Imaging – questions in need of addressing

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Method

- survey of STIR group
  - what are the key questions?
  - can they be addressed retrospectively vs prospectively?
  - if prospective can they be addressed by observational cohort vs RCT?
- distillation & personal view

Key Themes

- Refining the concepts of core & risk
  - improving definitions
  - accounting for location?
- Improving the technology
  - easier safety screening for MRI
  - better contrast to noise for CTP – hardware/software/contrast agent
  - faster reconstruction & post-processing
- Understanding value of imaging for treatment selection
  - Workshop 2 Tuesday – especially futility/NNT
  - role in standard vs extended time window reperfusion therapies
- MR vs CT comparisons
  - time delays, accuracy
- Applicability
  - proportion of stroke patients with LVO +/- collateral/core criteria

Refining the concept of core

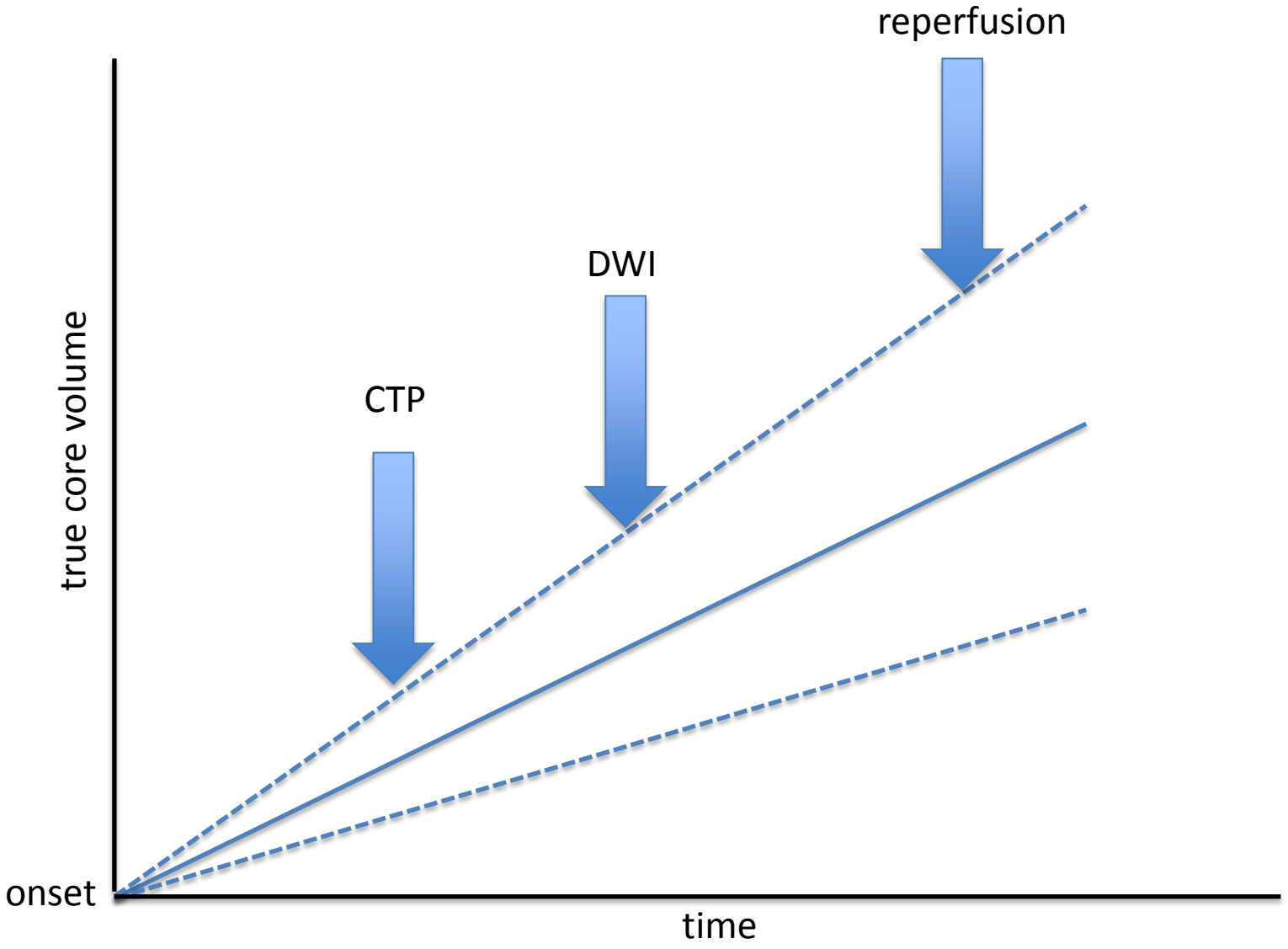
- Definitions/accuracy
  - **DWI**: little reversibility in traditional paradigm ?more with ultra-fast reperfusion,
  - **CTP relCBF** currently calibrated to maximal extent of "concurrent" DWI lesion ?re-calibrate vs final infarct* in rapid reperfusion group
  - **NCCT** – is the "lower sensitivity" of NCCT for core a product of delayed reperfusion rather than physiology? (especially if "core/collat-assisted" NCCT to reduce read errors)
- Relevance of core to predicted functional outcome if reperfusion successful
  - risk of SICH
  - incorporation of location information
  - is partial vs complete tissue infarction relevant to outcome?

