Stochastic Methods Can Resolve the Dilemma of Emergency Stroke Transport: A Case Study of Texas

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Objectives

- To create a generalized, stochastic model of time-dependent acute ischemic stroke growth based on realistic physiological mechanisms
- To apply the stochastic model in a case study of Texas to identify regions where one emergency stroke transportation (EST) method is significantly favored over another

Background

- **Primary Stroke Center (PSC):** has acute stroke imaging to identify severity of stroke and can treat non-LVO's with tPA (~70% of cases[1])
- **Comprehensive Stroke Center (CSC):** can do everything that PSC can and has resources to perform endovascular thrombectomy (EVT) to treat large-vessel occlusions (LVO, ~30% of cases[1])
- **Drip and Ship (DNS):** if the CSC is further away than the PSC, then EST goes to the PSC. If the patient scans at PSC show an LVO, then proceed to the CSC for EVT
- **Mothership (MS):** EST goes straight to the CSC, even if it is further away than the PSC
- **Bypass Time:** the absolute difference between the time from patient pick-up to CSC and the time from patient pick up to PSC

Methods

- We represent the physiology of infarct core growth as a first-order ordinary differential equation, enabling infarct volume $\boldsymbol{V(t)}$ for a single patient to be calculated and mapped to mRS at time of reperfusion given a simulated penumbra volume V_p and collateral score τ parameterized by penumbra volume[2,3]

$$\tau \frac{d\boldsymbol{V(t)}}{dt} + \boldsymbol{V(t)} = V_p, \; V(0) = 0$$

$$\tau = \left(-0.0013 \cdot (220 - V_p) \cdot \left(\frac{11}{220}\right) + 0.0179\right) \cdot (60)$$

The differential equation has the following solution,

$$\boldsymbol{V(t)} = V_p \cdot (1 - e^{-t/\tau}) \qquad \textit{Eqn. (1)}$$

$$\boldsymbol{mRS(t)} = 0.0376 \cdot \boldsymbol{V(t)} \qquad \textit{Eqn. (2)}$$

- The state's network of stroke centers is configured within 15,811 geographic block-groups as defined by **census data**, and travel time from stroke onset to reperfusion for MS and DNS is computed using the centroid of each block-group as the patient pick-up location
- For each block-group, **Monte-Carlo** methods generate a distinct Beta distribution of LVO V_p's and a second independently sampled Beta distribution of non-LVO V_p's
- For each block-group and for each of MS and DNS, Eqn. (1) is applied in an LVO-only model and an all-stroke (LVO & non-LVO combined) model. The resulting distributions of evolved patient infarct volumes are translated into **cumulative distribution functions** of mRS via Eqn (2). Continuous mRS is used for this analysis, but using the discretized scale does not vary results significantly
- For each block-group, we compute a **one-tailed, two-sample Kolmogorov-Smirnov test for statistical significance** and a **Cohen's d effect size statistic** for practical significance between the distributions of mRS outcomes for MS and DNS
- All model parameters, including probabilities of reperfusion dependent on treatment type, were established from large cohort studies

Results

- Of the 13,113 blocks where the PSC is the closest hospital from origin, DNS produces significantly better stroke outcomes than MS in 71.5% (1.7% std dev; $p < 0.01$; $n = 15{,}000$ per block-group)
- For the subset of only LVO patients, MS produces significantly better outcomes in 66.1% of blocks (0.6% std dev; $p < 0.01$; $n = 4{,}500$ per block-group)

Figure 1. All block-groups that statistically favor MS. Effect size of MS outcomes compared to DNS outcomes (left) and odds ratio of the probability of a good outcome (mRS 0-1) of MS over the probability of good outcome of DNS colored by magnitude of effect size (right)

