The Role of Hyperoxia in the Emergency Department Treatment of Acute Ischemic Stroke

Principal Investigator – Layne Dylla

NCT#03904017

Document Date 02/18/2022

Principal Investigator: Layne Dylla, MD, PhD
COMIRB No: 20-0486
Version Date: 11/30/21
Study Title: The Role of Hyperoxia in the Emergency Department Treatment of Acute Ischemic Stroke
Site: University of Colorado-Anshcutz Medical Campus

You are being asked to be in a research study. This form provides you with information about the study. A member of the research team will describe this study to you and answer all of your questions. Please read the information below and ask questions about anything you don't understand before deciding whether or not to take part.

Key Information:

- Being in this study is voluntary – it is your choice.
- You are being invited to participate in this study because you are exhibiting signs of a stroke, which is caused by problems with getting blood flow and oxygen to parts of your brain.
- The purpose of this study is to evaluate the potential therapeutic role of hyperoxia (a state in which oxygen supply is excessive) when applied just following a stroke in a controlled Emergency Department setting.
- Procedures will include the collection of blood at three time points: baseline, 4 hours after baseline, and 24 hours after baseline. Procedures will also include the collection of information about your ethnicity, age, and so forth (demographic information), past medical history, medication history, a measure of any problems you may have had beforehand (historical Modified Rankin Score (mRS)), as well as the collection of vital signs (for example your heart rate and blood pressure), MRI or CT in conjunction with your routine medical care. The images from these MRI and CTs will be processed with RAPID to determine the size of your stroke. Additional video-taped performance of the NIH stroke scale will also be obtained to see how much damage may have been caused by your stroke. Many of these activities will be done a part of your care while in the hospital for your stroke whether or not you participate in the study.
- You will be randomly, much like flipping a coin, placed in one of two treatment groups and followed for 90 days. One group will receive the study intervention, a brief amount of excessive oxygen (hyperoxia) for four hours. The other group (placebo) will receive normal air for four hours. This normal air is what you would normally get for your stroke, but through a special face-mask like those who are getting the extra oxygen.
- Your participation in this study will last up to three months. Most of the activities will occur while you are hospitalized for your stroke and one phone-call assessment with a review of your medical chart to identify potential complications from your stroke will occur at 3-months.
- There are risks from participating in the study: The most common risk is that you might produce more special oxygen and nitrogen molecules ("free radicals") than normal. This could lead to inflammation and tissue damage to the brain and lungs. You could also have pain, bleeding, and bruising at the needle site. Because we are collecting information about you, there is the possibility of losing your privacy or confidentiality.
- You will not benefit from being in this study.
- If you do not want to take part in this study, your standard medical care will not change in any way.

Why is this study being done?
This study plans to learn more about the potential role of given short periods of excessive oxygen ("brief hyperoxia") when applied in the immediate ischemic period following a stroke in the controlled Emergency Department setting.

You are being asked to be in this research study because you are exhibiting signs and physical examination findings suggestive of a stroke.

Other people in this study
Up to 400 people from your area will participate in the study.

What happens if I join this study?
If you join the study, a study team member will collect some demographic information about you (for example your age, sex, ethnicity and race) and information on your past medical history and medications. The study team will then randomize into one of two groups, like flipping a coin to see which of the two groups you will be in. One group will receive medical air, similar to what you breathe normally, and the other will receive brief excessive oxygen ("brief hyperoxia" therapy). Neither you nor your doctor will know which treatment you will receive.

Vital signs (for example your heart rate, blood pressure, respiratory rate, and pulse oximetry, or an estimate of the amount of oxygen in your blood) will be collected as part of this study. The study team will collect information to see how much damage your stroke may have caused through a physical exam similar to what you had done when you first arrived (the NIH stroke scale and a Modified Rankin Score (mRS)), and to see how the blood is flowing in your brain and the extent of damage to your brain (through the CT-perfusion which you already completed, and repeat MRI-head or CT-head which would normally be completed for most stroke patients in the hospital). These procedures will likely be performed even if you don't participate in the study.

In addition to the routine care you will receive, the study team will collect a very small amount of blood (5mL) of venous blood at three time points (baseline, 4 hours after baseline, and 24 hours after baseline) and a very small amount of blood from your artery (2ml) at a single time point (4 hours after baseline).

Your participation in the study will last up to 3 months. Your participation in this study will be completed in four visits (three will occur while you are still hospitalized and one will occur by phone at 3-months), and will end as soon as the final visit is complete.

