

## REVIEW

# Telestroke: the promise and the challenge. Part one: growth and current practice

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## ABSTRACT

Acute ischemic stroke remains a major public health concern, with low national treatment rates for the condition, demonstrating a disconnection between the evidence of treatment benefit and delivery of this treatment. Intravenous thrombolysis and endovascular thrombectomy are both strongly evidence supported and exquisitely time sensitive therapies. The mismatch between the distribution and incidence of stroke presentations and the availability of specialist care significantly affects access to care. Telestroke, the use of telemedicine for stroke, aims to surmount this hurdle by distributing stroke expertise more effectively, through video consultation with and examination of patients in locations removed from specialist care. This is the first of a detailed two part review, and explores the growth and current practice of telestroke, including the specific role it plays in the assessment and management of patients after emergent large vessel occlusion.

## INTRODUCTION

Despite significant advances in primary prevention, acute ischemic stroke (AIS) remains a major public health burden. AIS is the fourth leading cause of mortality in the USA and the top cause of serious long term disability.<sup>1 2</sup> Acute disease modifying treatment is founded on the recanalization hypothesis; recanalization of the occluded cerebral artery results in penumbral salvage, if accomplished early enough.

Prior to 1996, no Food and Drug Administration approved therapy directed to this goal existed, and acute management was supportive. The utilization of tissue plasminogen activator (tPA) in AIS revolutionized modern stroke therapy,<sup>3 4</sup> and in 1996 became the first directed therapy for AIS. Management of AIS has since rapidly evolved, both in application and understanding. The critical time dependence of tPA effect is well recognized,<sup>5</sup> but in 2009 the window for intravenous (IV) tPA was extended,<sup>6 7</sup> and dedicated stroke units<sup>8 9</sup> are now recognized to optimize stroke management and outcomes. Recently, endovascular therapies have entered the mainstream, providing an effective treatment for patients with proximal large vessel occlusions, with improved recanalization, functional outcomes, and survival,<sup>10–12</sup> a population of patients who may otherwise not benefit from tPA.

Despite these advances, a mere 5% of all ischemic stroke patients are treated with thrombolysis in the USA and Europe,<sup>13 14</sup> highlighting the need to optimize stroke care systems. Challenges exist at several

levels. Public awareness of stroke symptomatology and urgency remains limited,<sup>15 16</sup> and the overwhelming majority of eligible patients present outside of the therapeutic window for IV tPA.<sup>17</sup> Once a patient presents to medical attention, significant hurdles exist with treatment delivery. The mismatch between AIS incidence and subspecialty availability greatly affects access to care. Nationally, there is a prominent shortage of vascular neurologists, with only 1100 subspecialists despite an incidence of 800 000 strokes per year.<sup>18</sup> Nearly half of all hospitals in the USA do not have a neurologist on staff, and only 55% of all Americans live within 60 miles of a primary stroke center.<sup>19</sup> The discrepancy is most pronounced in the 'stroke belt' (southeastern USA), which has both the greatest incidence of AIS and lowest density of neurologists.<sup>20–22</sup> Even when neurologists live in the area, the increasing shift towards outpatient practices has decreased neurology coverage of local emergency departments.<sup>23–25</sup>

In the absence of a local specialist, management of AIS often is directed by local emergency medicine physicians who may be less comfortable administering tPA. Even under ideal conditions and clear indications, 40% of surveyed emergency medicine physicians would be unlikely to administer tPA.<sup>26</sup> The most commonly cited concerns are inexperience with tPA, concerns for intracranial hemorrhage (ICH), and medicolegal liability.<sup>26 27</sup> (even though malpractice claims for not treating IV tPA eligible patients far outweigh those when IV tPA was administered<sup>28</sup>).

