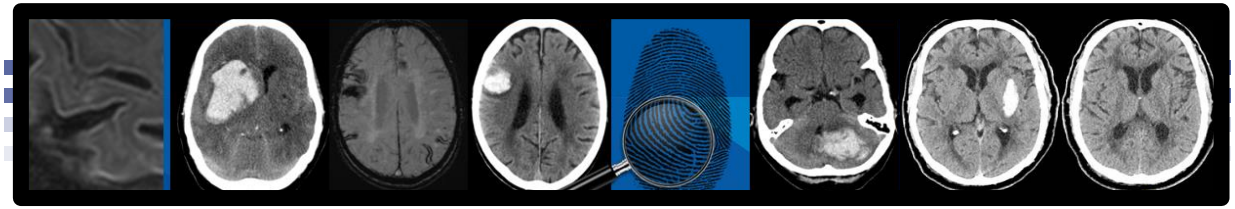


CHIRURGISCHE BEHANDELING VAN EEN INTRACEREBRALE BLOEDING

Neurovasculaire nascholing 19 januari 2024

Ruben Dammers
neurochirurg

Disclosure slide

- PI
  - DIST trial
    - RCT
    - ABC (Analysis of Budget-Impact and Cost-effectiveness)
    - INFLAME
- Speaker fee

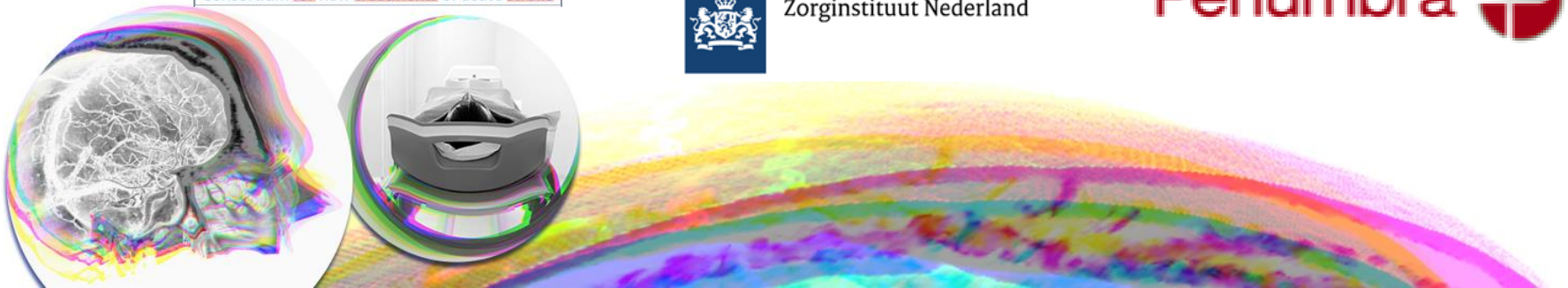
ZonMw

funded by the dutch heart foundation
Hartstichting

CONTRAST
Consortium for new treatments of acute stroke

Zorginstituut Nederland

Penumbra



Inhoud

Algemene introductie / impact van ICH

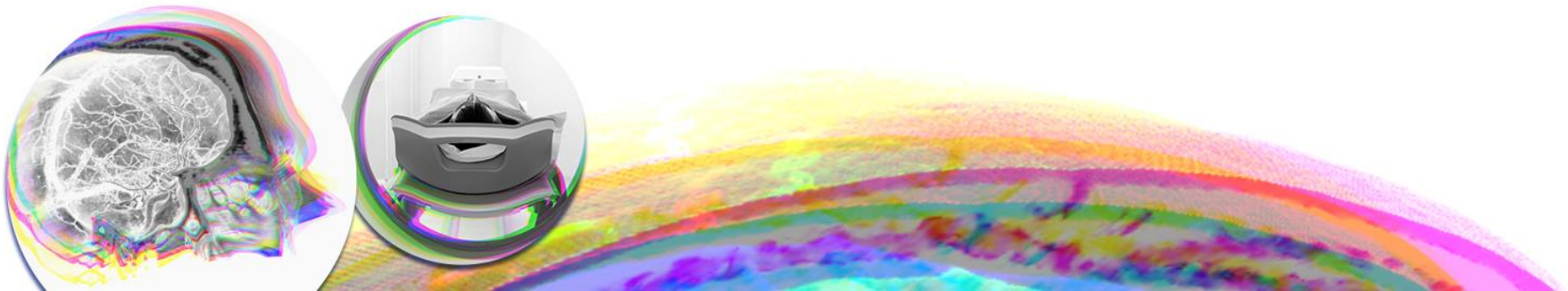
Diagnose

Indicatie chirurgie?

Welke chirurgie?

DIST studie

Conclusie



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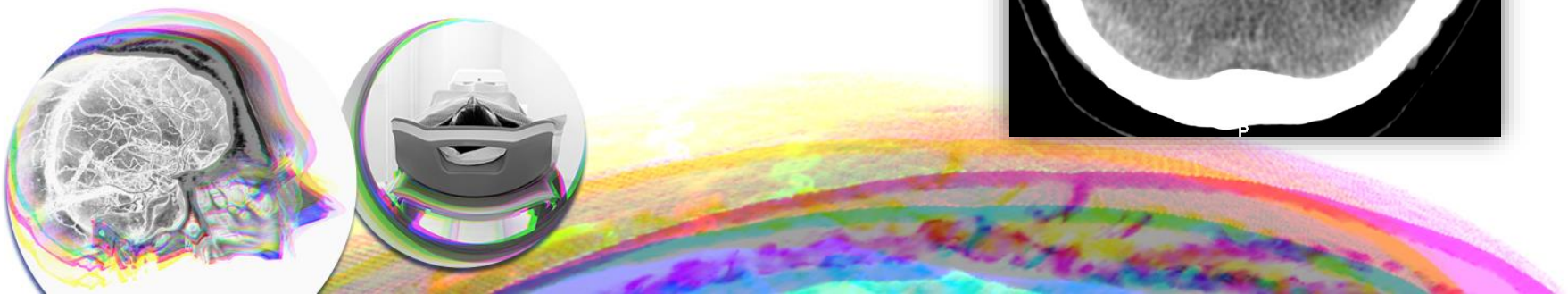
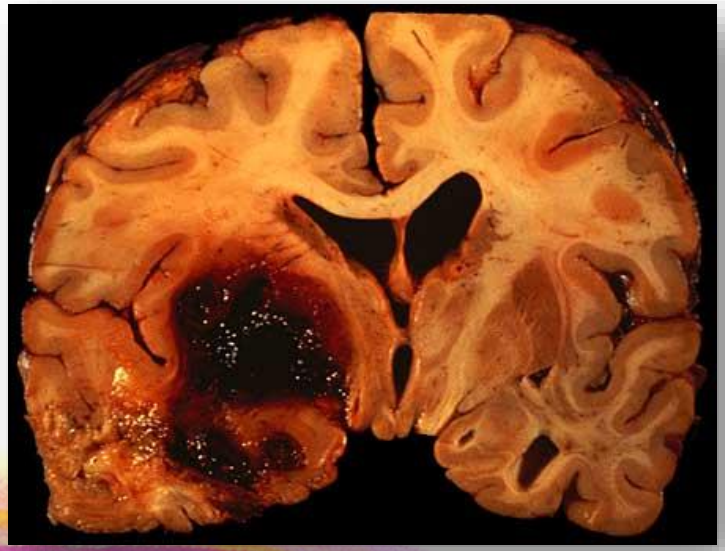
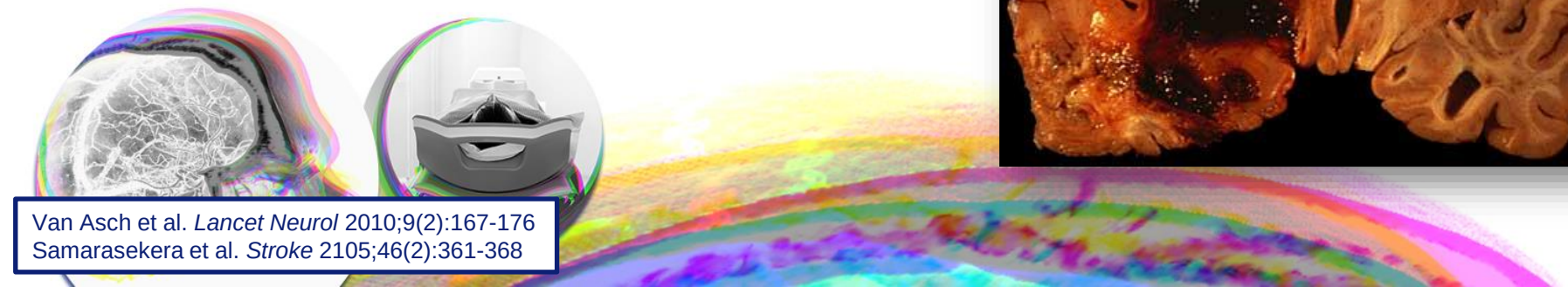


Algemene introductie / impact van ICH

- 10-15% van alle cerebrovasculaire accidenten
- Incidentie 25/100.000 persoon-jaren: 6000 in NL/jaar
- **Case-fatality 1 maand 40%**
- Life-time direct costs: 75k€ (Netherlands)





Van Asch et al. *Lancet Neurol* 2010;9(2):167-176
Samarasekera et al. *Stroke* 2105;46(2):361-368

Algemene introductie / impact van ICH

Ongeveer 3,4 miljoen gevallen wereldwijd in 2019

Verloren DALYs 68,6 miljoen

With conventional medical management (AHA or ESO guidelines), only 19 % of the patients live independently 1 year after.

Van Asch et al. *Lancet Neurol* 2010;9(2):167-176
Samarasekera et al. *Stroke* 2105;46(2):361-368
GBD 2016 collaborators. *Lancet Neurol* 2021;20(10);795-820

Algemene introductie / impact van ICH

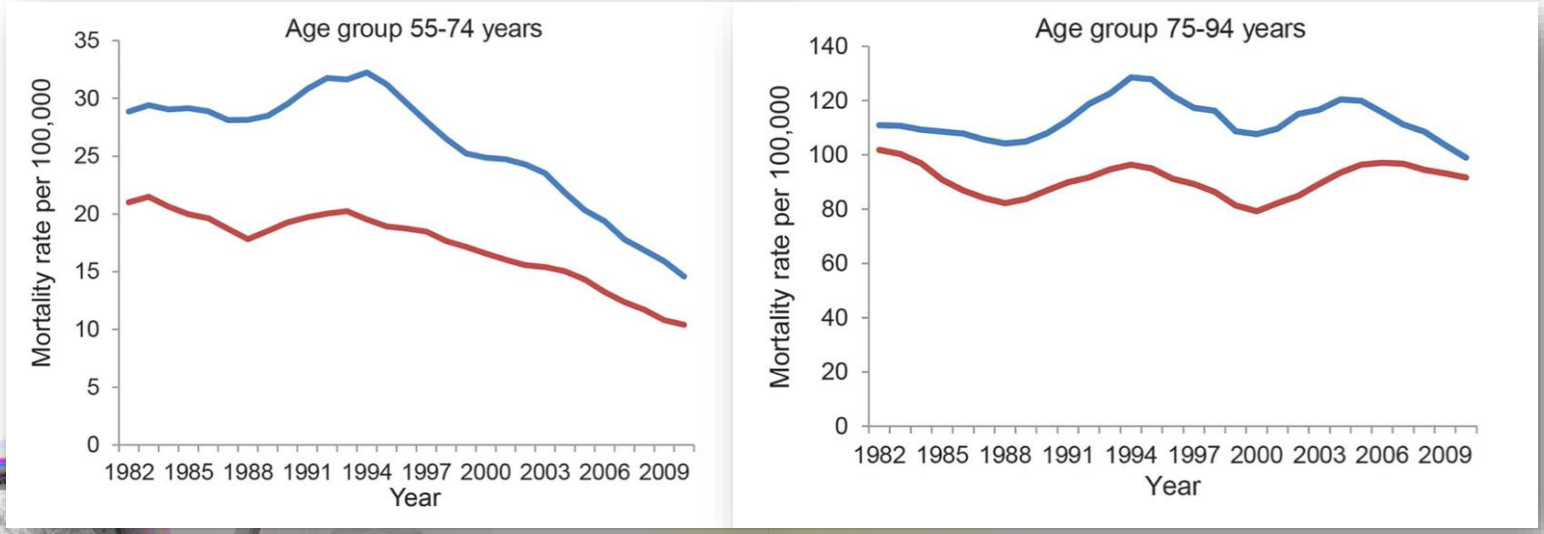
- Incidentie
  - 1983 → 2006 stabiel
  - Neemt toe met leeftijd

	Incidence per 100 000 person-years (95% CI)	Number of time periods	Incidence ratio (95% CI)
≤44 years[13,19]	1·9 (1·6–2·2)	16	0·10 (0·06–0·14)
45–54 years	19·1 (13·4–27·4)	15	Reference
55–64 years	36·5 (28·4–46·7)	16	1·8 (1·3–2·6)
65–74 years	77·1 (65·0–91·5)	18	3·8 (2·7–5·4)
75–84 years	136·9 (111·3–168·4)	18	6·8 (4·8–9·6)
≥85 years[19,23]	196·0 (148·3–259·1)	17	9·6 (6·6–13·9)

van Asch et al. *Lancet Neurol* 2010;9(2):167-176. Samarasekera et al. *Stroke* 2015;46(2):361-368

Algemene introductie / impact van ICH

- Mortaliteit
  - 1983 → 2009 stabiel in patiënten > 75 jaar
  - Afname in patiënten < 75 jaar



Jolink et al. *Neurol* 2015;85(15):1318-1324.

Inhoud

Algemene introductie / impact van ICH

Diagnose

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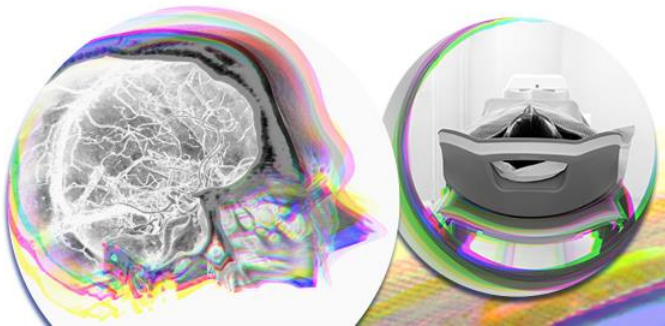
Welke chirurgie?

