Success With Telestroke: Speaking to Need

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National Stroke Statistics

- Annually, 795,000 people experience a new or recurrent stroke in the US.
- 5th leading cause of death
- Stroke is a leading cause of long-term disability and the leading *preventable* cause of disability.
- There are an estimated 7 million Americans who are stroke survivors (30% permanently disabled)
- Direct and indirect cost 33 billion

Minnesota Stroke Statistics (2014)

- 2.2% of adults reported ever having had a stroke in their lifetime – more than 90,000 people.²
- 5% of all deaths due to stroke (2,172 annually); fifth-leading cause of death in the state.³
- 12,000 hospitalizations for acute stroke events.⁴

Rural versus Urban - Mortality

- Ethnicity and Disease 2011, Sergeev AV
 - County based population study
 - 7 year time span (2000 to 2006)
 - Non-Strokebelt states
- Residents of rural counties had a 12% higher risk of stroke death than those living in urban counties (Adjusted RR = 1.12)
- Postulated reasons:
 - Disproportionate distribution of risk factors
 - Socioeconomic status
 - Availability and geographic barrier to receiving acute care options

Stroke and Rural Minnesota

- More than a third of Minnesotans live more than 60 minutes from a Primary Stroke Center
- Nearly one in three stroke victims in Minnesota present initially to a small rural hospital
- The rural population has a greater percentage of seniors at higher risk for stroke

MDH 2010 – Stroke Survey

Need for...

- Immediate treatment
- Timely expertise
- Team
 - Local team engagement / education
 - Broader team integration / coordination
- Going the second mile...

Immediate Treatment Need

>>> The play of time and Treatment options

IV tPA NINDS Study 1995 FDA approval – 1996

The New England Journal of Medicine

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TISSUE PLASMINOGEN ACTIVATOR FOR ACUTE ISCHEMIC STROKE

THE NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE IT-PA STROKE STUDY GROUP

- NINDS study (3hr time window)
 - 11% increase cures (MRS 0–1)
 - NNT = 8 (to achieve one "cure")
- Pooled analysis of tPA studies

ischemic stroke has been approached cautiously because there were high rates of intracerebral hemorrhage in early clinical trials. We performed a randomized, double-blind trial of intravenous recombinant tissue plasminogen activator (t-PA) for ischemic stroke after recent pilot studies suggested that t-PA was beneficial when treatment was begun within three hours of the onset of stroke. Methods. The trial had two parts. Part 1 (in which 291 patients were enrolled) tested whether t-PA had clinical activity, as indicated by an improvement of 4 points over base-line values in the score of the National Institutes of Health stroke scale (NIHSS) or the resolution of the neurologic deficit within 24 hours of the onset of stroke. Part

Abstract Background. Thrombolytic therapy for acute

Volume

2 (in which 333 patients were enrolled) used a global test statistic to assess clinical outcome at three months, according to scores on the Barthel index, modified Rankin scale, Glasgow outcome scale, and NIHSS. Results. In part 1, there was no significant difference

between the group given t-PA and that given placebo in

the percentages of patients with neurologic improvement at 24 hours, although a benefit was observed for the t-PA group at three months for all four outcome measures. In part 2, the long-term clinical benefit of t-PA predicted by the results of part 1 was confirmed (global odds ratio for a favorable outcome, 1.7; 95 percent confidence interval, 1.2 to 2.6). As compared with patients given placebo, patients treated with t-PA were at least 30 percent more likely to have minimal or no disability at three months on the assessment scales. Symptomatic intracerebral hem orrhage within 36 hours after the onset of stroke occurred in 6.4 percent of patients given t-PA but only 0.6 percent of patients given placebo (P<0.001). Mortality at three months was 17 percent in the t-PA group and 21 percent in the placebo group (P = 0.30).

Conclusions. Despite an increased incidence of symptomatic intracerebral hemorrhage, treatment with intrave nous t-PA within three hours of the onset of ischemic stroke improved dinical outcome at three months. (N Engl J Med 1995;333:1581-7.)

