



HRP-503B – BIOMEDICAL RESEARCH PROTOCOL (2017-1)

Protocol Title: Comparison of pain perception and incidence of intravascular injection during transforaminal epidural steroid injection (TFESI) using 22 gauge vs 25 gauge needle.

Principal Investigator: Dr. Robin Raju

Version Date: February 1, 2018

(If applicable) Clinicaltrials.gov Registration #: Not Available

INSTRUCTIONS

This template is intended to help investigators prepare a protocol that includes all of the necessary information needed by the IRB to determine whether a study meets approval criteria. **Read the following instructions before proceeding:**

1. Use this protocol template for a PI initiated study that includes direct interactions with research subjects. Additional templates for other types of research protocols are available in the system Library.
2. If a section or question does not apply to your research study, type “Not Applicable” underneath.
3. Once completed, upload your protocol in the “Basic Information” screen in IRES IRB system.

Section I: Research Plan

1. **Statement of Purpose:** State the scientific aim(s) of the study, or the hypotheses to be tested.

This is a pilot study to evaluate whether smaller bore 25 gauge needle can reduce the incidence of intravascular injection during TFESI compared to larger bore 22 gauge needle. Study will also evaluate any difference in patient pain perception between 2 needle types.

2. **Probable Duration of Project:** State the expected duration of the project, including all follow-up and data analysis activities.
1 year of enrolling subjects; 1 year of data analysis activities.
3. **Background:** Describe the background information that led to the plan for this project. Provide references to support the expectation of obtaining useful scientific data.
Transforaminal epidural steroid injection is very effective in placing injectate to ventral epidural space at the level of exact pathology, hence many practitioners prefer this technique over interlaminar approach, although there is no definitive evidence to suggest one is superior to the other. Rare but serious complications have been reported with TFESI including spinal cord infarction, hematoma, paralysis, and even death. Proposed mechanism of action behind these serious outcomes is inadvertent intravascular injections or the embolization of corticosteroid particulates. Although several needle types have been studied in the past, needle size has never been looked at in relation to intravascular uptake. It can be beneficial to know whether needle size plays a factor in intravascular uptake of injectate during TFESI. It can be hypothesized that 25 gauge needle due to its smaller diameter can potentially lead to less intravascular uptake. Practitioners tend to prefer 22 gauge needle for TFESI as it is easier to steer through tissue planes. There is also a notion that smaller 25 gauge needle tends to be less painful for patients.
4. **Research Plan:** Summarize the study design and research procedures using non-technical language that can be readily understood by someone outside the discipline. **Be sure to distinguish between standard of care vs. research procedures when applicable, and include any flowcharts of visits specifying their individual times and lengths.** Describe the setting in which the research will take place.
Prospective clinical trial. Goal is to recruit at least 250 patients. Patients will be given 2 forms to complete before and after the procedure. Patients will rate their pain before, during and after the procedure using VAS and/or similar ordinal scales. Patients will be blinded to what kind of needle being used. Practitioners will choose needle size randomly based on a computer-generated system. Live fluoroscopy to be utilized to confirm intravascular uptake on all cases. All practitioners to use similar approach for lumbar TFESI:
 1. S1 TFESI - target at superolateral aspect of posterior circular S1 foramen
 2. L1-L5 TFESI – target at supraneural ‘safe’ triangle (six o’clock position of the pedicle in the AP projection). May switch target to infraneural ‘Kambin’s’ triangle if injection cannot be safely administered with prior approach.
5. **Genetic Testing N/A #**
6. **Subject Population:** Provide a detailed description of the types of human subjects who will be recruited into this study.
Patients scheduled for lumbosacral TFESI at the Spine Center at YNHH Spine Center
7. **Subject classification:** Check off all classifications of subjects that will be specifically recruited for enrollment in the research project. Will subjects who may require additional safeguards or other considerations be enrolled in the study? If so, identify the population of subjects requiring special safeguards and provide a justification for their involvement. [Not Applicable]