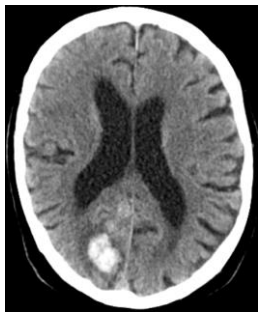
DIST studie

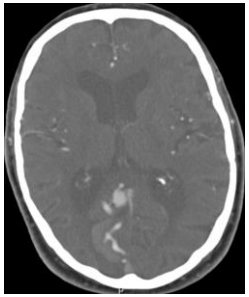
Conclusie

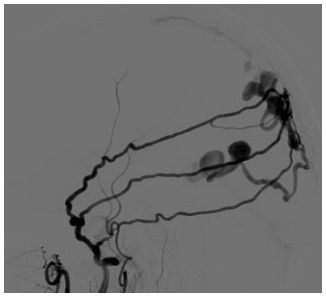


Diagnose

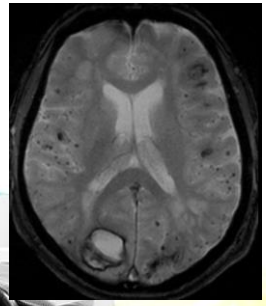
ICH is **geen diagnose**, maar een manifestatie van een onderliggende ziekte



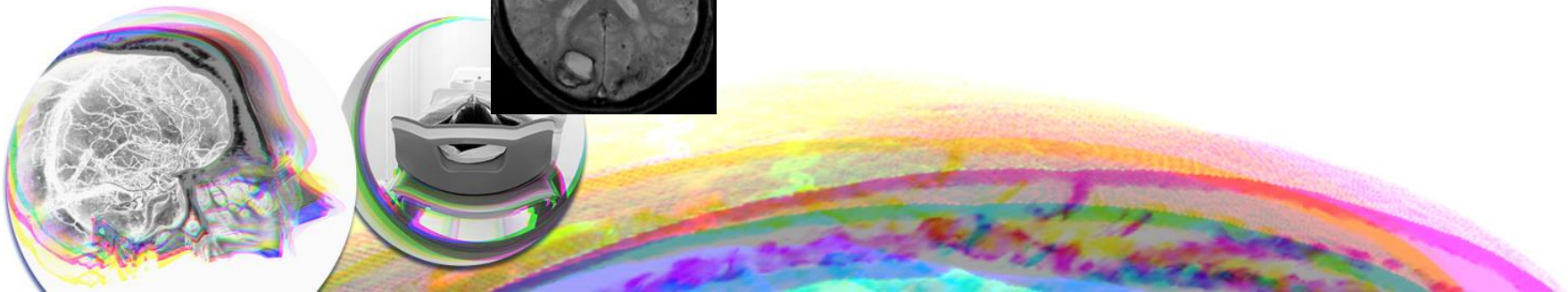




---> *85j M: durale AV fistul*



---> *66j M: cerebrale amyloid angiopathie*

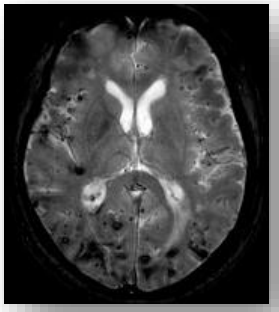


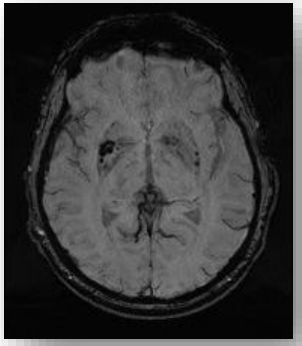
Diagnose

Oorzaken ICH

Meest voorkomend

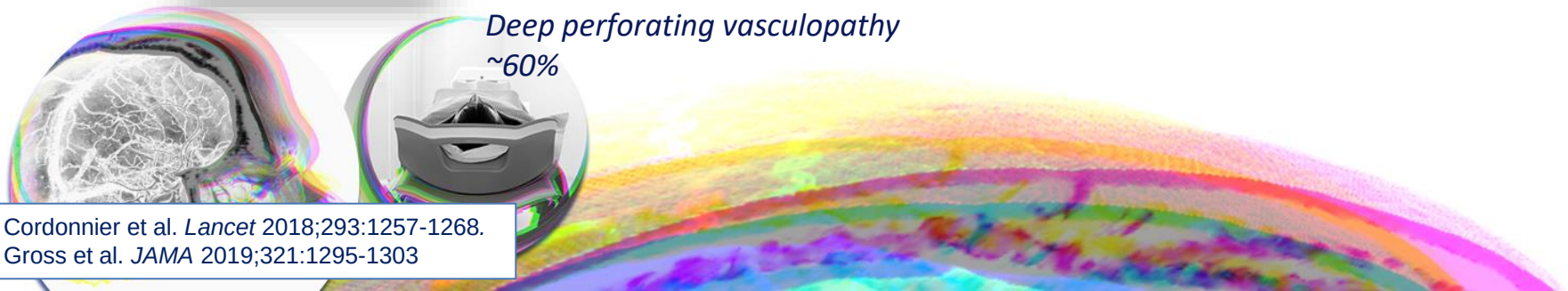
Cerebral amyloid angiopathy
~25%





"Secondary" ICH
~15%

Deep perforating vasculopathy
~60%

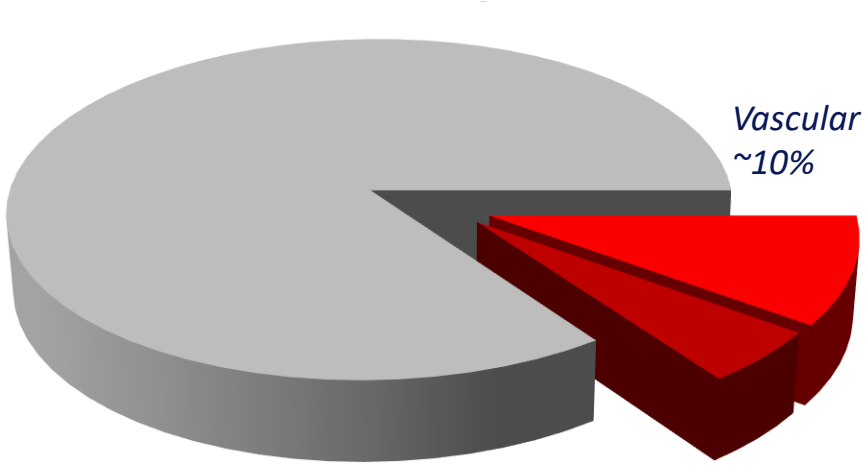


Cordonnier et al. *Lancet* 2018;293:1257-1268.
Gross et al. *JAMA* 2019;321:1295-1303

Diagnose

Oorzaken ICH

Meest voorkomende secundaire oorzaken



Vascular lesions
~10%

Non-vascular lesion
~5%

Cordonnier et al. *Lancet* 2018;293:1257-1268.
Gross et al. *JAMA* 2019;321:1295-1303

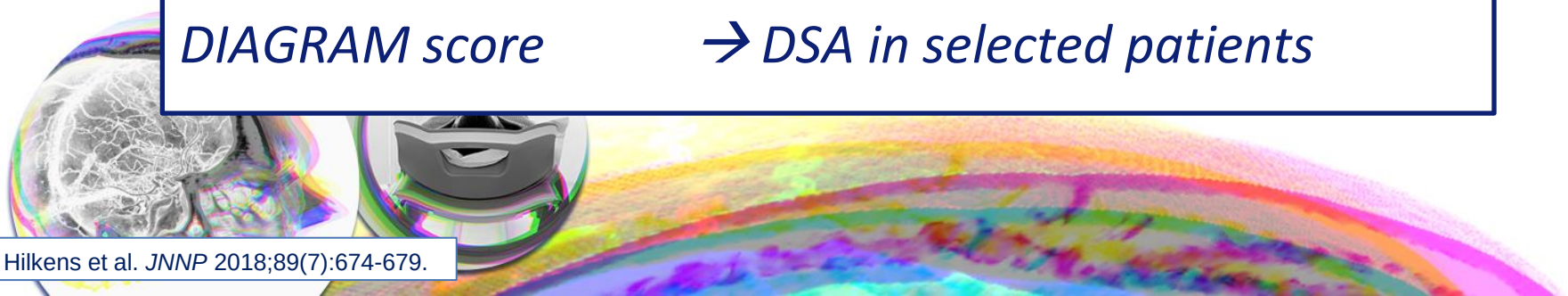
Diagnose

ICH is **geen diagnose**, dus zoek naar de onderliggende pathologie

(Chirurgische) interventie hangt hier ook van af

vasculaire laesie, tumor, *spontaan ICH*

CTA on admission	→ *macrovascular lesions*
MRI	→ *small vessel disease markers*
DIAGRAM score	→ *DSA in selected patients*



Hilkens et al. *JNNP* 2018;89(7):674-679.

Inhoud

Algemene introductie / impact van ICH

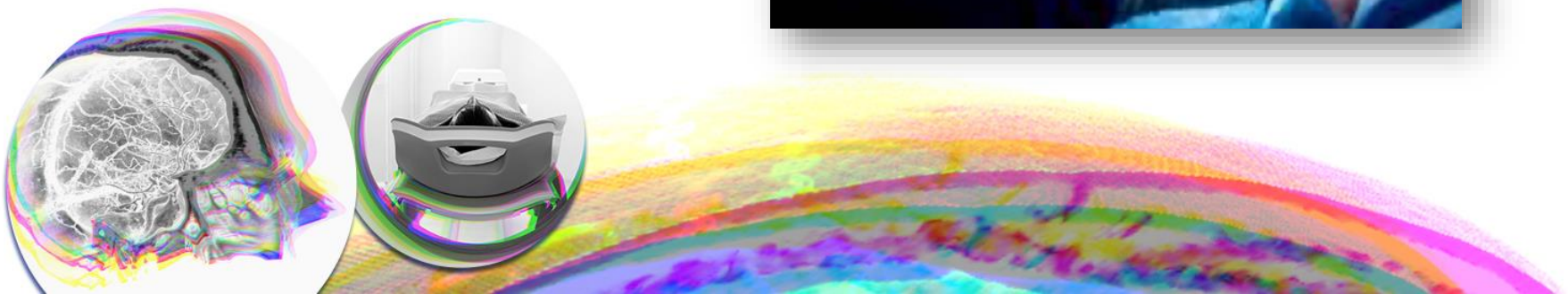
Diagnose

Indicatie chirurgie?

Welke chirurgie?

DIST studie

Conclusie



Indicatie chirurgie?

- Potentiële therapeutische targets

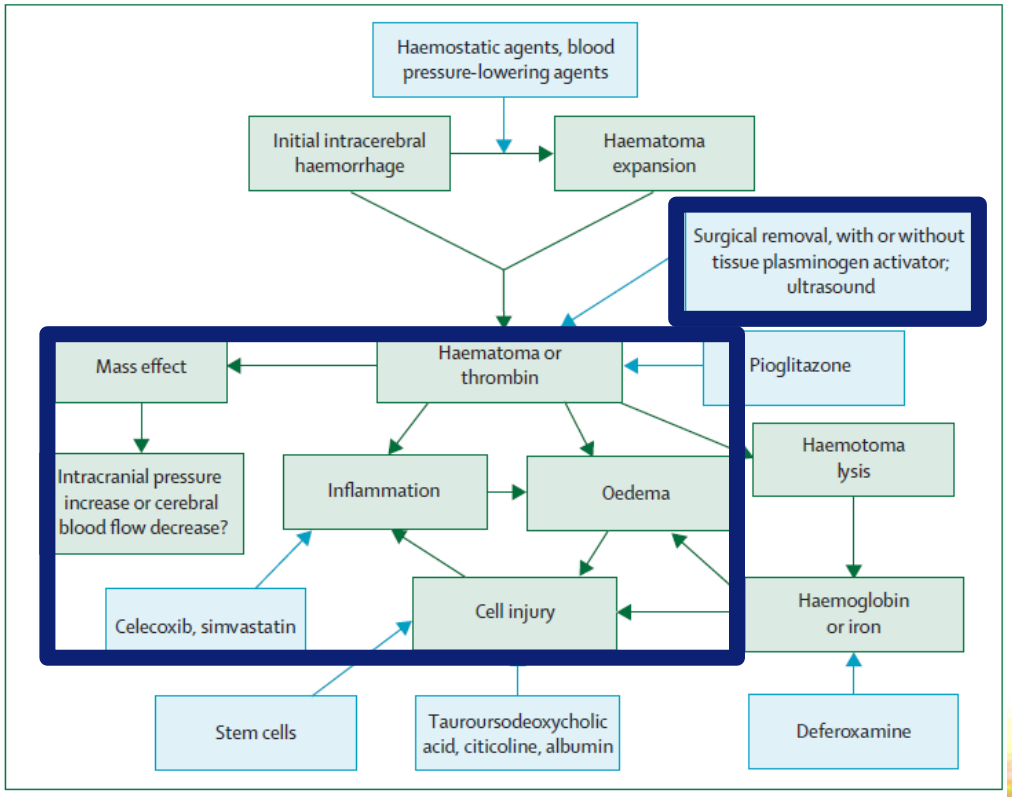


Figure 3: Current clinical trials for intracerebral haemorrhage in relation to proposed injury mechanisms

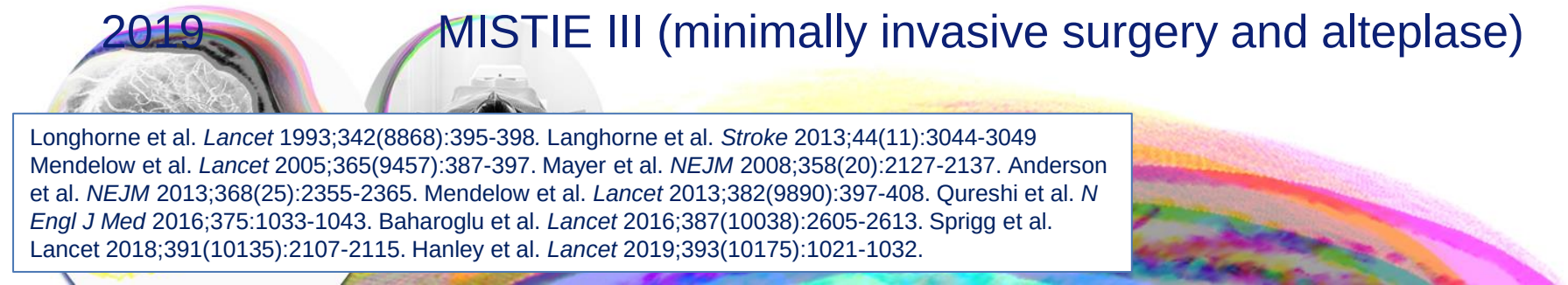
- **Primaire schade (0-4 hours)**
  - Directe mechanische schade door ICH
  - Cytotoxisch oedeem
  - Celdood
- **Secundaire schade (4 hours-7 days)**
  - Vasogeen & cytotoxisch oedeem
  - Apoptose
  - [illegible]toxiciteit
  - Bloed-hersenbarrière schade

Kans om secundaire schade te beperken

Keep et al. *Lancet Neurol* 2012;11(8):720-731. Zhou et al. *Prog Neurobiol* 2014;115:25-44

Indicatie chirurgie?