In particular, the mixed data correlating protocol violations with increased rates of ICH,<sup>29–31</sup> along with the concern for increased rates of observed ICH in routine practice compared with the National Institute of Neurological Disorders and Stroke (NINDS) trial,<sup>3 29 30</sup> have limited the willingness of non-neurologists to thrombolyse patients despite more recent data demonstrating parity between routine practice and clinical trial outcomes following appropriate training.<sup>32</sup>

Consequently, thrombolytics are grossly underutilized in rural and underserved communities. In a review of Medicare billing records of 4750 hospitals and nearly 500 000 cases of AIS over a 2 year period, 62% of surveyed hospitals never administered tPA.<sup>33</sup> Consistent with the lower specialist density,<sup>20</sup> patients in the midwest and southeast were least likely to receive tPA.<sup>33</sup> Even within a given state, thrombolysis rates were almost 10 times lower in remote communities than in urban settings.<sup>34</sup>



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## GENESIS AND GROWTH OF TELESTROKE

Telestroke,<sup>35</sup> the use of telemedicine for AIS care, is a modern strategy to overcome the practical limitations of stroke care delivery.

AIS is uniquely suited to telemedicine, for the following reasons.

1. A wide geographic and population distribution of disease.
2. Clearly visible clinical findings, often readily identifiable on video.
3. A narrow therapeutic window.
4. An existing, proven therapy that is predominantly IV and therefore can be administered in any facility with basic infrastructure.
5. Limited specialist availability.

With the aid of local hospital staff, a remote neurologist is able to use modern telecommunications networks to conduct a rapid clinical assessment, irrespective of locale, and based on this evaluation make treatment recommendations for the local clinician team.

Telestroke was initially pioneered in the USA, where a Boston based stroke center partnered with a hospital in Martha's Vineyard to demonstrate that remote neurologic assessment was reliable and increased the rates of thrombolysis.<sup>36–38</sup> Based on this proof of principle, a German effort led to the creation of the first telestroke network in which rural facilities in Swabia (TESS network) and Bavaria (TEMPiS network) were connected to central hubs with extended stroke care capabilities.<sup>39–40</sup> These pilot studies demonstrated the feasibility of a large scale telestroke network in facilitating remote thrombolysis. Telestroke models have since been widely adopted<sup>41</sup> and endorsed by the American Heart Association (AHA).<sup>42</sup>

## The rise of telestroke networks

Telestroke has quickly spread throughout the USA, with at least 56 networks in 27 states linking a stroke center with local hospitals that lack around the clock stroke expertise.<sup>41</sup> The particulars of each arrangement have led to network based experimentation as individual programs have explored a range of services and delivery models.

A remote neurologist can offer a range of services through a telemedicine platform, through either video or telephone contact. A variety of different models exist, but evidence suggests telestroke (or more broadly telemedicine), with audio and video, is superior to telephone consultation alone.<sup>43</sup> Practice models include the following:

1. Teleconsultation: a remote neurologist offers only advisory services,<sup>44</sup> and the referring hospital maintains responsibility and liability for the patient.
2. Telethrombolysis: a remote neurologist decides on thrombolysis and is responsible to varying degrees for the patient's course, typically in the context of a pre-existing agreement between hospitals.
3. Integrated telehealth system: exchange of patients, information, and therapeutic suggestions between centers involved in acute stroke care, often with disseminated responsibilities and no clearly dominant hub.

These services are offered through a variety of stroke networks, ranging from individual arrangements between hospitals to multilayered referral networks. The earliest American model was a one to one partnership, where a remote island hospital contracted with a tertiary referral center for around the clock stroke coverage.<sup>45</sup> Building on this, the early German pilot studies pioneered the classic spoke and hub model,<sup>39–40</sup> where a

central referral center partners with multiple local facilities to provide around the clock stroke coverage. This is now the dominant network model. The spoke and hub model has since become more nuanced, as rural hospitals partner with local primary stroke centers (sub-hubs) who are themselves partnered with a comprehensive stroke center (hub). The sub-hub provides routine stroke care services, but patients requiring subspecialty care or intervention are transferred to the hub, which is usually a comprehensive stroke center. More recently, an English telestroke network pioneered a horizontal telestroke model in rural hospitals that have local neurologists but lack both around the clock coverage and access to a tertiary referral center.<sup>46</sup> Through a reciprocal agreement, hospitals take turns providing after hours stroke coverage, and patients continue stroke therapy the following day at the local hospital.<sup>46</sup> By leveraging the speed and reach of telecommunication, all delivery networks are able to extend specialty and subspecialty care to broad geographic regions using preexisting resources.

