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Geographic modeling of best transport options for treatment of acute ischemic stroke patients applied to policy decision making in the USA and Northern Ireland

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ABSTRACT

Ischemic stroke is a treatable disease with alteplase, a clot-busting medical treatment, and endovascular therapy (EVT), mechanical removal of the clot through a minimally invasive procedure. The effectiveness of both treatments is time dependent, and they are usually given together. Alteplase is less effective than EVT, but is widely available at community hospitals; EVT is highly effective, but it is only available at large urban tertiary hospitals. There is uncertainty if it is better to receive alteplase early and delay EVT or vice versa. We developed a conditional probability model based on decay curves that were generated from pooled clinical trials, and then created a software solution using C# that interfaced with ArcGIS’s Software Development Kit and Google’s Distance Matrix API. The maps were developed based on pre-specified time interval variables to determine the best transportation for multiple US states (Colorado, Arizona, Tennessee, and Massachusetts/Rhode Island) and Northern Ireland. The overall objective of this work was to determine if these maps could be used to influence health policy decision making for acute stroke patients.

1. Introduction

Stroke causes a significant burden on society, as it is the leading cause of disability, the third leading cause of death in the developed world, and the second leading cause of death in developing countries (Kamal et al., 2015; Lozano et al., 2013). Ischemic stroke is the type of stroke where a blood clot moves to an artery in the brain and disrupts blood flow; it makes up approximately 85% of all strokes. Ischemic stroke can be treated with both alteplase, a clot-busting medical treatment, and endovascular treatment (National Institute of Neurological Disorders, 1995). Treatment with alteplase is available at hospitals that have a CT (computed tomography) scanner and access to adequately trained physicians, which makes the treatment available at smaller community hospitals as well as larger tertiary hospitals.

A major advancement in the treatment of ischemic stroke is the evolution of endovascular treatment (EVT) (Goyal et al., 2015, 2016). EVT is a minimally invasive surgery that mechanically removes the clot by threading a catheter through the artery and using a stent retriever device to snare and remove the clot, restoring blood flow. EVT is most often given with alteplase to ischemic stroke patients. However, EVT is only available in larger urban tertiary centers that have the required angio-suite and appropriate medical expertise to carry out the procedure. Treatment with alteplase is less effective than with EVT, and both treatments are highly time dependent (Emmerson et al., 2014; Menon et al., 2016; Saver et al., 2016). The probability of good outcomes from these therapies declines with time from onset of symptoms to when the treatment was started. This work will focus on patients who receive both treatments, although there are circumstances where a patient may only receive EVT. We are, however, including patients who receive only EVT when they are outside the time window for alteplase eligibility, as alteplase must be given within 4.5 hours of stroke onset. We are not focusing on the group of milder stroke patients who receive only alteplase, as this work focuses on the best transport option for accessing EVT. For
simplicity, we will refer to all hospitals that offer alteplase only as Primary Stroke Centers (PSC) and hospitals that offer both alteplase and EVT as Comprehensive Stroke Centers (CSC).

Since the success of the EVT clinical trials (Goyal et al., 2015, 2016), healthcare decision makers have been trying to better understand the best transportation route for patients who live outside the catchment area of a CSC (Jayaraman et al., 2017). There is uncertainty on how to access EVT—whether it is better to transport patients to a PSC first to receive early treatment with alteplase and then transport to a CSC for EVT—which delays the treatment with EVT (called “Drip and Ship”), or to bypass the closest PSC and take the patient directly to a CSC, delaying treatment with alteplase but ensuring that they receive EVT sooner (called “Mothership”) (Southerland et al., 2016). The answer to this question is not simple, as it depends on many factors, such as the drive time to each hospital and between each hospital, and the treatment efficiency of the hospitals.

