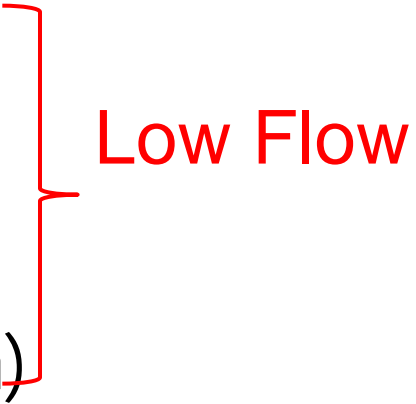


Disclaimer

- The copy in this file is protected by copyright of the author or authors. Consent was provided for the express purpose of educating attendees of the 2013 Registrars' Conference in Melbourne.
- You **MAY NOT COPY OR DISTRIBUTE** the contents or images in any form.
- You **MAY PRINT** the document for your own personal use as an educational resource

Low Flow Vascular Malformations

I.S.S.V.A. Classification

- Haemangioma – Proliferation
 - Vascular Malformation – Disorder of development
 - Arteriovenous malformations **High Flow**
 - Venous malformations
 - Lymphatic malformations
 - Glomuvenous malformations
 - Complex lymphovenous malformations
 - Capillary malformations (Port Wine stain)
- 
- Low Flow**

Low Flow Malformations

- Clinical Features
- Investigations
- Treatment
 - Conservative
 - Surgical
 - Interventional radiology
- Pathophysiology

Venous Malformation



Venous Malformations



Lymphatic Malformations



Lymphatic malformations



Venous v Lymphatic malformation

- Blood filled v Lymphatic fluid filled
- Continuous with circulation v isolated cysts
- Markers of lymphatic v vascular differentiation
 - VEGFR-3
 - D₂40 (Podoplanin)
 - CD31 / CD34

Investigations

- Medical Imaging
 - MRI
 - Ultrasound

0973120
22/09/2000
5 YEAR
M

MRI Brain - Congenital
t2_FS_tra_PAT2
21/09/2006 7:40:27 PM
06052492MRBCON

LOC: -27.56
THK: 4 SP: 5
HFS

R

L

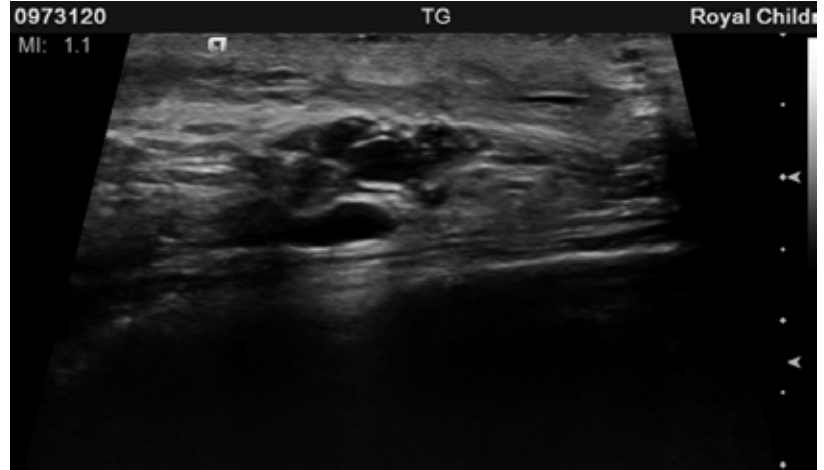
EC: 0
SE
FA: 150
TR: 3940
TE: 91
ACQ: 250\384