Possible Actions:

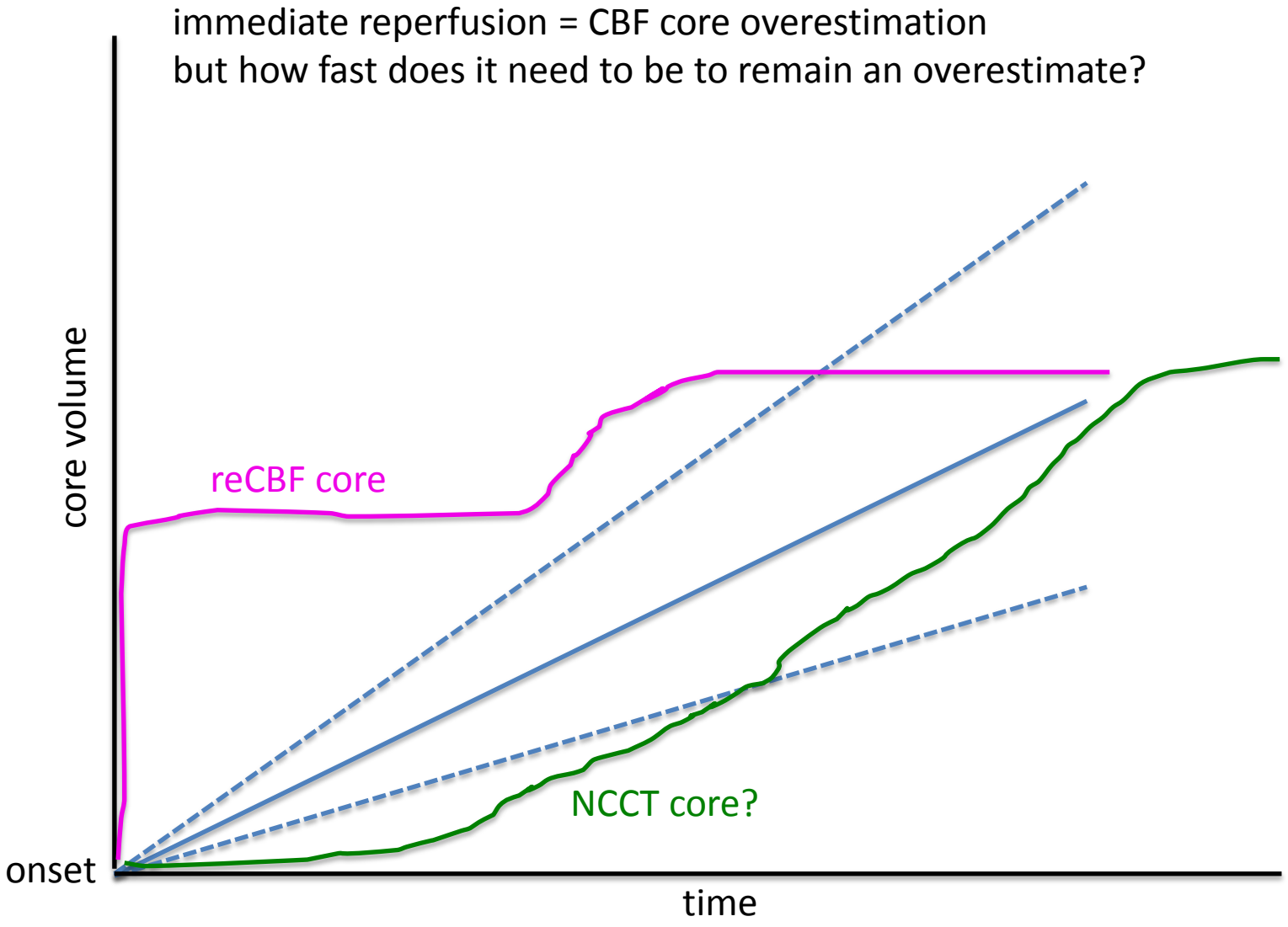
1. refine core definitions in *existing pooled trial datasets* using follow-up infarct on MRI* as reference standard in patients with short imaging to mTICI 3 reperfusion times *+ prospective data* as treatment gets even faster
2. develop a method to account for location - challenging