#Children # Healthy #Fetal material, placenta, or dead fetus
#Non-English Speaking # Prisoners #Economically disadvantaged persons
#Decisionally Impaired # Employees #Pregnant women and/or fetuses
#Yale Students # Females of childbearing potential

NOTE: Is this research proposal designed to enroll children who are wards of the state as potential subjects?
Yes # No #

8. Inclusion/Exclusion Criteria: What are the criteria used to determine subject inclusion or exclusion?

Inclusion Criteria:

Patients scheduled for lumbosacral TFESI
LBP with or without leg pain

Exclusion Criteria:

Patients with contrast/local anesthetic allergy
Patients with pregnancy,
Coagulopathy,
Systemic infection,
Mental disability
Inability to provide informed consent.
Prior surgery
Severe Anxiety

9. How will **eligibility be determined, and by whom?**

The PI, Dr. Robin Raju will determine eligibility

10. Risks: Describe the reasonably foreseeable risks, including risks to subject privacy, discomforts, or inconveniences associated with subjects participating in the research.

We are predicting that there may be increased risk for blood stream uptake of steroid particles with 22 gauge needle as opposed to 25 gauge needle. As mentioned earlier, this phenomenon has not been shown in any studies yet to date.

An inconvenience is lost time from filling out the questionnaire/consent form.

11. Minimizing Risks: Describe the manner in which the above-mentioned risks will be minimized.

Standard medical preparation and procedure will be utilized when giving the epidural injection, regardless of the needle gauge.

12. Data and Safety Monitoring Plan: Include an appropriate Data and Safety Monitoring Plan (DSMP) based on the investigator's risk assessment stated below. (Note: the HIC will make the final determination of the risk to subjects.)

a. What is the investigator's assessment of the overall risk level for subjects participating in this study? Minimal Risk

b. If children are involved, what is the investigator's assessment of the overall risk level for the children participating in this study? [Not Applicable]

c. Include an appropriate Data and Safety Monitoring Plan. Examples of DSMPs are available here <http://your.yale.edu/policies-procedures/forms/420-fr-01-data-and-safety-monitoring-plans-templates> for

- i. Minimal risk
- ii. Greater than minimal

The principal investigator is responsible for monitoring the data, assuring protocol compliance, and conducting the safety reviews at the specified frequency [*monthly*]. During the review process the principal investigator will evaluate whether the study should continue unchanged, require modification/amendment, or close to enrollment.

The principal investigator and the Institutional Review Board (IRB) have the authority to stop or suspend the study or require modifications.

This protocol presents minimal risks to the subjects and Unanticipated Problems Involving Risks to Subjects or Others (UPIRSOs), including adverse events, are not anticipated. In the unlikely event that such events occur, Reportable Events (which are events that are serious or life-threatening and unanticipated (or anticipated but occurring with a greater frequency than expected) and possibly, probably, or definitely related) or Unanticipated Problems Involving Risks to Subjects or Others that may require a temporary or permanent interruption of study activities will be reported immediately (if possible), followed by a written report within 5 calendar days of the Principal Investigator becoming aware of the event to the IRB (using the appropriate forms from the website) and any appropriate funding and regulatory agencies. The investigator will apprise fellow investigators and study personnel of all UPIRSOs and adverse events that occur during the conduct of this research project via email as they are reviewed by the principal investigator.

- d. For multi-site studies for which the Yale PI serves as the lead investigator: [Not applicable]
 - i. How will adverse events and unanticipated problems involving risks to subjects or others be reported, reviewed and managed? [not applicable]
 - ii. What provisions are in place for management of interim results? [not applicable]
 - iii. What will the multi-site process be for protocol modifications? [not applicable]

13. **Statistical Considerations:** Describe the statistical analyses that support the study design.