Z: 1.33
C: 458
W: 1024
DFOV: 18.7x23cm
Compressed 7:1
IM: 17 SE: 3

Page: 17 of 40

P

cm

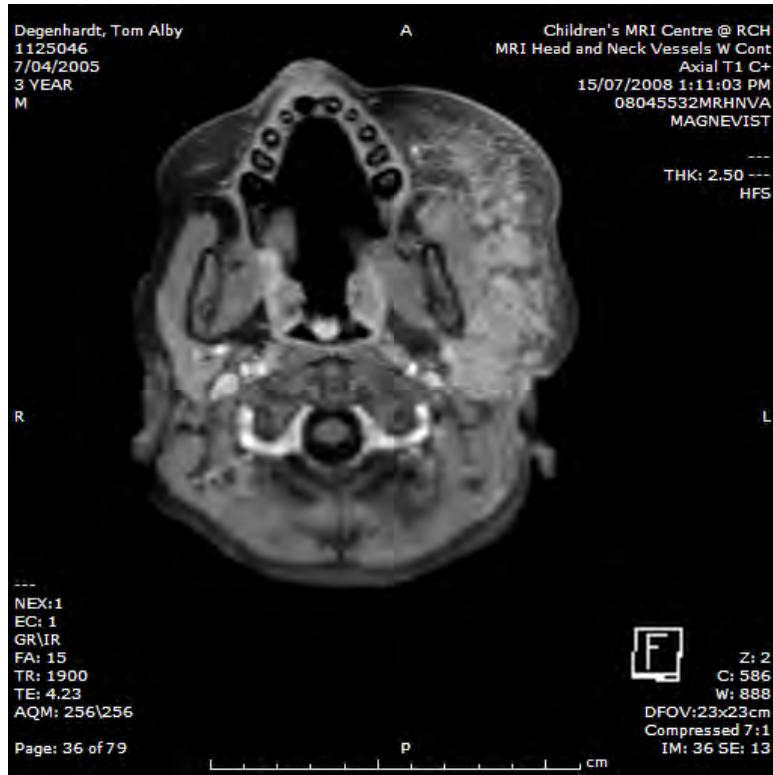
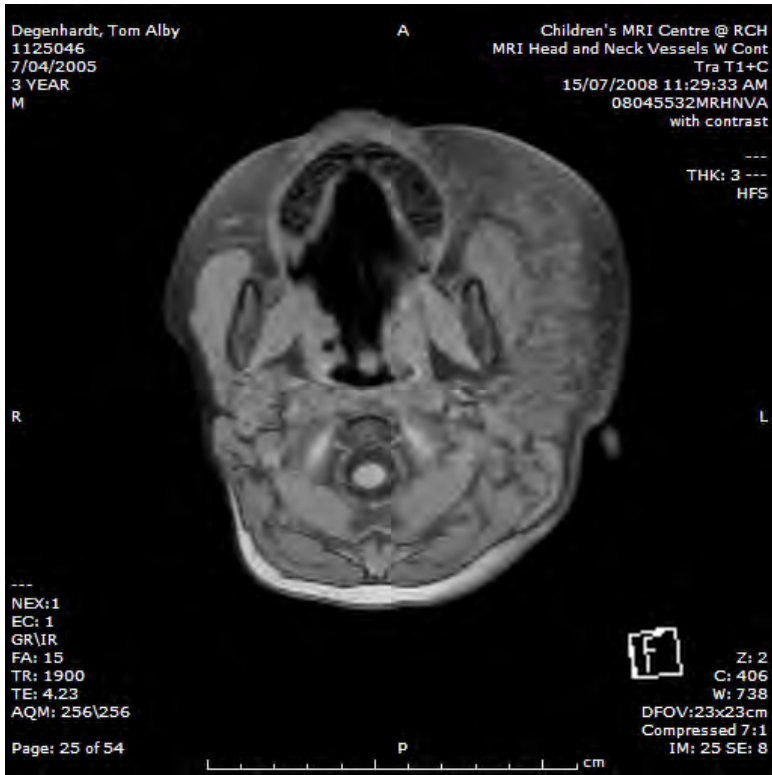




