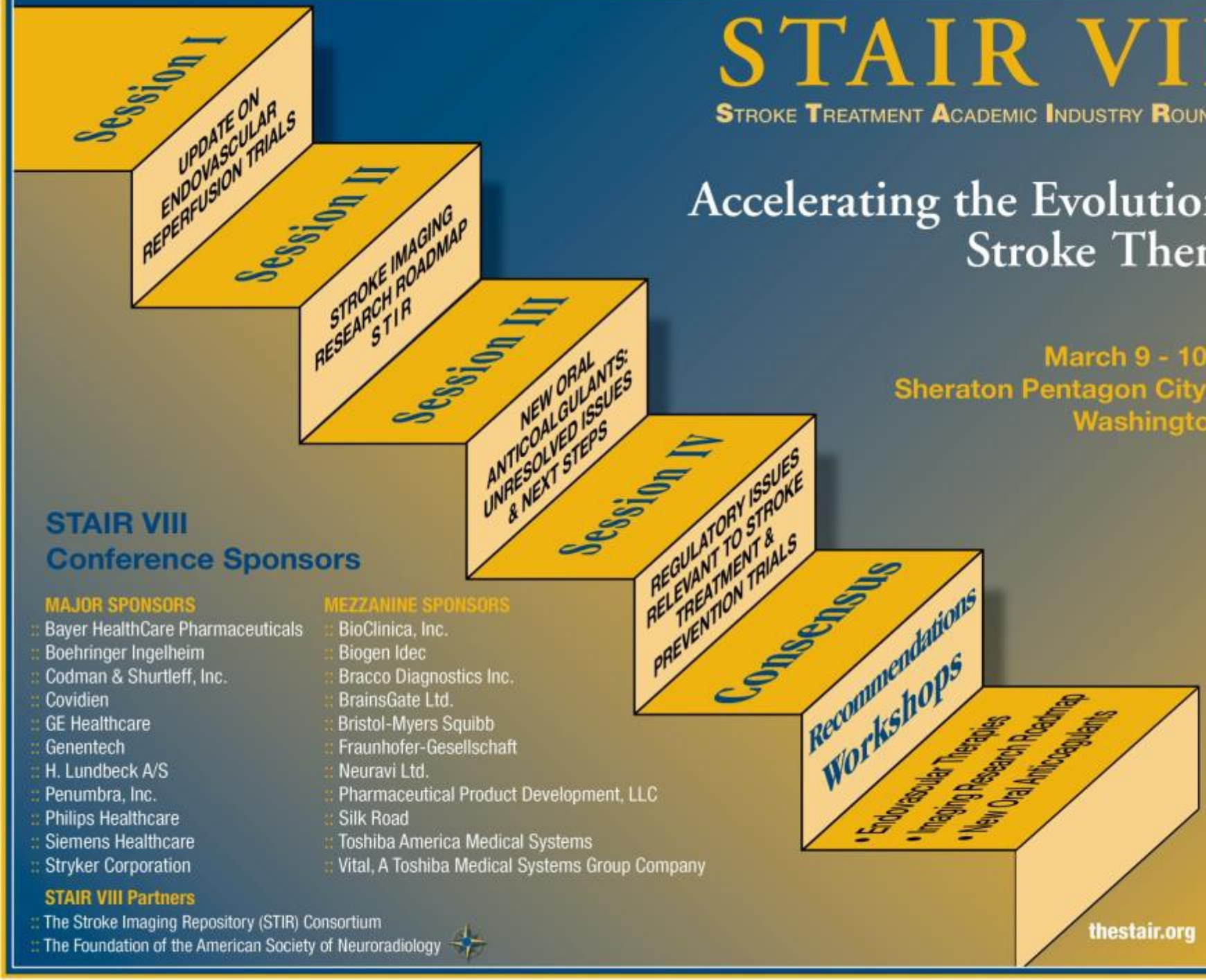
STAIR VIII

STROKE TREATMENT ACADEMIC INDUSTRY ROUNDTABLE

Accelerating the Evolution of Stroke Therapy

March 9 - 10, 2013
Sheraton Pentagon City Hotel
Washington D.C



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Research Imaging Workshop

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Standardization of the stroke imaging terminology:

Co-Chairs: Rüdiger von Kummer, Michael Lev

Members: Roland Bammer, Soren Christensen, Anthony Furlan, Kohsuke Kudo, David Liebeskind, Howard Rowley, Marie Luby