Figure 1 depicts the time intervals for Drip and Ship and for Mothership. The needle time is the point in time that alteplase administration begins, and the groin puncture and reperfusion time are related to the EVT procedure, where groin puncture is the start of the procedure and reperfusion is when blood flow is restored. As shown in the figure, the time intervals are dependent on geography: scene to PSC, PSC to CSC, and scene to CSC. Additionally, the time intervals are also dependent on the efficiency of the hospital:

![Drip and Ship: Early alteplase but later endovascular treatment](image1)

![Mothership: Delayed alteplase but faster endovascular treatment](image2)

**Figure 1** Time intervals of key processes within the Drip and Ship versus the Mothership transportation options. The red arrow depicts the time point when alteplase is administered.

<table>
<thead>
<tr>
<th>Table 1. Mothership and Drip and Ship Models (old model)</th>
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<tr>
<td>Model</td>
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<tr>
<td>Mothership</td>
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<tr>
<td>Drip and Ship</td>
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EVT: endovascular therapy.

Time X is the transportation time from the patient to the non-endovascular capable hospital (nECC). Time Y is the transportation time from the nECC to the endovascular capable hospital (ECC). Time Z is the transportation time from the patient to the ECC. Time A is the time from the patient’s arrival at the nECC to the administration of alteplase and time B is the time from alteplase administration to leaving the nECC. Time C is the time from the patient’s arrival at the ECC to the beginning of the endovascular procedure.

1.2. Research question

The research question that we are addressing here is: Can the development of a software to produce ideal transport maps for acute stroke patients assist health policy decision making? We explore this through a case study approach with two healthcare organizations.

2. Related work

Geographic information systems are increasingly important for decision-support tools (Church, 2002; Clarke, 1990), and these systems are assisting with understanding health service delivery and access (McLafferty, 2003). As described in the introduction, EVT was proven to be a highly effective therapy in 2015. Despite the relative novelty of EVT, there have been several related works examining the best transportation route for treatment of ischemic stroke patients. A conditional probability model was developed that yielded a generalized temporal-spatial visualization that showed how distance from PSC and CSC affected whether it was better for the patient to be transported via a Drip and Ship or Mothership route (Holodinsky et al., 2017b). This work found that health system efficiency affected when a patient should be transported via Drip and Ship or Mothership. The conditional probability model that yielded the generalized temporal-spatial visualization was put on to geographic maps for two Canadian provinces and one US state using the actual location of PSCs and CSCs; the maps showed where Drip and Ship or where Mothership yielded the better...
probability of good outcomes. Maps were developed for different efficiencies of the PSC’s door-to-needle time and different speed of symptom recognition (onset to first medical response or when paramedics arrive on scene) (Milne et al., 2017). These studies created models based on the assumption that all patients underwent EVT and that they were not re-admitted; the decay curves for good outcomes were derived using previous studies for this patient group (Emberson et al., 2014; Menon et al., 2016). Table 1 shows the formulas that were used to create this model, which is based on a patient population that has received EVT and reperfused (Holodinsky et al., 2017b; Milne et al., 2017).

Further research is now being done to examine the patient population in the field, as there is no way of confirming if a patient will be eligible for EVT in the field. There are quick clinical assessment scales that have been developed that provide good sensitivity in identifying patients that would be eligible for EVT; this includes the Los Angeles Motor Scale, LAMS (when LAMS >3, there is a higher probability of being eligible for EVT) (Nazliel et al., 2008), and the RACE (Rapid Arterial Occlusion Evaluation) Scale (De la Ossa et al., 2014). There have been policy changes made in Rhode Island based on the LAMS score. When a patient is within 30 minutes of the CSC and the LAMS is greater than 3, the closest PSC will be bypassed and the patient will be transported directly to the CSC (Mothership) (Jayaraman et al., 2017). A new conditional probability model has been developed to account for the full population in the field based on different field tests (Holodinsky et al., 2017a). Table 2 shows the formulas that were used to create this model, based on a field patient population showing those who received EVT or only received alteplase (Holodinsky et al., 2017a).

Related work also includes a modelled approach to understanding when different RACE scores should be used for Drip and Ship or Mothership to yield a higher probability of good outcomes (Schlemm et al., 2017). Additionally, a geographic model was developed to look at how traffic patterns alter the shortest time to a CSC (Phan et al., 2017).