T1



T2 FS



+C

Investigations

- Medical Imaging
 - MRI
 - Ultrasound
 - **NOT:** MRA/MRV; CT angio; Angiogram

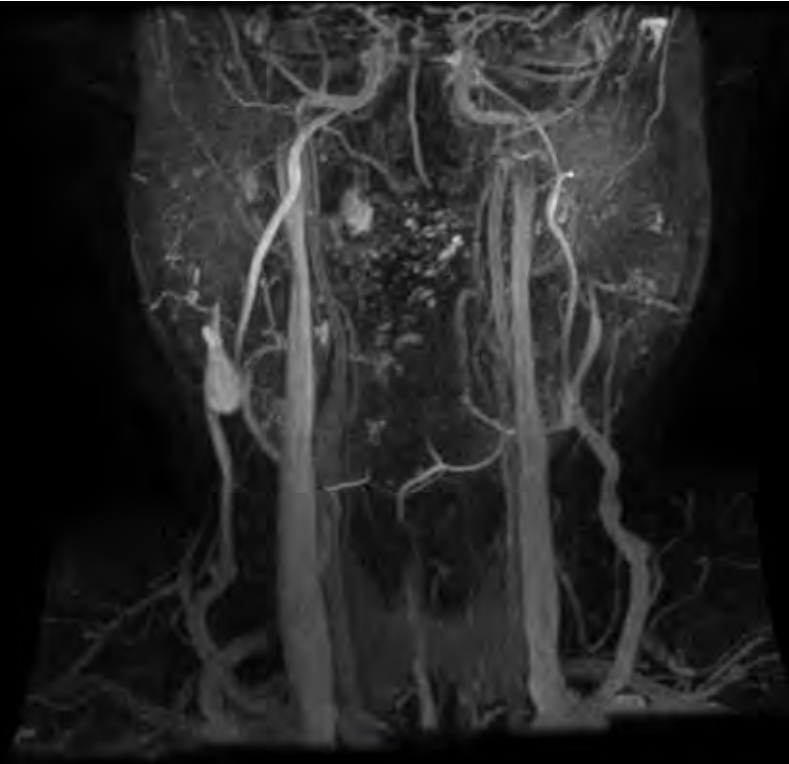
BAIG, Mirza
200902534
M 523/1970
Scan Nr. 2 - Slice 9/30
TE 1ms - TR 3ms
Flip Angle 25°

Royal Hobart Hospital
Scan Thk 2.2 / 1.1
FOV 240 mm
Zoom 100%

L-R P-170 H-2

I: 4342
W: 9886

H
R A L
F
8:00 AM
2/1/2011



Investigations

- Medical Imaging
 - MRI
 - Ultrasound
 - NOT: MRA/MRV; CT angio; Angiogram
- CT Scanogram for leg length
- Bloods
 - D-Dimer – breakdown product of fibrinogen

Management

- Define the Problem



Management

- Define the Problem
 - Pain
 - Continuous, use related, episodic
 - Appearance
 - Intermittent swelling
 - Infection
 - Functional impairment
- Treat the problem

Acute swelling in low flow malformations

- Haemorrhage
- Thrombosis
- Infection
 - Acute infection can reduce size of macrocystic LM
 - Recurrent infections lead to increase in size



Treatment

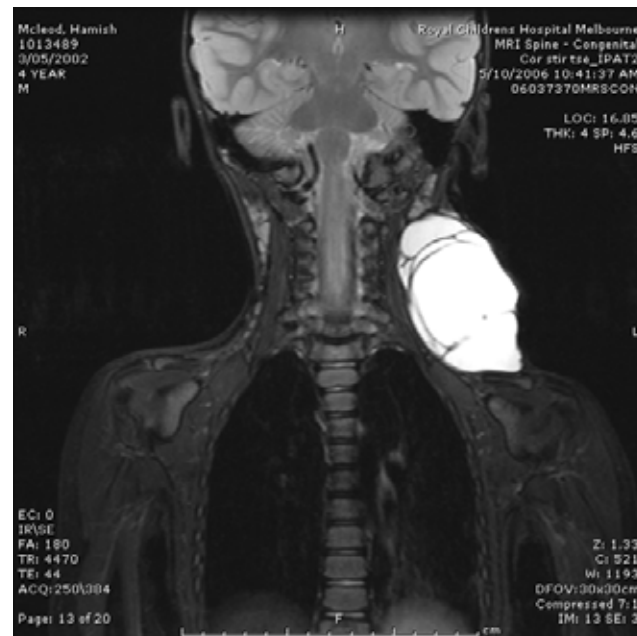
- Interventional radiology
- Surgery

Injection Sclerotherapy

- Needle access under ultrasound
- Direct puncture angiography
- Injection
 - Sodium Tetradecol
 - Polidocanol
 - Ethanol
 - Bleomycin
 - Doxycycline
 - OK432