Literature evidence shows general incidence of intravascular uptake is 8.5% to 13% for TFESI depending on the level of injection. If one were to presume intravascular uptake rates for 22G vs 25G needle to be 11% versus 4%, 80% power to detect an effect at $p < .05$, 1-tailed, requires 125/group (250 total patients).

Section II: Research Involving Drugs, Biologics, Radiotracers, Placebos and Devices

If this section (or one of its parts, A or B) is not applicable, check off N/A and delete the rest of the section.

A. RADIOTRACERS **N/A**

B. DRUGS/BIOLOGICS **N/A**

C. DEVICES **N/A**

Section III: Recruitment/consent and assent procedures

1. **Targeted Enrollment:** Give the number of subjects: 250

- a. Targeted for enrollment at Yale for this protocol: 250
- b. If this is a multi-site study, give the total number of subjects targeted across all sites: [not applicable]

2. **Indicate recruitment methods below. Attach copies of any recruitment materials that will be used.**

# Flyers	# Internet/web postings	# Radio
# Posters	# Mass email solicitation	# Telephone
# Letter	# Departmental/Center website	# Television
# Medical record review*	# Departmental/Center research boards	# Newspaper
# Departmental/Center newsletters	# Web-based clinical trial registries	# Clinicaltrails.gov
# YCCI Recruitment database	# Social Media (Twitter/Facebook):	
# Other:		

* Requests for medical records should be made through JDAT as described at <http://medicine.yale.edu/ycci/oncore/availableservices/datarequests/datarequests.aspx>

3. Recruitment Procedures:

- a. Describe how potential subjects will be identified. Patients will be identified when they see their physician at the Yale New Haven Hospital Spine Center.
- b. Describe how potential subjects are contacted. Subjects will be approached in the Spine Center clinic.
- c. Who is recruiting potential subjects? PI-Dr. Robin Raju and the study team

4. Assessment of Current Health Provider Relationship for HIPAA Consideration:

Does the Investigator or any member of the research team have a direct existing clinical relationship with any potential subject?

#Yes, all subjects

#Yes, some of the subjects

#No

If yes, describe the nature of this relationship. PI's own clinic patients who is getting an injection may be eligible for study enrollment.

5. Request for waiver of HIPAA authorization: (When requesting a waiver of HIPAA Authorization for either the entire study, or for recruitment purposes only. Note: if you are collecting PHI as part of a phone or email screen, you must request a HIPAA waiver for recruitment purposes.)

Choose one:

For entire study

For recruitment/screening purposes only

For inclusion of non-English speaking subject if short form is being used and there is no translated HIPAA research authorization form available on the University's HIPAA website at hipaa.yale.edu.

- i. Describe why it would be impracticable to obtain the subject's authorization for use/disclosure of this data: A phone call potentially needs to be made after the injection (within 30 days of injection) to make sure there are no complications (if those patients haven't been followed up by a physician in that time span).

- ii. If requesting a waiver of **signed** authorization, describe why it would be impracticable to obtain the subject's signed authorization for use/disclosure of this data: A phone call potentially needs to be made after the injection (within 30 days of injection) to make sure there are no complications (if those patients haven't been followed up by a physician in that time span).

The investigator assures that the protected health information for which a Waiver of Authorization has been requested will not be reused or disclosed to any person or entity other than those listed in this application, except as required by law, for authorized oversight of this research study, or as specifically approved for use in another study by an IRB.

Researchers are reminded that unauthorized disclosures of PHI to individuals outside of the Yale HIPAA-Covered entity must be accounted for in the "accounting for disclosures log", by subject name, purpose, date, recipients, and a description of information provided. Logs are to be forwarded to the Deputy HIPAA Privacy Officer.

6. Process of Consent/Accent: Describe the setting and conditions under which consent/assent will be obtained, including parental permission or surrogate permission and the steps taken to ensure subjects' independent decision-making.

