FVIIa for Acute hemorrhagic Stroke Administered at Earliest Time (FASTEST) Trial

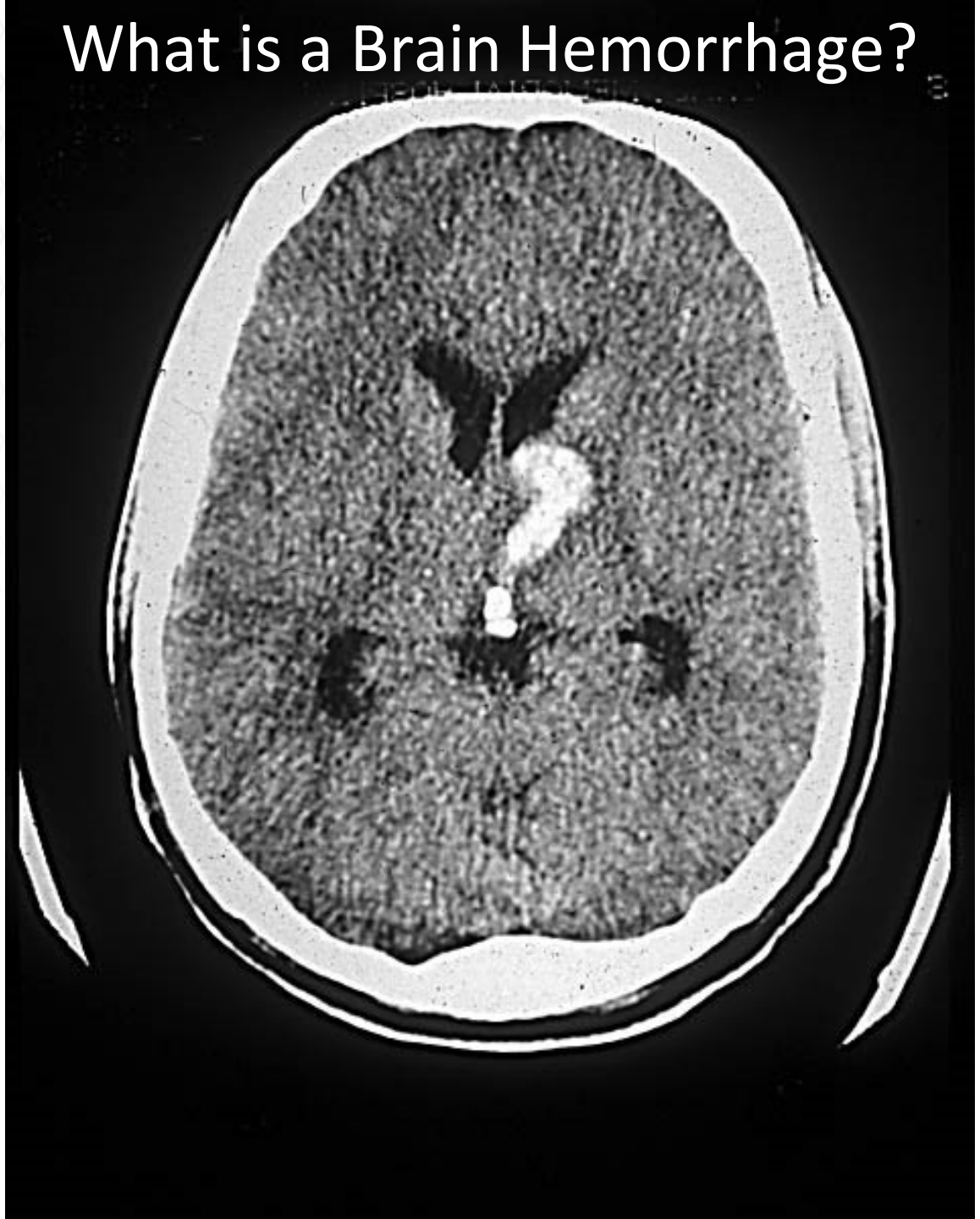
<<Insert Site Principal Investigator Name>>

NIH StrokeNet
PREVENTION | TREATMENT | RECOVERY

Topics for Today

- Discuss what is a brain hemorrhage (bleeding in the brain) or intracerebral hemorrhage (ICH)?
- Explain what recombinant Factor VIIa is.
- Explain the FASTEST Trial and what it is trying to accomplish.
- Discuss emergency research and consent and why we need to hear from you.

What is a Brain Hemorrhage?



