

Update on the ACST-2 MRI substudy

ACST-2 Collaborators' Meeting

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Overview

- Brain MRI as a surrogate outcome measure in carotid interventions
- Design of the ACST-2 MRI substudy
- Plaque instability
- Update on enrolment & power considerations

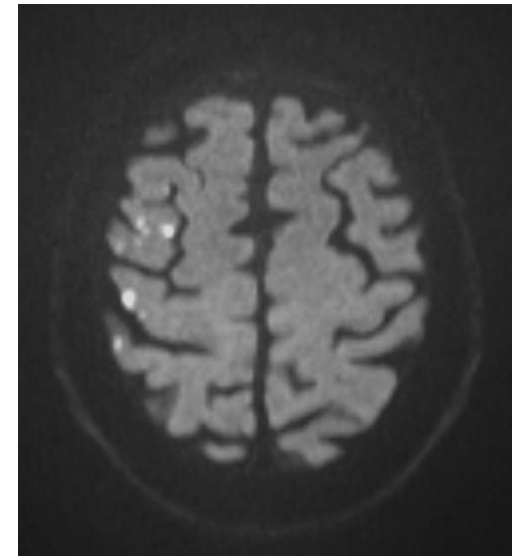
Brain MRI in carotid interventions

ICSS-MRI substudy: New ischaemic brain lesions after treatment

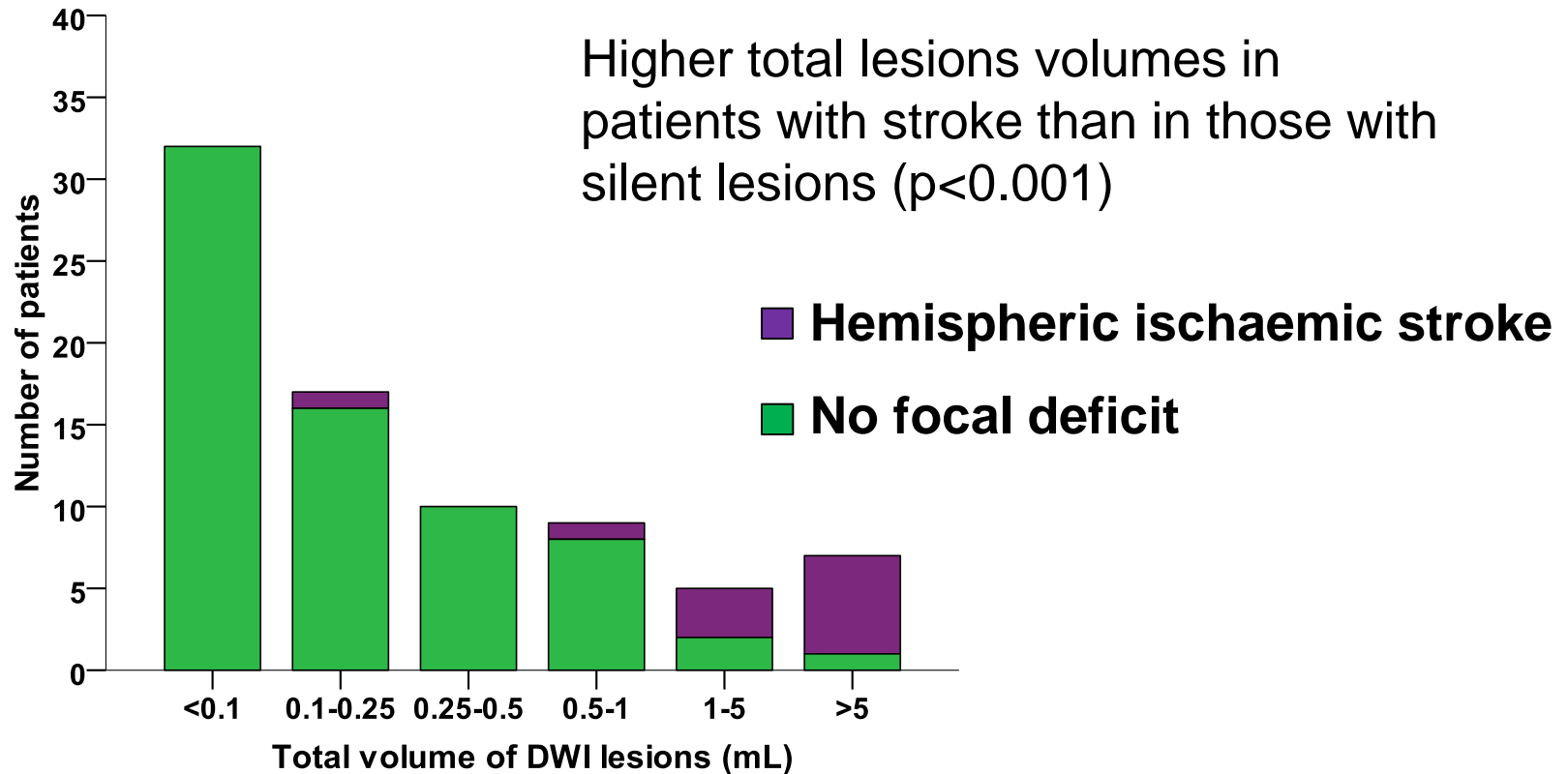
	CAS (n=124)	CEA (n=107)	Adjusted OR (95% CI), p
≥1 new DWI lesion <i>N patients (%)</i>	62 (50%)	18 (17%)	5.21 (2.78-9.79), p<0.001