Patients will meet with the PI or any other designated consenting individual in a private clinic room, after they have been determined as a possible subject for the study. The study will be presented to the patient along with a copy of the informed consent. The patient and any other individuals as appropriate will have the opportunity to ask any questions they may have and all questions will be

answered completely. The patient will be given the opportunity to consider the trial and then sign if they are comfortable doing so.

7. **Evaluation of Subject(s) Capacity to Provide Informed Consent/Accent: Indicate how the personnel obtaining consent will assess the potential subject's ability and capacity to consent to the research being proposed.**
Individuals obtaining consent will evaluate the subject's ability to sign consent by evaluating their comprehension of the study procedures being presented and by the questions the subject asks regarding the study.

8. **Non-English Speaking Subjects: Explain provisions in place to ensure comprehension for research involving non-English speaking subjects. If enrollment of these subjects is anticipated, translated copies of all consent materials must be submitted for approval prior to use.**
Enrollment of non-English speaking participants is not anticipated.

As a limited alternative to the above requirement, will you use the short form* for consenting process if you unexpectedly encounter a non-English speaking individual interested in study participation and the translation of the long form is not possible prior to intended enrollment? YES # NO #

Note* If more than 2 study participants are enrolled using a short form translated into the same language, then the full consent form should be translated into that language for use the next time a subject speaking that language is to be enrolled.

Several translated short form templates are available on the HRPP website (yale.edu/hrpp) and translated HIPAA Research Authorization Forms are available on the HIPAA website (hipaa.yale.edu). If the translation of the short form is not available on our website, then the translated short form needs to be submitted to the IRB office for approval via modification prior to enrolling the subject. *Please review the guidance and presentation on use of the short form available on the HRPP website.*

If using a short form without a translated HIPAA Research Authorization Form, please request a HIPAA waiver in the section above.

9. **Consent Waiver: In certain circumstances, the HIC may grant a waiver of signed consent, or a full waiver of consent, depending on the study. If you will request either a waiver of consent, or a waiver of signed consent for this study, complete the appropriate section below.**

#Not Requesting any consent waivers

#Requesting a waiver of signed consent:

Recruitment/Screening only (if for recruitment, the questions in the box below will apply to recruitment activities only)
Entire Study (Note that an information sheet may be required.)

Requesting a waiver of consent:

Recruitment/Screening only (if for recruitment, the questions in the box below will apply to recruitment activities only)
Entire Study

Section IV: Protection of Research Subjects

Confidentiality & Security of Data:

1. What protected health information (medical information along with the HIPAA identifiers) about subjects will be collected and used for the research? *Age, Sex, Medical Diagnosis, Pain Questionnaire*
2. How will the research data be collected, recorded and stored? *Data will be collected via the patients' medical record and patient questionnaire. Data will be stored in locked file cabinets, only accessible to members of the research staff.*
3. How will the digital data be stored? #CD #DVD #Flash Drive #Portable Hard Drive #Secured Server #Laptop Computer #Desktop Computer #Other
4. What methods and procedures will be used to safeguard the confidentiality and security of the identifiable study data and the storage media indicated above during and after the subject's participation in the study?

All electronic data are stored in password encrypted computers. Computers and any paper study materials will be stored in the PIs office, which is locked.

All portable devices must contain encryption software, per University Policy 5100. If there is a technical reason a device cannot be encrypted please submit an exception request to the Information Security, Policy and Compliance Office by clicking on url <http://its.yale.edu/egrc> or email it.compliance@yale.edu

5. What will be done with the data when the research is completed? Are there plans to destroy the identifiable data? If yes, describe how, by whom and when identifiers will be destroyed. If no, describe how the data and/or identifiers will be secured.
When the research and all data analysis is complete, all identifiers will be destroyed by the PI, Both by deleting electronic files and shredding paper copies.
6. If appropriate, has a Certificate of Confidentiality been obtained? *[not applicable]*

Section V: Potential benefits

Potential Benefits: Identify any benefits that may be reasonably expected to result from the research, either to the subject(s) or to society at large. (Payment of subjects is not considered a benefit in this context of the risk benefit assessment.)