ICH: Old or Damaged Blood Vessels Break Under Pressure

Background

- Brain Hemorrhage (bleeding) or intracerebral hemorrhage (ICH) is a type of stroke that accounts for more than 10% of the estimated 17 million strokes worldwide each year or about 1,700,000 cases per year.
- More than 40% of patients die and only 20% of survivors are functionally independent at 6 months.
- The size of blood in the brain is the most important determinant of outcome and most bleeding occurs within 2-3 hours.
- Patients with brain hemorrhage are also at risk for other vascular diseases and blood clots where there are damaged blood vessels.
- There is no scientifically proven effective treatment for ICH.

Growth of bleeding in the Brain Leads to Bad Outcomes

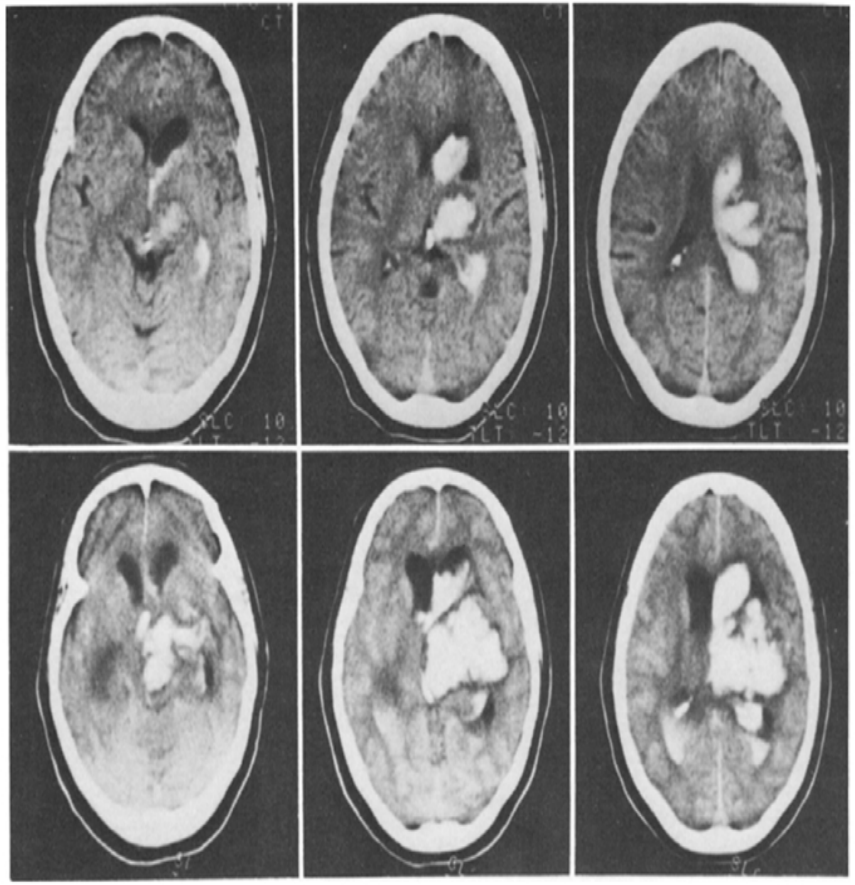


FIG. 2. Serial computerized tomography (CT) scans in Case 3. An increase in volume of hemorrhage from 8 to 35 cc was recorded between the first CT scans *(upper)*, obtained 50 minutes after onset of symptoms, and the second CT scans *(lower)*, obtained 210 minutes after onset.