Standardized assessment of infarct and penumbral imaging methods:

Chair: Mark Parsons

Members: Andrew Bivard, Joseph Broderick, Bruce Campbell, Soren Christensen, James Grotta, Ting Lee, David Liebeskind, Marie Luby, Howard Rowley, Steven Warach, Max Wintermark, Ona Wu, Albert Yoo

Consensus Thrombolysis in Cerebral Infarction (TICI) scale for revascularization in acute ischaemic stroke trials:

Co-Chairs: Andrew Demchuk, Tudor Jovin, David Liebeskind, Albert Yoo

Members: Greg Albers, Joseph Broderick, Pooja Khatri, Michael Lev, Jeffrey Saver, Thomas Tomsick, Steven Warach, Max Wintermark, Osama Zaidat

Rosters

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Outline

- Deliverable
- Proposed Authorship Plan
- Terminology
- Imaging in Stroke Trials
- Revascularization
- mTICI
- STIR certification
- STIR network

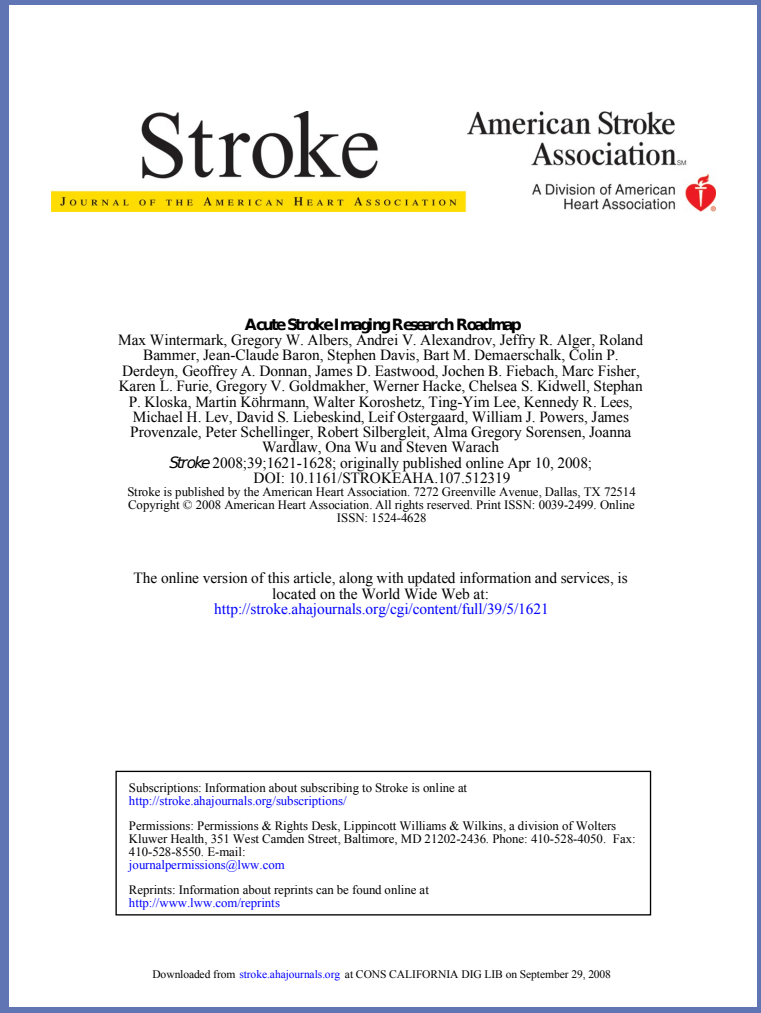
Deliverable

- 1 imaging manuscript
- Separate from the other STAIR paper
- To be published both in Stroke and in AJNR

- Timeline: feed-back by Sunday March 24
- Incorporation of revisions by Sunday March 31
- Final revisions submitted by Sunday April 7
- Manuscript ready to submit by Monday April 10

Proposed Authorship Plan

- All STIR members who were actively involved in the drafting of this manuscript will be co-authors
- Group chairs and task force leaders higher up in the authorship list
- All STIR members and STAIR participants are welcome to endorse the recommendations and will be listed in the acknowledgement
- Acknowledgements will also list the rosters for the different groups and task forces



Stroke
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American Stroke Association
A Division of American Heart Association