- NNT = 2 (to improve one grade on MRS in pts treated under 3hrs) 0 (BMI 2004:324:723-9)
- ECASS III European study extending time window to 4.5 hours (NEJM 2008;359:1317-29)

Pooled Analysis of IV TPA Studies

Odds of excellent outcome (mRS 0-1) decreasing with time even within the effective time

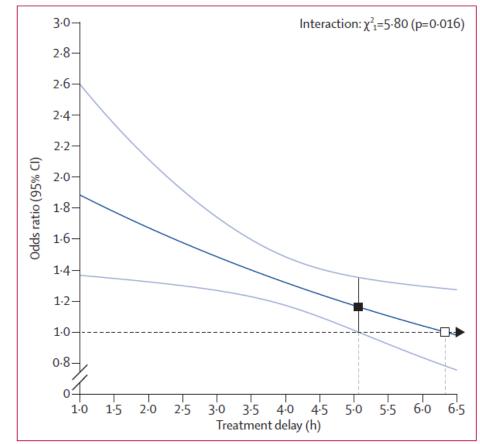


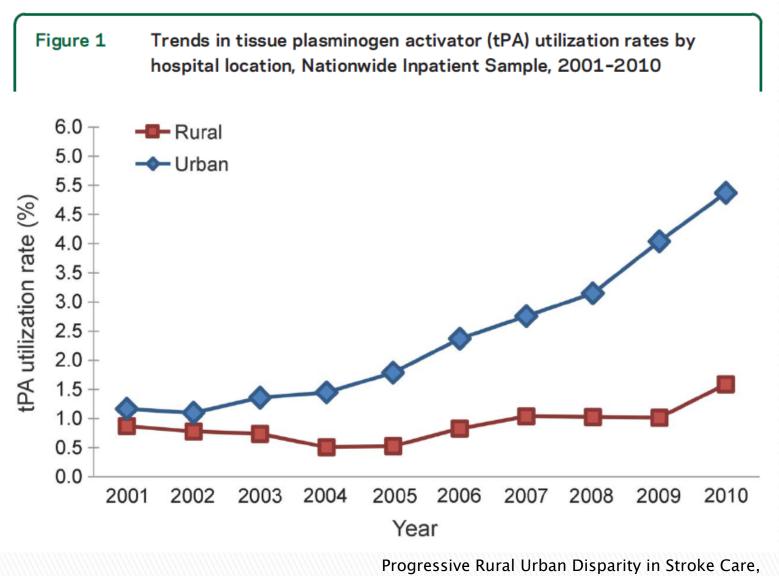
Figure 1: Effect of timing of alteplase treatment on good stroke outcome (mRS 0-1)

Emberson J et al. Lancet 2014;384:1929-1935.

Intravenous tPA – Rescue treatment for the stroke victim – available since 1996

ARE WE DELIVERING?

National estimates of tPA use 1%
2004 survey/One fifth of US hospitals (370Kpts)
GWTG hospitals 2010–2013 6.5%
1030 hospitals – ASA quality surveillance
MDH registry 2011 13%
IV tPA or catheter based treatment
Centers of excellence in acute care of stroke 20–30%



Neurology 2017;88:441-448

How fast are we treating? AHA/ASA recommendation DTN 60 min

- National Stroke Registry
 - GWTG- 1030 US hospitals 2010-2013
 - 43,850 patients treated (6.5% of all ischemic stroke)
- Results:
 - Median DTN time 67 min
 - 41% receiving TPA within 60 min
 - Outcomes if DTN time < 60min
 - Lower in-hospital mortality by 1.7%
 - Lower bleeding rate decreased by 1%
 - Higher rate of discharge to home increased by 5%
 - Every 15 minutes saved, results in 5% relative risk reduction in inpatient mortality

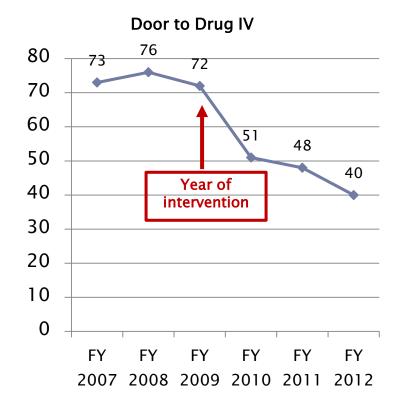
Fonarow GC et al. JAMA 2014;311:105. 140 Khatri P et al. Neurology 2009;73:1066-1067.