### 3. Methods

We used a case study approach to study whether generated maps from our conditional probability model can assist healthcare systems to make policy decisions for stroke patients to access EVT. There were two healthcare organizations that were identified for this study: the Society of NeuroInterventional Surgery (SNIS) and Health and Social Care Board (HSCB) of Northern Ireland. These healthcare organizations were chosen as they represent two divergent types of organizations in two very different health systems and geographies. SNIS, in the US, is leading a major initiative called the Get Ahead of Stroke campaign. They are aiming to change legislation in all 50 states to triage patients to the most appropriate center based on a field severity assessment. These maps would allow SNIS to put forth legislation with greater certainty of the distance between a PSC and CSC, and where a PSC should be bypassed (Mothership transport enacted). HSCB wanted to make policy decisions on the optimal hospital efficiency for door-to-needle time to ensure good outcomes for patients who will access EVT. They needed to look at both their current door-to-needle times at each of their stroke hospitals and compare the results of the map to the ideal door-to-needle time of 30 minutes. These two case studies allowed us to answer our key research question about whether the maps that our software produces can influence health policy decisions. Based on the conditional probability work that was previously developed (Holodinsky et al., 2017a, 2017b; Milne et al., 2017), we were contracted to develop maps that displayed the best transport options for several US states by SNIS and for Northern Ireland by HSCB.

### 3.1. Software to create maps

To create the maps, software was developed in C# using Microsoft’s Visual Studio.NET framework (versions Community and up). Visual Studio.NET was chosen because of its ability to develop in many different languages (C# and JavaScript) and platforms (desktop, web, and mobile), as well as the processing power of the selected languages. Using this framework, a Universal Windows Platform (UWP) application was developed where the NuGet package manager was used to add Esri’s ArcGIS Software Development Kit (SDK) to grant access to ArcGIS’s resources (maps of different regions) and to allow one to work with and manipulate the imagery of the imported maps. Additionally, the Newtonsoft.JSON package was used for (de)serializing all data used, and GeoCoordinate.NetStandard1 package was used to programatically work with coordinates. Furthermore, Google’s Distance Matrix API (application programming interface) was used to determine the travel times between stroke centers, as well as the times from stroke patient locations to the...
nearest stroke centers. ArcGIS also has this capability, but Google was more cost-effective and accurate as it is derived from actual traffic patterns (ZevRoss, 2014). These travel times were input into a conditional probability model that has been previously developed (Holodinsky et al., 2017a, 2017b; Milne et al., 2017). Using the calculated probabilities of good outcomes, a grid was created to display a radial gradient showing the distribution of these probabilities for both the Drip and Ship option and Mothership options. Figure 2 shows the software architecture diagram.

Using the ArcGIS’s SDK, a street base map was loaded. A feature service of international boundaries was also loaded, and a query was performed to return the geometry information of the region of interest. The geometry data were converted to a polygon object, and passed into a method along with a polyline object to generate an array of geometries. Each entry in this array is a square that, when displayed together, creates a grid of regular intervals over the region of interest. Each geometry in this array has a centroid calculated in WGS-84 coordinate format to use in the call to the Google Distance Matrix API. Both the geometry array and centroid collection can be serialized/cached for later use.

Using the tabulated hospital data (location of each PSC and CSC), a comma separated value (CSV) file was created with the name, hospital type, latitude and longitude and, if available, the median door-to-needle time for each hospital. This CSV file was used to instantiate a list of hospital data. Making calls to the Google API and using the latitude and longitude, the travel time from each PSC to each CSC was calculated and serialized into its own file. From the centroid file created (see previous paragraph), travel times to the closest PSC and closest CSC were calculated for each centroid location. The best travel time option for 5:00 AM was requested from Google’s API to simulate the light-and-sirens drive time of an ambulance. This time was chosen as there would be minimal traffic congestion, but it has not been validated as a close approximation to an ambulance driving in moderate traffic with lights and sirens on.

Once all travel times were found, they were passed into the probability model service, along with the other chosen time interval variables. The probabilities for Drip and Ship and for Mothership were calculated and compared for each centroid. The transportation option (Drip and Ship or Mothership) with the highest probability of good outcomes was assigned to each grid section, along with the probability. Based on the best transportation option and probability, a color value was assigned to each grid section. The grid was refreshed and displayed on top of the street map.