1993	Stroke unit care
2005	STICH (surgery)
2008	FAST (rFactor VIIa)
2013	INTERACT2 (intensive hypertension treatment)
2013	STICH II (surgery)
2016	ATACH-II (very intensive hypertension treatment)
2016	PATCH (platelets)
2018	TICH-2 (tranexamic acid)
2019	MISTIE III (minimally invasive surgery and alteplase)



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Indicatie chirurgie?

1993	Stroke unit care
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2013	INTERACT2 (intensive hypertension treatment)
2013	STICH II (surgery)
2016	ATACH-II (very intensive hypertension treatment)
2016	PATCH (platelets) → harmful
2018	TICH-2 (tranexamic acid)
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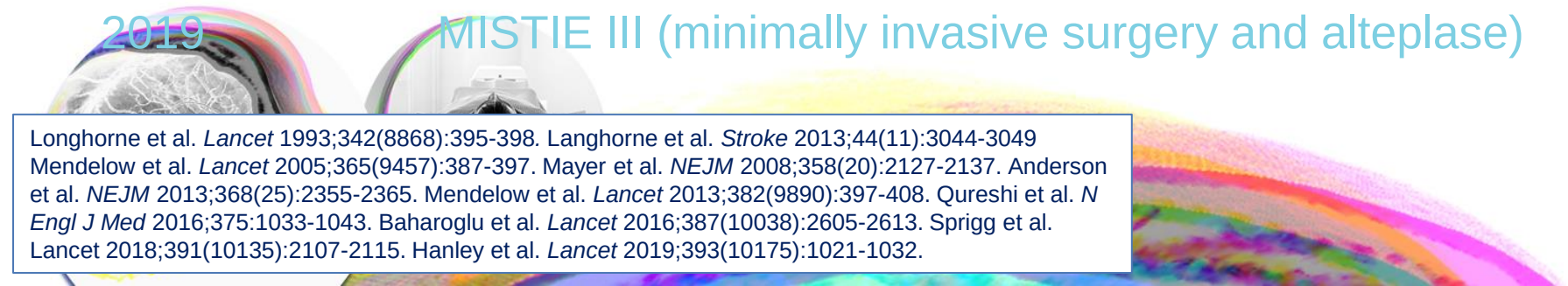

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Indicatie chirurgie?

AHA/ASA Guideline

Guidelines for the Management of Spontaneous Intracerebral Hemorrhage

A Guideline for Healthcare Professionals From the American Heart Association/American Stroke Association

- General ICU Monitoring and Nursing Care
- BP control
- Glucose Management
- Seizure Management
- IVH - CSF drain

- *Supportive care and multi-system homeostasis*
- ***Surgery only with neurological decline or hydrocephalus***
- *Rehabilitation and recovery via access to a multidisciplinary approach*

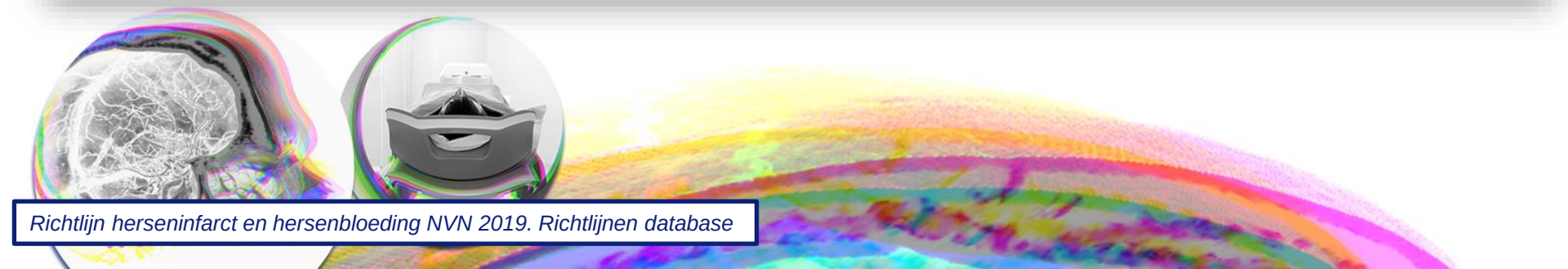
Hemphill JC, Greenberg SM, Anderson CS, Becker K, Bendok BR, Cushman M, et al. Guidelines for the Management of Spontaneous Intracerebral Hemorrhage. Stroke. 2015;46(7):2032-2060.

Indicatie chirurgie?

Supratentorieel

Wees zeer terughoudend met het opereren van patiënten met een spontaan intracerebraal hematoom.

Overweeg een operatie bij patiënten met progressieve neurologische achteruitgang met een oppervlakkig gelegen hematoom.



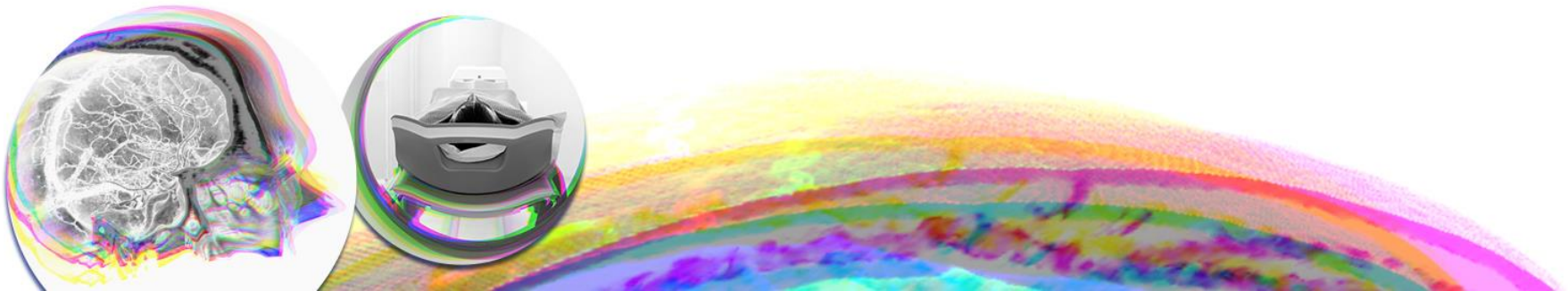
Richtlijn herseninfarct en hersenbloeding NVN 2019. Richtlijnen database

Indicatie chirurgie?

Indicatie chirurgie?

Waarom is evacuatie van het ICH niet effectief gebleken?

- verkeerde techniek?
- operatie te laat?
- te weinig hematoom verwijderd?
- verkeerde target?



Indicatie chirurgie?

Systematisch review en meta-analyse

21 RCTs chirurgie *vs*. standaardbehandeling

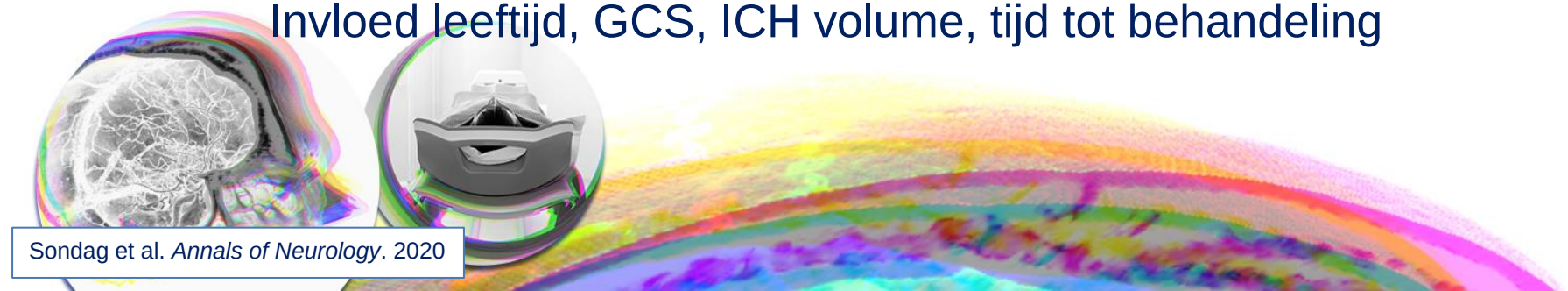
4 van 21 (19%) hoogste kwaliteit studies

13 studies minimaal invasieve chirurgie

4.145 patients

Primaire uitkomst: goede functionele uitkomst op 6 maanden

Invloed leeftijd, GCS, ICH volume, tijd tot behandeling

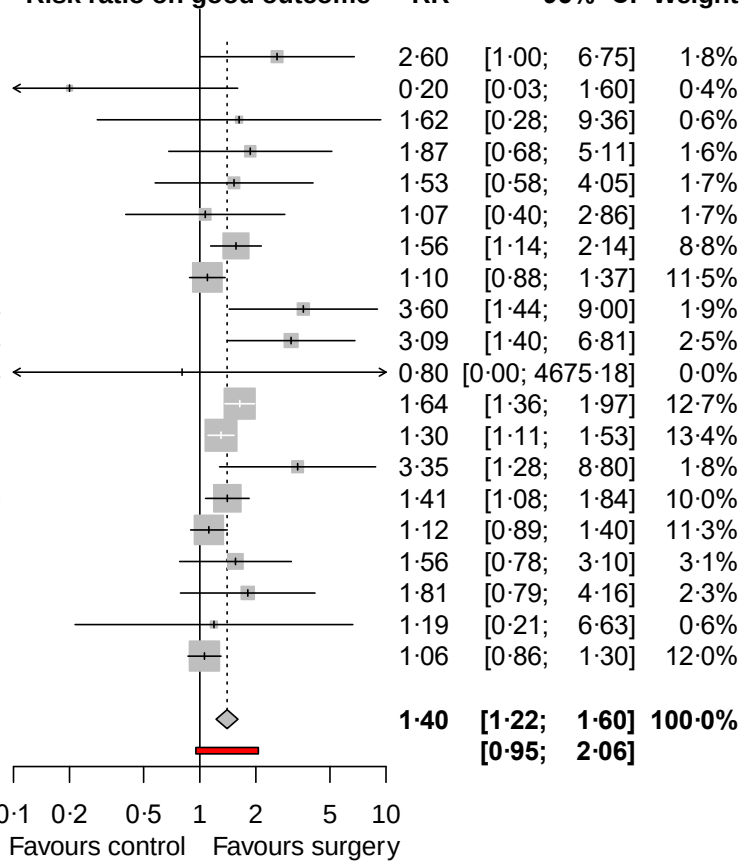


Sondag et al. *Annals of Neurology*. 2020

Indicatie chirurgie?

Study	Surgery Events	Surgery Total	Control Events	Control Total	RR	95%−CI	Weight
Auer 1989	13	50	5	50	2·60	[1·00; 6·75]	1·8%
Juvela 1989	1	26	5	26	0·20	[0·03; 1·60]	0·4%
Batjer 1990	2	8	2	13	1·62	[0·28; 9·36]	0·6%
Morgenstern 1998	7	15	4	16	1·87	[0·68; 5·11]	1·6%
Zuccarello 1999	5	9	4	11	1·53	[0·58; 4·05]	1·7%
Teernstra 2003	7	36	6	33	1·07	[0·40; 2·86]	1·7%
Hattori 2004	61	121	39	121	1·56	[1·14; 2·14]	8·8%
Mendelow 2005	122	468	118	497	1·10	[0·88; 1·37]	11·5%
Pantazis 2006	18	54	5	54	3·60	[1·44; 9·00]	1·9%
Luo 2008	18	33	6	34	3·09	[1·40; 6·81]	2·5%
Miller 2008	0	5	0	4	0·80	[0·00; 4675·18]	0·0%
Young 2009	148	204	81	183	1·64	[1·36; 1·97]	12·7%
Wang 2009	138	194	99	181	1·30	[1·11; 1·53]	13·4%
Wei 2010	26	64	4	33	3·35	[1·28; 8·80]	1·8%
Wang 2011	30	32	20	30	1·41	[1·08; 1·84]	10·0%
Mendelow 2013	107	297	92	286	1·12	[0·89; 1·40]	11·3%
Hanley 2016	18	54	9	42	1·56	[0·78; 3·10]	3·1%
Vespa 2016	6	14	9	38	1·81	[0·79; 4·16]	2·3%
Bhaskar 2017	3	34	2	27	1·19	[0·21; 6·63]	0·6%
Hanley 2019	110	249	100	240	1·06	[0·86; 1·30]	12·0%
Random effects model	**840**	**1967**	**610**	**1919**	**1·40**	**[1·22; 1·60]**	**100·0%**
Prediction interval						**[0·95; 2·06]**	