*optimal definition to be discussed in session on Final Infarct Volume as outcome

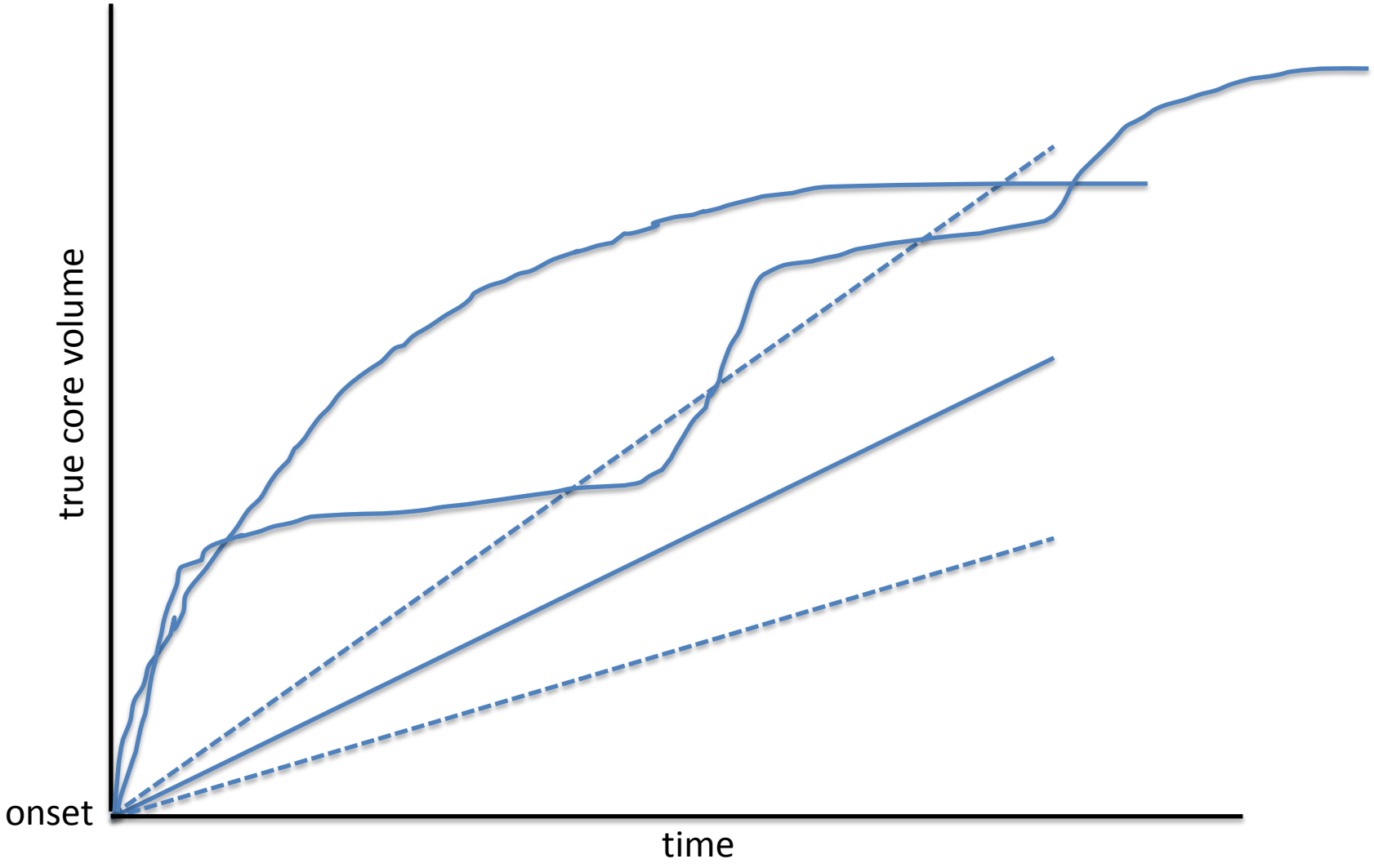
Current workhorse ultra-fast deep learning



…but with ultra-fast reperfusion



…and what are the core development kinetics?



