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Meta-analysis and Late Results of Randomized Trials in Carotid Interventions

K. Mathias
Department of Radiology
Teaching Hospital of Dortmund - Germany

Presenter Disclosure Information

Name: Klaus Mathias MD.

Within the past 12 months, the presenter or their spouse/partner have had the financial interest/arrangement or affiliation with the organization listed below.

None

Actual Situation

- some single center reports
- many registries
- few trials
- very few randomized trials

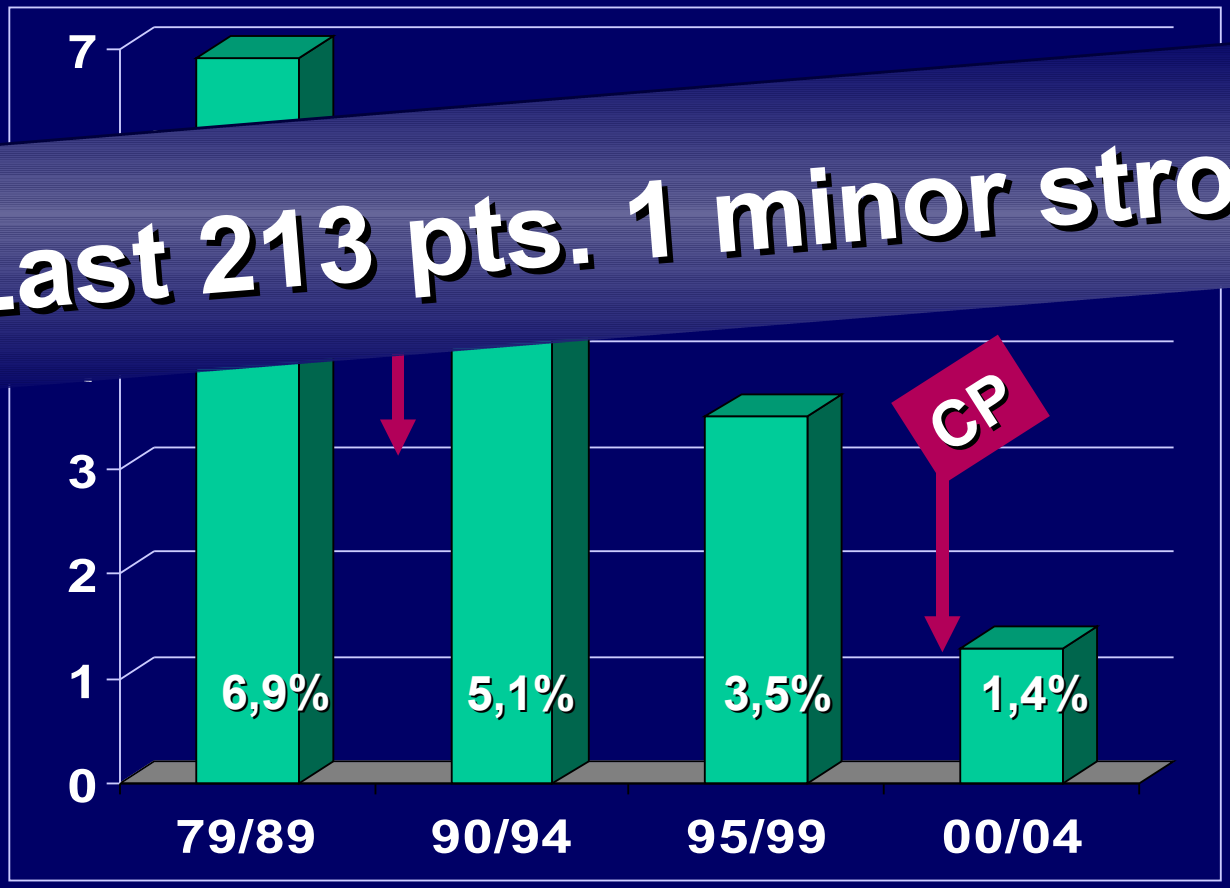
Own Results with CP

patients	1.194	
treated arteries	1.327	100.0%
[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]
cerebral hemorrhage	1	0.1%
MI	2	0.2%
30-day mortality	1	0.1%
others (e.g. amaurosis)	6	0.6 %
Stroke & Death	**18**	**1.4 %**