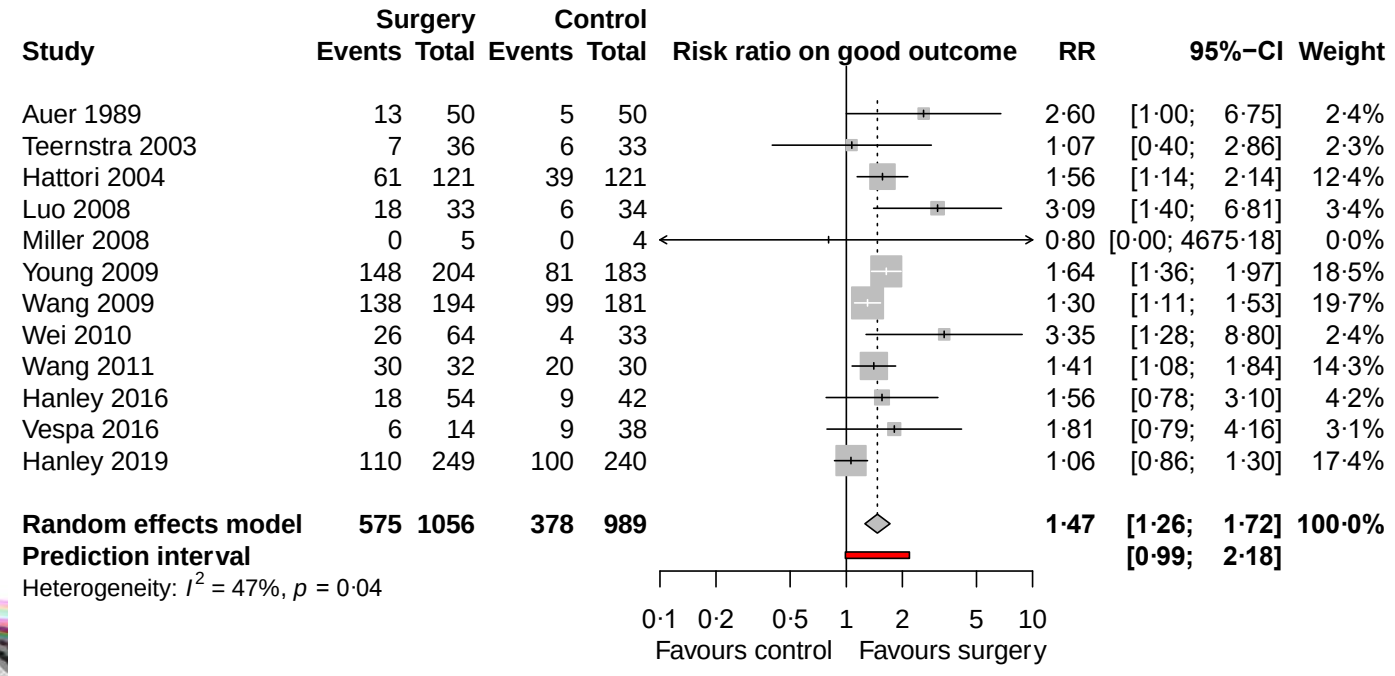
Heterogeneity: I^2 = 46%, p = 0·01



Sondag et al. *Annals of Neurology*. 2020

Indicatie chirurgie? Verkeerde techniek?

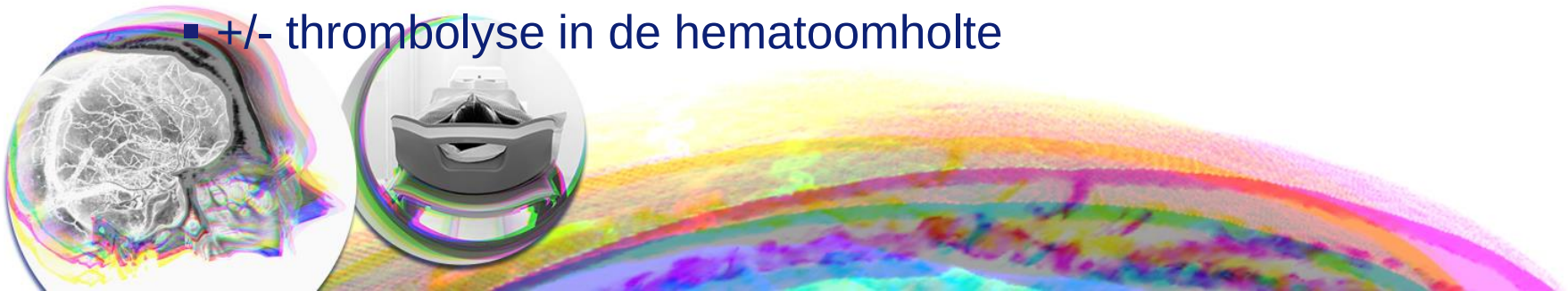
- Minimaal invasieve chirurgie alleen



Sondag et al. *Annals of Neurology*. 2020

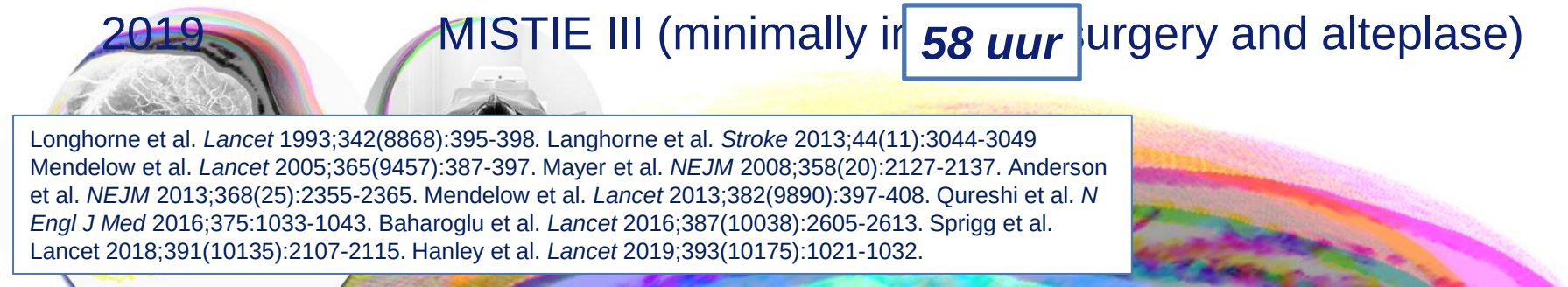
Indicatie chirurgie? Verkeerde techniek?

- Hydrocephalus behandeling
  - EVD +/- thrombolyse IVH
- ”Open” chirurgie
  - Hemicraniectomie
  - (mini-)Craniotomie met evacuatie hematoom
- “Minimaal invasieve” chirurgie
  - Stereotactische aspiratie
  - Endoscopie-geleide evacuatie hematoom
  - +/- thrombolyse in de hematoomholte



Indicatie chirurgie? Te laat?

1993	Stroke unit care	
2005	STICH (surgery)	***30 uur***
2008	FAST (rFactor VIIa)	
2013	INTERACT2 (intensive hypertension treatment)	
2013	STICH II (surgery)	***28 uur***
2016	ATACH-II (very intensive hypertension treatment)	
2016	PATCH (platelets)	
2018	TICH-2 (tranexamic acid)	
2019	MISTIE III (minimally i	***58 uur*** urgery and alteplase)



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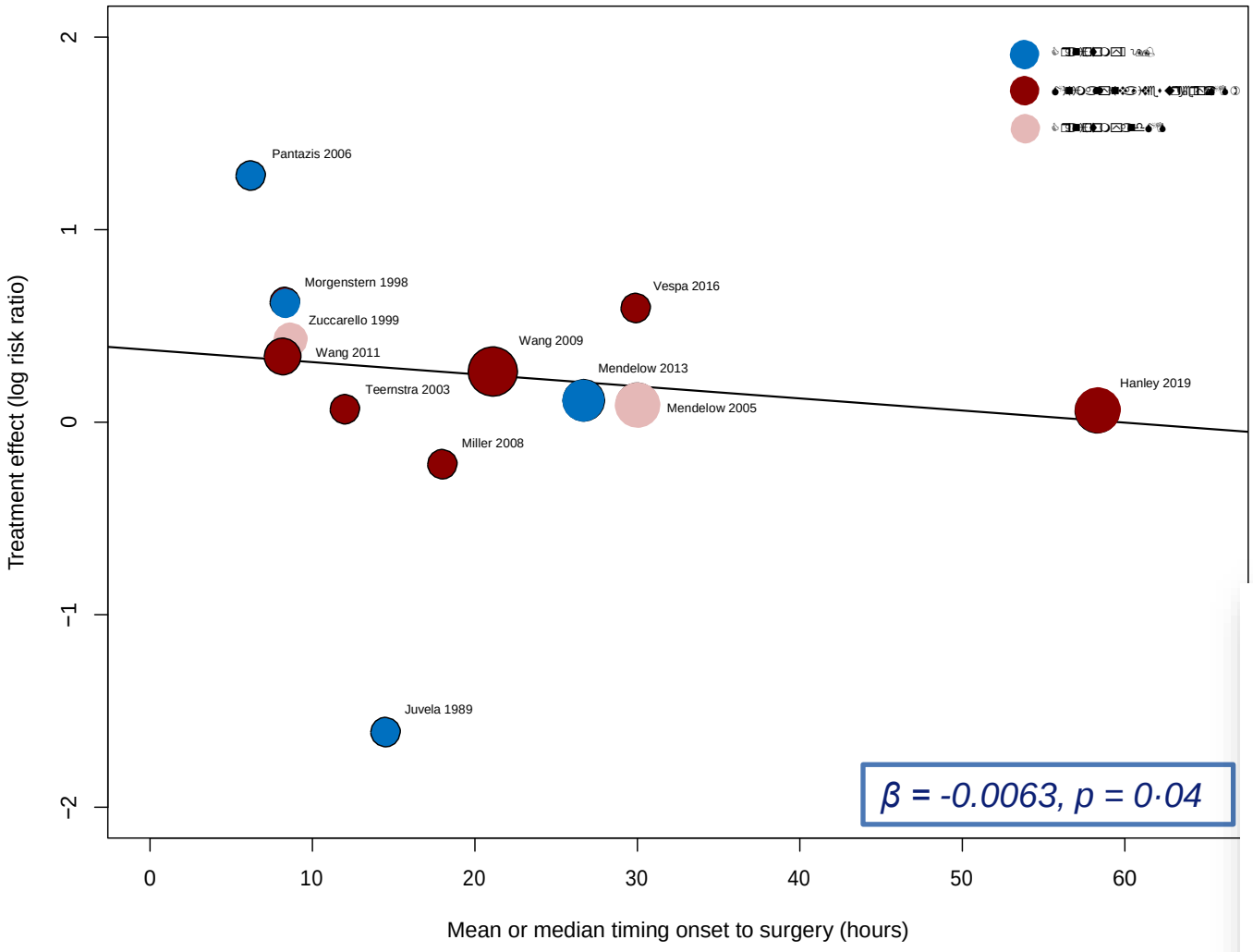
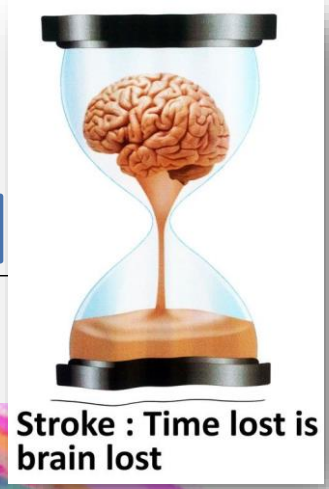
Indicatie chirurgie? Te laat?





Sondag et al. *Annals of Neurology*. 2020

Indicatie chirurgie? Te laat?

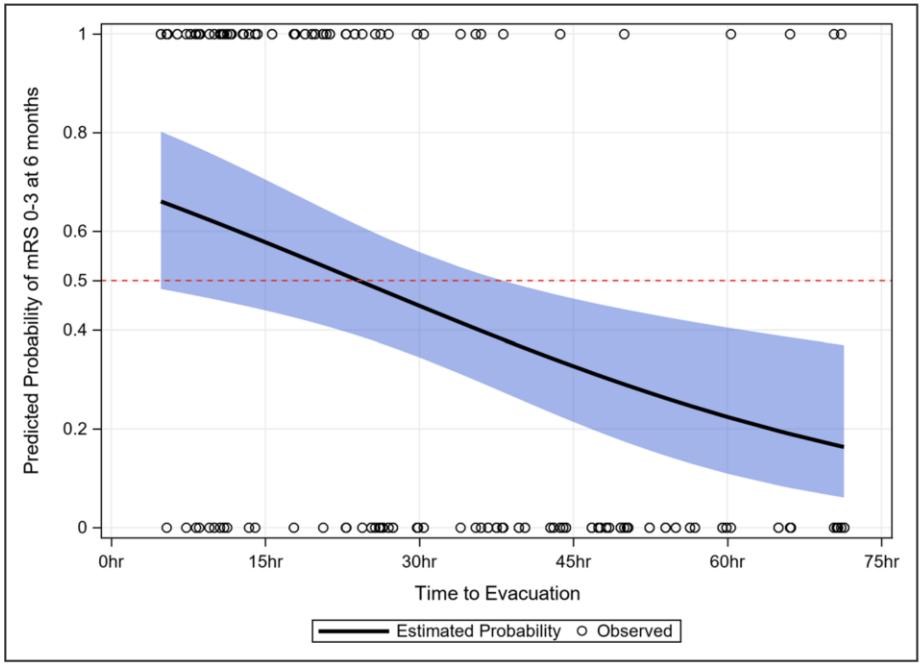
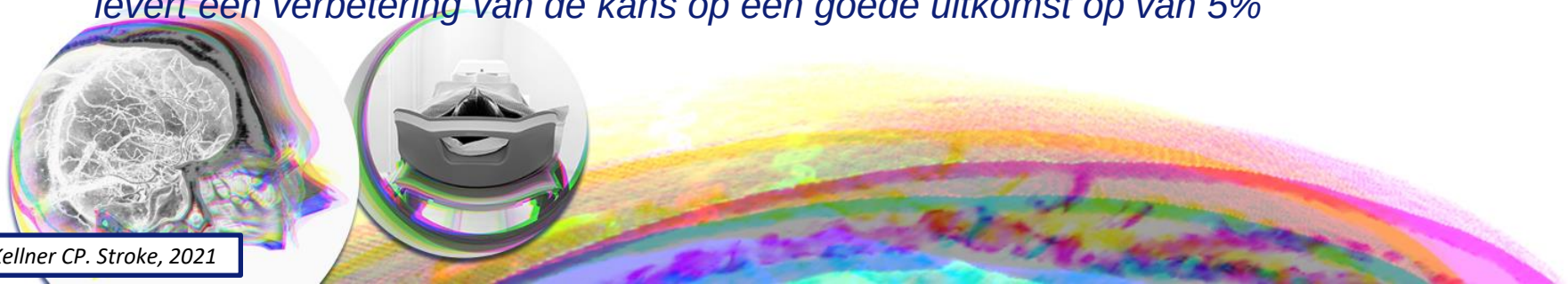