Associated ischaemic events between initiation of treatment and post-treatment scan:

Stroke	8	3
Retinal infarct	1	0
TIA	0	0
None	53	15

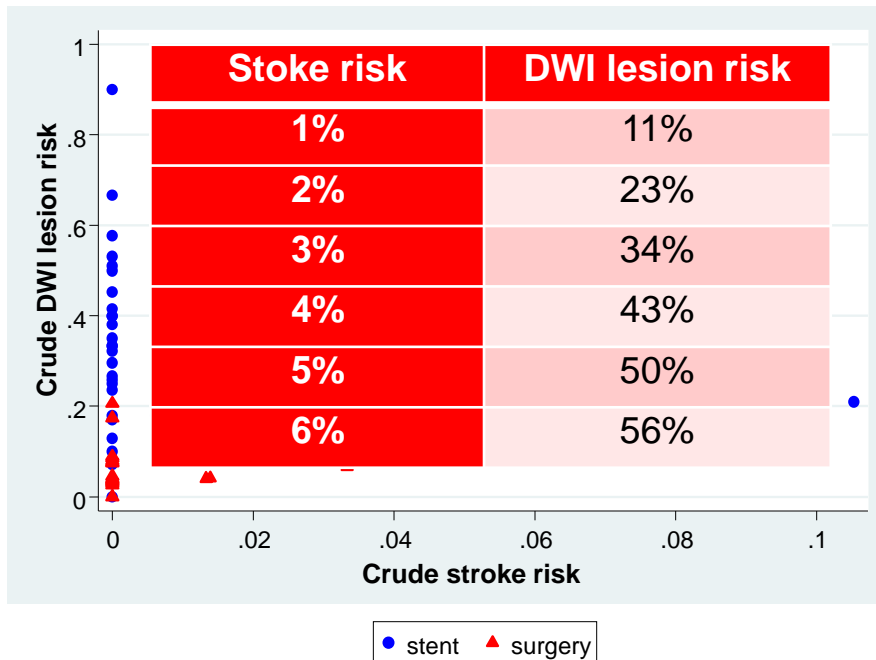


ICSS-MRI substudy: Total DWI lesion volume and symptoms (both treatment groups combined)

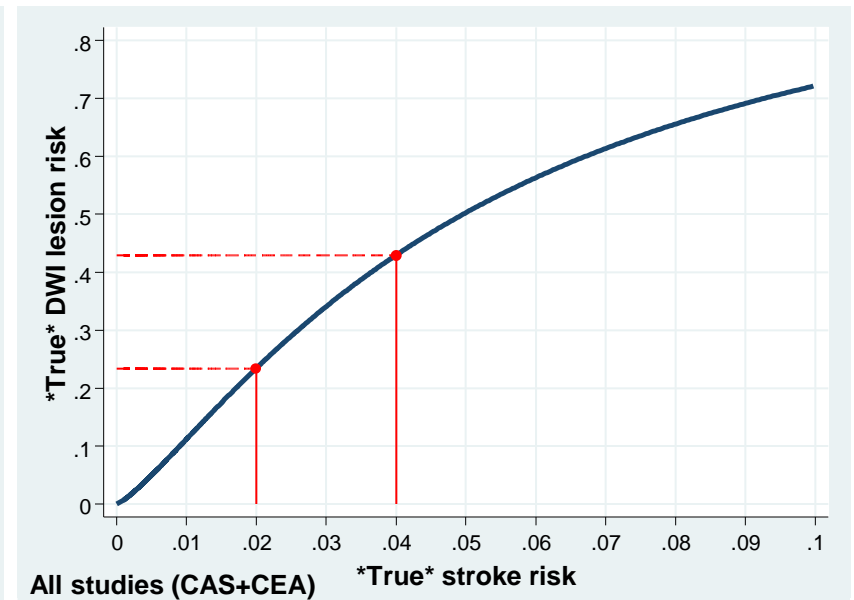


DWI lesions correlate with stroke risk in carotid interventions

71 studies, reporting 75 separate CAS treatment groups (4455 procedures) and 29 separate CEA treatment groups (1708 procedures)



Observed crude risks of stroke and DWI+ in all 104 treatment subgroups



Correlation between log odds of DWI lesions and log odds of stroke (coefficient 0.68 [95% CI 0.36-0.88], $p=0.00024$)

Correlation between true risks of stroke and DWI+ in all included studies (corrected for measurement error and study size)

Brain MRI in carotid interventions

- MRI is sensitive in detecting cerebral embolism
- Most MRI lesions are asymptomatic
- Across studies, MRI lesions correlate with stroke risk
- MRI is a useful **surrogate outcome** measure to investigate treatment effects and potential modifiers thereof (subgroup analysis) within clinical trials
- MRI can be analysed **blinded** to treatment (blinding of patients and investigators performing treatment and follow-up not feasible in carotid trials)