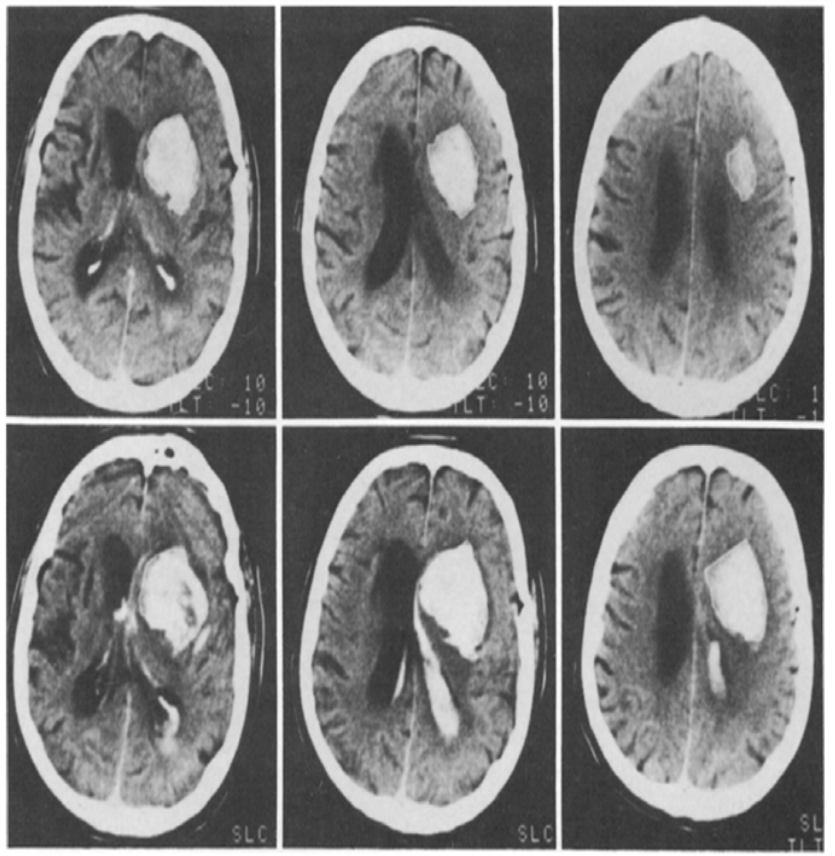


FIG. 1. Serial computerized tomography (CT) scans in Case 1. Measurement of the volume of hemorrhage revealed an increase from 25 to 44 cc between the first CT scans *(upper)*, obtained 35 minutes after onset of symptoms, and the second CT scans *(lower)*, obtained 105 minutes after onset.

J. Neurosurg: 72: 195-199, 1990

Has anyone here had or know of someone who has had a stroke? A brain hemorrhage?

Treatment of Brain Bleeds (Hemorrhage)

- Admission to an intensive care unit.
- Treatment of blood pressure, which is often very elevated.
- Often ventilator machine to help breathe.
- Treatments to help relieve pressure in the brain.
- Occasionally surgery to remove blood.
- THERE IS NO SCIENTIFICALLY PROVEN TREATMENT FOR BRAIN HEMORRHAGE.

What is Recombinant Factor VIIa

- Factor VIIa is normal protein in our body that helps stop bleeding.
- Recombinant Factor VIIa (identical to Factor VIIa but given in much larger amounts) is the only medication that has been shown to substantially decrease bleeding in patients with hemorrhage in the brain.
- Recombinant Factor VIIa (rFVIIa) stimulates formation of blood clots.
- The medicine is easily administered into a patient's vein, through an IV line (small flexible tube inserted into a vein).
- The medicine works rapidly.
- Recombinant Factor VIIa is approved for other medical conditions that involve bleeding (such as hemophilia) but not for brain hemorrhage.
- Prior research studies of Recombinant Factor VIIa showed that it slowed bleeding in the brain but the benefits are most likely to improve outcome when given within 2 hours of start of symptoms.

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What is a placebo?

- A placebo is a substance that looks just like the study medicine but contains no active ingredient.
- The placebo is easily administered into a patient's vein, through an IV line (small flexible tube inserted into a vein), just like the study medicine.
- Neither the patients, nor the researchers know who is getting a placebo and who is getting the study treatment.

Primary Specific Objective – FASTEST Trial

- The *goal* of the FASTEST Research Trial is to determine if a medicine used to treat and prevent bleeding can also improve outcomes after a stroke caused by bleeding in the brain.

NIH Funded: 1U01NS110772-01

Enrollment of Study Population

- Participants to be enrolled - 860.
- Anticipated number of study locations– 100 hospitals including 15 mobile stroke units.
- Countries participating: USA, Canada, Germany, Spain, UK, and Japan.

Who would be in the FASTEST Study?

- Persons aged 18 through 80 years of age with spontaneous bleeding in their brain.
- Able to be treated with study medication within 120 minutes of stroke start or last known well

Who would not qualify for the FASTEST Study?

- Persons who already are in deep coma or who have very large areas of bleeding in the brain who are already destined to die.
- Person with recent heart attacks, strokes, or blood clots within prior 3 months.
- Persons on blood thinners such as warfarin.
- Women known to be pregnant.
- Persons carrying an Opt-Out Card for the study.
- Persons conscious and able to refuse or if a legally authorized representative, or a family member, is available to decline for the patient.

FASTEST

How to Minimize Time to Treatment

- Mobile Stroke Units

At some locations, this study is also being conducted in Mobile Stroke Units. The Mobile Stroke Units are special types of ambulances, with CT scanners (special type of X-ray machine) on board.

