e-METHODS

Development of the UIATS model

The following factors assumed to increase the risk of UIA rupture were not included in the UIATS model due to their low relevance ratings (mean of 2 or less) during the Delphi consensus: *Female sex, the post-menopause phase, concomitant treatment with platelet inhibitors or anticoagulants, aneurysm sphericity or ellipticity and chronic headaches*. Additionally, the following treatments or lifestyle modifications considered to reduce the risk of UIA rupture were not included in the UIATS model due to their low overall relevance ratings (mean of 2 or less): *Prophylactic treatment with aspirin or statins, regular exercise and avoidance of rigorous physical activity*. The only feature potentially influencing the treatment risk not included in the model due to a low relevance rating (mean of 2 or less) during the Delphi consensus was *diabetes mellitus* as a comorbid disease.

For the development of the UIATS model each category or feature was assigned to one or two of a total of three domains; patient-, aneurysm-, and/or treatment-related. Depending on how categories or items may affect UIA management, they could generate individual scores (e.g. patient age, aneurysm size, and the corresponding risk factors etc.) in favor of aneurysm repair, while others (e.g. chronic diseases/comorbidities, aneurysm size and patient age in relation to treatment risk) could generate scores in favor of conservative management. Individual scores for each item within the categories were derived from pooled medians from 0-10 (0 indicating not relevant or important and 10 indicating critically important) based on ratings of these items in round two and three. Items were ranked and assigned a score from 0-4 in accordance with the following definition (0 indicating low relevance and 4 highest relevance): 0 (median 0-2), 1 (median 2-4), 2 (median 5-6), 3 (median 7-8) and 4 (median 9-10). Since items with a score of 0 would then be defined to have low relevance for the assessment of a UIA, each item with a score of 0 was omitted unless it reflected one feature within a continuous variable category (e.g. aneurysm size or patient age range).

After round five, age categories were adjusted (1 point) to account for the potentially higher relevance of young age to UIA management and the higher treatment risk in elderly patients. To account for the overall risk of treatment in the score, pooled data from two meta-analyses on risk of surgical or endovascular repair of UIAs were used, which estimated a pooled mean risk of repair of 7%. A score of seven was then used to represent the mean distribution of aneurysms 6-10 mm in size and patients with a mean age of 52 years based on the underlying data set.[1, 2] Accordingly, the treatment risk scores were ranked higher or lower than six, for patient ages and aneurysm sizes that differed from the mean distribution above within the cohort of the underlying meta-analyses, in a step-wise relation manner. The score itself was designed like a Forest plot for illustrative purposes so that scores of each feature would ultimately add up to one value "supporting aneurysm repair" and one value "supporting conservative management". This sum or ratio of factors supporting aneurysm repair (i.e. surgical or endovascular treatment) or conservative management for UIAs, based on individual patient and aneurysm characteristics, illustrates the relation of arguments for or against UIA treatment. For cases that result in similar aneurysm repair and conservative management scores (+/- 2 points difference or less), the consensus was a recommendation category in which either management approach could be supported. For such cases additional features that are not accounted for in the present score may need to be considered.

Validation of the UIATS

Validation of the UIATS was performed using a selected set of 30 representative UIA patients, who sought consultation at the primary authors institution (NE) between January 2013 and February 2014. The UIA cases were selected by one investigator (AA), who did not participate in the Delphi process or the UIATS development to provide a cross-sectional set of common variations in patient age distributions, incidence of risk factors or comorbid diseases and aneurysm features **(Table-e1 and Table-e2, see below).** The level of agreement among internal and external reviewers with resulting UIATS-derived management recommendations was then analyzed using a five point Likert scale (1=strongly disagree, 2=disagree, 3=neutral, 4=agree, 5=strongly agree). Reviewers were presented with

radiological imaging including catheter angiograms in two projections and 3-dimensional reconstructions to illustrate aneurysm morphology. All relevant patient, aneurysm or treatment-related features accounted for in the UIATS model were provided. For each case the panel member was first asked whether they would have personally recommended aneurysm repair (answers: yes, no, uncertain). After they provided that answer, the individual scores based on UIATS and the resulting UIA recommendation were presented and panel members were asked to rate the level of agreement with the proposed recommendation. The first question on the reviewers' personal recommendation was blinded to the subsequent question on the agreement with the UIATS recommendation for each case, to minimize bias. Round five was designed to test agreement among the 39 panel members using 15 selected UIA cases. Validation focused on analysis of agreement with the UIATS per case and per reviewer. Round six was used to re-evaluate agreement of the panel members with the UIATS recommendations following minor adjustment of the score by using the same 15 plus 15 additional UIA cases. Subsequently, 30 cerebrovascular specialists, not involved and blinded to the development and design of the UIATS were recruited as external reviewers. The external reviewers, who were only given a short description of the UIATS development, were asked first whether they would have personally recommended aneurysm repair or conservative management and then asked for agreement with UIATS-derived recommendations using the same UIA cases as the panel members (round seven).