no significant difference between symptomatic and asymptomatic patients

1999-2004

Learning Curve & Technical Development



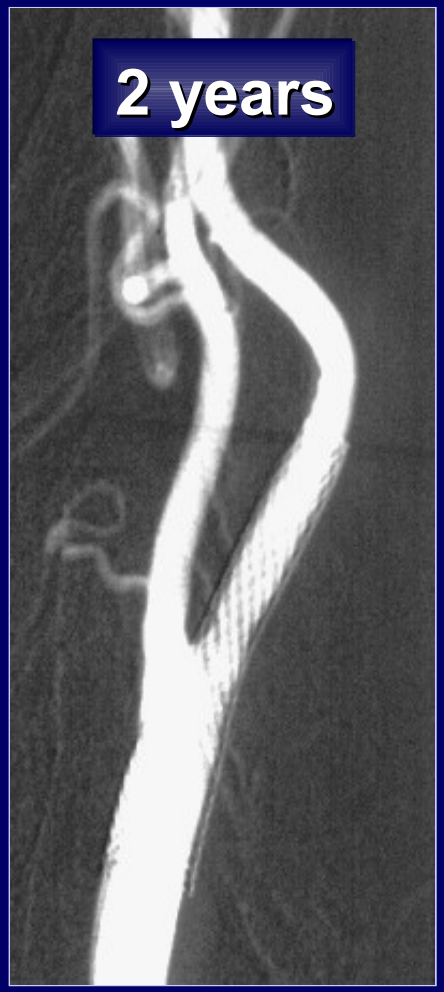
Last 213 pts. 1 minor stroke

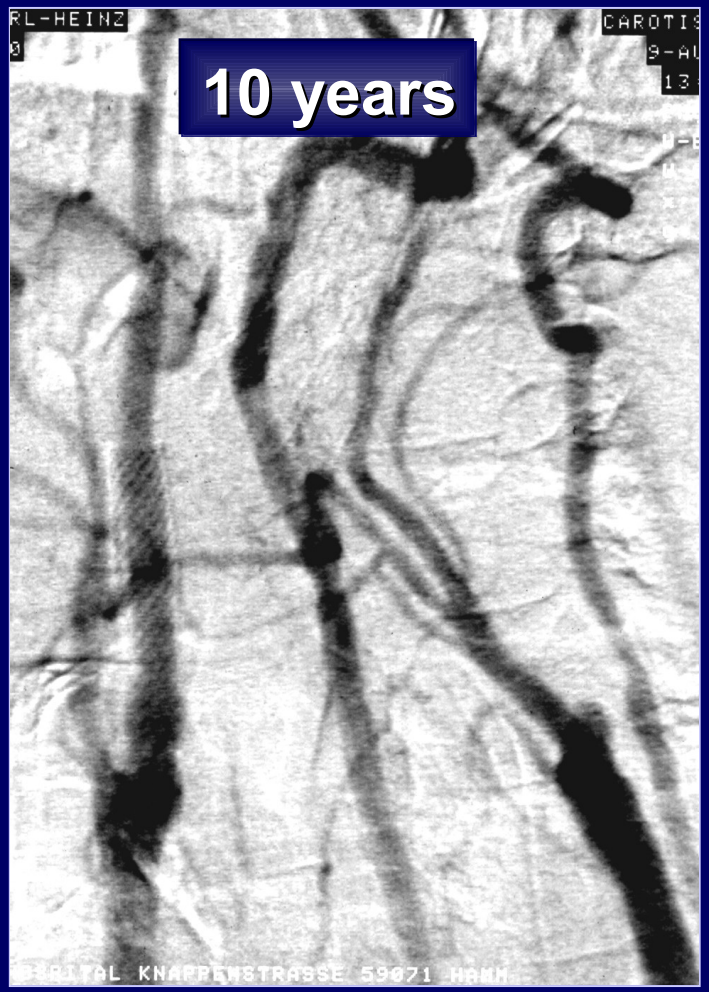
Follow-up Findings

69- year old man 10 months after CEA: recurrent stenosis of left ICA

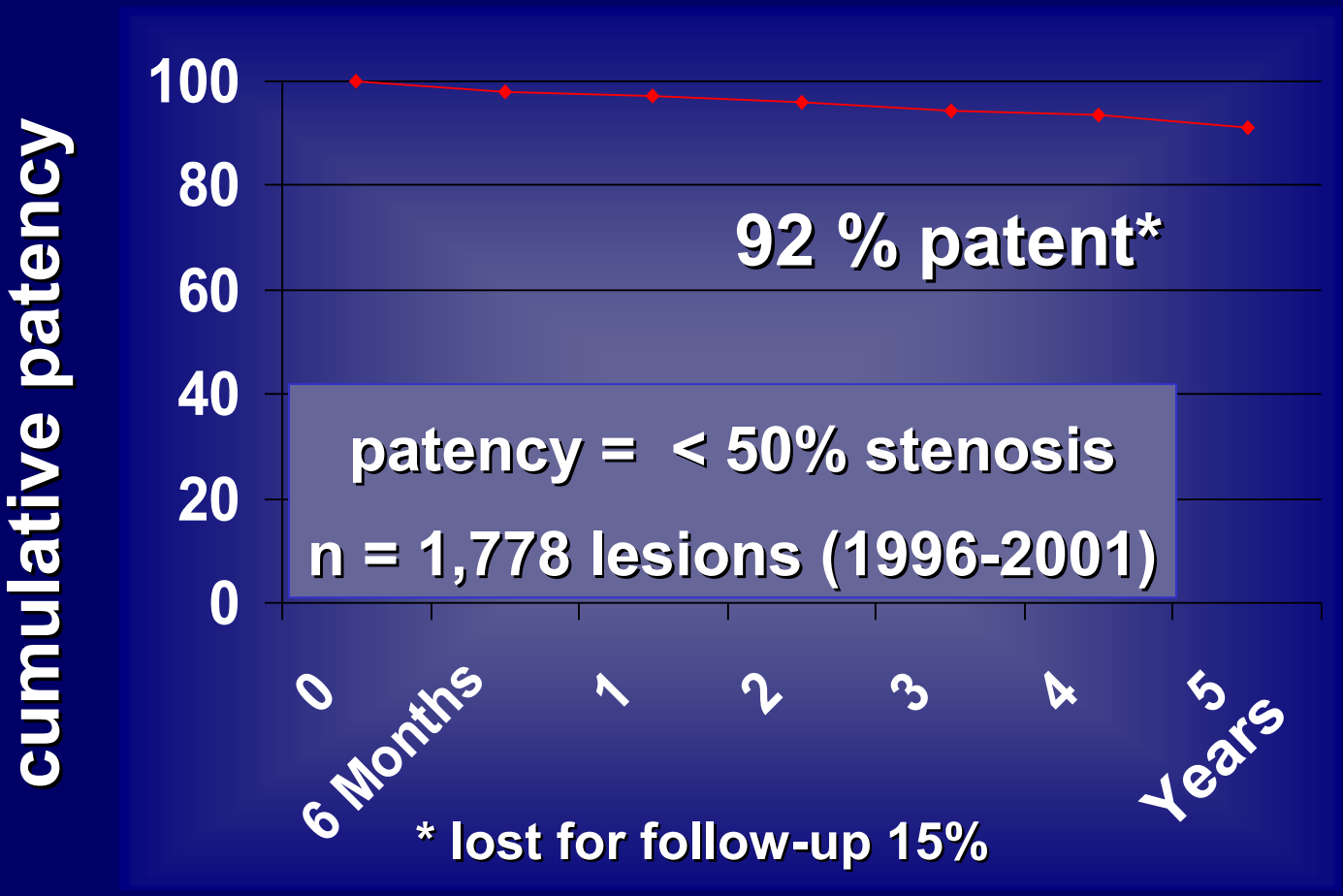
6 months after CAS: durable good result

Follow-up Angiograms

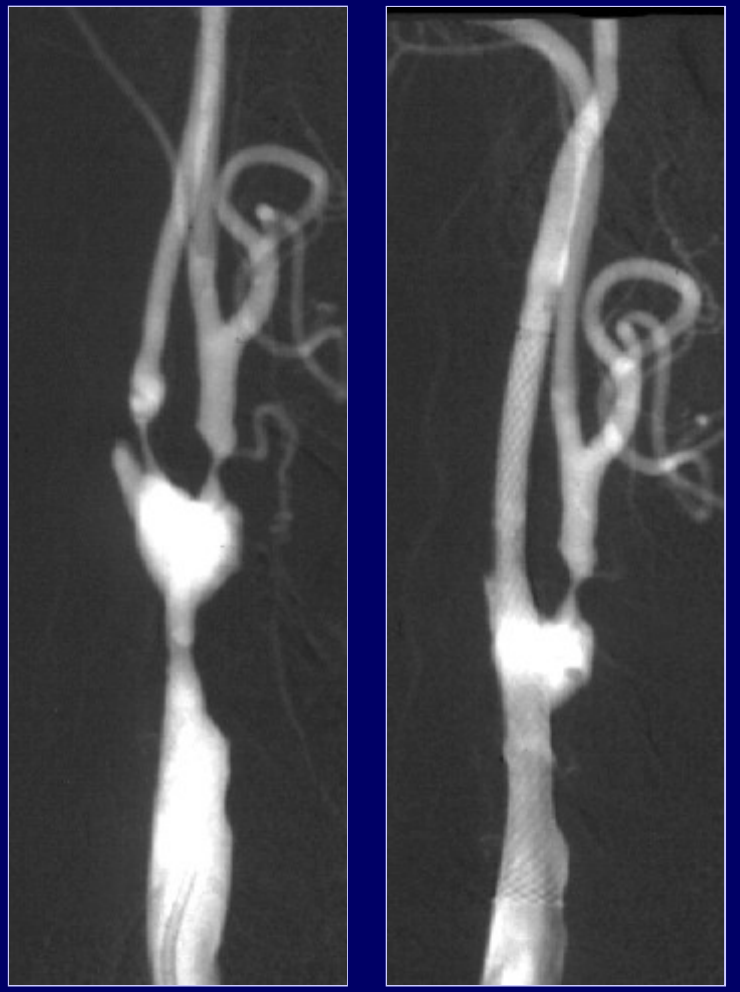




5-Y Patency Rate*



CEA Recurrence Rate 5- 10%*



8 months after CEA

* S Rugonfalvi-Kiss et al.