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How does the study work?

- All patients will get a CT of the brain (a way to make x-ray images), to make sure that they have bleeding in the brain and qualify.
- All patients will receive the best medical care, including control of blood pressure and careful management of breathing in mobile stroke units when available, the emergency department and intensive care unit.
- Patients will have an intravenous line, a small flexible tube placed inside the vein, as part of standard care. The Recombinant Factor VIIa or the placebo is given through this line.

Participants will be put into one of two groups.

- One group will receive rFVIIa in an intravenous line (a soft, flexible tube placed inside a vein used to give medications or fluids).
- One group will receive placebo (an non-active substance made to look like an active medicine).
- This will be determined by chance (like flipping coin).
- Everyone will receive the best standard of medical care

Intervention: What else will happen?

- Participants will get another CT of the brain (special type of X-ray) within the first 24 hours to measure if the bleeding has increased in size.
- Participants will receive treatment in the intensive care unit for as long as necessary.
- They will have follow-ups with the study team by phone at 30 and 90 days and in person at 180 days.

What are potential benefits?

- Because the purpose of the study is to determine the effectiveness of rFVIIa compared to a placebo, it is not known whether or not you will benefit from being in this study.
- If rFVIIa slows bleeding and improves outcome, participants may benefit from this study.
- Future patients with bleeding in the brain may benefit from what is learned in the study.

What are potential risks?

- Since rFVIIa helps stop bleeding by enhancing blood clots, there is a risk of heart attacks, stroke due to blockage of brain arteries, and clots in the lung.
- In prior studies, this occurred about 5 % more commonly in persons treated with rFVIIa as compared to placebo. In other words, if 100 persons were treated with rFVIIa as compared to 100 persons treated with placebo, 5 more patients would have heart attack, stroke due to blockage of brain arteries or clots in lungs.

Has anyone here been involved in a research study? What was it like?

What is EFIC? Why are we here today?

EFIC is **E**xception **F**rom **I**nformed **C**onsent for Emergency Use

How are emergency studies different?

- In most studies, investigators describe what will happen, discuss potential risks and benefits, answer questions, and then eligible patients decide whether or not to participate. This process is called informed consent.
- In this study, most eligible patients will almost always be unable to say whether or not they wish to participate in the study.
- Also, treatment is needed to be started often before family or patient legal representative are available to decide for the patient.

So, how do we do emergency research?

EFIC

- Specific federal regulations allow for **exception from informed consent for emergency research or EFIC**
- EFIC is only allowed when:
  - The condition under study is life threatening.
  - Existing treatment are unproven or inadequate.
  - There is potential benefit for patients.
  - Informed consent cannot be obtained**.**

  - Before researchers may do a study using EFIC, they must provide information about the study to the community and get their feedback. That is why we are talking with you today!

FASTEST

Requirement for EFIC

- Community consultation (why we are here)!
- Public disclosure before and after the study.
- Oversight during study.
  - The research is monitored by an Independent Review Board for safety and protection of human subjects.

How does EFIC work in FASTEST?

- If the patient is able to consent for themselves, they will be asked! Most patients with brain bleeds are not able to communicate and give consent.
- If a representative (LAR) or a family member is available within the 2 hour time window, they will decide for the patient.
- If an LAR, or family member, is not available, eligible patients will be started in the study without consent.
- Patients, family members and representatives are told about the study as soon as possible and asked if they want the patient (or themselves) to continue in the study.

What if I don't want to be in FASTEST?

- Ask for an Opt-Out Card that says that you don't want to be in the FASTEST Research Study and let your family members know your wishes.
- Call your local study team to have a card sent to you.
- Go to the Stroke Net website to print an Opt-out Card

  https://nihstrokenet.org/fastest/community-resources
- If you have bleeding in the brain, first responders will look for this card and you will not be enrolled, if you are carrying this Opt-Out Card when you arrive at the hospital.

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What do you think about FASTEST?

- The study hasn't started yet, so…
  - We want to hear your thoughts.
  - Tell us about your experiences.
  - Do you think that it is OK for the study to be done?
  - The study team and medical review board will consider your input in deciding whether it is OK for this study to be done in our community.
  - Please take the study survey to tell us about your feelings!

Questions?

- If you have any concerns or questions please call us or contact us.
- Principal Investigator:

Name phone number, email

- Study Coordinator:

Name, phone number, email

<<Insert QR code to study survey>>