Early Results with Telestroke Code

- First telestroke treatment case 2006, Glencoe MN...
- % treated with tPA of all ischemic stroke discharges in the first year of telestroke
 - My metro site 12% versus My first rural partner 21%
- Convinced me within a few years of the need to get
 Neuro expertise early in code to make these decisions

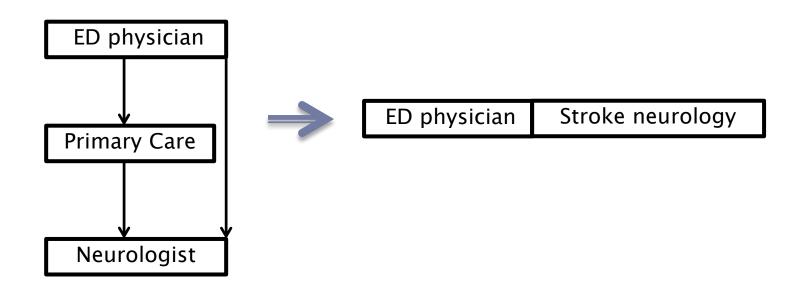
Overcoming the barriers at a Metropolitan Hub Hospital

- % of all ischemic stroke treated
 - 24% FY 2012
 - Reasons:
 - Stroke code process
 - Educated/aggressive triage cast a wide net
 - Stroke neurology leadership
 - Eyes on the patient
 - Expertise
 - Accessing newer options
 - Finding ways around previous factors excluding patients
 - Extending time window with imaging



Stroke Neurology PHILOSOPHY of PRACTICE

Subspecialty care when and where it is needed



NEED for TIMELY EXPERTISE



>>> What does the local application of subspecialty expertise offer

Treating with tPA Straightforward Decision ???

The New England Journal of Medicine

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DECEMBER 14, 1995 Number 24

TISSUE PLASMINOGEN ACTIVATOR FOR ACUTE ISCHEMIC STROKE

THE NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE [t-PA STROKE STUDY GROUP*

Abstract Background. Thrombolytic therapy for acute ischemic stroke has been approached cautiously because there were high rates of intracerebral hemorrhage in early clinical trials. We performed a randomized, double-blind trial of intravenous recombinant tissue plasminogen activator (t-PA) for ischemic stroke after recent pilot studies suggested that t-PA was beneficial when treatment was begun within three hours of the onset of stroke.

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Methods. The trial had two parts. Part 1 (in which 291 patients were enrolled) tested whether t-PA had clinical activity, as indicated by an improvement of 4 points over base-line values in the score of the National Institutes of Health stroke scale (NIHSS) or the resolution of the neurologic deficit within 24 hours of the onset of stroke. Part 2 (in which 333 patients were enrolled) used a global test statistic to assess clinical outcome at three months, according to scores on the Barthel index, modified Rankin scale, Glasgow outcome scale, and NIHSS.

Results. In part 1, there was no significant difference between the group given t-PA and that given placebo in the percentages of patients with neurologic improvement at 24 hours, although a benefit was observed for the t-PA group at three months for all four outcome measures. In part 2, the long-term clinical benefit of t-PA predicted by the results of part 1 was confirmed (global odds ratio for a favorable outcome, 1.7; 95 percent confidence interval, 1.2 to 2.6). As compared with patients given placebo, patients treated with t-PA were at least 30 percent more likely to have minimal or no disability at three months on the assessment scales. Symptomatic intracerebral hemorrhage within 36 hours after the onset of stroke occurred in 6.4 percent of patients given placebo (P<0.001). Mortality at three months was 17 percent in the t-PA group and 21 percent in the placebo group (P = 0.30).