Table 1: Schedule of Activities:

Procedures	Baseline/Enrollment ED presentation -T0 (ED arrival +/-60min)	T1 (T0+4hours +/- 20min)	T2 (T0+24hours +/- 4hours)	T3 - Final Assessment (T0+3mo +/- 2weeks)
Informed consent	X			
Demographics	X			
Medical Chart Review	X			X
Randomization	X			
Administer study intervention		X		
Vital signs: HR, BP, RR, SpO2	X	X	X	
ABG		X		
CT-perfusion or non-contrast CT-head with RAPID ASPECT	X			
Repeat MRI-head (CT-head if unable to get MRI)[a]			X	
Serum sample[b]	X	X	X	
NIHSS	X	X	X	
mRS	X			X
Adverse event review and evaluation		X	X	X

[a] only routine re-imaging will be obtained
[b] tested for selected biomarkers (IL-6, IL-8, and MMP-9)

What are the possible discomforts or risks?
Discomforts you may experience while in this study include pain, bleeding and bruising, or an infection at the needle site where we draw blood for the study. When possible, we will try draw blood from your IV catheter. However, at the end of the treatment period we must also get blood from an artery. Getting blood from an artery carries these same risks, but can also cause the artery to spasm causing the blood flow to your hand to be disrupted. You may also feel lightheaded or even to faint after giving blood. Only approved, trained personnel will collect blood samples to minimize these risks.

Other possible risks include the increased amount of oxygen and the production of types of oxygen and nitrogen molecules (“free radical”) that can harm your tissue, lungs and/or heart.

You will be assigned to a study treatment by chance, and the study treatment you receive may prove to be less effective or to have more side effects than the other study treatment(s) or other available treatments.

There is a risk that people outside of the research team will see your research information. We will do all that we can to protect your information, but it cannot be guaranteed.

The study may include risks that are unknown at this time.

Certificate of Confidentiality:

This study has been issued a Certificate of Confidentiality from the federal government to help protect your privacy. The Certificate prohibits the researchers from disclosing your name, or any

identifiable information, document or biospecimen from the research, with the exceptions listed below. A certificate provides protections against disclosing research information in federal, state, or local civil, criminal, administrative, legislative or other proceedings.

These protections apply only to your research records. The protections do not apply to your medical records.

The researchers may disclose your name or identifiable information, document or biospecimen, under the following circumstances:

To those connected with the research,
If required by Federal, State or local laws,
If necessary for your medical treatment, with your consent,
For other scientific research conducted in compliance with Federal regulations,
To comply with mandated reporting, such as a possible threat to harm yourself or others, reports of child abuse, and required communicable disease reporting, or
Under other circumstances with your consent.

A Certificate of Confidentiality does not protect information you or a member of your family voluntarily release.

What are the possible benefits of the study?
This study is designed for the researcher to learn more about the possible benefits of excessive amounts of oxygen may have on how someone recovers from an ischemic stroke and their body responses to a stroke.

Are there alternative treatments?
Your only alternative is to not participate in this study. If you do not want to take part in this study, your standard medical care will not change in any way. You may leave this study and still have these other choices available to you.

Who is paying for this study?

The University of Colorado and the Principle Investigator are receiving payment from the sponsor, the American Heart Association and the National Institutes of Health Building Interdisciplinary Research Careers in Women's Health K12 program, to support this research. The sponsor will only pay for procedures not considered standard of care. Specifically, the sponsor will only pay for the analysis of your imaging results using the RAPID software, the collection of blood specifically for this study.

Will I be paid for being in the study?
You will receive a gift card or check for $25.00 for completing the study. You will be paid at the completion of the final study visit at 3-months. If you are unable to complete the study, you will not be paid for participation in the study.

Will I have to pay for anything?
It will not cost you anything to be in the study.

Is my participation voluntary?
Taking part in this study is voluntary. You have the right to choose not to take part in this study. If you choose to take part, you have the right to stop at any time. If you refuse or decide to withdraw later, you will not lose any benefits or rights to which you are entitled.

If you leave this study, you will still receive your normal medical care. The only medical care that you will lose is the medical care you are getting as part of this study. You might be able to get that same kind of medical care outside of the study. Ask your study doctor.

Can I be removed from this study?
The study doctor may decide to stop your participation without your permission if the study doctor thinks that being in the study may cause you harm, or for any other reason. Also, the sponsor may stop the study at any time.

What happens if I am injured or hurt during the study?
We will arrange to get you medical care if you have an injury that is caused by this research. However, you or your insurance company will have to pay for that care.

Who do I call if I have questions?

The researcher carrying out this study is Layne Dylla. You may ask any questions you have now. If you have questions, concerns, or complaints later, you may call Dr. Dylla at 720-848-6777. You will be given a copy of this form to keep.

You may have questions about your rights as someone in this study. You can call Dr. Dylla with questions. You can also call the responsible Institutional Review Board (COMIRB). You can call them at 303-724-1055.