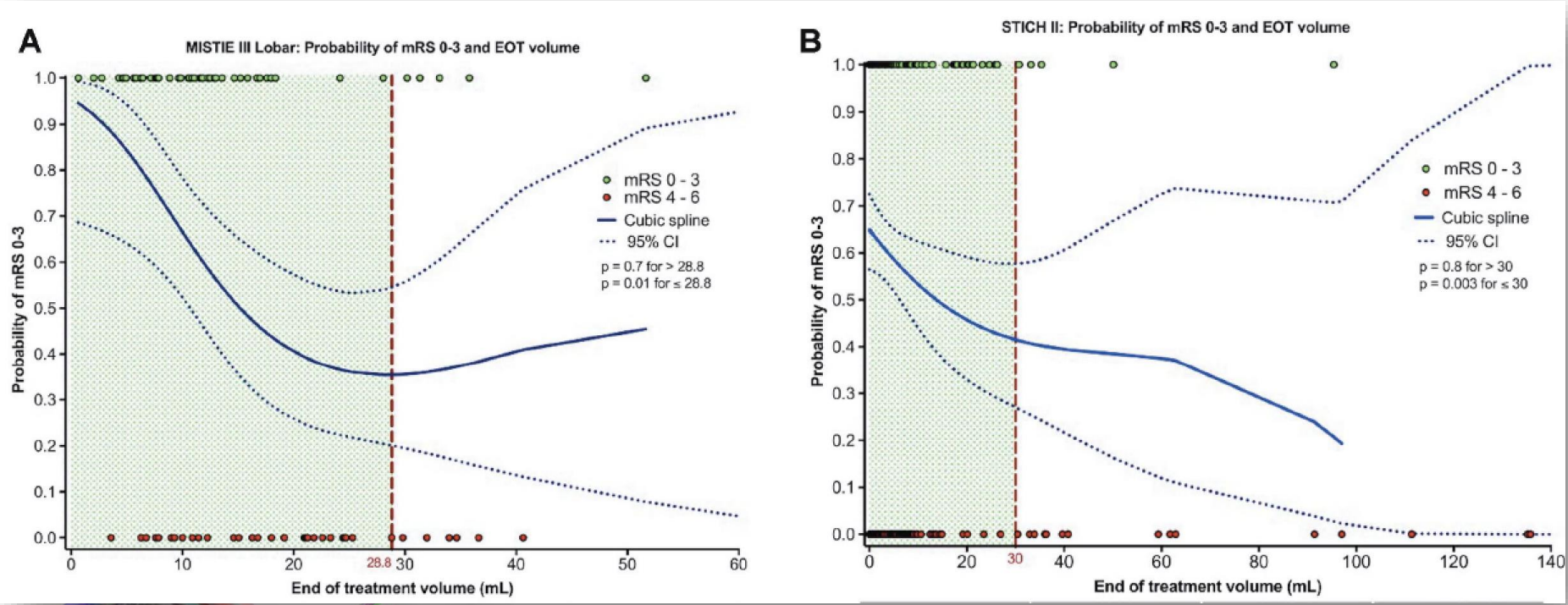
Figure. Decreased time to evacuation is independently associated with a decrease in the probability of achieving a good outcome at 6 mo (shade: 95% CI).
mRS indicates modified Rankin Scale.

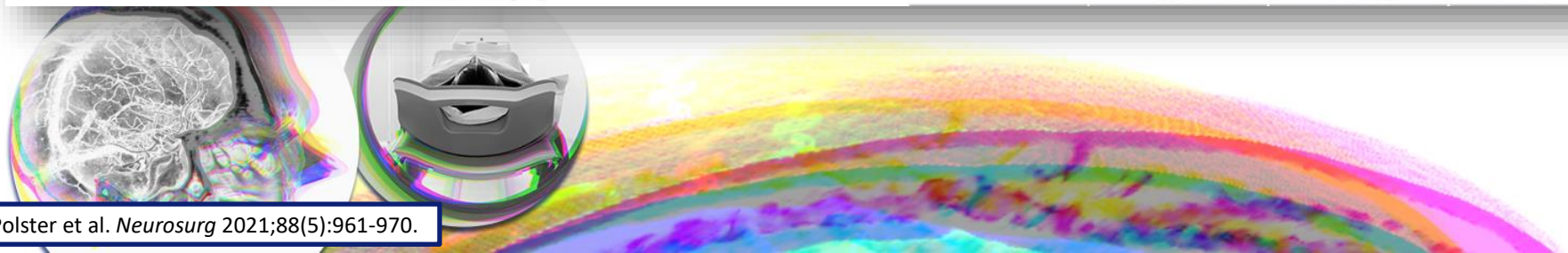
Ieder uur dat eerder wordt geopereerd,
levert een verbetering van de kans op een goede uitkomst op van 5%



Kellner CP. Stroke, 2021

Indicatie chirurgie? Te weinig?

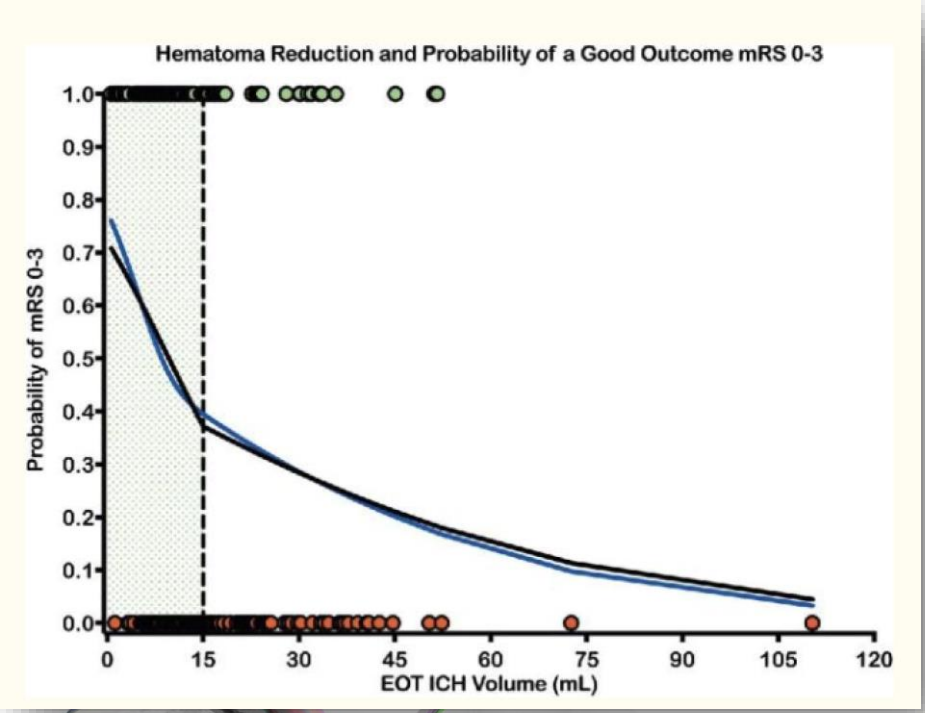




Polster et al. *Neurosurg* 2021;88(5):961-970.

Indicatie chirurgie? Te weinig?

MISTIE III



5i. Graphical Relationship between Probability of mRS 0-3 Outcome and Clot Remaining at EOT

Inclusion criterion: ICH ≥30mL

Presentation: 42.7mL (30.4-54.4)
Stability scan: 45.8 mL (35.4-59.6)

Surgery:

>80% reduction:	33%
Mean reduction:	69%
Percentage ≤15mL:	58%
Median vol removed:	32mL (24-42)
Median vol remaining:	13mL (8-21)

Awad et al. *Neurosurg* 2019;84(6):1157-1168.

Inhoud

Algemene introductie / impact van ICH

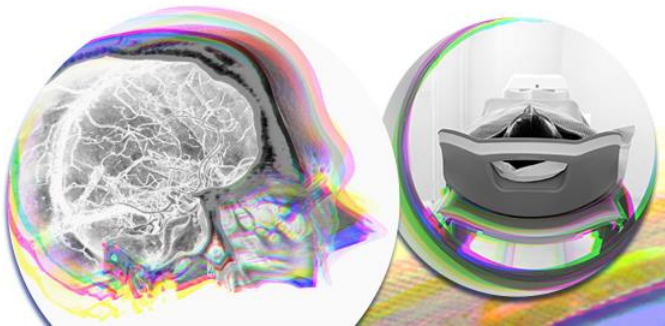
Diagnose

Indicatie chirurgie?

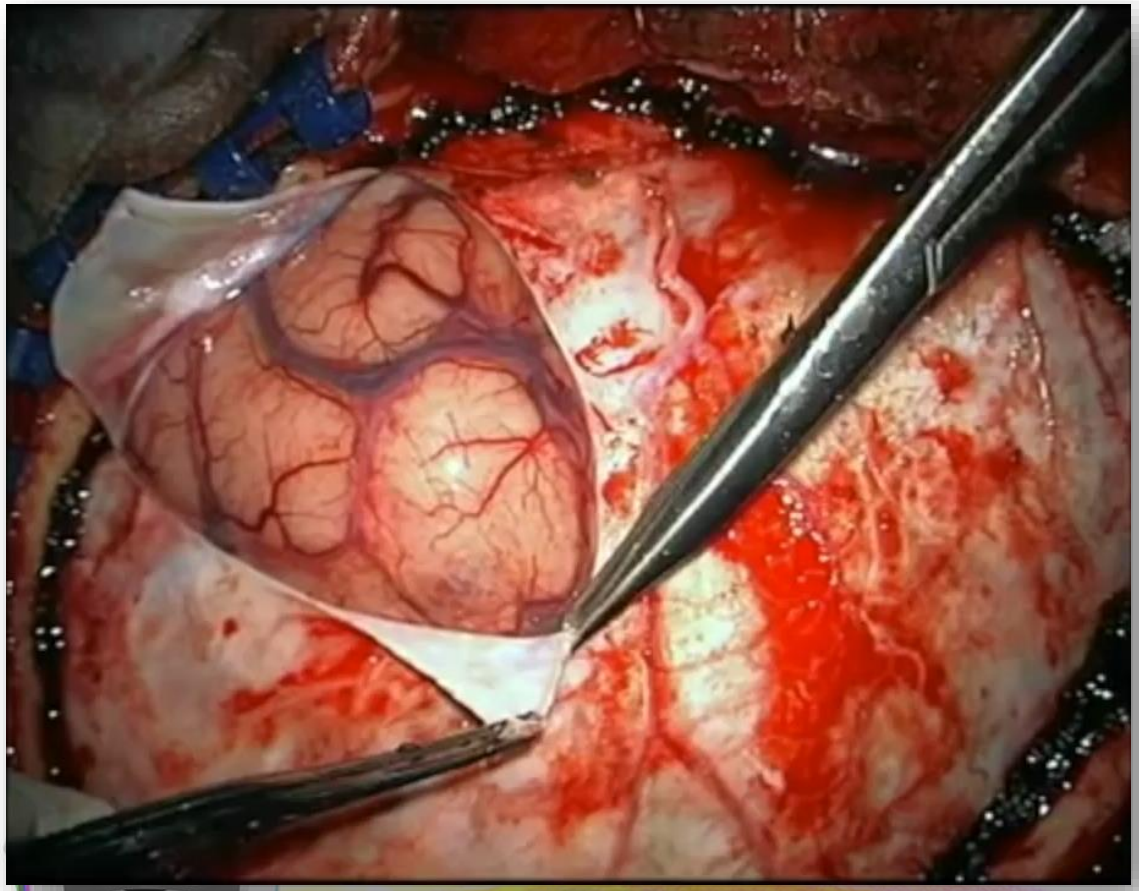
Welke chirurgie?