Conclusions. Despite an increased incidence of symptomatic intracerebral hemorrhage, treatment with intravenous t-PA within three hours of the onset of ischemic stroke improved clinical outcome at three months. (N Engl J Med 1995;333:1581-7.)

NINDS study (3hr time window) 11% absolute increase in very good outcome (MRS 0-1) NNT = 8 (to achieve one "cure")

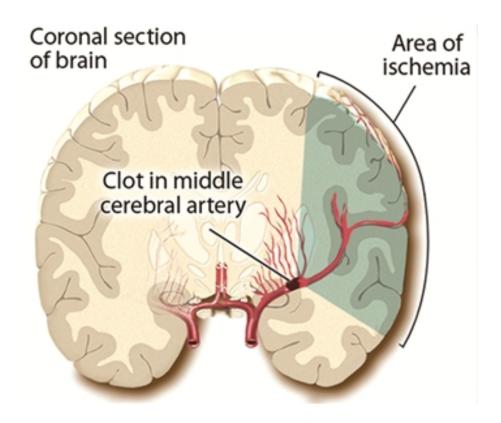
EXCLUSION CRITERIA

- TIME > 3hrs from onset
- Mild or resolving deficit
- Seizure at onset
- Presentation of SAH
- SBP>185 or DBP>100 despite attempts to treat
- Glucose >400, <50
- Recent use heparin and abn. aPTT
- Platelet count <100,000</p>
- Recent use warfarin and INR>1.7
- CT showing hemorrhage
- History of intracranial hemorrhage
- Untreated aneurysm, AVM
- Stroke or serious head trauma within 3 mos
- Presentation of acute MI or post-MI pericarditis
- GI or GU hemorrhage within 3 wks
- Arterial puncture noncompressible site within 1wk
- LP within 3 days
- Major surgery within 2 wks

So what has changed:

- Time window for IV tPA expanded to 4.5hrs
- Intraarterial treatment (mechanical thrombectomy)
- Changes in treatment criteria with new data about the safety profile
 - Treating mild and rapidly improving stroke
- Multimodal imaging
- Improvements in triage
 - Recognizing the hard to recognize
 - Distinguishing the imitators

What about Intra-arterial (IA) therapies? Mechanical Thrombectomy

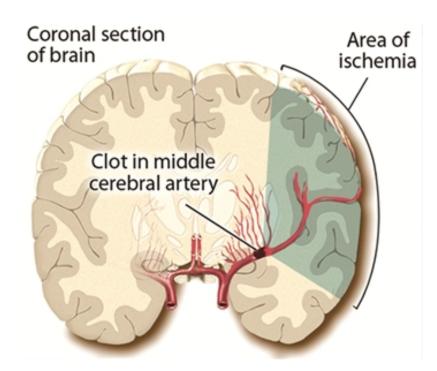


Summary of 2015 Trials - Clinical Benefit Adding mechanical thrombectomy to tPA

Trial	90-day mRS 0-	2 (or good	d outcome)	
n=1288	Endovascular (most tPA+MT)	Control (most tPA)	OR (95% CI)	NNT
MR CLEAN (n=500)	32.6%	19.1%	2.16 (1.39– 3.38)	7
EXTEND-IA (n=70)	71%	40%	4.2 (1.4–12) p=0.01	3.2
ESCAPE (n=316)	53%	29.3%	1.8 (1.4–2.4) p<0.001	4
SWIFT PRIME (n=196)	60.2%	35.5%	2.75 (1.53– 4.95) p=0.008	4
REVASCAT (n=206)	43.7%	28.2%	2 (1.1-3.5)	6

Campbell BC et al. N Engl J Med 2015;372:1009-1018. Goyal M et al. N Engl J Med 2015;372:1019-1030. Saver JL et al. N Engl J Med 2015;372:2285-2295. Jovin TG et al. N Engl J Med 2015;372:2296-2306. Berkhemer OA. N Engl J Med 2015;372(1):11-20.

Why not go with the catheter then?