A description of this clinical trial will be available on http://www.Clinical Trials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Additional Optional Study Procedure

The following is an additional optional study procedure that you are being asked to consider. Your decision to participate, or to not participate, in this additional procedure will not affect your ability to participate in the main study you agreed to above.

The research team, Dr. Layne Dylla, would like to keep some of the data and your blood samples that is taken during the study but is not used for other tests. If you agree, the data and samples will be kept and may be used in future research to learn more about stroke. The research that is done with your data and samples is not designed to specifically help you. It might help people who have a stroke and other diseases in the future. Reports about research done with your data and samples will not be given to you or your doctor. These reports will not be put in your health records. The research using your data and samples will not affect your care.

The choice to let Dr. Layne Dylla keep the data and samples for future research is up to you. No matter what you decide to do, it will not affect the care that you will receive as

part of the study. If you decide now that your data and samples can be kept for research, you can change your mind at any time and contact your study doctor to let him or her know that you do not want Dr. Dylla to use your data and samples any longer, and the will no longer be used for research. Otherwise they may be kept until they are used up or until Dr. Dylla decides to destroy them.

When your data and samples are give to other researchers in the future, Dr. Dylla will not give them your name, address, phone number or any other information that will let the researchers know who you are.

Sometimes data and samples are used for genetic research (about disease that are passed on in families). Even if your data ans samples are used for this kind of research, the result will not be told to you and will not be put in your health records. Your data and samples will only be used for research and will not be sold. The research done with you data and samples may help to develop new products in the future, but there is no plan for you to be paid for this.

We may share data from our research with other researcchers or data banks. On such data bank is called dbGAP, which collects genetic and other data and is sponsored by the National Institutes of Health. By broadly sharing data in data banks like this, we can make our discoveries more accessible to other researchers. Information which directly identifies you will not be sent to these data banks.

Because your genetic information is unique to you, there is a small risk that someone could connect the information back to you. Also, genetic research and broadly sharing data may involve risk to you or people like yourself that are unknown at this time.

The possible benefits of research from your dta and samples included learning more about what causes strokes and other dieseases, how to prevent them, and how to treat them. The greatest risk to you is the release of your private information. Dr. Dylla will protect your records so that your name, address, and phone number will be kept private. The chance that this information will be given to someone else is very small. There will be no cost to you for any data or sample collection and storage by Dr. Dylla.

Please read each sentence below and think about your choice. After reading each sentence, check “yes” or “no”. If you have questions, please talk to your doctor or nurse. Remember, no matter what you decide to do about the storage and future use of your data and samples, you may still take part in the study.

I give my permission for my data and blood to be stored in a central sample bank at the University of Colorado for future use by the study investigators:

☐ Yes ☐ No _____Initials

I give my permission for my data and blood samples to be kept by Dr. Dylla for future research to learn more about how to prevent, detect, or treat stroke.

☐ Yes ☐ No _____Initials

I give my permission for my data and blood samples to be used fore research about other health problems (for example: causes of heart disease, osteoporosis, diabetes).

☐ Yes ☐ No _____Initials

I give my permission for my study doctor (or someone she chooses) to contact me in the future to ask me to take part in more research.

☐ Yes ☐ No _____Initials

Who will see my research information?

The University of Colorado Denver | Anschutz Medical Campus (the University) and its affiliated health systems have rules to protect information about you. Federal and state laws including the Health Insurance Portability and Accountability Act (HIPAA) also protect your privacy. This part of the consent form tells you what information about you may be collected in this study and who might see or use it.

The institutions involved in this study include:

- University of Colorado Denver | Anschutz Medical Campus
- University of Colorado Health
- The sponsor of this study, the American Heart Association
- The Department of Health and Human Services

We cannot do this study without your permission to see, use and give out your information. You do not have to give us this permission. If you do not, then you may not join this study.

We will see, use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside the University and its affiliate hospitals may not be covered by this obligation.

We will do everything we can to maintain the confidentiality of your personal information but confidentiality cannot be guaranteed.

The use and disclosure of your information has no time limit. You can cancel your permission to use and disclose your information at any time by writing to the study's Principal Investigator (PI), at the name and address listed below. If you do cancel your permission to use and disclose your information, your part in this study will end and no further information about you will be collected. Your cancellation would not affect information already collected in this study.

Dr. Layne Dylla
12401 E. 17th Ave., Mail Stop B-215
Aurora, CO 80045

Both the research records that identify you and the consent form signed by you may be looked at by others who have a legal right to see that information, such as:

- Federal offices such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP) that protect research subjects like you.
- The Institutional Review Board that is responsible for overseeing this research
- The study doctor and the rest of the study team.