Acute Stroke Imaging Research Roadmap

Max Wintermark, Gregory W. Albers, Andrei V. Alexandrov, Jeffry R. Alger, Roland Bammer, Jean-Claude Baron, Stephen Davis, Bart M. Demaerschalk, Colin P. Derdeyn, Geoffrey A. Donnan, James D. Eastwood, Jochen B. Fiebach, Marc Fisher, Karen L. Furie, Gregory V. Goldmakher, Werner Hacke, Chelsea S. Kidwell, Stephan P. Kloska, Martin Köhrmann, Walter Koroshetz, Ting-Yim Lee, Kennedy R. Lees, Michael H. Lev, David S. Liebeskind, Leif Ostergaard, William J. Powers, James Provenzale, Peter Schellinger, Robert Silbergleit, Alma Gregory Sorensen, Joanna Wardlaw, Ona Wu and Steven Warach

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Terminology

- Stroke imaging terminology must be specific to the clinical context, acknowledging that different imaging modalities may be optimal for different methods of treatment (IV versus IA) and in different time windows (early versus late).
- Different modalities, parameters, and thresholds may have differing roles for determination of the potential risks of treatment (e.g., hemorrhagic risk) versus the potential benefits of treatment (e.g., salvageable penumbral tissue volume).
- "Treatment-Relevant Acute Imaging Targets" (TRAITs) are meant to capture imaging elements needed for inclusion into specific treatment algorithms.

Terminology

- It is important to distinguish pathophysiological concepts from operational definitions that use imaging to assess these concepts as part of research studies or clinical trials.
- Therefore, when the terms of infarct and penumbra are employed, there should be an explicit qualification as to the specific imaging technique, parameter(s) and threshold(s) under discussion.
- Also, one should recognize the probabilistic nature of operational CT and MRI definitions
- All the imaging-based operational methods to assess infarct and penumbra only provide with a snapshot of a complex, dynamic process.

Imaging in Stroke Trials

- In general, imaging design for stroke clinical trials should be adjusted to the individual requirements of the trial, depending on its exact goal, and kept to a minimum.
- The understanding of appropriate imaging modalities, acquisition parameters, thresholds, and post-processing approaches is evolving as experience accrues.
- No single imaging approach addresses all issues.

Imaging in Stroke Trials

Regardless of the imaging techniques used, trials should ensure that

- in therapeutic trials, the balance of imaging time (including acquisition, processing and interpretation) against potential detriment of treatment delay, has to be considered in planning the trial design and its imaging component; workflow should be optimised based on best practice;
- acquisition parameters and post-processing are standardized or conform to minimum, protocol-defined, common standards;
- central analysis of imaging outcomes should be undertaken in multicenter trials;
- if imaging is used to define patient selection then either a system for standardised central image processing and automated analysis, or appropriate training for radiological raters at participating centers, should be undertaken;
- imaging methods should have demonstrated acceptable interobserver reliability;
- the bias introduced by imaging selection on the population recruited has to be considered.

Imaging in Stroke Trials

- *Imaging as a Biomarker for Efficacy Outcome in Stroke Clinical Trials*
- *Imaging as a Biomarker for Safety Outcome in Stroke Clinical Trials*
  - Intracranial haemorrhage on post-treatment CT is widely used as a safety outcome in trials of revascularization therapies (drug or mechanical). Definitions have varied among trials, and trials commonly report multiple definitions. Different sensitivities of imaging depending on modality (e.g. MRI versus CT; susceptibility weighted imaging (SWI) versus gradient recalled echo (GRE)) and timing of follow-up are not yet clearly defined.
  - Other safety-related outcomes lack standardized definitions for timing, imaging modality or reporting (e.g. brain swelling/malignant edema).

Imaging in Stroke Trials

- *Imaging for Patient Selection in Stroke Clinical Trials*
- Eventually, a clinical trial should be conducted to assess what imaging adds in terms of information compared to what could have been extracted just from clinical information alone. This trial should consider the potential harm caused by the delay to treatment caused by the imaging.
- This trial of imaging should use an intent-to-treat approach. Because it may difficult to find centers willing to randomize patients to different imaging protocols, the trial may course to a cluster randomization approach.
- The trial should test a particular type of intervention and a particular time window.

