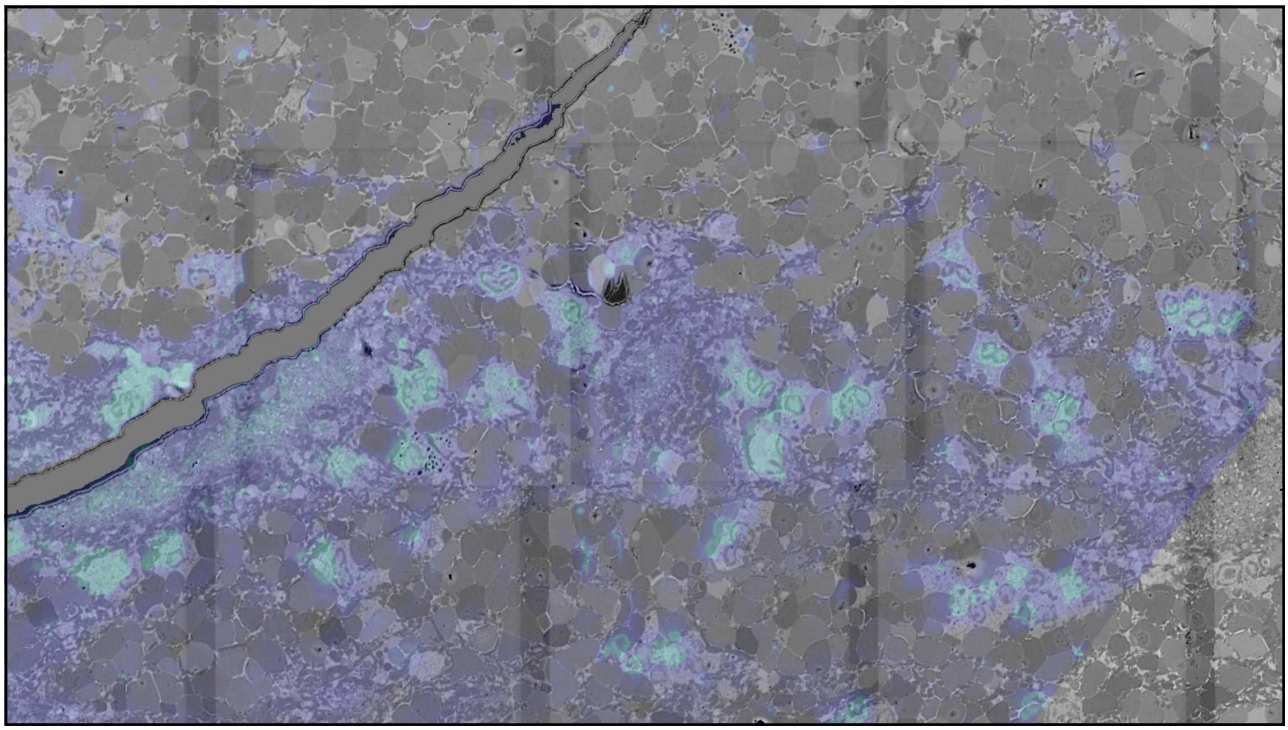

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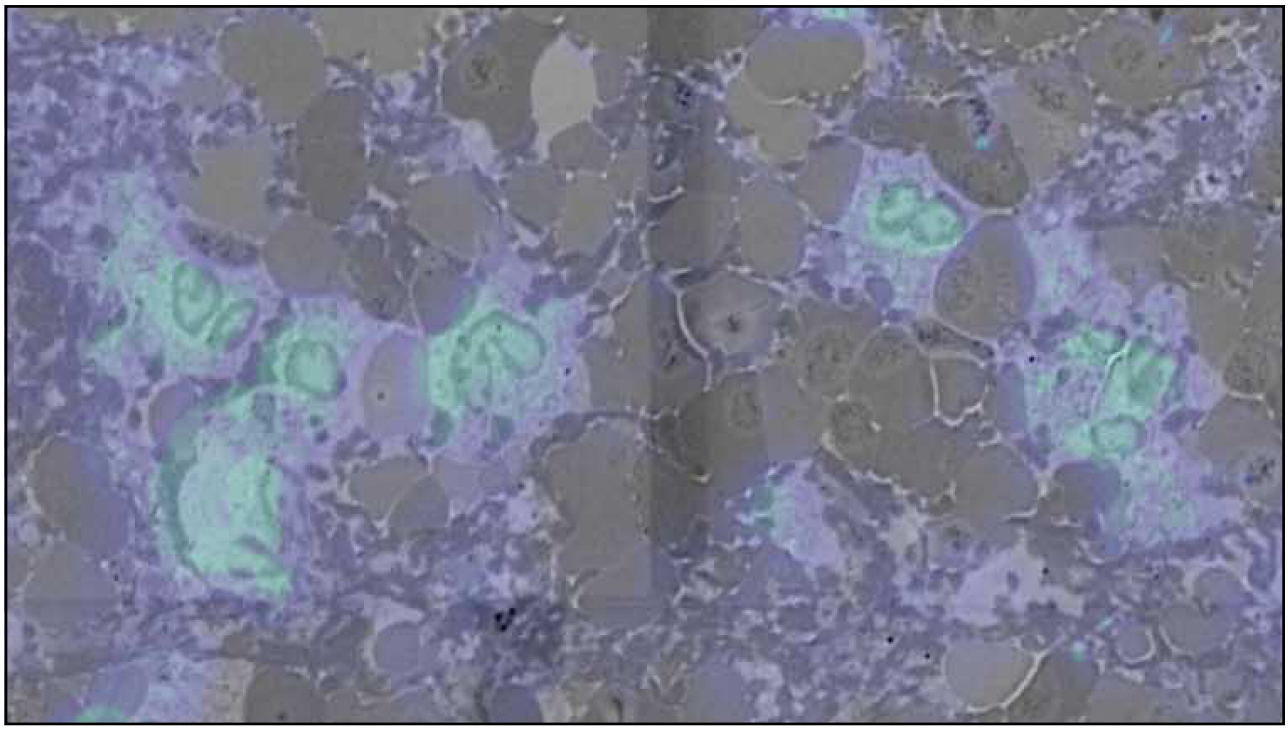