- The American Heart Association, who is the company paying for this research study.
- Officials at the institution where the research is conducted and officials at other institutions involved in this study who are in charge of making sure that we follow all of the rules for research

We might talk about this research study at meetings. We might also print the results of this research study in relevant journals. But we will always keep the names of the research subjects, like you, private.

You have the right to request access to your personal health information from the Investigator. To ensure proper evaluation of test results, your access to these study results may not be allowed until after the study is completed.

The investigator (or staff acting on behalf of the investigator) will use you information for the research outline in this consent form. They will also make all or some of the following health information about you collected in this study available to: iSchema, Inc (RAPID AI)

Information about you that will be seen, collected, used and disclosed in this study:

- Name and Demographic Information (age, sex, ethnicity, address, phone number, etc.)
- Portions of your previous and current Medical Records that are relevant to this study, including but not limited to Diagnosis(es), History and Physical, laboratory or tissue studies, radiology studies, procedure results
- Research Visit and Research Test records
- Blood samples and the data with the samples.

What happens to Data and Blood Specimens that are collected in this study?

Scientists at the University and the health systems involved in this study work to find the causes and cures of disease. The data and blood specimens collected from you during this study are important to this study and to future research. If you join this study:

- The data and blood specimens given by you to the investigators for this research no longer belong to you.
- Both the investigators and any sponsor of this research may study your data and blood specimens collected from you.
- If data and blood specimens are in a form that identifies you, the University or the health systems involved in this study may use them for future research only with your consent or Institutional Review Board (IRB) approval.
- Any product or idea created by the researchers working on this study will not belong to you.
- There is no plan for you to receive any financial benefit from the creation, use or sale of such a product or idea.

Agreement to use an eConsent Process
I understand that I have the option to use an electronic consent process in order to minimize the possible transmission of COVID-19. I will be given a signed electronic version of this consent fom to keep. I may also request a paper copy of this signed/dated consent.

Signature:_____ Date:_____

Printed Name:_____

HIPAA Authorization for Optional Additional Study Procedures
In this form, you were given the option to agree to additional, optional research procedures. You must also give us your permission, under HIPAA rules, to use and disclose the information collected from these optional procedures, as described above.

Some of these optional procedures may involve genetic testing or the use of your genetic information. Your genetic information will not be released to others.

If you decline to give use permission to use and disclose your information, you cannot take part in these optional procedures, but you can still participate in the main study. Please initial next to your choice:
_____ I give permission for my information, from the optional procedures I have agreed to above, to be used and disclosed as described in this section.

_____ I do not give my permission for my information for any optional procedure to be used and disclosed; I understand that I will not participate in any optional procedures.

Agreement to be in this study and use my data
I have read this paper about the study or it was read to me. I understand the possible risks and benefits of this study. I understand and authorize the access, use and disclosure of my information as stated in this form. I know that being in this study is voluntary. I choose to be in this study: I will get a signed and dated copy of this consent form.

Signature:_____ Date:_____

Printed Name:_____

Consent form explained by:_____ Date:_____

Print Name:_____ Time:_____

----------Use the following only if applicable----------

Signature:_____ Date:_____

(Select one: ☐*Legally Authorized Representative* **OR** ☐*Proxy Decision Maker*)

Print Name:_____

----------Use the following only if applicable----------

A signature of a witness is required for consent of non-reading subjects and consent using a short form.

Witness Signature: _____ Date:_____

Print Name:_____

Witness of Signature ☐ Witness of consent process ☐

Consent for Continued Research Participation
You have been taking part in the research study: The Role of Hyperoxia in the Emergency Department Treatment of Acute Ischemic Stroke. Consent for your participation was obtained from your legal representative because you were unable to provide consent at that time. We are now asking for you to consent to continue being in the study. Your continued participation is entirely voluntary. If you decide not to continue in this study, it will not affect your relationship with your doctor or with the University of Colorado Hospital and will not result in any penalty or loss of benefits to which you are otherwise entitled.

Statement of Voluntary Consent
I have read this form and the attached consent or have had them read to me. I have been told what to expect if I take part in this study, including risks and possible benefits. I have had a chance to ask questions and have had them answered to my satisfaction. I have been told that the people listed in this form will answer any questions that I have in the future. By signing below, I am volunteering to continue to be in this research study.

Signature:_____ Date:_____

Printed Name:_____

Consent form explained by:_____ Date:_____

Print Name:_____ Time:_____

----------Use the following only if applicable----------

A signature of a witness is required for consent of non-reading subjects and consent using a short form.

Witness Signature: _____ Date:_____

Print Name:_____

Witness of Signature ☐ Witness of consent process ☐