The ACST-2-MRI substudy

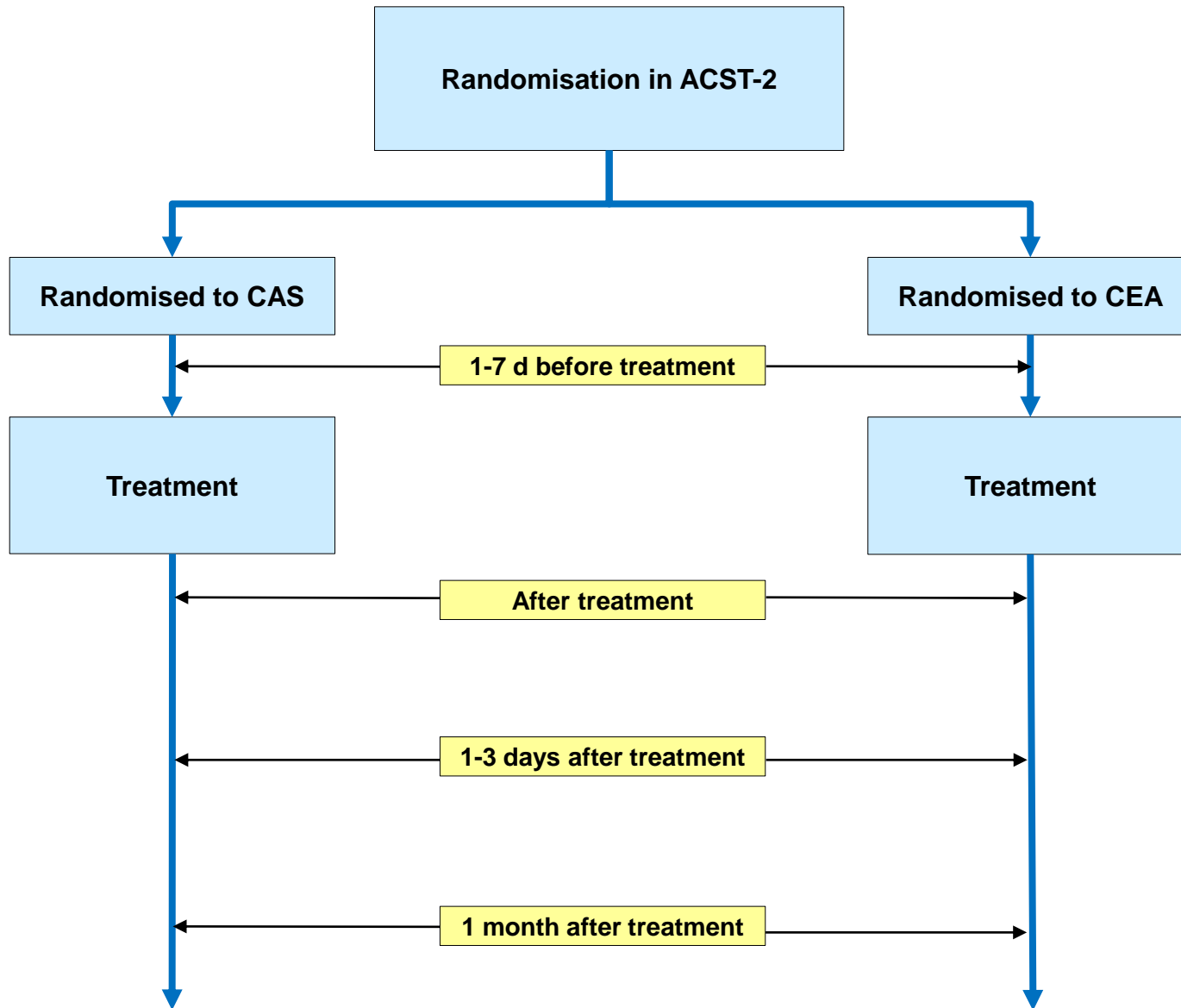
ACST-MRI substudy: Objectives

1. To compare the incidence of symptomatic and silent cerebral ischaemia between CAS and CEA using MRI as blinded, surrogate outcome assessment