REASONS:

- Only about 30 % of our patients treated with some sort of rescue treatment are candidates for mechanical thrombectomy. The rest receive IV tPA alone for smaller artery blockages.
- IV tPA is much faster and more available and has some level of success
- Studies utilized a combined approach (tPA followed by mechanical thrombectomy) vs tPA alone

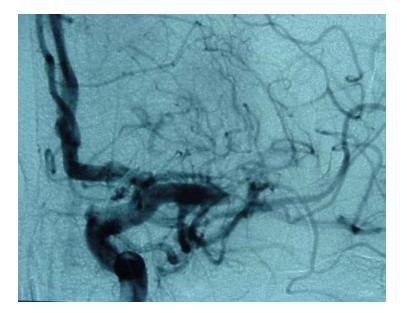
Case

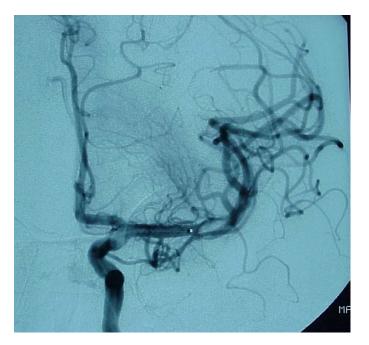
- Young woman with sudden onset speech difficulty, right face, arm and leg paralysis
- CT scan "clot" sign indicating this was a large vessel blockage
- Intravenous tPA started 110 minutes after stroke had started



Case

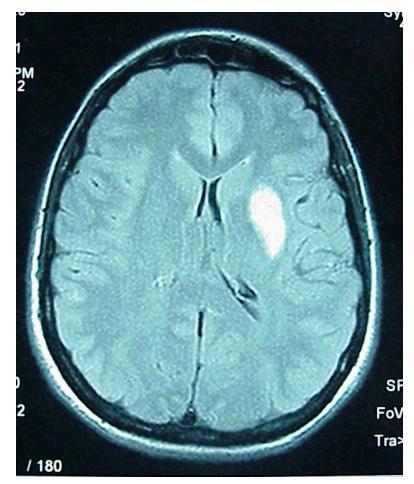
She was taken to the "cath lab" for an angiogram where this large vessel occlusion was still documented to be present despite IV tPA and then a catheter based intraarterial treatment was successful in opening the vessel.





Case

- Immediate improvement in speech and weakness when large artery was opened
- No stroke symptoms or disability 2-3 months later despite the small stroke seen on MRI



Strict Exclusion vs Common Sense "The List"

- TIME > 3hrs (now 4.5hrs for IV)
- Mild or resolving deficit
- Seizure at onset
- Glucose >400, <50

Imaging and Clinical picture

- Presentation of SAH
- Presentation of acute MI or post-MI pericarditis
- SBP>185 or DBP>100 despite attempts to treat
- CT showing hemorrhage
- History of intracranial hemorrhage

- Recent use warfarin and INR>1.7
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- GI or GU hemorrhage within 3 wks
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IA or Device treatment

Wake Up Stroke and thrombolysis

- Approximately 20% of patients wake up with their symptoms
- Since time of onset unknown, time last normal time patient went to sleep.
- Excludes many patients that might otherwise be good thrombolytic candidates
- Meta-analysis of 31 studies reporting timing of 11,816 strokes the onset of symptoms was 55% more likely to occur between 6 am to noon.

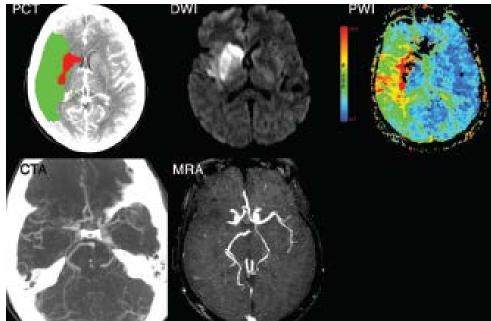
Next area of change that will increase our use of tPA, but will likely require some rapid imaging review requiring expertise.