3.2. Requirements for SNIS

The Society for NeuroInterventional Surgery (SNIS) contracted us to develop maps for Arizona, Colorado, Tennessee, and Massachusetts/Rhode Island, showing where Drip and Ship or Mothership would yield the better outcomes. SNIS is the leading professional society for neuro-interventional surgery, focusing on EVT for stroke and other minimally invasive, image-guided procedures of the head, neck, and spine. A current major initiative led by SNIS in the US is the Get Ahead of Stroke campaign, aiming to change legislation in all 50 states to triage patients to the most appropriate center based on a field severity assessment. In many cases, the closest center is not the most appropriate. To assist stakeholders in healthcare policy to visually understand the benefit of transporting patients directly to EVT-capable centers, maps depicting two different scenarios based on PSC DTN times of 30 and 60 minutes were created for the five regions, using a previously described model (Holodinsky et al., 2017b; Milne et al., 2017). This model accounts only for patients who received EVT (Table 1), which is what SNIS requested. Other than the DTN times, other variables remained constant: onset to first medical response of 60 minutes; on-scene time of 25 minutes (time that paramedics remain at scene of stroke to conduct clinical screens and ready the patient for transport); needle-to-door-out time at PSC of 60 minutes (valid for Drip and Ship option only); and a door-to-reperfusion time of 115 minutes at the CSC. These hospital efficiency times were chosen based on current performance of these hospitals; they were provided by SNIS to be representative of the performance of the hospitals in these jurisdictions.

3.3. Requirements for HSCB

Similar to SNIS, the Health and Social Care Board (HSCB) of Northern Ireland contracted us to develop maps to assist with their policy decision making. HSCB arranges health and social care services for the population of Northern Ireland. HSCB requested that their maps depict the actual stroke patient population in the field for two scenarios: (1) those with a LAMS greater than 3; and (2) all potential stroke patients recognized by paramedics. We updated the model to calculate the probabilities of good outcomes based on the patient population in the field, which is described in previous work (Table 2) (Holodinsky et al., 2017a). The estimated distribution of patients with a LAMS greater than 3...
is as follows: 45% have a large vessel occlusion (eligible for EVT); 12% have a medium/small vessel occlusion (eligible for alteplase only); 34% are hemorrhagic strokes; and 9% are stroke mimics. For all potential stroke patients in the field, the estimated distribution of patients is as follows: 14.5% have a large vessel occlusion; 31% have a medium/small vessel occlusion; 10.4% are hemorrhagic strokes; and 44.1% are stroke mimics. The HSCB also requested that we develop three maps for each model. One map uses an ideal DTN time at the PSCs (30 minutes) and needle-to-door-out time (30 minutes). The second map uses the actual median DTN time at the hospitals and a needle-to-door-out of 30 minutes. The third map uses the actual median DTN time at the hospitals and a needle-to-door-out time of 60 minutes. The other time intervals were kept constant: onset to first medical response of 40 minutes; on-scene time of 20 minutes; and a door to groin puncture of 30 minutes for Drip and Ship and 60 minutes for Mothership. These constants were derived from actual performance in Northern Ireland.

4. Results

4.1. Maps for multiple US states

The maps for SNIS are shown in Fig. 3. The maps are color coded such that the location where Mothership yields higher probability of good outcome is in green; the red areas show the locations where Drip and Ship yield higher probability of good outcome; and the orange indicates the area where both options predict similar outcomes (within 2.5% of each other). The colors fade as the probability of good outcome declines, with the legend showing the exact probability for all color hues. For the smaller states of Tennessee and Massachusetts/Rhode Island, the Mothership transportation scenario almost always was better than Drip and Ship, regardless of location or PSC efficiency. For Arizona and Colorado, there are areas in the state where Drip and Ship is better for patient outcomes; however, these areas diminish as the efficiency at the PSC drops (door-to-needle at PSC is 60 minutes versus 30 minutes). The Arizona and Colorado maps also show considerable areas where the probability of good outcome is lower, as shown by the faded colors.