Once a telestroke service identifies an AIS case, patients can either be transported to a referral hospital or kept at the local hospital. In the 'drip and ship' model, a remote neurologist decides to initiate thrombolysis and transfer the patient for admission to their service. The patient immediately receives tPA and is then transferred to the hub or sub-hub facility. This most frequently occurs with small local hospitals without the staff or capacity to provide stroke care. Alternatively, many remote hospitals have stroke care capacity, but lack around the clock stroke coverage. In these circumstances, teleconsultations for mild to moderate strokes may result in 'drip and keep,' where tPA is administered and patients remain at the local hospital with local neurology coverage the following morning. A remote specialist can also continue to advise regarding a patient's care through a telemedicine enabled local hospital unit. Patients with severe strokes, requiring endovascular intervention, surgical intervention (e.g., hemicraniectomy), and critical care should be transferred to the tertiary center in the absence of local expertise or facilities. In all models, network hospitals have specific agreements and protocols to transfer patients with stroke or thrombolysis complications.

## TELESTROKE IN CLINICAL PRACTICE

With the increasing adoption of telestroke, a growing body of evidence has evaluated the technical feasibility, diagnostic fidelity, safety, and efficacy of telestroke in AIS management.

### Telestroke technology

Telemedicine is dependent on the technology that makes it possible. Initial experiences with video teleconferencing were limited by the transmission rates of integrated services digital network (ISDN) or dedicated local area network (LAN) connections.<sup>38–40</sup> Rare but notable interruptions complicated initial pilot studies.<sup>37</sup> The proliferation of broadband and cellular access, combined with high resolution video capability, has since facilitated high resolution, low latency audiovisual connections.<sup>47</sup> Initial videoconferencing technology required the remote neurologist to be present at a fixed workstation,<sup>38–40</sup> but technical advances have since led to laptop<sup>47–48</sup> and even smartphone based videoconferencing.<sup>49–51</sup> Now that telemedicine capability is routine with a low barrier to entry, the principle concern has shifted away from technical to practical limitations over the implementation and utility of remote assessment.

### Telestroke and diagnostic accuracy

Initial experimentation with telestroke has consistently demonstrated that video teleconference facilitates rapid and accurate

remote diagnosis. In an initial pilot study done in the non-acute setting, remote application of the National Institutes of Health Stroke Scale (NIHSS) was assessed in tPA ineligible AIS patients.<sup>38</sup> Nurse assisted remote evaluation by a neurologist was comparable with that of a bedside neurologist, with a discordance rate similar to that observed between two bedside examiners.<sup>52 53</sup> Nonetheless, while remote diagnostic assessment is rapid, it is slower than a bedside assessment (9.7 vs 6.5 min, respectively).<sup>38</sup> The reliability of remote NIHSS assessment has since been replicated in the acute setting,<sup>54 55</sup> demonstrating the fidelity of telestroke assessment in AIS. In an attempt to further optimize remote diagnosis, video teleconference and telephone consultation were directly compared in the prospective Stroke Team Remote Evaluation Using a Digital Observation Camera (STRoKE DOC) trial.<sup>43</sup> Using a mobile, laptop based system, video teleconference led to a correct diagnosis and thrombolysis in over 97% of cases, with an OR for a correct diagnosis of 10.9 compared with telephone consultations. Based on initial experiences with telestroke, the AHA now endorses remote clinical and radiographic assessments of patients in underserved medical settings as safe and reliable (class IA).<sup>42</sup>

### Safety of remote thrombolysis

The emphasis on accuracy of remote diagnosis is essential because of the safety concerns of remote thrombolysis. Given the potential for tPA induced ICH, the risk is that inappropriate thrombolysis could precipitate an iatrogenic ICH. The most likely reasons for inappropriate thrombolysis are protocol violations and misdiagnosis of a stroke mimic. Stroke mimics are equally common among local and referral hospitals,<sup>56 57</sup> and telestroke is effective in identifying cases of stroke mimics.<sup>56</sup> Even when stroke mimics are inappropriately thrombolysed, ICH is extremely rare and less likely to occur than in thrombolysed AIS patients.<sup>58</sup> Alternatively, protocol violations could result in either inappropriate thrombolysis or inadequate perithrombolysis management, increasing the risk of ICH.<sup>29-31</sup> While protocol violations are not uncommon in community practice,<sup>29</sup> violations are rare at local hospitals in a telestroke network<sup>36 40 43</sup> and are comparable with rates observed in the network hub.<sup>40 43</sup> This is likely due to the fact the same pool of hub based neurologists are deciding on thrombolysis for the entire telestroke network. Ultimately, the safety of telestroke is measured by rates of ICH, irrespective of the appropriate diagnosis or management. Multiple telestroke networks have now demonstrated that remote thrombolysis does not increase the risk of ICH compared with either in-person thrombolysis at a referral center or published trial data.<sup>43 59-62</sup> Remote thrombolysis is therefore both accurate and safe.