Large RCTs- THAWS (Japanese study - 0.6mg/kg)

- WAKE-UP (European study 0.9mg/kg)
- I-WITNESS (North American study 0.9mg/kg)
- DAWN (US mechanical thrombectomy in wakeup)
- NORTEST

Adding Newer Imaging Options

- Standard noncontrast CT ischemic vs hemorrhagic
- CT Perfusion and CT angio
- MR DWI/Perfusion and MR angio
- Large vs small vessel
- Mismatch pattern on perfusion suggesting "brain to save"
- Excluding imitators



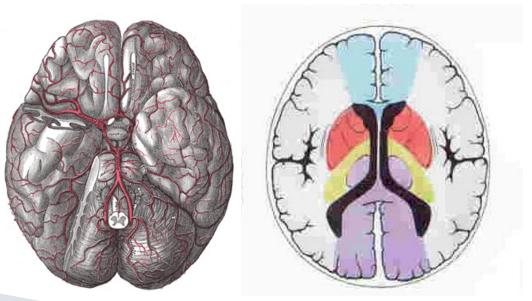
Serious cases we can miss in triage that may seem nonfocal at first

- Isolated aphasia "confusion" left MCA delirium
- Isolated VF cut "blurred vision"

migraine, nonspecific blurred vision complaint

Abulia, monoparesis

ACA Seizure (CPS), peripheral nerve



PCA

Serious cases we can miss in triage that may seem nonfocal at first

Isolated vertigo

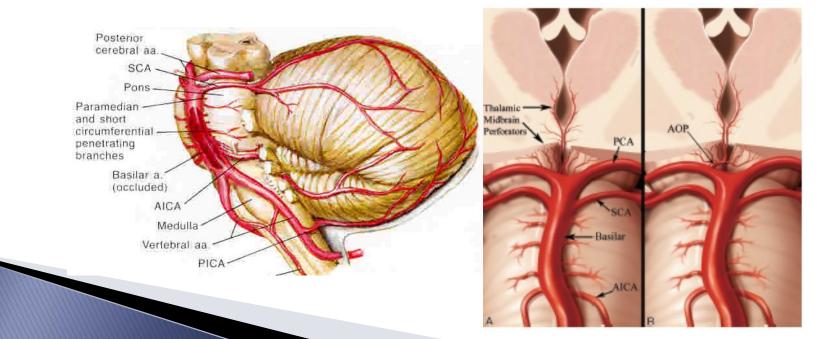
- PICA
- Coma, fluctuating deficit w bilateral signs

Basilar

labyrinthitis, Meniere's

Seizure w posturing of limbs ataxia -may appear drunk

 Hypersomnia, eye mvmt disturbance bilateral motor symptoms Artery of Persheron Post-ictal state, other encephalopathy, basilar artery thrombosis



Improved Accuracy of Stroke Diagnosis with Telemedicine

- StrokeDOC trial compared the accuracy of diagnosis and treatment decisions of Stroke Neurologists using:
 - Telestroke video/audio connection and CT review
 - Versus telephone consultation alone
- Correct treatment decisions were made more often when telemedicine was used than with telephone alone (same practitioners):
 - 98% (n=108)
 - 82% (n=91) (p=0.0009)

A complex triage/treatment plan:

- Call a stroke code if within 7-8 hrs of onset or "wake-up" stroke and let the expert team review the case for:
- 1) Correctness of diagnosis and 2) Imaging 3) Treatment choices

Tx can start within 4.5hrs

- 1) Small vessel IV tPA
- 2) Large vessel 1) IV tPA followed by mechanical thrombectomy

2) IV tPA alone 3) mechanical thrombectomy alone

Tx would start after 4.5 hrs or wake-up stroke

- 1) Small vessel aspirin
- 2) Large vessel large vessel occlusion but minimal infarct core

4.5 to 8 hours – mechanical thrombectomy

Beyond 8 hours w basilar artery thrombosis - mechanical thrombectomy

Complex decision tree

- Large artery versus small artery
- Time frame and treatment choices
- Newer imaging strategies with rapid interpretation within the clinical context
- Recognizing stroke imitators
- Recognizing unusual stroke presentations
- Not the simple CT scan/IV access and recipe for treatment we thought in 1996!