ACST-MRI substudy: Objectives

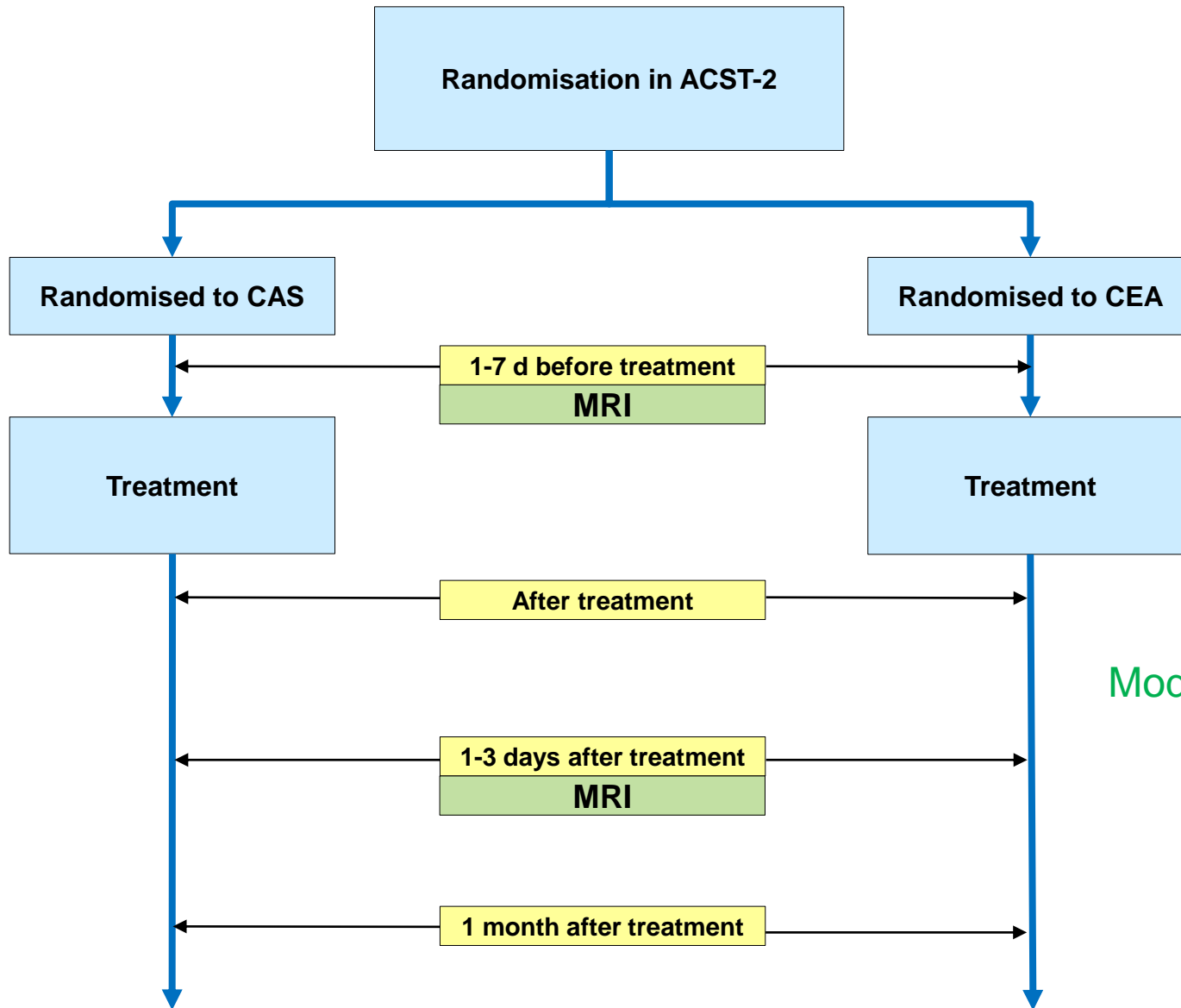
1. To compare the incidence of symptomatic and silent cerebral ischaemia between CAS and CEA using MRI as blinded, surrogate outcome assessment
2. To investigate whether plaque imaging predicts cerebral ischaemia in CAS or CEA

Study flow chart



CAS: carotid artery stenting, **CEA:** carotid endarterectomy,
MRI: magnetic resonance imaging