4.2. Maps for Northern Ireland

The maps for HSCB are shown in Fig. 4. These maps immediately show the reduced probability of good outcome when only looking at patients with a LAMS greater than 3 compared to all stroke patients, which is because those patients who have a LAMS of more than 3 are the most severe patients, and typically have poorer outcomes. Additionally, there is a green band to the north where patients with LAMS >3 are more likely to benefit if transported directly to the CSC, rather than to their nearest PSC. However, despite these differences, the two models yield very similar locations of when the Drip and Ship or Mothership transportation option should be used. The maps show that there is an area to the north and south of the CSC in Belfast that should always transport directly to the CSC, and patients should always be transported directly to the two PSCs to the west of Northern Ireland prior to moving to the CSC.

The maps confirm the importance of optimal efficiency at PSCs in the era of EVT. For example, if the PSC in the north were able to improve its performance to the idealized scenario, this PSC could provide early alteplase treatment prior to rapid transfer to the CSC for EVT, a Drip and Ship transportation option. However, the current performance of this PSC provides equivalent patient outcomes via Drip and Ship or Mothership.
4.3. Healthcare policy decision making

Both SNIS and HSCB used these maps to make specific decisions about their acute stroke system of care. These maps allowed SNIS greater certainty in putting forth legislation that would allow PSCs to be bypassed when there was a higher likelihood that the patient would be eligible for EVT (e.g., LAMS > 3). Additionally, these maps also provided impetus for PSC to improve their door-to-needle times, especially for those hospitals that were further from the CSC, as the patient had greater probability of good outcomes via Drip and Ship, but only if the PSCs performed optimally. These maps show that a door-to-needle time of 30 minutes is optimal compared to 60 minutes, which is the performance of many US centers. The HSCB is in the process of reviewing stroke services in Northern Ireland and, in particular, the number and distribution of PSCs. These maps identify regions in which equivalent outcomes can be expected, either by transport to the nearest PSC or the CSC in Belfast. This means that other factors can be taken into account in deciding the location of PSCs in these areas.

5. Discussion and future directions

Software solutions can provide meaningful geographic modeling of clinical information to assist policy decision makers in designing their health systems. This article provides two case examples of how geographic modeling assisted policymakers in implementing the best transportation options for stroke patients based on geographic location using conditional probability models developed with clinical trial data. The impetus for this work was to operationalize a health system for acute stroke patients to access EVT, which was recently proven to improve outcomes for ischemic stroke patients through a series of randomized clinical trials that provided the highest level of evidence for EVT.

The examples provided show how the patient population (e.g., only patients who receive EVT versus all potential stroke patients in the field) can alter the resultant maps. Additionally, changing time intervals can also create substantial changes in the maps. Therefore, these maps only provide a single picture of a specific clinical scenario. There are potentially hundreds of maps that can be generated for each potential time interval and patient population. For example, a patient may react to their stroke symptoms late and the time from onset to first medical response may be 130 minutes, rather than the 40 minutes that was assumed in the maps for HSCB. This would substantially change the transport decision for the patient.

Similarly, we have examined performance at the PSC, but how do these maps change if the performance at the CSC is below optimal? In order for decision makers to be able to explore the full scope of variables, a completely interactive version of the software is needed. This interactive software would allow for visualization of the map showing the best transport decision using their own entered time intervals and chosen patient population. By extension, the interactive software can also be used by paramedics to make the most appropriate transport decision based on onset time of the stroke, current traffic patterns, and the efficiency of the closest PSC and CSC. An interactive software would allow for a transport decision that would result in the greatest probability of good outcomes for the stroke patient.

6. Conclusion

Software was developed to show map visualizations using previously developed conditional probability models,
demonstrating the transport option that will result in the best outcomes for stroke patients. This software was used to develop maps for two health policy decision makers, and the maps helped these organizations to make health policy decisions. A fully interactive software will further assist health policy decisions and real-time transport decision by paramedics. Additional features can be added to the software, such as the population distribution, to allow health policy-makers to see which populations would be most affected by either a Drip and Ship or Mothership transport scenario.

References


