

Imaging of Revascularization (Recanalization and Reperfusion)

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Baseline Vascular Imaging

- **Non-invasive vascular imaging prior to invasive imaging**
 - limit unnecessary invasive procedures (ie. CTA before DSA)
 - more homogeneous patient population
- **“Thrombus” imaging** may supplant vascular imaging for patient selection if practical/time considerations (ie. PSC delays to CTA)
 - Disappearance of “thrombus” reliability?/
recan assessment impacted

Revascularization imaging protocols

- **Same modality throughout study design** when possible
 - Avoid “apples and oranges” scenario for revascularization endpoint (ie. TCD/CTA or CTA/MRA)
 - Practical considerations: contraindications to one modality (ie. agitation/metal-MRA; low CrCl-CTA; no bone windows -TCD)
- **Technical considerations for standardizing imaging protocols** to allow comprehensive assessment (overlap with other STIR subgroups)
 - Perfusion – whole brain coverage; non-truncated
 - Angiography – extracranial and intracranial at baseline depending on research question

3 Vascular Components must be assessed separately

- **Recanalization** (arterial patency)
- **Reperfusion** (antegrade tissue level perfusion)
- **Collaterals** (retrograde tissue level perfusion)

TICI/TIMI Confusion

COMMENTARY

TIMI, TIBI, TICI: I Came, I Saw, I Got Confused

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Protocol for the perfusion and angiography imaging sub-study of the Third International Stroke Trial (IST-3) of alteplase treatment within six-hours of acute ischemic stroke

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re-perfuse. One score for initial occlusion was described by Mori and colleagues based on IAA of the cerebral circulation but again became confused with recanalization (71); the TIMI score (70) was adapted to the cerebral circulation as the Thrombolysis in Cerebral Infarction (TICI) score and then further modified to describe degrees of distal arterial patency (54,75); the TICI and Arterial Occlusive Lesion (AOL) scales were then edited and used for categorizing degrees of recanalization after therapy and not the primary occlusion; these scores also muddle arterial patency with tissue perfusion, a cardinal cause of confusion (76); finally there are several further variations on the TICI score (Table 2).

Recanalization

Arterial patency and grading

- **One standard recanalization scale** for each imaging modality (TCD, CTA, MRA, DSA) to assess patency of arteries
 - TCD -TIBI
 - DSA- **TICI angio taskforce to report out tomorrow- AOL recan?**
- **Primary lesion: most proximal intracranial occlusive segment** that is likely to be the cause of stroke symptoms
 - **Standardize definitions of different sites** of primary lesion -
 - Carotid T/L; Tandem ICA+ MCA
 - Proximal vs distal M1 vs prominent anterior temporal branch
 - M2; M3/M4

Recanalization

Arterial patency and grading

- **‘Occlusion’ definition** includes complete and partial arterial obstruction:
 - Complete – abrupt cutoff/no forward flow
 - Partial – contrast opacifying through thrombus/hairline lumen
- **Secondary lesion(s)** are occlusive segments:
 - proximal +/- extracranial to primary lesion (ie. vert, cervical ICA)
 - tandem lesion distal to primary lesion (ie. M2/M3)
 - other territory arteries (ie. ACA, PCA)
 - important side branches (ie. SCA)

Tissue level antegrade reperfusion grading

- **One standard reperfusion measure** for each imaging modality (CTP, MRP, DSA) to assess tissue level antegrade (re)perfusion within affected vascular territory.
 - DSA- **TICI angio taskforce to report out tomorrow- mTICI?**
- **Distinguishing anterograde from retrograde** considered to be an important distinction therapeutically
 - Is quite difficult to differentiate on CTA/MRA unless dynamic/4D acquisition available

Tissue level antegrade reperfusion grading

• **Visual method versus computational method?**

- appropriate to trial question and trial stage
- avoid unnecessarily complex analysis steps
- Be robust and reliable within measurement tolerance limits

Collaterals retrograde perfusion grading

- **One standard collaterals scale** for each imaging modality (CTA, MR, DSA) to assess tissue level retrograde perfusion within affected vascular territory.
 - Single snapshot imaging may underestimate collaterals- if imaging timing very early
 - Difficulty in distinguishing retro- from anterograde flow on CTA/MRA acknowledged

Timing and number of assessments

- **Timing of assessments should be similar in all treatment arms** for direct comparison
 - Important considerations include reocclusion or partial/slow recanalization
- **Number of assessments** relevant to trial questions; avoid unnecessary excess radiation/disruption to patient care
 - **2 CTA/CTP studies maximum**

When to do assessments?

Baseline (vascular status)

- Preferably pre-randomization
- Should be as close in time as possible to the administration of treatment – in general more than two hours time lapse would be too long

Post-treatment

- Early revascularisation – “nutritional”
- Exact timing depends on treatment but similar in both arms
 - Endovascular: 2-3 hours
 - Systemic Thrombolysis: 3-6 hours

Next day

Ex: 24-36 hr – ceiling effect with some occlusion sites (M1 and iv tPA)?

Argument for early (few hours) vs next day balances clinical relevance with practicality

How revascularization should influence stroke clinical trial design

- Phase 1- ???

- **Proof of Concept Phase 2**

- **Prove revascularization generally comparable** and no more hazardous than current standard treatment before Phase 3
 - **biologic effect confirmed**

How revascularization should influence stroke clinical trial design

- **Pivotal Phase 3 trials**

- **Training of local investigators**

- Patient selection (ie. collateral assessment; baseline primary lesion; baseline AOL/TICI)
 - Revascularization local interpretation (when to abort procedure)

- **Credentialing investigators/** standardizing imaging protocols/ strict timelines for data transfer to core lab

- **Standard set of definitions across trials** for primary lesion and revascularization scales (recanalization and reperfusion)

Conclusion

- **3 distinct vascular components**
 - **Recanalization**
 - **Reperfusion**
 - **Collaterals**
- **Simplicity and standardization**