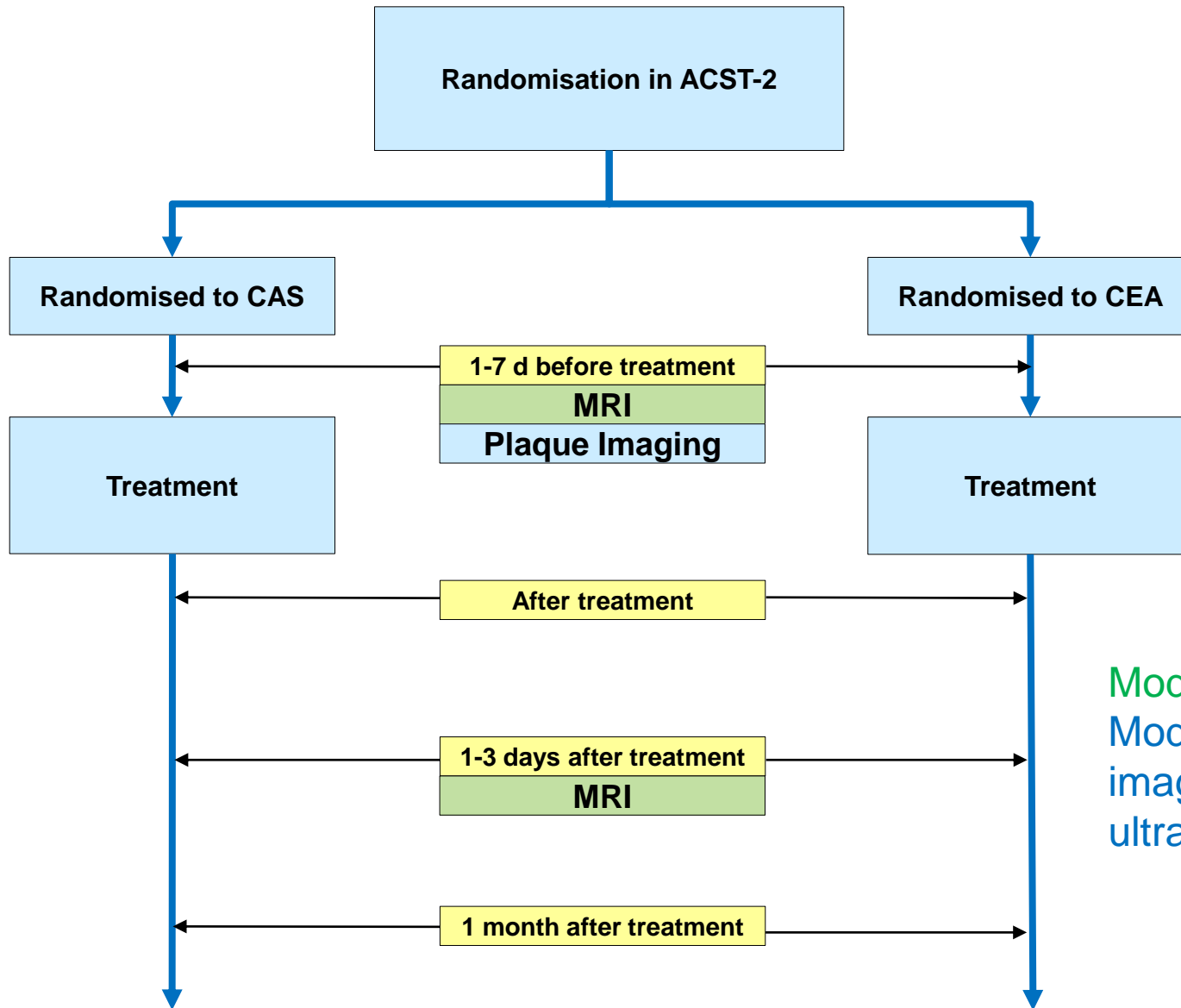
Study flow chart



Module 1: Brain MRI

CAS: carotid artery stenting, **CEA:** carotid endarterectomy,
MRI: magnetic resonance imaging

Study flow chart

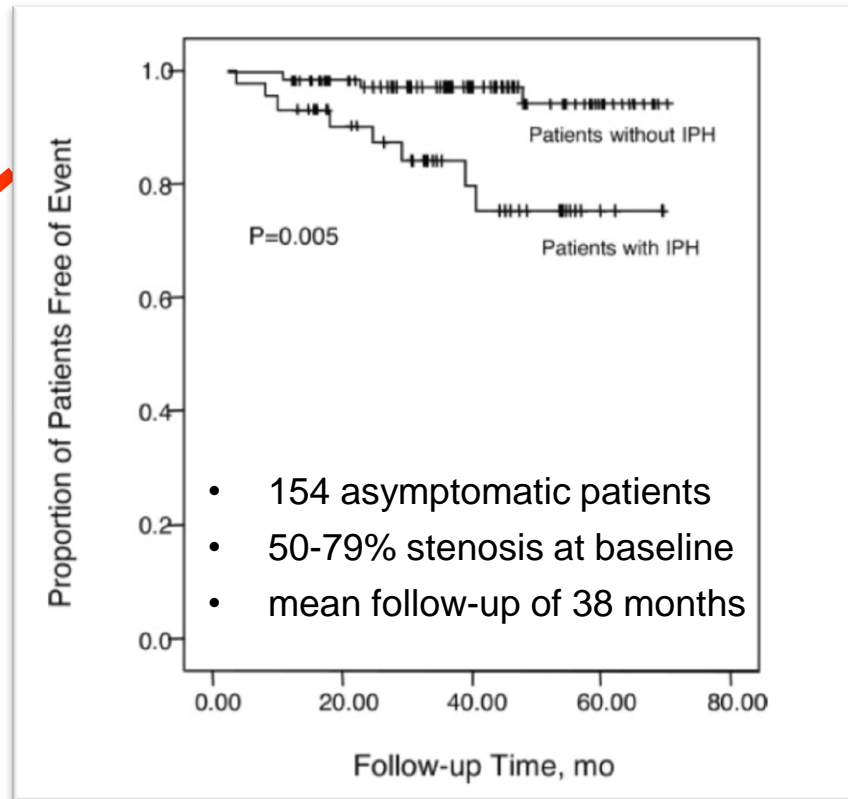
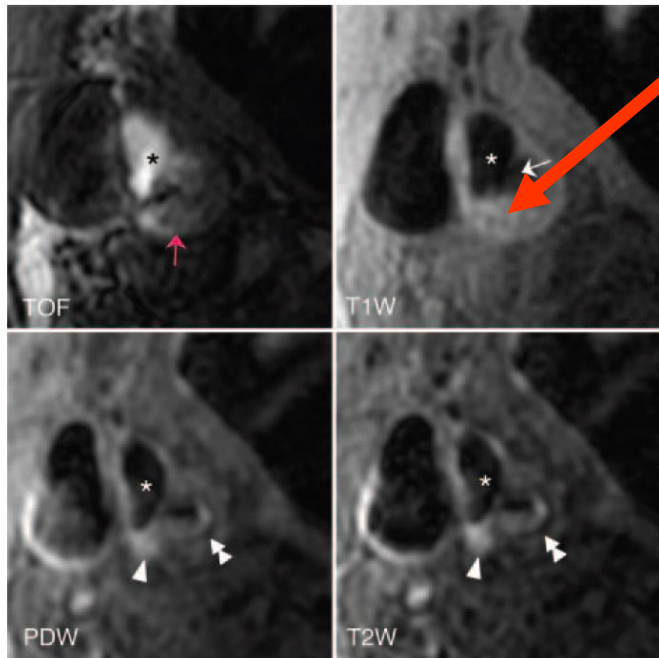