Stroke, 2005; 36:944-8

St. Louis Data

	CAS n=42	**NASCET med** n=331	**NASCET surg** n=328
Any ipsilateral stroke	9.5%	26%	9%
Any stroke	14.3%	27.6%	12.6%
Any stroke or death	19%	32.3%	15.8%

Mean follow-up 1.7 years (range 1 – 62 months): no ipsilateral strokes,
2 contra-lateral strokes

D. F. Fox et al.: Long-term outcomeafter angioplasty for symptomatic extracranial carotid stenosis in poor surgical candidates. Stroke 2002; 33: 2877-2880

Registries

Clinical Trials

Study Status	Study Design	Sample Size
ARCHER 1-3 completed	high-risk registry	581
BEACH completed	high-risk registry	480
CABERNET completed	high-risk registry	488
CASES enrolling	hig	1,500
CREATE I+II completed	high-risk registry	579
CAPTURE enrolling	Acculink registry	1,500
MAVERIC I+II completed	high-risk registry	498
MOMA completed	EU registry	157

15,170 tx

Purpose of the Clinical Trials

- **Feasibility and safety of**
  - stents and delivery device
  - embolic protection devices
- **Clinical outcome**
  - no randomization
  - success and complication rate
  - 30 day m & m rate
  - 1-y follow-up
- **Appoval of devices**
  - FDA
  - EU-CE