Imaging in Stroke Trials

- *Imaging for Patient Selection in Stroke Clinical Trials*
- The trial may include some basic imaging (for instance NCT, or NCT and CTA depending on the type of intervention selected) that would be common to all trial arms.
- The trial should have three arms: 1) an arm with control patients who do not receive any additional (tested) imaging and do not receive the intervention (only best medical care); 2) an arm with patients who do not receive any additional (tested) imaging but do receive the intervention; and 3) an arm with patients who do receive the additional (tested) imaging and the intervention.
- The main outcome of the trial should be a clinical outcome (typically mRS), but an imaging endpoint could be acceptable for phase 2 trials.
- Also, the trial should include a cost-benefit analysis, to integrate the cost of the intervention and the cost of the imaging.

Revascularization

- Pathophysiology of acute ischaemic stroke should be routinely documented at baseline angiography using systematic description of arterial occlusions and collateral perfusion. In general, non-invasive vascular imaging with sufficient sensitivity and specificity should be performed prior to any invasive vascular imaging to limit the number of unnecessary invasive procedures.
- Timing of assessments should be recorded and must be the same in all arms of the trial to avoid disparities in revascularization assessment timing between treatment arms. Number of assessments should be relevant to the trial question to avoid unnecessary excess radiation/disruption to patient care.

mTICI scale for reperfusion

0	**no reperfusion**
1	flow beyond occlusion without distal branch perfusion
2a	downstream perfusion <50% of target arterial territory
2b	downstream perfusion >50% of target arterial territory
3	near? complete and normal perfusion of downstream territory

Revascularization

- M1 definition:
  - horizontal segment or
  - definition based on branching
- M2 configurations:
  - single versus multiple

STIR Certification

- STIR therefore proposes the creation and population of a cloud-based repository of clinical and imaging data that can be used to compare head to head different software packages in their attempts to define infarct and penumbra, and determine which software package is “good enough”. More specifically, we will describe below:
  - the minimum criteria/standards/standards that software packages measuring infarct and penumbra should be evaluated against, and the results of this evaluation that need to be disclosed to the stroke community;
  - the standard study design that needs to be used to conduct the evaluation of the software packages measuring infarct and penumbra;
  - the characteristics of the clinical and imaging data to be compiled into the repository.

STIR Certification

- The *first recommended analysis* is to use existing digital phantoms to ensure that the PCT and Perfusion MRI software produces five perfusion results in an acceptable ballpark.

STIR Certification

- The *second recommended analysis* is a comparison of acute PCT and DWI to determine the optimal PCT parameter(s)/threshold(s) to determine infarct
- For this analysis, the required characteristics for the dataset include:
  - a maximal delay of 60 minutes between the PCT and the DWI studies (this is particularly an issue where eligible patients will need to have IV tPA lysis commenced after the PCT and before the MRI, which will be performed during tPA infusion);
  - criteria for satisfactory data will be concurrent CTA (NCT assumed) and MRA to confirm lack of recanalization between exams;
  - if no baseline occlusion can be detected on the initial CT, then follow-up perfusion MRI will be required to confirm the absence of reperfusion;
  - thus, ideally, MRI data should contain both MRA and perfusion MRI.

STIR Certification

- The *third recommended analysis* will involve acute CT and MRI datasets to determine optimal parameters/thresholds to determine infarct and penumbra in two groups of patients: one with no recanalization and one with early recanalization.
- The baseline dataset should include NCT, PCT, CTA (ideally dynamic CTA) or DWI, perfusion MRI, FLAIR, GRE or SWI, MRA.
- In the first group, patients should demonstrate persistent occlusion on follow-up CTA or MRA or complete lack of reperfusion (persistent PCT or perfusion MRI lesion of similar size to baseline).
- In the second group (“early” recanalization), the issue is the timing of documentation of recanalization/reperfusion.

STIR Certification

Baseline imaging study	**- NCT/PCT/(dynamic) CTA** **- DWI, PWI, FLAIR, GRE or SWI, MRA**
Revascularization imaging study	- DSA after clot retrieval - NCT/PCT/(dynamic) CTA between 2 and 24 hours - DWI, PWI, FLAIR, GRE or SWI, MRA between 2 and 24 hours
Follow-up imaging study	- 3-7 day FLAIR - 3-7 day NCT - 24-hour DWI

STIR Network

- The two logistic priorities for promoting translation of new imaging research are:
  - (1) establishment and population of a STIR/VISTA-Imaging clinical and image data repository, and
  - (2) establishment of an international stroke trial imaging network.
- What would be the optimal structure/components of a central imaging coordinating/data center to support imaging-based clinical trials of acute reperfusion therapies?

Any other suggestion??