Module 1: Brain MRI
Module 2: Plaque imaging (MRI, ultrasound)

CAS: carotid artery stenting, **CEA:** carotid endarterectomy,
MRI: magnetic resonance imaging

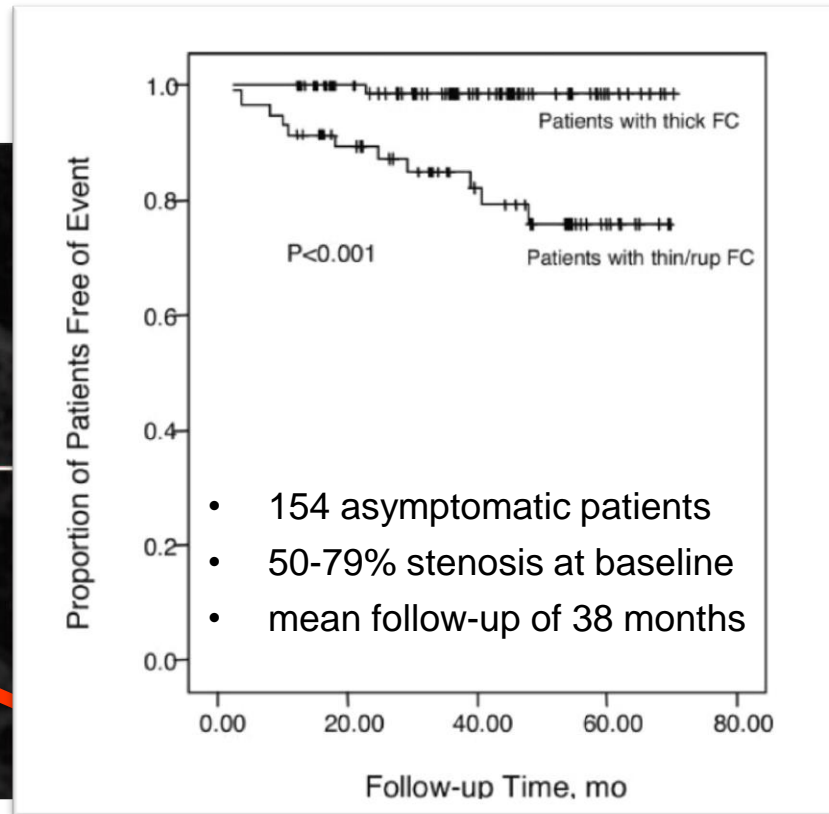
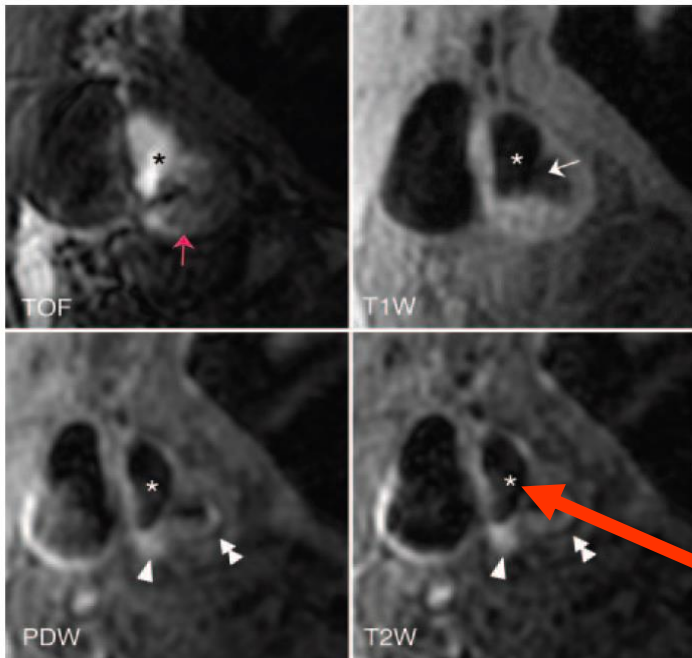
Imaging of carotid plaques: 2D phase-contrast MRI