ELOCAS*

intenton to treat	2,172	100%
technical success	2,165	99.7%
no EPD	306	14.1%
with EPD	1,859	85.9%
5-y stroke/death rate	1,356	4.1%
recurrence rate		
1-y	1,363	1.0%
3-y	480	2.0%
5-y	139	3.4%

*European Long Term CAS Registry; J Cardiovasc Surg 2005;46:241-7

Prospective Randomized Studies

Randomized Clinical Trials

Study Status	Study Design	Sample Size
ACT I enrolling	asymptomatic	1,540
CAVATAS completed	sy	504
CREST enrolling	symptomatic	2,500
EVA3S enrolling	asymptomatic symptomatic	2,400
SAPPHIRE	high-risk	724

11,868 tx

CAVATAS

Inclusion criteria

- symptomatic patients
- > 70% stenosis
- patients with increased risk accepted

Enrollment

1992 – 1996

504 patients randomized

M. Brown et al. Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomised trial. Lancet 2001;357:1729-37

CAVATAS

Technique

balloon angioplasty	100%
stent placement	25%
cerebral protection	0%

OTW technique

device profile 7 – 9F

M. Brown et al. Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomised trial. Lancet 2001;357:1729-37

CAVATAS

Type of Procedure	Technical Success	Neurological Deficits	All Compli-cations	3-Year Patency
CAS	>95%	6.4%	10.0%	no significant difference
CEA	>95%	6.3%	9.9%	

M. Brown et al. Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomised trial. Lancet 2001;357:1729-37

SPACE

SPACE = Stent protected angioplasty versus carotid endarterectomy

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Prospective multicenter trial

Participating centers must be certified
Devices must be certified

1.800 patients will be enrolled
Start March 2001
presently > 1.100 pts enrolled

SPACE

Inclusion criteria:
>70% symptomatic stenosis

Primary endpoints
stroke & death in 30 days

Secondary endpoints:
stroke & death after 1 year

SPACE

Preliminary results:

no statistical difference

M&M rate ~5%

1-year patency no difference

SAPPHIRE

Follow-up:

- 30-days
- 6 months
- 1 year
- 2 years
- 3 Years

SAPPHIRE

Statistical Assumption

The purpose was to compare carotid stenting to CEA and to demonstrate 'non-inferiority' of stenting to CEA based on a -3% delta

SAPPHIRE

Primary Endpoints

- Death, any Stroke, and MI at 30-days post-procedure
- 30 day MAE plus Death and Ipsilateral Stroke between 31-days and 12-months post-procedure