### Telestroke and thrombolysis rates

The increasing use of telestroke has created a body of data to test the assumption that telestroke would increase thrombolysis rates (and by extension improve clinical outcomes).<sup>63</sup> Universally, implementation of a telestroke network is associated with a significant increase in thrombolysis in remote or underserved hospitals.<sup>40 43 59 61 62 64-67</sup> Consider rural Georgia, where as recently as 2002, tPA was simply not administered to patients with AIS due to the lack of available neurologists. After a telestroke network was implemented the following year, tPA utilization rates immediately increased to 16% in networked hospitals.<sup>54 68</sup> Similarly, in rural Bavaria, Germany, tPA utilization increased nearly 10-fold after the implementation of a telestroke network while out of network tPA utilization lagged

behind.<sup>67 69</sup> Critically, remote hospitals in a telestroke network use tPA at equivalent rates to referral centers, demonstrating a tractable response to the rural penalty in AIS.<sup>54 66 69</sup>

### Telestroke and stroke outcomes

Telestroke improves stroke outcomes. This is the most important component of this therapeutic modality. The increased use of tPA with telestroke has led to direct comparisons of clinical outcomes in networked and out of network hospitals. In a prospective study comparing 3 month outcomes after an AIS in 3122 cases, the composite outcome of death, institutionalization, or disability was significantly less likely in telestroke hospitals than comparable out of network hospitals (44% and 54%, respectively).<sup>60</sup> In a multivariate regression analysis, presentation to a telestroke hospital was independently associated with a reduced risk of a poor outcome.<sup>60</sup> The benefit of telestroke also extends beyond thrombolysis, as demonstrated in a separate German telestroke network.<sup>39</sup> Remote consultation led to higher rates of diagnostic and therapeutic interventions in cases of AIS, with at least 75% of consultations resulting in a meaningful change in management. This is consistent with a previous observation from the Veterans Administration Acute Stroke study where neurologist management of AIS was associated with both increased testing and improved clinical outcomes, including reduction in death and disability.<sup>70</sup>

Consequently, the availability of telestroke not only improved clinical outcomes relative to other remote hospitals, but it has also closed the rural gap in outcomes compared with large referral centers. Multiple telestroke networks throughout Europe and the USA have reported comparable rates of disability and mortality between stroke centers and telestroke hospitals.<sup>59-61 64 69 71 72</sup> In a retrospective review of 296 cases of thrombolysis in a Boston based telestroke network, there was no difference in symptomatic ICH, mortality, discharge disposition, and long term functional outcomes between patients thrombolysed remotely in small community hospitals or at a regional stroke center.<sup>59</sup> Notably, all thrombolysed patients were transferred in this network, but improved clinical outcomes do not require patient transfer. This was demonstrated in a Finnish telestroke network that was based on a drip and keep delivery model.<sup>61</sup> Even when patients were kept at small remote hospitals, there was no difference in mortality or functional outcome. Telestroke therefore improves clinical outcomes across multiple delivery models, providing subspecialty care to underserved communities. Effectively, the functional characteristics of the specialist center are brought to the local hospital emergency room.

### Telestroke and endovascular therapy

It is now clear from recent data that in selected patients with emergent large vessel occlusions, endovascular management improves functional outcomes and mortality.<sup>10-12 73</sup> Similar to IV thrombolysis, remote and underserved communities have limited access to endovascular therapy,<sup>74</sup> but limited access is also a concern in urban regions with eccentric service provision. Telestroke provides an opportunity to extend the reach of endovascular therapy evaluation to patients who would otherwise do poorly.