Intra-plaque haemorrhage

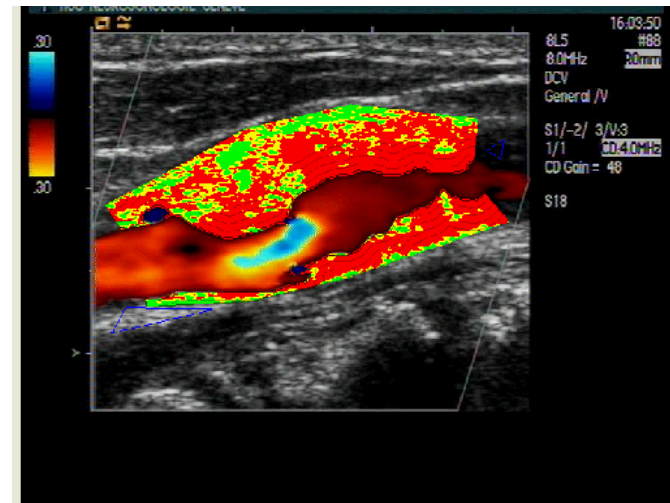


Imaging of carotid plaques: 2D phase-contrast MRI

Fibrous cap rupture



Imaging of carotid plaques: Plaque echolucency on carotid ultrasound



«Plaque instability» determined procedural risk in CREST: Death or any stroke within 30 days of treatment

■ Symptomatic stenosis

n= 1'321

□ **Stent: 6.0% +/- 0.9%**

VS

□ **CEA: 3.2% +/- 0.7%**

HR = 1.89

95%CI: 1.11- 3.21

p= 0.019

■ Asymptomatic stenosis

n=1'181

□ **Stent: 2.5% +/- 0.6%**

VS

□ **CEA: 1.4% +/- 0.5%**

HR = 1.88

95%CI: 0.79 – 4.42

p= 0.15

«Plaque instability» determined procedural risk in CREST: Death or any stroke within 30 days of treatment

■ Symptomatic stenosis

n= 1'321

≈ **unstable plaque**

□ **Stent: 6.0% +/- 0.9%**

VS

□ **CEA: 3.2% +/- 0.7%**

HR = 1.89

95%CI: 1.11- 3.21

p= 0.019

■ Asymptomatic stenosis

n=1'181

≈ **stable plaque**

□ **Stent: 2.5% +/- 0.6%**

VS

□ **CEA: 1.4% +/- 0.5%**

HR = 1.88

95%CI: 0.79 – 4.42

p= 0.15

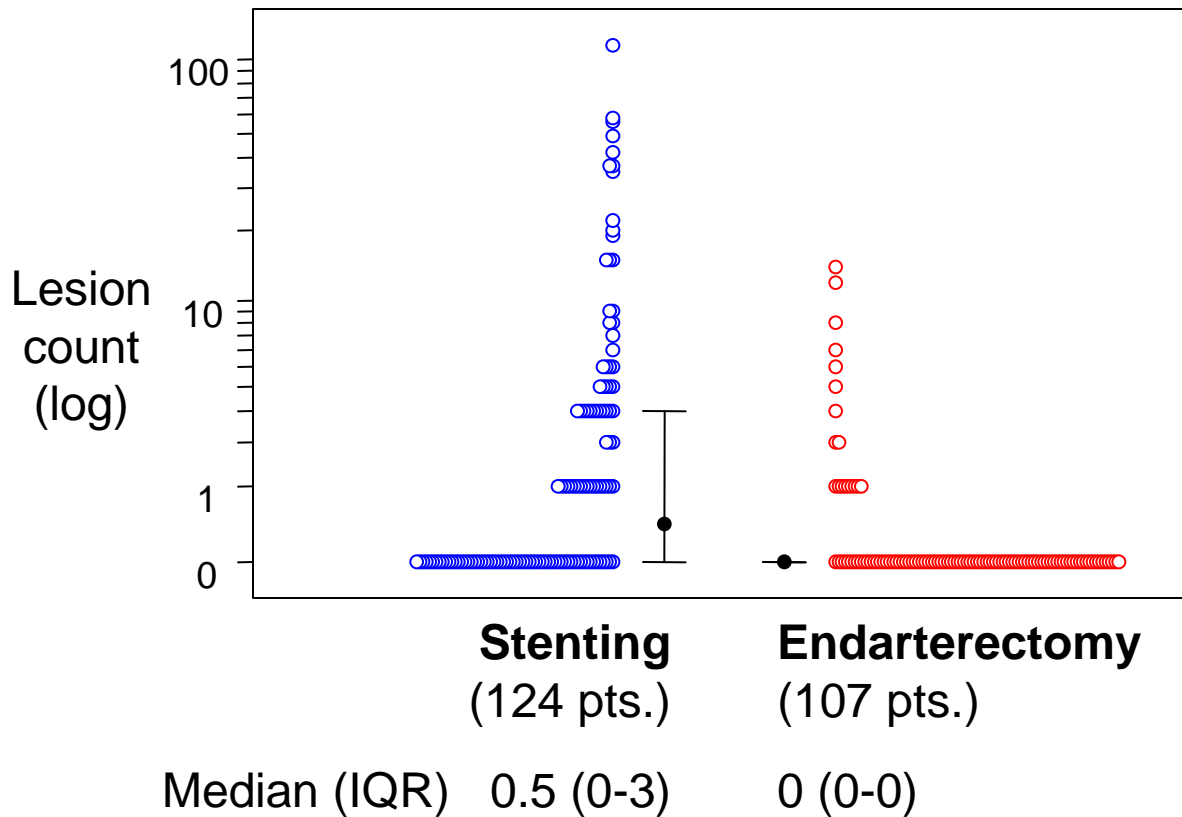
Participating centres & enrolment

- Currently enrolled: 81 patients
- Active centres:
 - University Hospital Basel (n=30)
 - University Hospital of Larissa (n=14)
 - Serbian Clinical Centre Belgrade (n=11)
 - UMC Utrecht (n=9)
 - Istituto Auxologico Milano (n=11)
 - Klinikum rechts der Isar, Munich (n=4)
 - La Sapienza Rome (n=2)