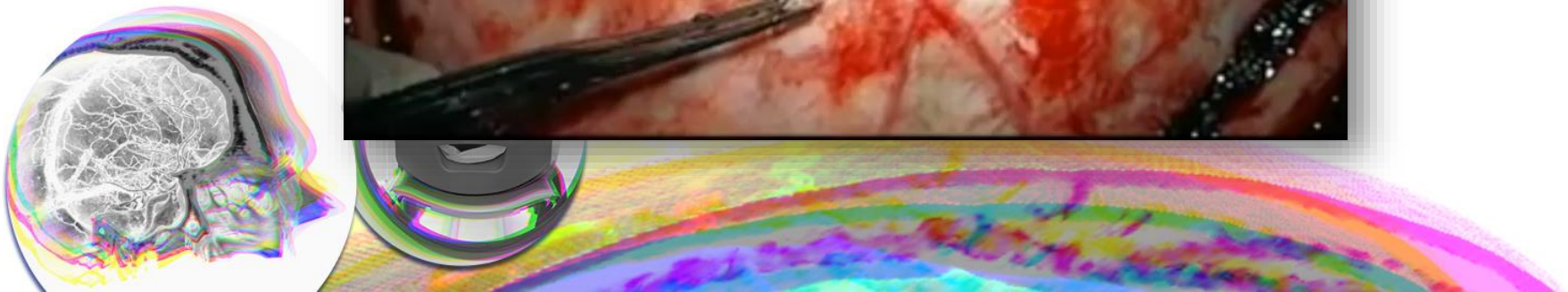
DIST studie

Conclusie

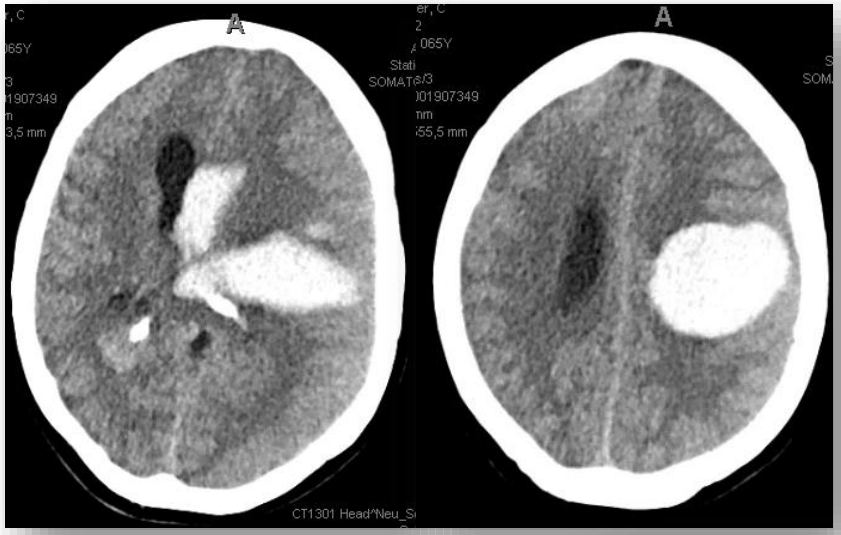


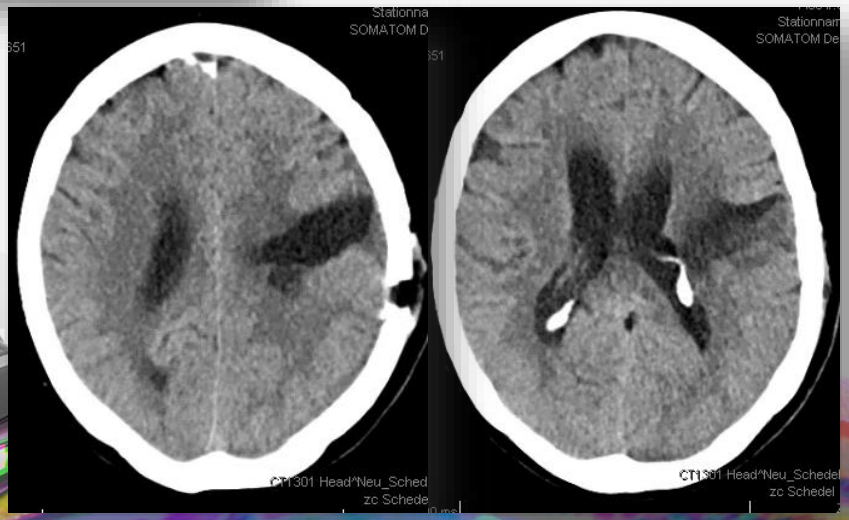
Welke chirurgie? Open chirurgie

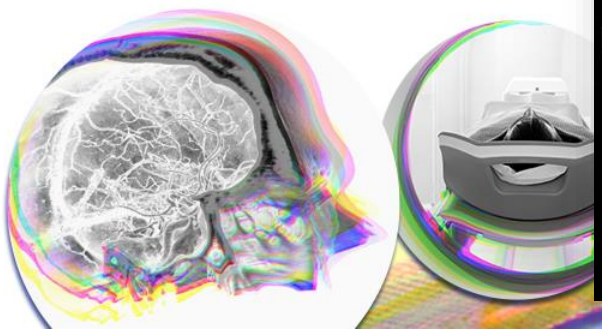




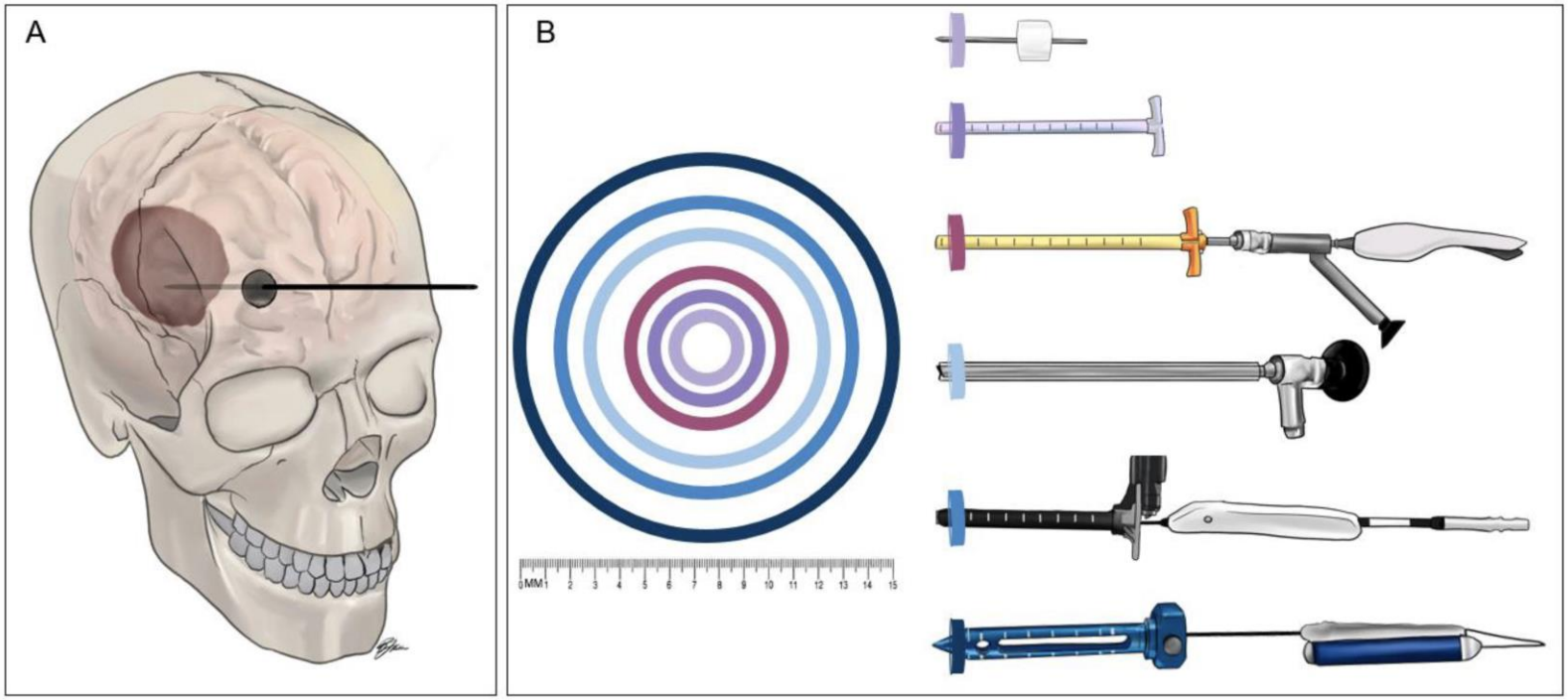
Welke chirurgie? Open chirurgie

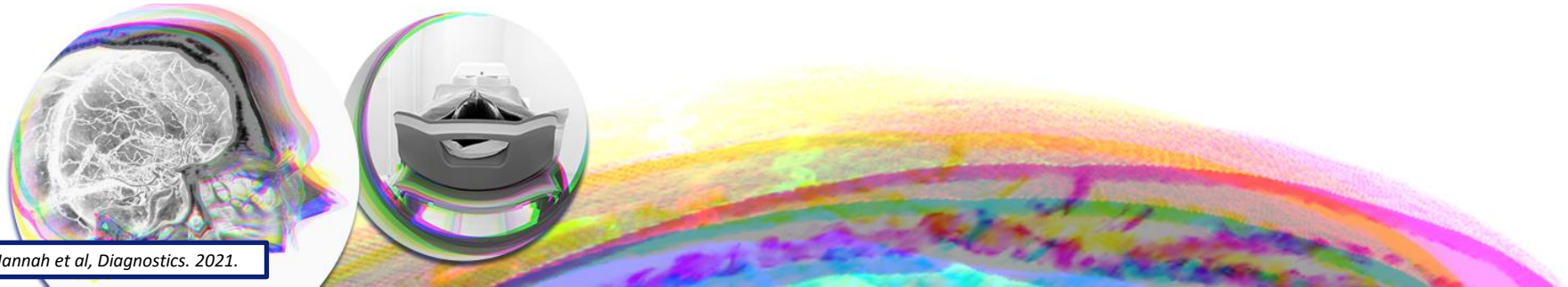






Welke chirurgie? Minimaal invasief

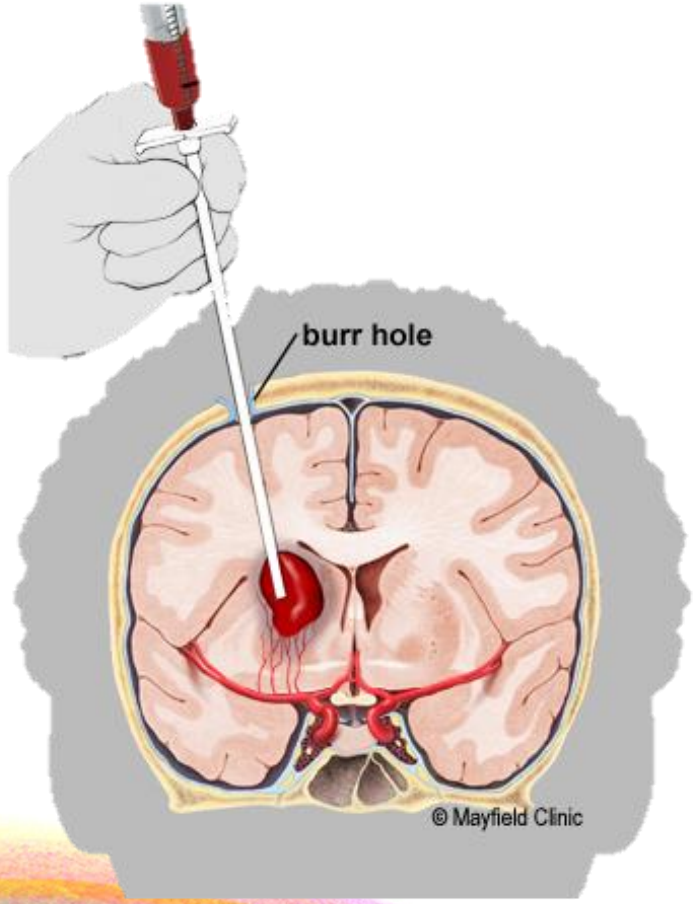


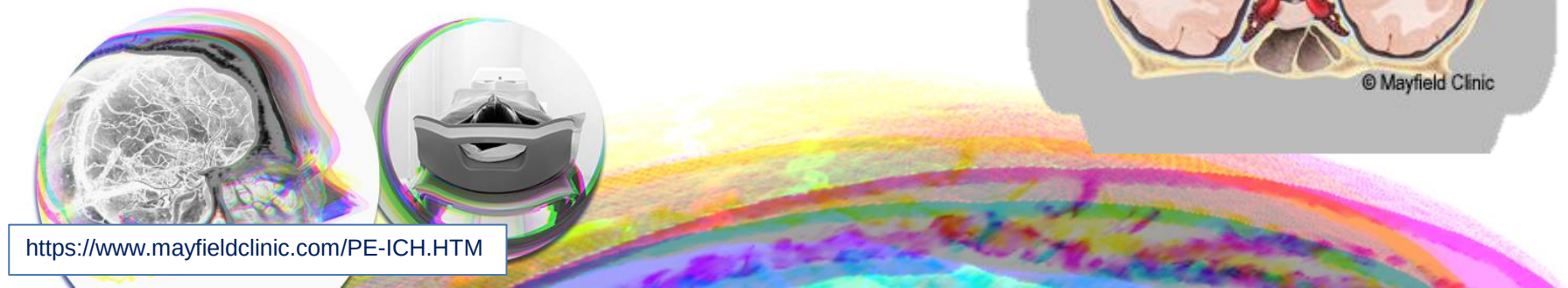


Hannah et al, Diagnostics. 2021.

Welke chirurgie? Minimaal invasief

- Verschillende technieken
  - Ultrasone aspiratie
  - Hoge druk irrigatie
  - Endoscopische aspiratie
  - Catheter aspiratie met lokale applicatie van thrombolytica





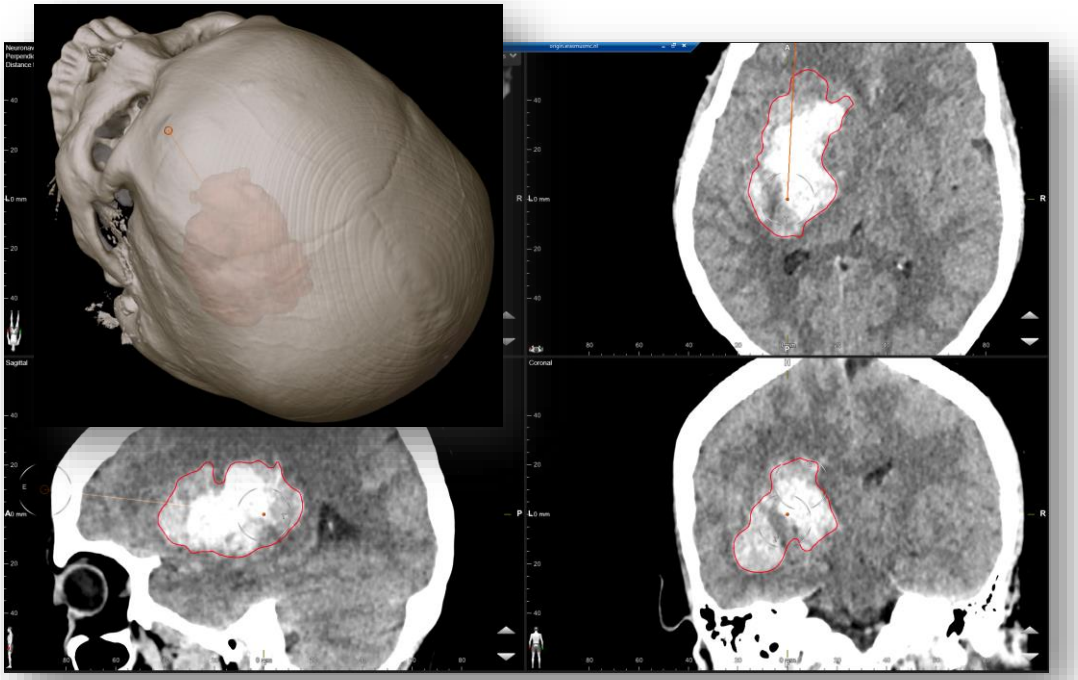
https://www.mayfieldclinic.com/PE-ICH.HTM