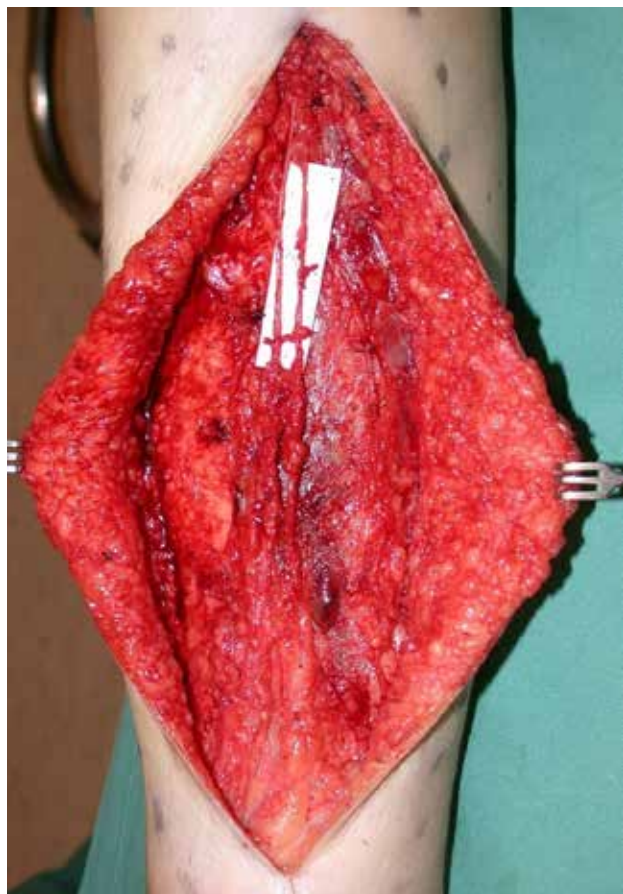
Injection Sclerotherapy

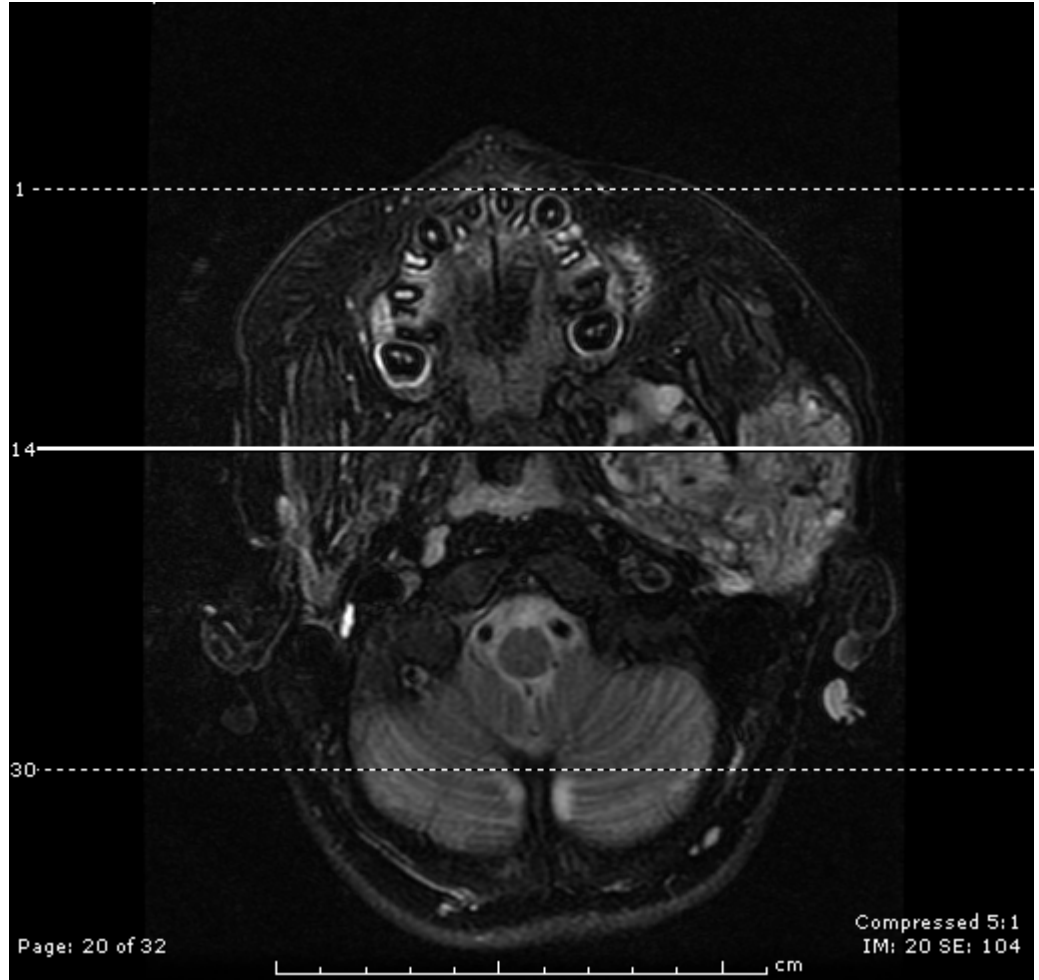
- Multiple treatments
- Not a 'cure'
- Best for macrocystic LM
- Can be good for pain in VM
- Highly specialised interventional radiology