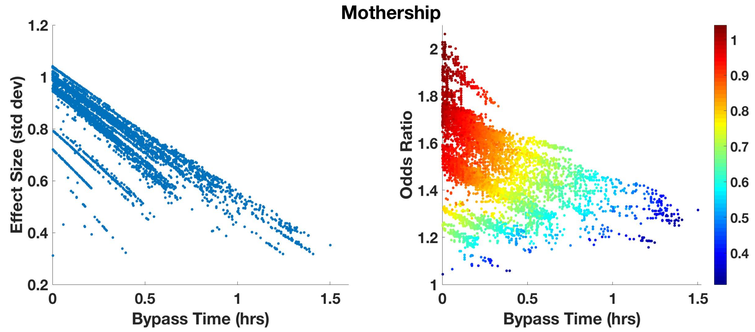


Figure 2. All block-groups that statistically favor DNS. Effect size of DNS outcomes compared to MS outcomes (left) and odds ratio of the probability of a good outcome (mRS 0-1) of DNS over the probability of good outcome of MS colored by magnitude of effect size (right)

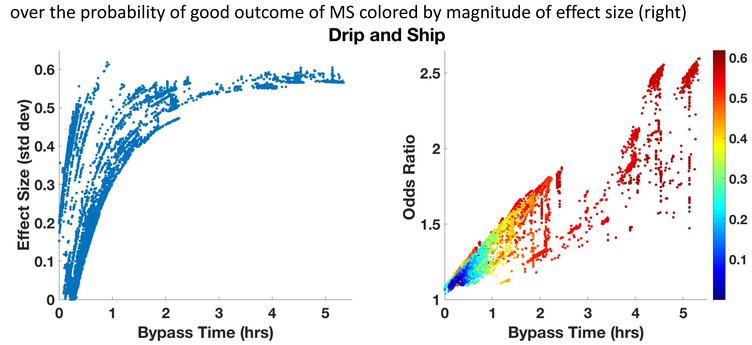
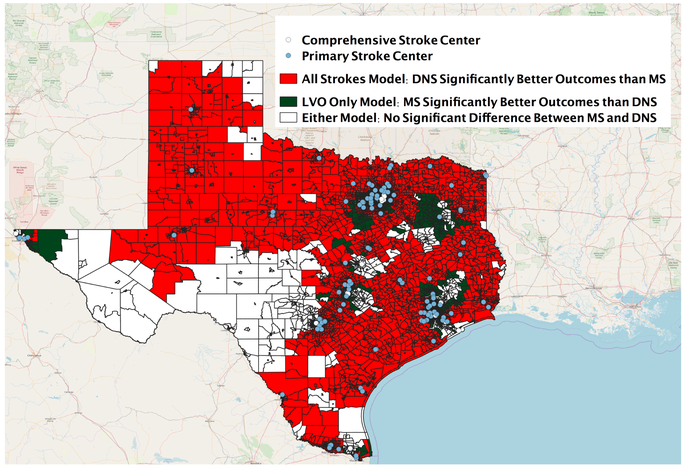


Figure 3. Heat map of block-groups showing regions that statistically favor an EST method



Discussion

Assumptions

- EST decision (MS or DNS) at time of pick-up is carried through completely
- Onset defined as time of first-noticed symptoms
- Probability of reperfusion given EVT is independent of time from onset of acute ischemic stroke
- Reperfusion occurs immediately at time of treatment
- Patients in population start with initial mRS = 0
- All non-travel times are taken as constants (e.g. door-to-needle, door-to-puncture, call-to-pickup, etc.)
- All non-LVO and LVO patients are eligible for tPA and all LVO patients are eligible for EVT. Patients are ineligible to receive tPA if onset-to-treatment time >4.5 hrs. If patient is outside of eligibility time window or does not reperfuse from treatment, then $\boldsymbol{V(t)} = V_p$

Strengths

- Can compute the probability of any mRS on a continuous or discretized 0-6 scale, whereas previous models can only compute the probability of a good outcome
- Can compute comparative significance to directly compare efficacy of the two emergency transport strategies (existing models define time-dependent outcomes but cannot compute statistical significance because their independent variables are deterministic[4])

Limitations of Current Model

- Simulated n may be an unrealistic sample size depending on block-group
- Time calculations use the centroid of each block-group (i.e. resolution)
- Does not include stroke mimic cases, intracerebral hemorrhage cases

Future Work

- Improve resolution from block-group to smaller geographical unit
- Optimize outcomes with distributions of pre-hospital times, hospital triage times, and patient factors such that an ideal bypass time can be determined
- Build a learning algorithm to predict probabilities of an LVO or non-LVO, then incorporate into the stochastic model

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