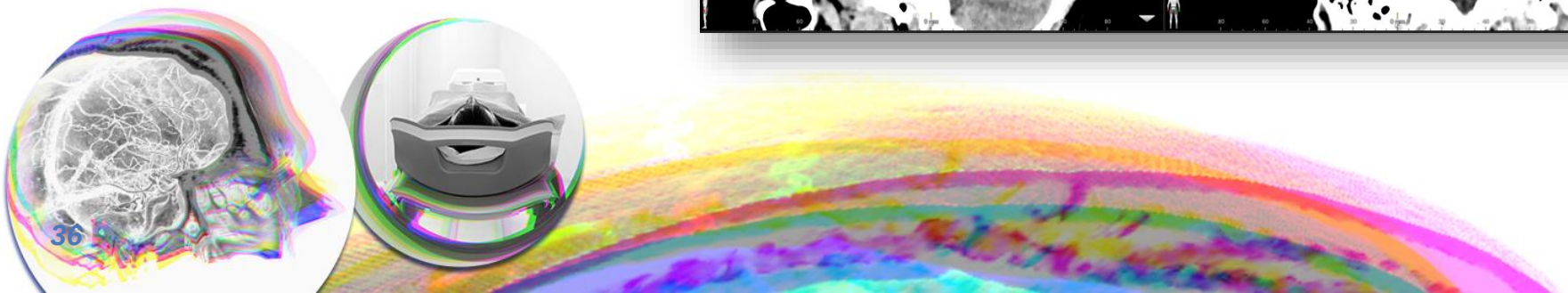
Welke chirurgie? Endoscopisch

Neuronavigatie

Kortste route, rekening houdend met hersenstructuren

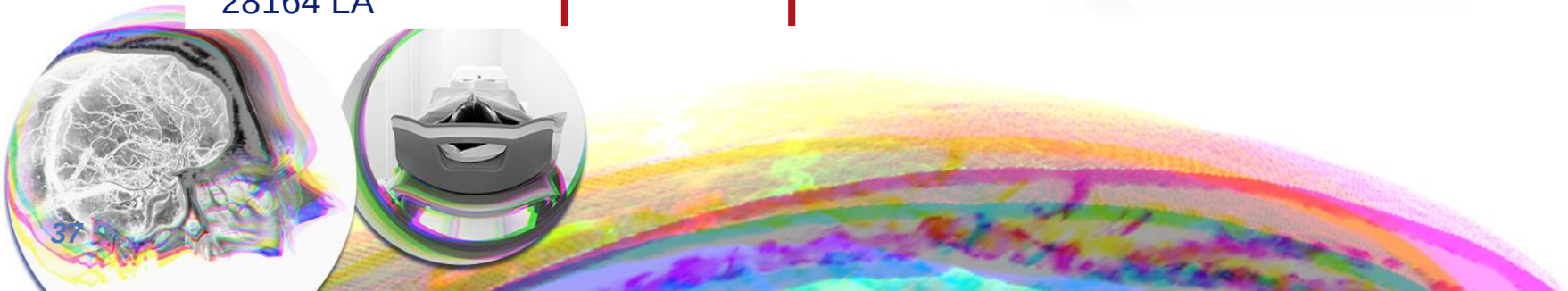
Bij voorkeur ICH lange as



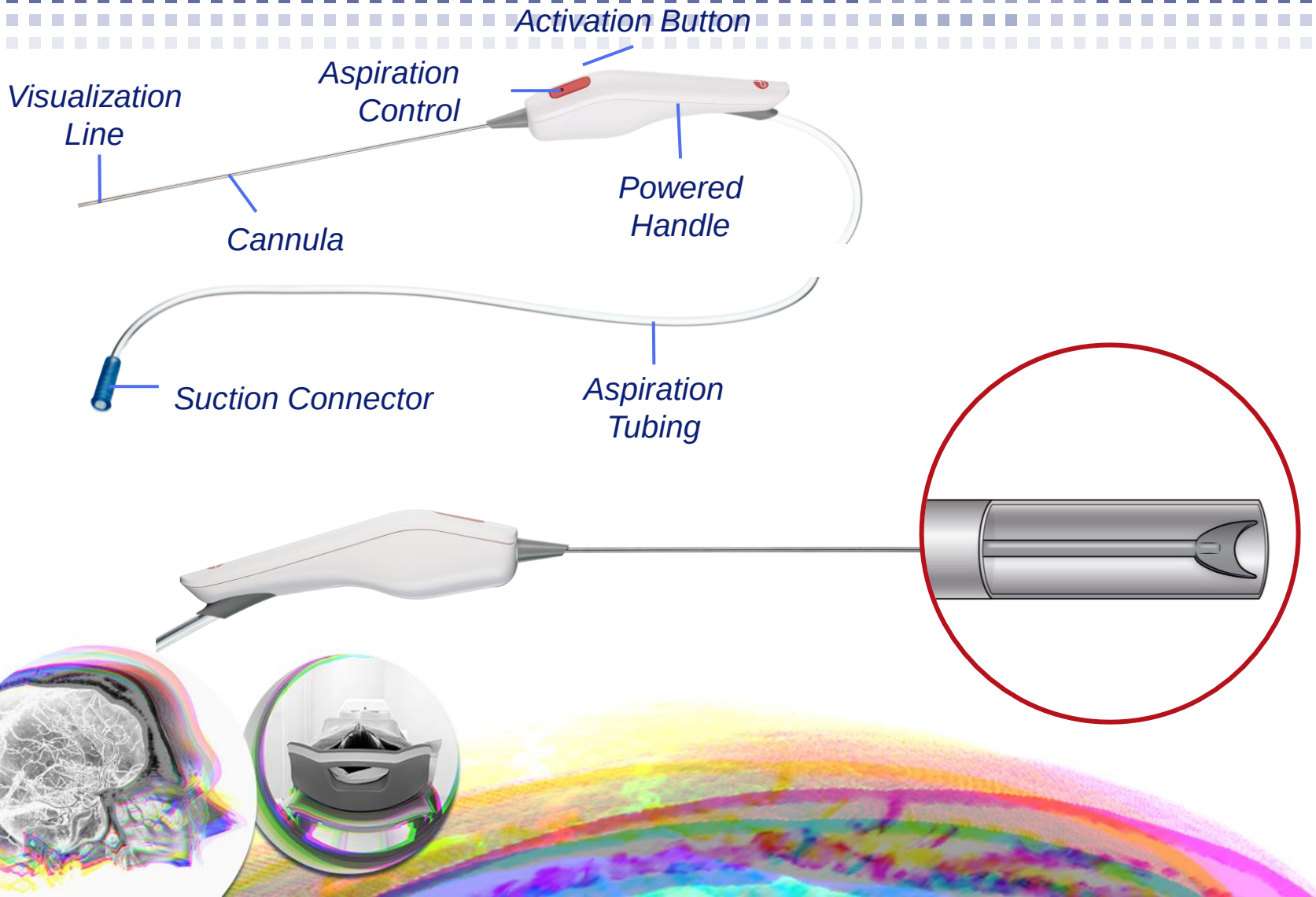


Welke chirurgie? Endoscopisch

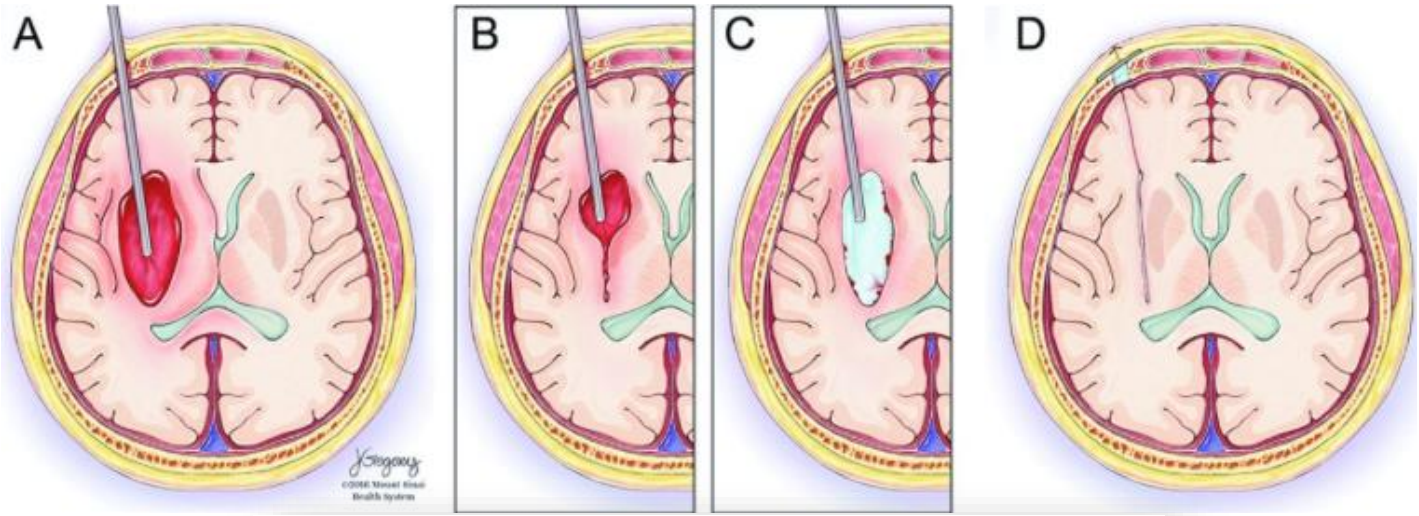
		Artemis
STORZ® LOTTA® 28164 LA	2.9 mm ID	AP28 (2.8 mm OD)



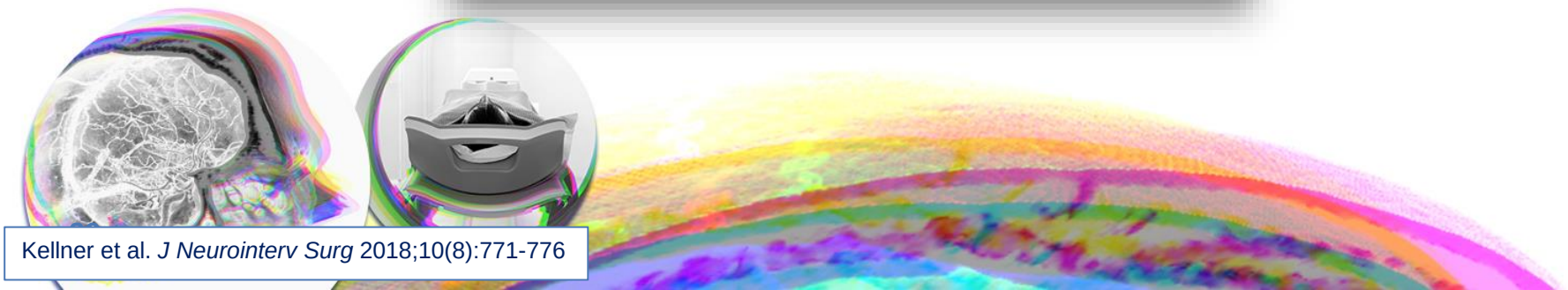
Welke chirurgie? Endoscopisch



Welke chirurgie? Endoscopisch



The Stereotactic Intracerebral Hemorrhage Underwater Blood Aspiration (SCUBA) technique



Kellner et al. *J Neurointerv Surg* 2018;10(8):771-776

Welke chirurgie? Endoscopisch

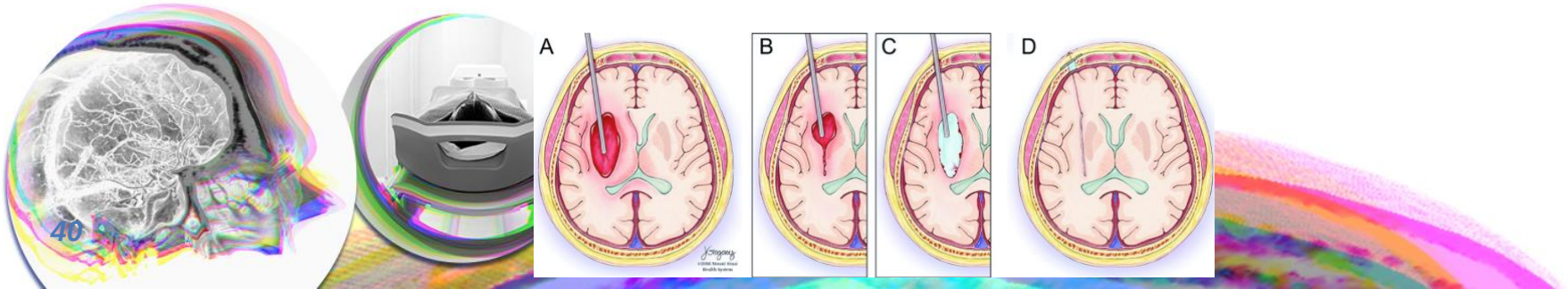
6 uur na ictus

NIHSS 18

Duur ok 1,5 uur

Dutch ICH Surgery Trial
pilot study

NIHSS 5

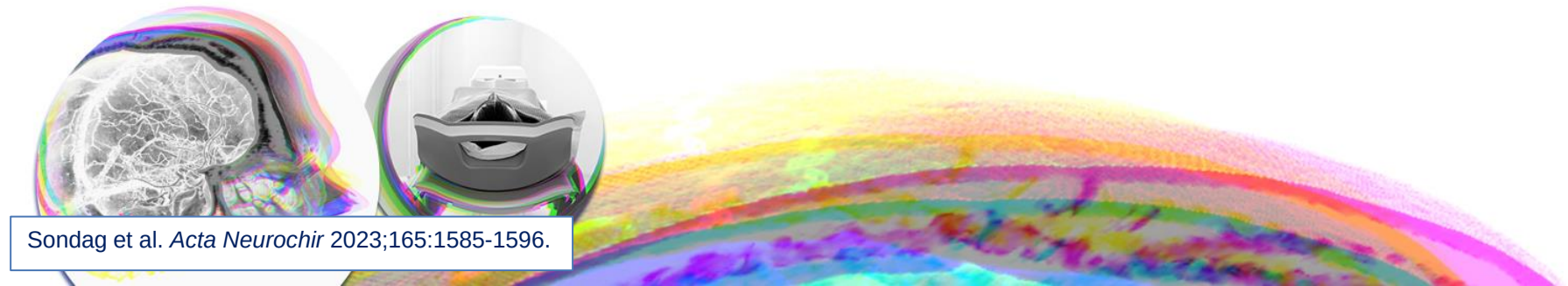


Welke chirurgie? Endoscopisch

Dutch ICH Surgery Trial
pilot study

Safety and technical efficacy of early minimally invasive endoscopy-guided surgery for intracerebral haemorrhage: the Dutch Intracerebral haemorrhage Surgery Trial pilot study

Conclusions Minimally invasive endoscopy-guided surgery within 8 h after symptom onset for supratentorial ICH appears to be safe and can effectively reduce ICH volume. Randomised controlled trials are needed to determine whether this intervention also improves functional outcome.