Surgery

- Have a defined objective
- Clear one area as completely as possible
- Preserve cutaneous nerves
 - Meticulous dissection







Lymphatic Malformations



Venous Malformation surgery







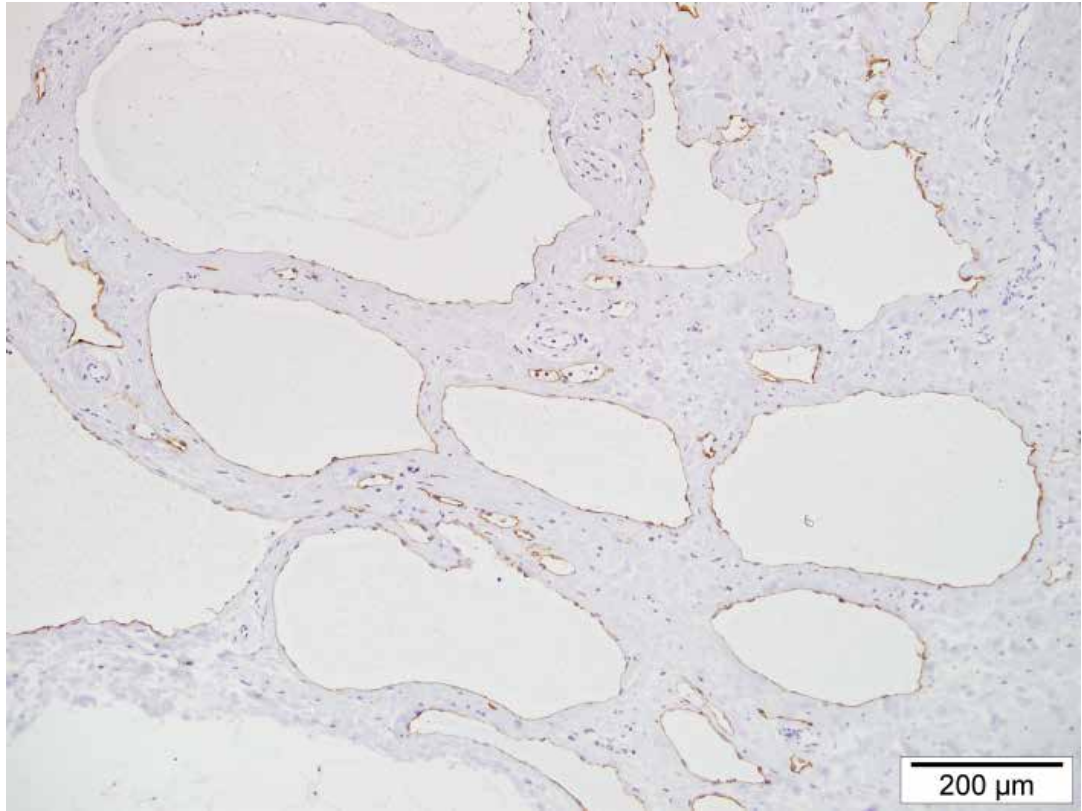
Pathophysiology of low flow malformations

- Familial Venous malformation
 - Activating germline mutation in TIE-2 gene
 - Presumed 'second hit' somatic mutation to cause lesion