e-REFERENCES

e1. Kotowski M, Naggara O, Darsaut TE, et al. Safety and occlusion rates of surgical treatment of unruptured intracranial aneurysms: a systematic review and meta-analysis of the literature from 1990 to 2011. Journal of Neurology, Neurosurgery, and Psychiatry 2013;84:42-48.

e2. Naggara ON, Lecler A, Oppenheim C, Meder JF, Raymond J. Endovascular treatment of intracranial unruptured aneurysms: a systematic review of the literature on safety with emphasis on subgroup analyses. Radiology 2012;263:828-835.

Table e-1: Single aneurysm cases used to test agreement with UIATS

Case no·	Age (y) /Sex	risk factors	chronic/malignant disease (Life expectancy years) /other comorbidities	aneurysm location	Size (mm)	AR	SR	Clinical symptoms/ other radiological findings	UIATS recommendation points		v_r*
									Treatment	Conservative management	
1	75/F	ATH	malignant disease (5-10) /dementia	AcomA	4.8	1.1	2.1	--/irregular shape	9	15	.024
2	48/F	SMO	--/--	MCA right	7.4	1.3	3.0	thromboembolic events/--	14	7	.024
3	62/M	--	malignant disease (5-10)/--	ACA left	3.8	1.3	1.7	--/--	2	11	.024
4	47/F	ATH	--/--	AcomA	7.6	2.1	3.8	--/irregular shape	13	7	.006
5	65/F	SMO	--/--	Para ICA right	48.2	7.2	13.8	CN deficit (II), mass effect/giant aneurysm, partially thrombosed	20	16	.031
6	62/F	ATH	mild AI (>10)/--	PcomA left	9.2	2.3	2.6	CN deficit (III)/irregular shape	15	9	0
7	78/M	ATH	mild CHD (>10)/--	SCA right	5.6	1.7	2.1	--/--	6	10	.061
9	79/M	ATH	AI, CRI, malignant disease (<5) /--	MCA left	26.0	--	--	--/Mass effect, giant aneurysm, partially thrombosed	15	21	.031
10	49/M	SMO	--/--	MCA right	6.3	0.7	1.2	--/irregular shape	10	7	.031
11	74/F	--	--/--	PICA left	4.0	1.7	2.4	--/--	6	9	.031
13	55/F	ATH	--/--	BasA bifurcation	5.7	0.6	1.4	--/wide neck	13	9	.031
14	45/F	SMO, Fx	--/--	PcomA left	8.4	1.2	1.5	--/lobulated	15	7	0
15	48/F	--	--/--	BasA bifurcation	15.0	1.4	5.0	--/wide neck, irregular shape	16	12	.024
17	61/F	SMO, ATH	--/--	AcomA	7.3	1.0	1.4	--/--	13	8	.024
18	25/F	--	--/--	para ICA left	3.0	0.7	0.7	--/wide neck	4	8	.061
19	71/F	SMO, ATH	--/--	PcomA right	8.5	2.5	2.8	--/irregular shape	14	9	.024

Table e-1: Single aneurysm cases used to test agreement with UIATS (continued)

Case no·	Age (y) /Sex	risk factors	chronic/malignant disease (Life expectancy years) /other comorbidities	aneurysm location	Size (mm)	AR	SR	Clinical symptoms/ other radiological findings	UIATS recommendation points		v_r*
									Treatment	Conservative management	
20	77/M	ATH	--/--	BasA	3.9	0.7	0.8	--/wide neck	7	12	.024
21	52/F	SMO	CRI (>10)/--	MCA right	7.5	1.8	2.8	--/--	11	8	.024
22	60/F	ATH	--/--	para ICA left	7.8	1.6	3.0	--/irregular shape	14	7	.024
23	73/F	--	2 malignant diseases (<5)/--	MCA right	23.9	--	--	mass effect/irregular shape, partially calcified	11	21	.031
24	47/F	SMO	--/--	SCA right	3.3	2.3	4.1	--/--	10	6	.061
28	32/M	--	--/--	MCA left	4.4	0.9	1.3	--/irregular shape, wide neck	8	8	.061
29	48/M	ATH	--/--	MCA left	40.7	4.9	14.7	thromboembolic events mass effect/ giant aneurysm, partially thrombosed	17	14	.031
30	31/F	SMO, ATH	--/--	para ICA right	5.0	1.4	2.6	--/irregular shape, wide neck	14	8	.031
Means ±SD/ Frequencies	56.8 ±15.2/ 17 F 7 M	--	--/--	--	11.1 ±11.6	1.8 ±1.5	3.4 ±3.6	--	11.5 ±4.3	10.4 ±4.1	