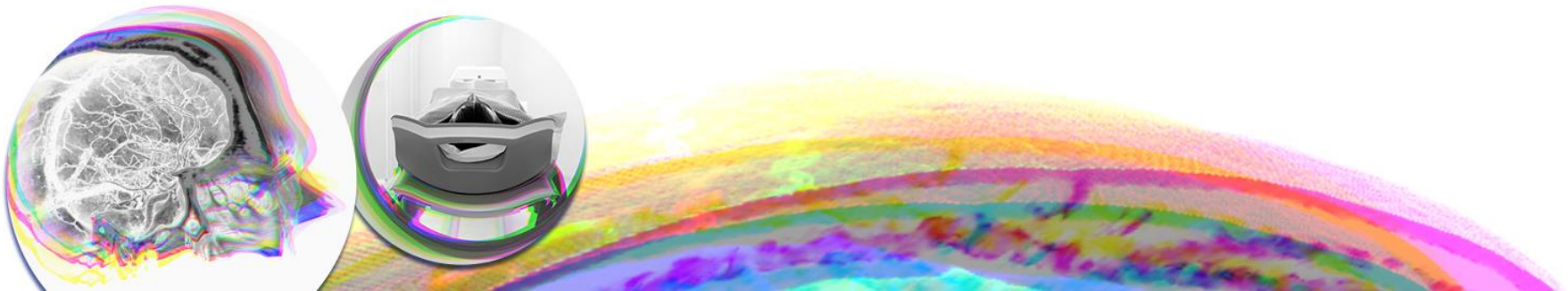
Sondag et al. *Acta Neurochir* 2023;165:1585-1596.

Welke chirurgie? Tubular retractor chirurgie

Welke chirurgie? Tubular retractor chirurgie

ENRICH

Outcome under embargo



Welke chirurgie?

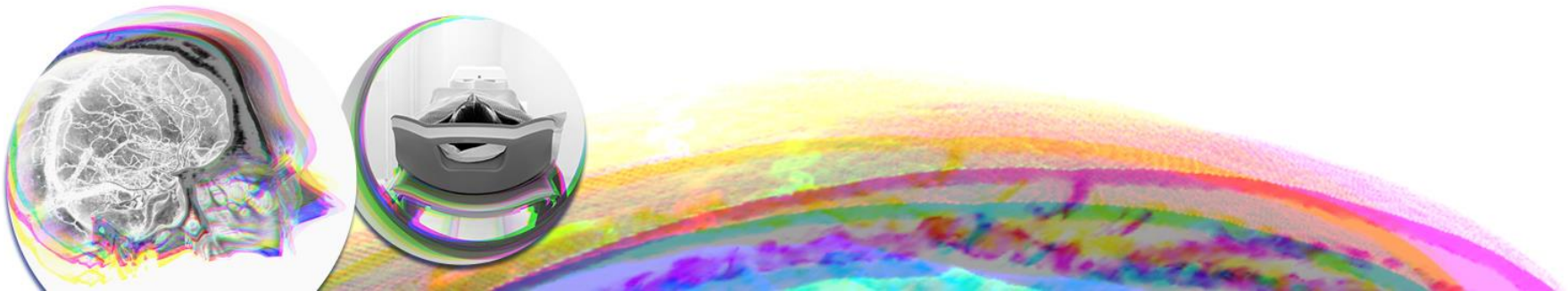
Surgical treatment may be beneficial, in particular with **minimally invasive procedures** and when **performed early**

But:

- Methodological shortcomings trials
- Heterogeneity due to different inclusion criteria

Recommendations:

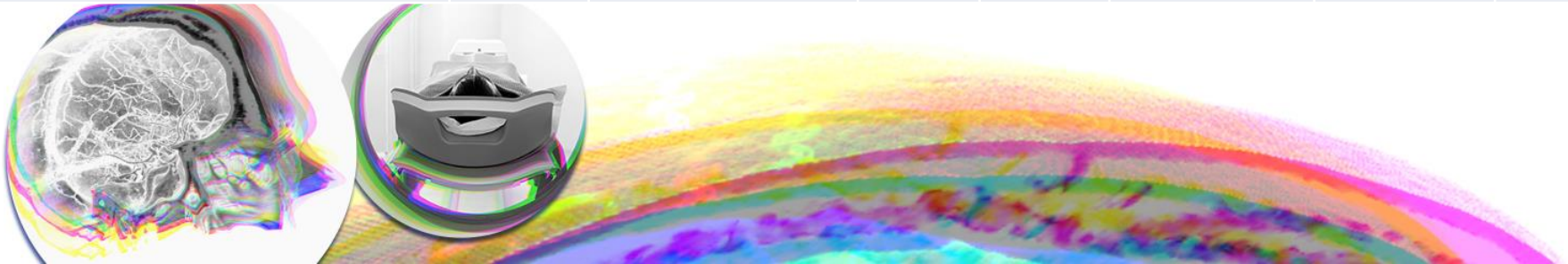
- New research is needed to investigate minimally invasive surgery, without locally administered alteplase in different time windows (especially early after symptom onset)



Welke chirurgie?

RCTs met neurochirurgische behandeling van ICH

	Technique	Control	ICH volume	GCS	Timing	Primary outcome	N (centres)	
MIND NCT03342664	Artemis	MM (2:1)	20-80 mL	≥5	<72 h	mRS 6mo Death	500 (>20)	recruiting
ENRICH NCT02880878	Brainpath	MM	30-80 mL	5-14	<24 h	uw-mRS 6mo	300 (>30)	stopped early
SWITCH NCT02258919	Decompressive hemicraniectomy	MM	30-100 mL BG, thalamus only	8-14	<72 h	mRS 5-6	300 (34)	recruiting
MISICH NCT02811614	Endoscopic vs stereotactic	**CT** (1:1:1)	> 20 mL Hypertensive ICH	≥5	<24 h	mRS 6mo	900	recruiting
EVACUATE NCT04434807	Surgiscope, mini-craniotomy	MM	≥ 20 mL	NIHSS ≥5	**< 8 h**	mRS 0-3	240	recruiting
DIST	Endoscopic	MM	**≥ 10 mL**	Any[#]	**< 8 h**	mRS 6mo	600 (11)	starting soon



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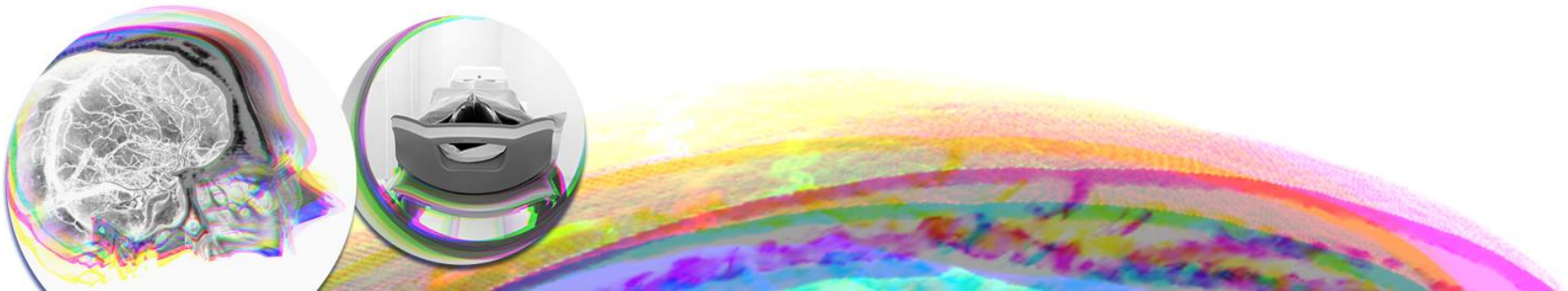
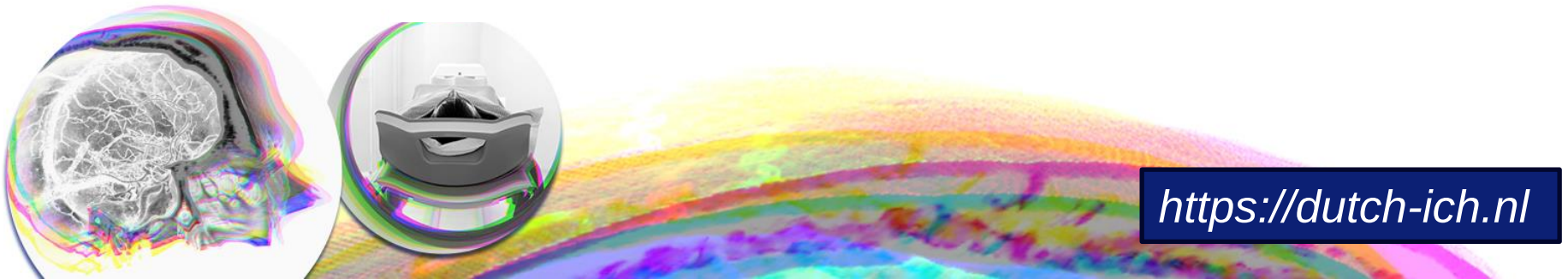


DIST studie

Dutch
ICH
Surgery
Trial



https://dutch-ich.nl

DIST studie

Doel: effect op functionele outcome verbeteren

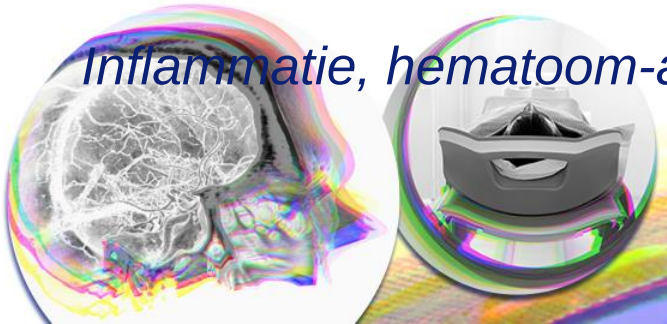
Interventie: endoscopie-geleide minimaal invasieve chirurgie binnen 8 uur na start symptomen; minimaal volume 10 mL; NIHSS ≥ 2

Design: RCT met blind endpoint assessment

Sample size: n = 600, 11 centers and > 36 referring hospitals

Primary outcome: efficacy: mRS na 180 dagen

Inflammatie, hematoom-analyse, kosten-effectiviteit….



Dutch ICH Surgery Trial

Inhoud

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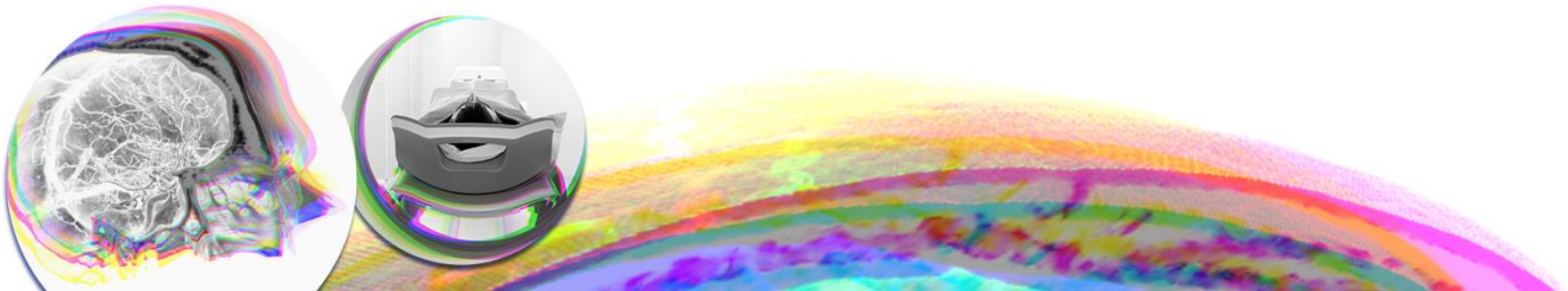

Conclusie

- ICH: hoge incidentie, mortaliteit en kans op afhankelijk leven
- Meta-analysis mogelijk verbetering functionele uitkomst na minimaal invasieve chirurgie
- Is minimaal invasief beter dan open chirurgie (wat is open chirurgie)?
- Endoscopische chirurgie is veilig en effectief
- Grote, goed opgezette RCTs nodig
- Volume reductie tot minder dan 15 mL lijkt van belang
- Timing < 8 uur of nog sneller als mogelijk?

Rol van chirurgie blijft onzeker/onduidelijk
Meerdere trials wereldwijd lopen op dit moment

Dutch ICH Surgery Trial

Erasmus MC

Participating centers

Amsterdam UMC
University Medical Centers

Jonathan Coutinho
Peter Vandertop

Erasmus MC
Universitair Medisch Centrum Rotterdam

Ruben Dammers
Diederik Dippel
Paula Janssen
Nadia Colmer

Radboudumc

Lotte Sondag
Floor Wilting
Floris Schreuder
Jeroen Boogaarts
Axel Wolsink

isala

Wilmar Jolink
Mahrouz Foumani

ETZ

Ben Jansen
Bram van der Pol

H+MC

Jelis Boiten
Wouter Moojen

LUMC

Marieke Wermer
Radboud Koot

MST

Renate Arntz
Paul Brouwers
Kuan Kho

UMCG

Gert-Jan Luijckx
Marc van Dijk

Maastricht UMC+

Inger de Ridder
Roel Haeren

UMC Utrecht

Bart van der Worp
Friso Hoefnagels