Refining the concept of risk

- Definitions/accuracy
  - new Heidelberg classification of SICH

- Relevance to functional outcome
  - large infarct = futile but not harmful? (malignant edema?)
  - SICH may be actively harmful - ?sufficiently predictable to exclude

Possible Actions:

1. *re-assess IA trials using Heidelberg classification*
2. *baseline core & hypoperfusion assessment for SICH risk*

existing + prospective data in less favorable imaging profiles likely to have higher SICH risk (Bern series etc)

Improving the technology

- MRI
  - **key barrier = effective fast safety screening**
  - rapid protocols – reasonably established
  - gadolinium risks – ASL development etc
- CTP
  - **key limitation: poor contrast to noise**
    - hardware – detector sensitivity etc
    - software – iterative recon, smoothing etc
    - contrast agent – more concentrated?
  - **faster reconstruction and post-processing**
    - combined CTP and arch-vertex CTA?
    - dynamic CTA in <1min post-acquisition?
- NCCT
  - could even better resolution of subtle loss of grey-white/hypodensity improve core detection?

Possible Actions:

1. *requires manufacturer commitment to continue developing the technology* ***urgent need*** *– risk that the requirement for speed will trim out advanced imaging from routine protocols – reducing potential future pathophysiologic insights and treatment advances*

Understanding value for treatment selection

- Endovascular <6h?
- IV thrombolysis <4.5h?
- Extended time window reperfusion
  - **prognosis versus treatment effect**: at some point the absolute improvement in good outcome becomes meaningless, despite potentially having the same ”treatment effect”
  - Denominator = **all** LVO patients (avoid discounting potential benefit in those excluded from treatment by imaging).

Possible Actions:

1. ***consensus on “futile” outcome*** *– Workshop 2 Tuesday*
2. *options*
   - *existing observational - compare occlusion vs collat vs CTP selection effect*
   - *RCTs of Tx in extended window ongoing only in “favorable” group, adding unfavorable would be ethically challenging and costly*
   - *RCT of Tx in “non-target” early window patients – need large sample size & need to be doing imaging in all to identify “non-target”*
   - *prospective observational – “DEFUSE-style” but focused on non-favorable imaging group: Tx all imaging profiles, analyze those with vs without reperfusion by imaging profile status*

MR vs CTP vs mCTA comparisons

- Speed vs accuracy
  - predicated on there being a benefit from selection
    - if can't identify a futile subgroup there's little point
    - current debate is whether any more than CT/CTA is necessary…
  - rapidly obsolete as technology evolves
    - faster MRI or better CTP core would invalidate old results
  - methodology challenging
    - few sites can do both CTP and MRI well → cluster RCT
  - *realistically* how often do Tx decisions differ between modalities?

Possible Actions:

1. *is this the right time to do this?*
2. *?cluster RCT in extended time window once proven vs embed in an extended window RCT*

Applicability/Generalizability

- proportion of stroke patients who have
  - LVO
  - LVO + good collat
  - LVO + “small core”
  - if only excluding a small % in whom treatment is genuinely futile is it worth bothering?
  - *e.g. is 6% ASPECTS 0-4 in MR CLEAN consecutive vs selected?*
  - *what potential numbers of patients will we be treating?*

Possible Actions:

1. *limited screening logs in recent trials but could pool large institutional databases already in existence to rapidly answer*

Conclusions

- Great potential for technological advancement
  - urgently needed to avoid loss of potential future insights from advanced imaging due to speed-driven “minimalist” approach
- Existing observational pooled data
  - assist addressing “core” definition and location issue
  - assist with futility question (but limited numbers of large core/poor collaterals in trials)
- Prospective data with even faster imaging-reperfusion times
  - test frontiers of reversibility & outcomes in “unfavorable” core/collateral group
- Extended window reperfusion trials ongoing
- RCT by imaging modality??