Table e-1: Single aneurysm cases used to test agreement with UIATS recommendations in round 6 and 7 (main data is shown). ACA indicates anterior cerebral artery; AcomA, anterior communicating artery; AI, aortic valve insufficiency; AR, aspect ratio; ATH, arterial hypertension; BasA, basilar artery; CHD, coronary heart disease; CN, cranial nerve; CRI, chronic renal insufficiency; F, female sex ; Fx, familial history for intracranial aneurysms or subarachnoid haemorrhage; ICA, internal carotid artery, M, male sex ; MCA, middle cerebral artery; para ICA, paraophalmic ICA; PcomA, posterior communicating artery; PICA, posterior inferior cerebellar artery; SCA, superior cerebellar artery; SMO, smoking; SR, size ratio; v_r*= Standardized coefficients of disperson for inter-rater agreement.

Table e-2: Multiple aneurysm cases used to test agreement with UIATS

Case no·	Age (y) /Sex	risk factors	chronic/malignant disease (Life expectancy years) /other comorbidities	aneurysm location	Size in [mm]	AR	SR	Clinical symptoms/ other radiological findings	UIATS recommendation points		v_r*
									Treatment	Conservative management	
8	51/F	SMO, ATH	--/coagulopathy	MCA left	3.6	0.9	1.4	--/wide neck	11	11	
			--/--	ACA right	2.7	1.0	1.1	--/--	11	11	.031
			--/--	ACA left	3.9	1.0	2.0	--/wide neck	11	11	
12	68/F	SMO, ATH	--/--	ICA left	26.6	3.7	4.9	Mass effect/wide neck, partially calcified	19	15	0
			--/--	PcomA right	3.5	0.8	0.8	--/wide neck	8	9	
16	62/F	ATH, SAH Hx	--/--	MCA left	5.0	1.0	1.7	--/--	12	8	0
			--/--	AChoA right	3.6	1.4	0.7	--/wide neck	11	9	
25	44/F	ATH, Fx	--/--	MCA right	2.3	1.2	1.1	--/--	11	9	0
			--/--	ICA left	5.2	1.1	1.5	--/--	12	6	
26	71/F	ATH	--/--	PcomA right	8.5	1.2	2.2	--/irregular shape	12	9	0
			--/--	BasA bifurcation	6.0	1.2	1.6	--/--	11	9	
27	70/F	SMO, ATH	--/--	AcomA	12.2	6.8	6.8	steno-occlusive disease	14	11	.031
			--/--	MCA left	3.0	1.3	1.5		8	11	
Means ±SD/ Frequencies	61.0 ±10.2 6 F 0 M				6.6 ±6.1	1.7 ±1.6	2.1 ±1.7		11.6 ±2.6	9.9 ±2.1	

Table e-2: Multiple aneurysm cases used to test agreement with UIATS recommendations in round 6 and 7 (main data is shown). AChoA indicates anterior choroidal artery; ACA, anterior cerebral artery; AcomA, anterior communicating artery; AI, aortic valve insufficiency; AR, aspect ratio; ATH, arterial hypertension; BasA, basilar artery; CHD, coronary heart disease; CN, cranial nerve; CRI, chronic renal insufficiency; F, female sex ; Fx, familial history for intracranial aneurysms or subarachnoid haemorrhage; ICA, internal carotid artery, M, male sex ; MCA, middle cerebral artery; para ICA, paraophalmic ICA; PcomA, posterior communicating artery; PICA, posterior inferior cerebellar artery; SCA, superior cerebellar artery; SMO, smoking; SR, size ratio; v_r*= Standardized coefficients of disperson for inter-rater agreement.

Figure e-1.

Figure e-1: Geographic distribution of the 69 cerebrovascular specialists participating in the development and validation of the UIATS.