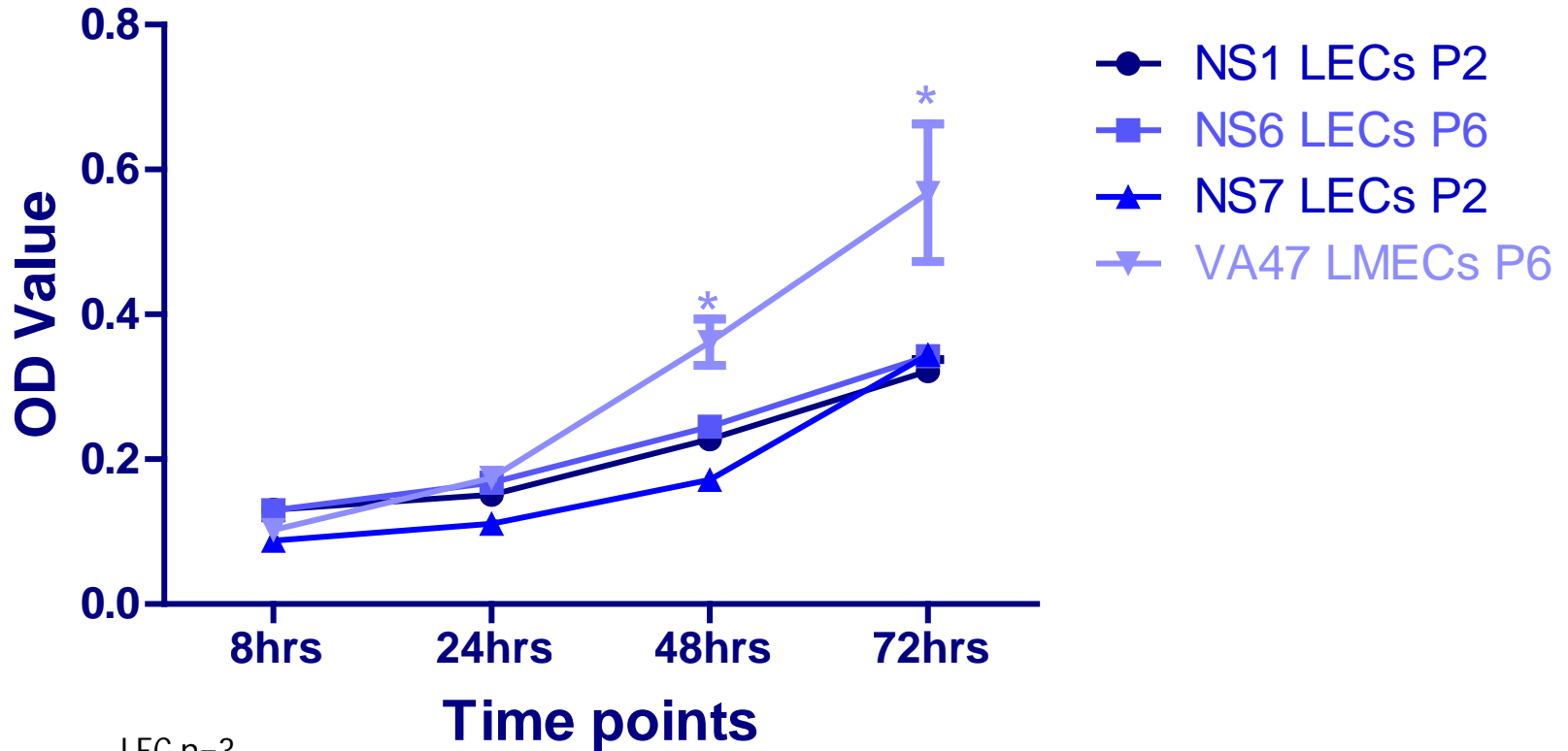


Pathophysiology of low flow malformations

- Familial Venous malformation
 - Activating germline mutation in TIE-2 gene
 - Presumed 'second hit' somatic mutation to cause lesion
- Sporadic lesions may be due to intersection of two separate somatic mutations.