It can be beneficial to know whether needle size plays a factor in intravascular uptake of injectate during TFESI. It can be hypothesized that 25 gauge needle due to its smaller diameter can potentially lead to less intravascular uptake. Practitioners tend to prefer 22 gauge needle for TFESI as it is easier to steer through tissue planes. There is also a notion that smaller 25 gauge needle tends to be less painful for patients.

Section VI: Research Alternatives and Economic Considerations

1. **Alternatives:** What other alternatives are available to the study subjects outside of the research?
The patient can choose not to participate in this study.
2. **Payments for Participation (Economic Considerations):** Describe any payments that will be made to subjects, the amount and schedule of payments, and the conditions for receiving this compensation.
There is no payment for participating in this study.
3. **Costs for Participation (Economic Considerations):** Clearly describe the subject's costs associated with participation in the research, and the interventions or procedures of the study that will be provided at no cost to subjects.
There are no charges to the participant or their insurance carrier for study visits or tests that are part of this research.

4. **In Case of Injury:** This section is required for any research involving more than minimal risk, and for minimal risk research that presents the potential for physical harm (e.g., research involving blood draws).

- a. Will medical treatment be available if research-related injury occurs? **Yes**
- b. Where and from whom may treatment be obtained? *The participant can seek treatment from and hospital or medical facility.*
- c. Are there any limits to the treatment being provided? **No**
- d. Who will pay for this treatment? *Participants' Insurance Company*
- e. How will the medical treatment be accessed by subjects? *Participant will seek medical care, if needed.*

IMPORTANT REMINDERS

Will this study have a billable service? **Yes #** **No #**

A billable service is defined as any service rendered to a study subject that, if he/she was not on a study, would normally generate a bill from either Yale-New Haven Hospital or Yale Medical Group to the patient or the patient's insurer. The service may or may not be performed by the research staff on your study, but may be provided by professionals within either Yale-New Haven Hospital or Yale Medical Group (examples include x-rays, MRIs, CT scans, specimens sent to central labs, or specimens sent to pathology). Notes: 1. There is no distinction made whether the service is paid for by the subject or their insurance (Standard of Care) or by the study's funding mechanism (Research Sponsored). 2. This generally includes new services or orders placed in EPIC for research subjects.

If answered, "yes", this study will need to be set up in OnCore, Yale's clinical research management system, for Epic to appropriately route research related charges. Please contact oncore.support@yale.edu

Are there any procedures involved in this protocol that will be performed at YNHH or one of its affiliated entities? **Yes #** **No #**

If Yes, please answer questions a through c and note instructions below.

- a. Does your YNHH privilege delineation currently include the **specific procedure** that you will perform? **Yes #** **No #**
- b. Will you be using any new equipment or equipment that you have not used in the past for this procedure? **Yes #** **No #**
- c. Will a novel approach using existing equipment be applied? **Yes #** **No #**

If you answered "no" to question 4a, or "yes" to question 4b or c, please contact the YNHH Department of Physician Services (688-2615) for prior approval before commencing with your research protocol.

IMPORTANT REMINDER ABOUT RESEARCH AT YNHH

Please note that if this protocol includes Yale-New Haven Hospital patients, including patients at the HRU, the Principal Investigator and any co-investigators who are physicians or mid-level practitioners (includes PAs, APRNs, psychologists and speech pathologists) who may have direct patient contact with patients on YNHH premises must have medical staff appointment and appropriate clinical privileges at YNHH. If you are uncertain whether the study personnel meet the criteria, please telephone the Physician Services Department at 203-688-2615. **By submitting this protocol as a PI, you attest that you and any co-investigator who may have patient contact has a medical staff appointment and appropriate clinical privileges at YNHH.**