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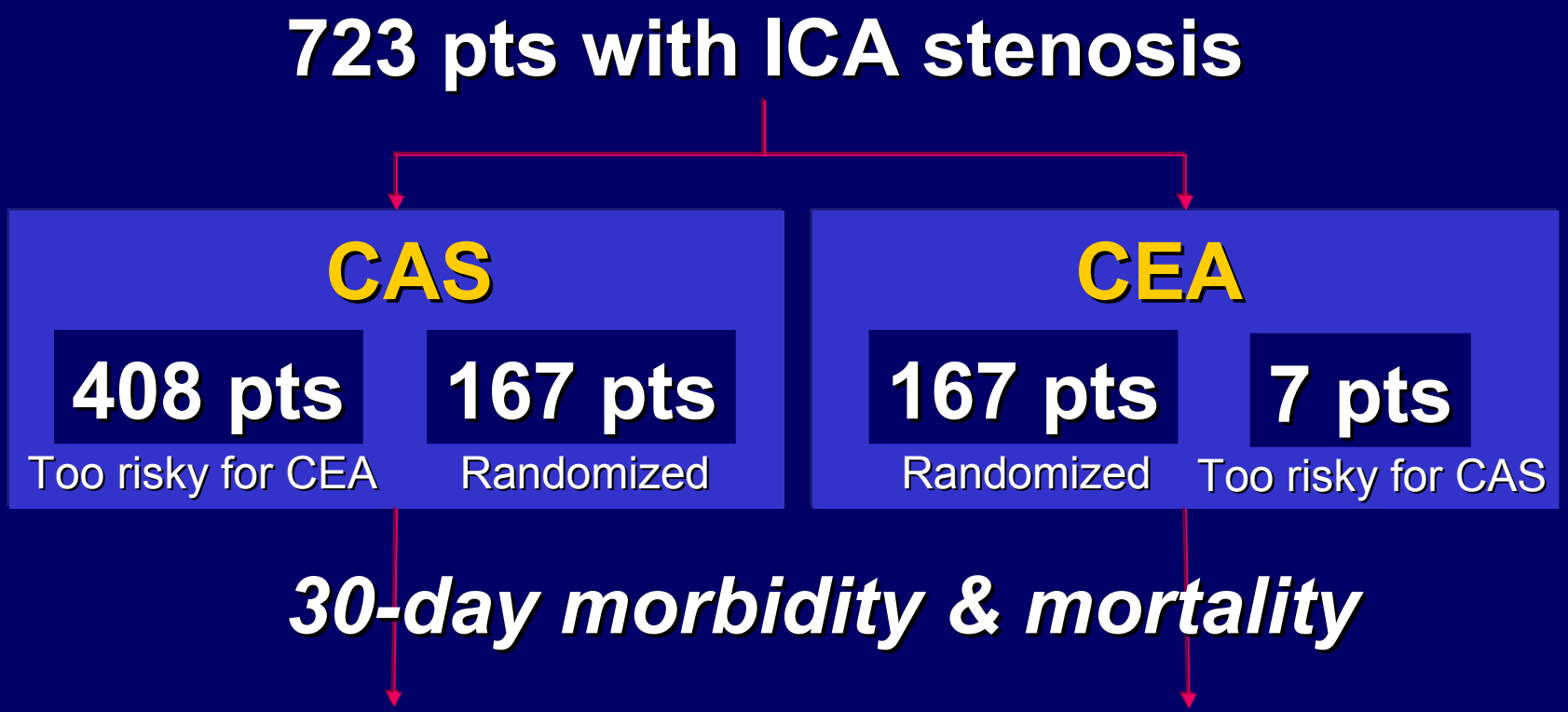
SAPPHIRE



NEJM, 2004

30-Day Events Symptomatic Pts

Events %	CAS 48 pts 95% CI	CEA 39 pts 95% CI	p-Value
death	0.0	5.1	0.2
stroke	2.1	7.7	0.32
major ipsilateral	0.0	0.0	
major non-ipsilateral	0.0	2.6	
minor ipsilateral	2.1	5.1	
minor non-ipsilateral	0.0	0.0	
MI	2.1	5.1	0.58
death & stroke	2.1	10.3	0.17
death & stroke & MI	4.2	15.4	0.13

Long Term Results

	Recurrence rate*	
	CAS	CEA
CAVATAS (3-y)	equal	
SAPPHIRE (3-y)	0.7%	4.6%
Dortmund (5-y)	2.1%	5.4%

*more than 50% restenosis

Comparison

	CAS	CEA
high-risk sympt. patient general medical condition	better	inferior
high-risk sympt. patient local high-risk	better	inferior
high-risk asympt. patient	no benefit	no benefit
normal-risk sympt. patient	equal	equal
normal-risk asympt. patient	equal?	benefit proven

Conclusions

- level A evidence for high-risk sympt. patient
- level B evidence for normal-risk sympt. patient

Prospective randomized trials are still running

ACT	normal-risk	asymptomatic
CAVATAS II	normal-risk	symptomatic
CREST	normal-risk	symptomatic
		asymptomatic
EV3S	normal-risk	symptomatic
SPACE	all-risks	symptomatic
TACIT	normal-risk	asymptomatic

Conclusions

Highest level of evidence will be established in 2 – 5 years

The „informed“ patient endangers sufficient enrollment in the trials preferring CAS