Accurate identification of potential embolectomy candidates is the primary focus, most readily through accurate video assessment of NIHSS. Any patient with an NIHSS score greater than 6 is a potential endovascular candidate,<sup>75</sup> but higher NIHSS thresholds more accurately predict proximal vessel occlusions.<sup>76</sup> Additionally, if vascular imaging is obtained at the referral

source, central review of images can be performed remotely to determine anatomic candidacy for therapy (level of occlusion, tortuosity, collateral vasculature, etc). Telestroke in this fashion provides effective triage of patients likely to benefit from more invasive treatment options.

Beyond appropriate identification and triage of endovascular candidates, telestroke availability may potentially facilitate prompt transfer, potentially overcoming time delays that represent a major barrier to endovascular therapy<sup>77 78</sup> by allowing preparation for the endovascular case to occur while the patient is in transit. In addition, telestroke based consent from family members for mechanical thrombectomy can be accomplished through a video interface, allowing a detailed discussion of the planned intervention. This has been demonstrated in a Spanish telestroke network where remote assessment facilitated prompt thrombolysis and transfer for endovascular management of AIS.<sup>79</sup> In this 'drip, ship, and retrieve' model, informed consent was obtained remotely and the angiography suite was prepared while the patient was en route, facilitating faster groin puncture times in telestroke versus out of network transfers. Three months post-infarct, functional outcomes were comparable between patients initially treated at the referral center or via telestroke, but significantly worse in patients in out of network facilities.

Telestroke is therefore a strategy with the potential to bridge the geographic gap in access to both pharmacologic and mechanical recanalization (box 1).

### Box 1 Role of telestroke for potential endovascular stroke treatment candidates and for endovascular practice

#### *Clinical identification of candidacy for endovascular intervention*

- ▶ Presence/nature of deficit
- ▶ Magnitude of deficit (NIHSS)
- ▶ Clarification/determination of symptom onset timing

#### *Radiological identification of candidacy for endovascular intervention*

- ▶ Exclusion of hemorrhage
- ▶ Presence of ELVO (hyperdense vessel on NCHCT or vessel occlusion on CTA)
- ▶ Adequacy of collaterals
- ▶ Volume of established core
- ▶ Arterial access considerations (tortuosity, etc)

#### *Facilitated patient transfer decisions*

- ▶ Helicopter vs road

#### *Advance procedural preparation*

- ▶ Angiographic suite
- ▶ Equipment preparation
- ▶ Anesthesia mobilization

#### *Video based procedural consent from family*

#### *Feedback/follow-up to referring hospital*

- ▶ Logistics of transfer
- ▶ Patient evaluation and course
- ▶ Patient outcome
- ▶ Quality improvement efforts

#### *Expanded general endovascular referrals*

- ▶ Hemorrhagic pathology
  - ▶ Non-acute ischemic pathology
- CTA, CT angiogram; ELVO, emergent large vessel occlusion; NCHCT, non-contrast head CT; NIHSS, National Institutes of Health Stroke Scale.

### Impact of telestroke beyond acute stroke treatment

Beyond the acute phase, telestroke has led to improvements in a range of overall AIS management at network hospitals. Critically, these interventions benefit both thrombolysed and untreated patients. For instance, a German telestroke network implemented local stroke units in all networked hospitals, providing standardized treatment protocols and medical education to the local staff on optimal stroke management and secondary prevention.<sup>80</sup> Compared with out of network hospitals, telestroke hospitals had a decreased composite risk of death, disability, or institutionalization.<sup>80</sup> Similarly, evidence based guideline implementation interventions in the USA, such as the Get With the Guidelines-Stroke program, are likely more accessible in telestroke hospitals than non-telestroke centers. In the subacute setting, telestroke has also been used to remotely provide transient ischemic attack management and secondary prevention.<sup>81 82</sup> By harnessing the reach of telecommunication, telestroke has the potential to provide both preventative and acute management to underserved communities.

### Summary

Despite the advent of effective pharmacologic and mechanical treatments, healthcare delivery for AIS is limited by the current allocation of resources. Telestroke was developed as a response to geographic disparities, leveraging modern telecommunication technology to extend existing resources into underserved communities. Now, with more than a decade of experience, the safety, efficacy, and improved long term outcomes demonstrated by telestroke have firmly established it as a durable healthcare delivery model. With the advent of data strongly supporting the use of endovascular therapy in stroke, the relevance of telestroke has never been greater. In the second part of this two part review, we will discuss the challenges telestroke faces for wider adoption.

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