Need for Team



Local team engagement/education Broader team integration/coordination

United Hospital Allina Health Telestroke

- Videoconferencing equipment at a primary site and remote site allowing stroke clinicians to remotely offer consultation on an emergent basis
- Purpose: Full participation of a stroke clinician in a "stroke code" at a remote site for the purpose of aiding the local "stroke team" in making a thrombolytic or interventional treatment decision



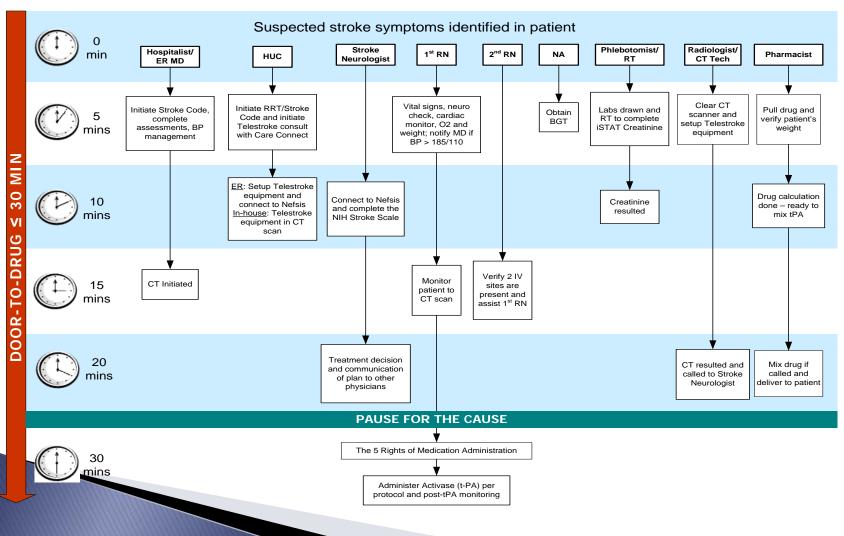
Developing a partnership "Hub and Spoke"

- > Meetings to garner support and interest
- > Gain administrative and clinician agreement to go forward / contract
- > Credentialing TS physicians

- Team meetings with partner hospital staff (Telestroke team) to formulate a telemedicine stroke response process – a local "Stroke code team response
 - Code team development nursing, physician, lab, pharmacy, radiology
 - > Paperwork design flow sheet, standing orders, other tools
 - Administrative quality/nursing staff to develop plans for quality improvement work
- > Technology acquire equipment, set up unit, downloading software
- Go live..... 2 days of in-services with ER staff review roles in stroke code process and TS equipment use, participate in mock stroke code, NIHSS training, stroke recognition
- Quarterly review Rural hospital Telestroke team / Hub hospital leadership

Stroke Code Algorithm

Stroke Code Protocol



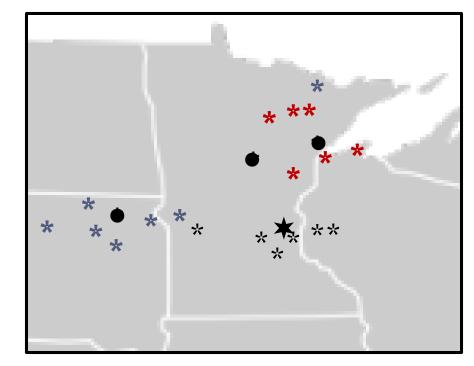
Direction of United Hospital Telestroke Progam

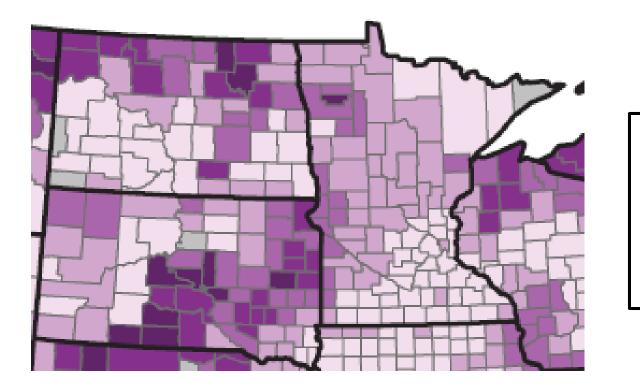
Conclusions

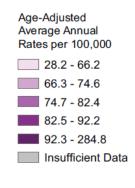
Telemedicine Work Now and Going Forward United Hospital Network