Proliferation Assay LECs vs. LMECs



LEC n=3

LMECs n=1

$p < 0.001$

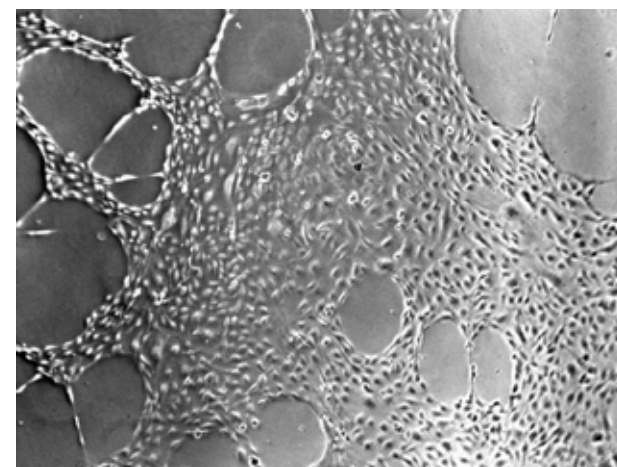
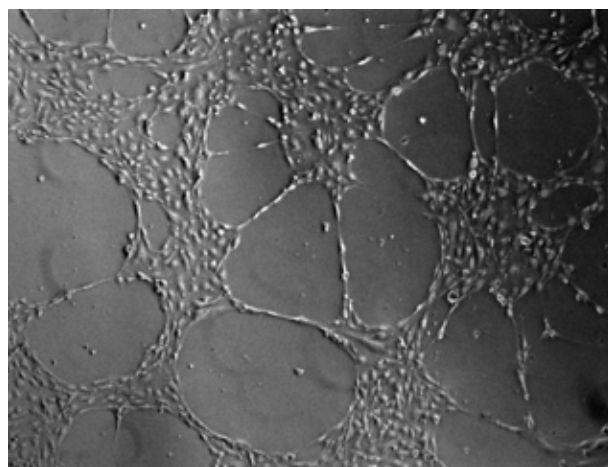
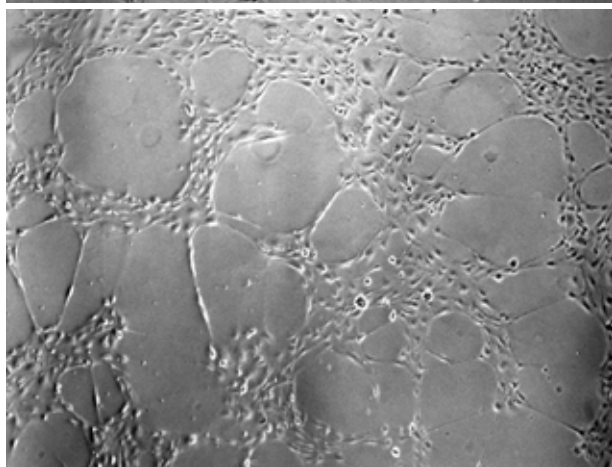
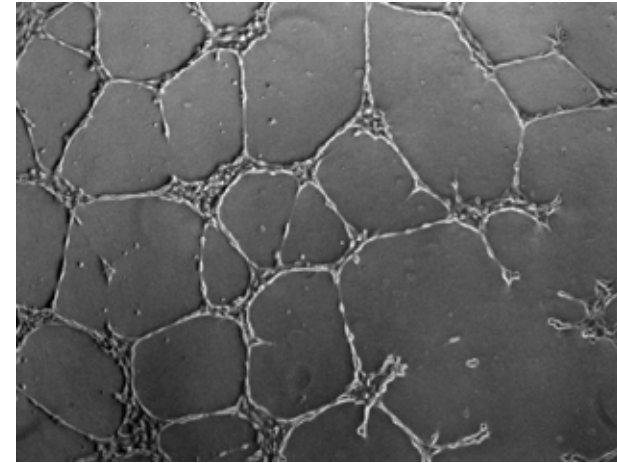
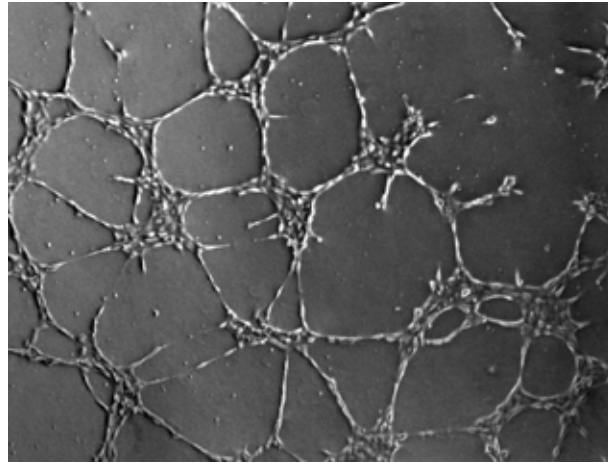
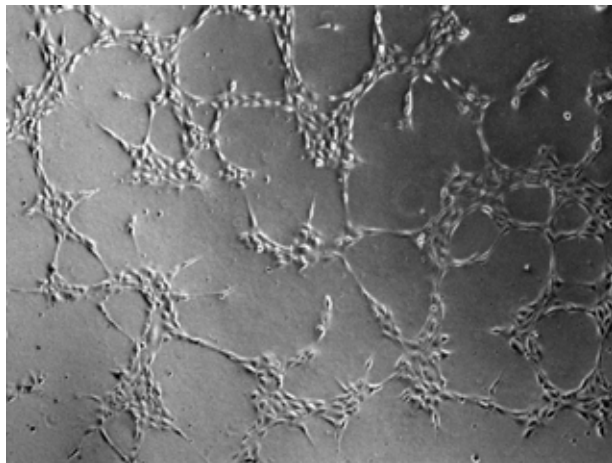
Error bars = SD