Power considerations

- Currently enrolled: $n=81$
- With 120 patients we can pick up an absolute difference in risk of DWI lesions between groups of about 20% (e.g. 30% versus 10%) with 80% power
- With 240 patients: risk difference of about 15%

Comparing DWI lesion count in the ICSS-MRI Substudy

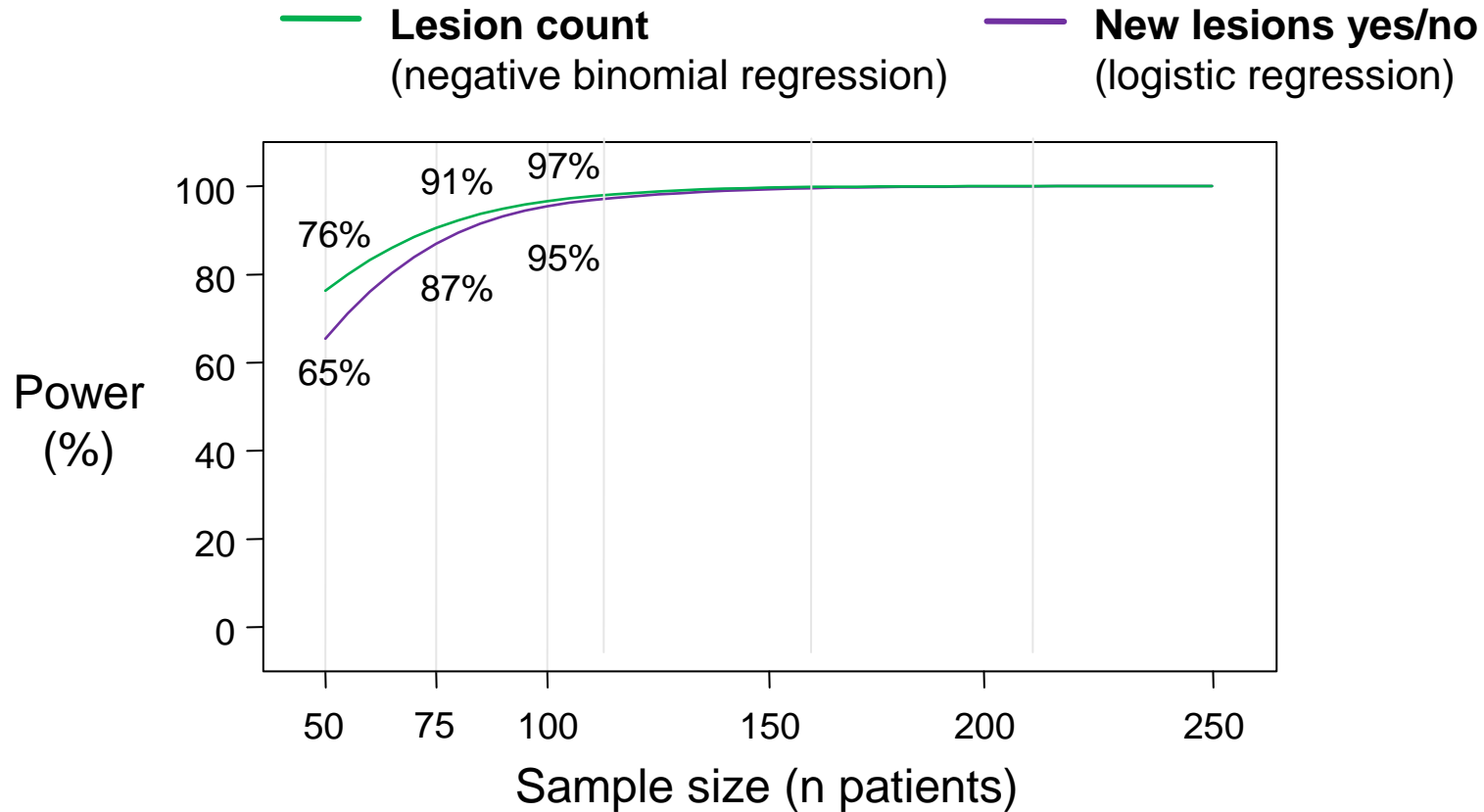


Risk ratio 8.8 (4.4-17.5)
*for a higher lesion count
with CAS than CEA*

***p<0.001**

(*P-value from negative binomial regression model)

Comparing DWI lesion count had higher power than DWI lesion yes/no



Centre remuneration

400 Euros per patient with completed pre- and postprocedural scan
(Swiss Heart Foundation)

Interested in joining or need further information?

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Thank you for your attention