- Telestroke Service Site Expansion
 - Sites active in 2015 *
 - Sites developed 2016 *
 - Sites invited for 2017 *
- Active stroke code projects
 - EMS prealert / shorten DTN
 - Improve transfer coordination for IA
 - Keeping IV tPA patients on site 24hr FU
- Add nonurgent stroke consultation for subacute care
- Mini–Hub concept
 - Duluth
 - Brainerd
 - Aberdeen

Teleneurology







Telestroke Clinical Model, Results, and Administrative Discussion

Clinical benefits for patients A national comparison

- Allina Health Clinical Model (January 2014–Q1 2015)
 - Percent treated with tPA
 - 26%
 - Door-to-needle time mean
 - 56 minutes
 - Symptomatic intracerebral hemorrhage rate
 - <2%

- Get With the Guidelines US Experience – before and after intervention:
 - Percent treated with tPA¹
 - 4% (2003–2005)
 - 7% (2010-2011)
 - Door-to-needle time mean²
 - 79 minutes (2003–2009)
 - 67minutes (2010–2013)
 - Symptomatic intracerebral hemorrhage rate²
 - 5.68% (2003–2009)
 - 4.68% (2010-2013)

1. Circulation: Cardiovascular Quality and Outcomes. 2013; 6: 543–549c 2. JAMA. 2014;311(16):1632–1640.

Clinical Model to Achieve These Results

<u>Clinical features of TS Code:</u>

- Comprehensive triage process casting a wider net (hub educates team to this process)
- Earlier engagement of Stroke Neurology in the beginning of the code and code leadership for diagnostic accuracy and partnership in decision making
- In-depth consultative work performed on all stroke code cases including those excluded from tPA during the stroke code to enhance the value of the service to the patient and local hospital

Benefits to regional site:

- "Wider net" captures the hard to recognize strokes or those that may have been excluded without the applied expertise.
- Early subspecialty expertise applied to both the diagnostic and treatment questions in "just in time" approach
 - Increases % treated
 - decreases door-to-drug time
- Keeping patients close to home when possible
 - decreasing unnecessary transfers when higher level of care not needed.
 - Expertise added to local care.

AllinaHealth Telestroke Team United Hospital



Stroke Neurology

MD



<u>Jesse Corry, MD</u> Stroke Neurology



<u>Sandy Hanson, MD</u> Stroke Medical Director



Stroke Neurology



<u>Amy Castle, RN</u> *Telestroke Nurse Coordinator*

- This practice had its beginning in 2006 as the first telestroke practice in Minnesota
- Collectively 36 years of post training practice experience in the acute management of stroke and 3 of the 4 providers with fellowship training

Cost-Effectiveness of Hub-and-Spoke Telestroke Networks for the Management of Acute Ischemic Stroke From the Hospitals' Perspectives (CIRCOUTCOMES.112.967125)

"Contrary to the common perception that a telestroke referral network poses a substantial financial burden on hospitals, our study revealed that it is likely to be a cost-saving strategy from the hospitals' perspectives while also improving patient

outcomes in terms of home discharges. To improve its generalizability, our model included the costs of maintaining round-the-clock coverage with stroke experts from the hub. Which hospitals, then, should bear the cost burden of a telestroke network?

The results of this economic research have implications on the assignment of financial responsibility between hub-and-spoke partners.

a. In a network that is fundamentally designed to transfer patients from spoke to hub, the hub hospital should subsidize the costs of the telestroke

b. whereas in a network designed predominantly to aid spoke hospitals' capability to effectively maintain more AIS patients, the spoke hospitals should finance the system.

c. In the base-case model, targeting a spoke to hub transfer rate of $\approx 30\%$ resulted in an economic benefit for the hub, the spokes, and the telestroke network overall."