NS6 LECs x 4

8hrs

12hrs

16hrs



8hrs

12hrs

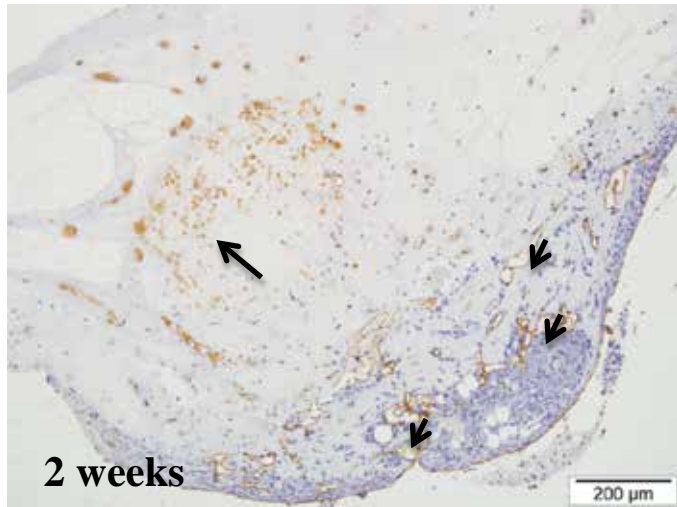
16hrs

VA47 LMECs x 4

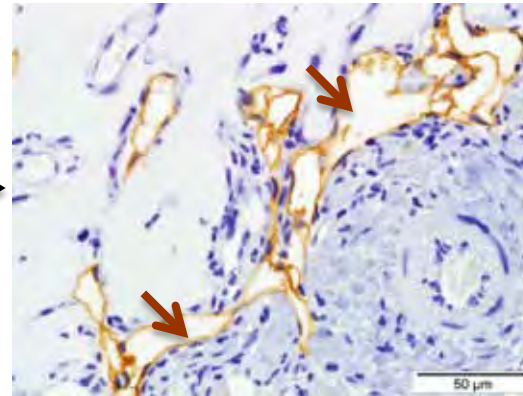


Murine Model: Histology and Immunophenotypic Characterisation

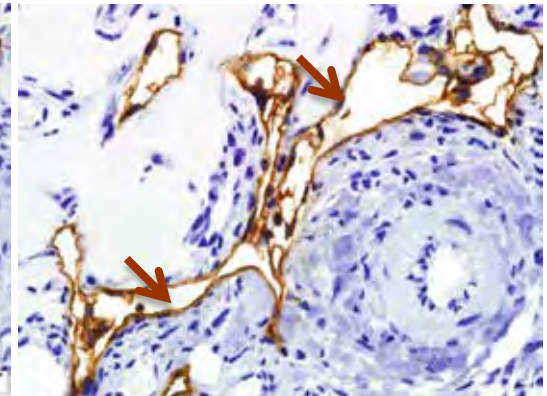
D2-40



D2-40

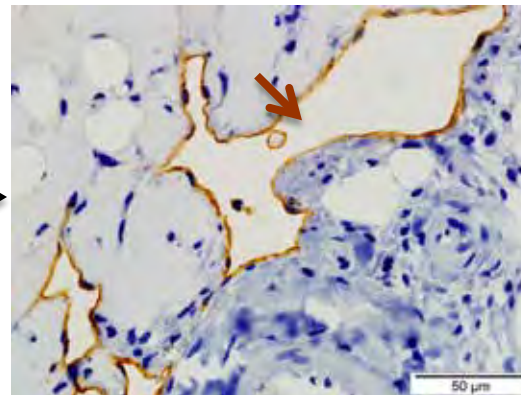


VEGFR3

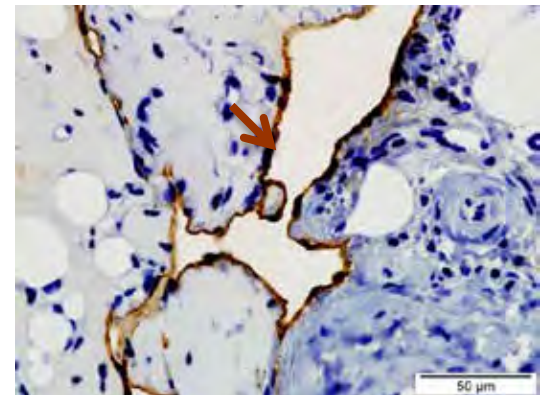


2 weeks

D2-40



VEGFR3



4 weeks

*Indirect immunohistochemistry visualised with **diaminobenzidine (DAB)***