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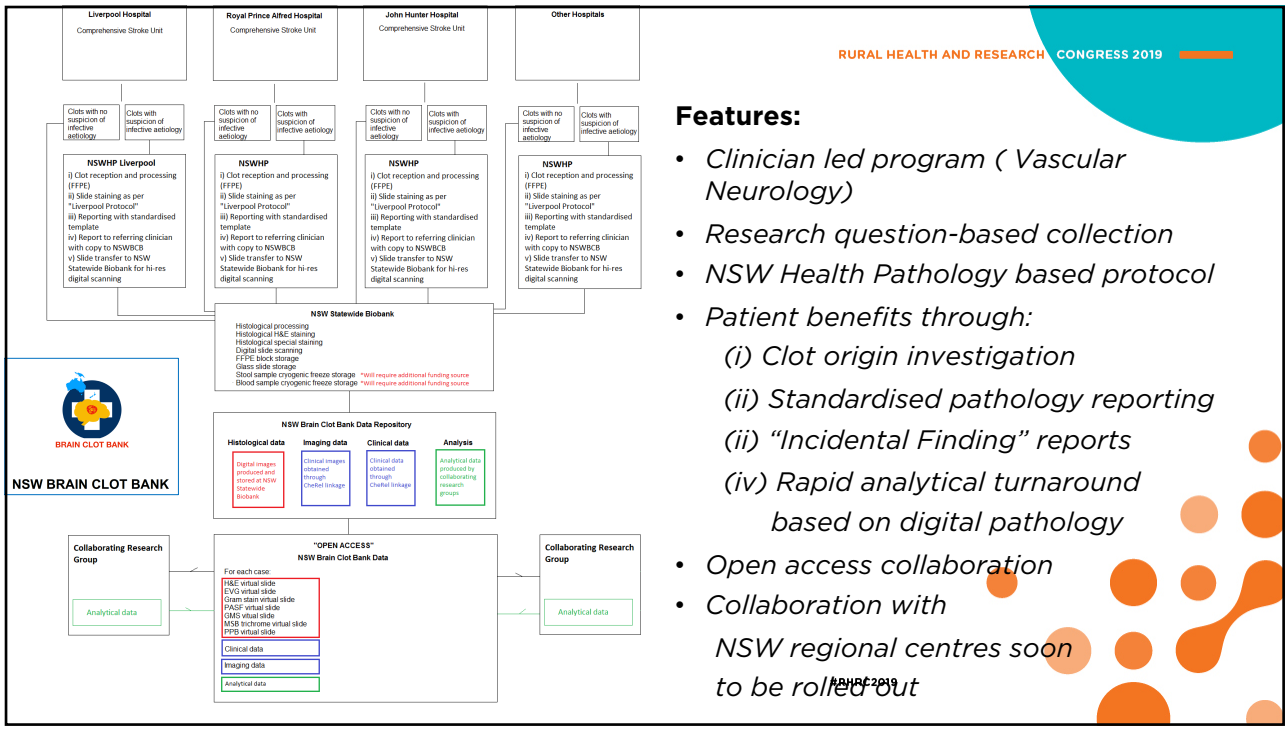

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Features:

- *Clinician led program (Vascular Neurology)*
- *Research question-based collection*
- *NSW Health Pathology based protocol*
- *Patient benefits through:*
  - *(i) Clot origin investigation*
  - *(ii) Standardised pathology reporting*
  - *(ii) "Incidental Finding" reports*
  - *(iv) Rapid analytical turnaround based on digital pathology*
- *Open access collaboration*
- *Collaboration with NSW regional centres soon to be rolled out*

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Questions?

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