HealthEast
Care System

# NCT07187362

# Study Protocol Document Date: October 3, 2015

## Title

**Stem cell containing bone graft options and bone morphogenetic protein (BMP) compared to iliac autograft for single level posterior spinal fusion**

HealthEast
Care System

# RESEARCH/PROJECT REVIEW APPLICATION

__ *HMRI*
__ *HealthEast*
__ *Non HealthEast*

*This form fulfills both Research and IRB requirements for HealthEast. Please complete all questions, even if you are not applying for IRB approval.*

## 1 Project Title:

***Bone graft options for single level posterior spinal fusion***

## 2 Contact Information

a. Principal Investigator(s): Glenn Buttermann, MD
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Please indicate the training or education completed in the protection of human subjects (***this is required***):

*CITI Human Subjects Research Curriculum*

b. Co- Investigator(s):
Mailing Address:
Telephone:
FAX:
Email:

Indicate the training and education completed in the protection of human subjects (***this is optional***):

c. Research Staff (personnel you wish to include in correspondence related to this study, e.g. study coordinators):
Mailing Address:
Telephone:
FAX:
Email:

## 3 Abstract (500 words or less, do not refer to "see protocol" for abstract):

This abstract should consist of two paragraphs, written in lay language, labeled Background and Methods. They should briefly describe the problem being addressed in the study, including the hypothesis or study question and how the study will be performed.

***Background****. Achieving spinal fusion requires bone graft and is most reliable using an anterior/posterior technique. The bone graft is placed between the vertebral bodies during the anterior fusion and placed in and adjacent to the facet joints for the posterior fusion. Because there is greater bony surface area between the vertebral*

*bodies, this area has a more reliable fusion success rate. Instrumentation which helps stabilize the vertebra during the healing period also increases the fusion rate. The bone graft for the posterior fusion may come from a variety of sources. Historically, bone graft was obtained from the iliac portion of the patient own pelvis, IBG, but this resulted in additional postoperative pain (sometimes worse than the fusion wound). Alternatives are currently the most common form of bone graft, but there is very little knowledge as to the superiority of one alternative over another. The purpose of this research is to determine the ability to achieve a solid posterior spinal fusion using sources to bone graft coming from the patient's own iliac crest, or from bone morphogenic protein (BMP), which is costly, but known to give very high fusion rates when applied anteriorly, or from donor bone combined with stem cells derived from either donor bone, fat, or amniotic membrane/fluid (placenta or "afterbirth" tissue).*

***Methods**. Patients who are surgical candidates for a one-level anterior/posterior lumbar fusion will be randomized to IBG or one of 4 types of bone graft alternatives (small Medtronic Infuse BMP, Orthofix Trinity allograft bone marrow derived stem cells combined with morcelized cancellous allograft, Allosource Allostem fat derived stem cells combined with morcelized cancellous allograft, or Nutech Nucel amnion derived stem cells combined with morcelized cancellous allograft). There will be 20 patients in each group. All anterior fusions will use BMP; the study only applies to the posterior fusion. Neither patient nor surgeon is blinded to the posterior type of bone graft. The volume of bone graft is the same for each type, approximately 5cc. The decortication part of the fusion is identical for all patients, as is the type of instrumentation (anterior plate and posterior facet screws). Limited CT scans of the fusion will be obtained at approximately one year postoperatively to assess fusion success of both anterior and posterior regions. The limited CT scan results in approximately 2.88 mSv radiation exposure, or similar to one year's worth of background radiation. Secondary endpoints are patient outcomes for pain and function using standard VAS pain scales and Oswestry. Disability Index at one year postoperatively will be assessed to ascertain the relationship between clinical success and fusion success since prior studies suggest that success is only related to the status of anterior fusion.*

**4 Study Design/Protocol** (Please answer the questions below and attach the study protocol):

a. What are the objectives of the proposed research/project?

*Evaluate the effectiveness of 5 types of bone graft material in obtaining a solid posterior fusion for one level anterior/posterior lumbar spinal fusion.*

b. What is the significance of the proposed study? (Provide the context for the study, and the rationale. What is known about the topic? Why is the study important? What kind of answers will the study provide)?

*Iliac bone autograft is an additional procedure with known morbidity and high rate of residual pain postoperatively at the graft donor site leading to reduced outcomes. Bone morphogenic protein is effective in obtaining fusion but is used off label, has multiple side effects, and is expensive to hospital systems. Stem cell bone products are an attractive alternative that avoids pain related to the graft donor site and have a far better safety profile than BMP.*

- What will subjects be asked to do?

  *Patients who are scheduled to undergo a single level lumbar anterior/posterior spinal fusion with instrumentation will be eligible to participate. Subjects will be asked to agree to be randomized to one of five types of bone graft for the posterior portion of their fusion surgery.*

- What is the study design?

  *Prospective, non-blinded, randomized study design of 5 types of bone graft material applied to 100 patients (20 patients per group).*

c. Describe the proposed data collection procedures. Attach any forms such as surveys, chart abstraction or other data collection forms.

*Data collection includes age, date of surgery, date of follow-up CT scan (>9 months postop), assessment of fusion at follow-up, smoking and osteoporosis status (which may affect fusion status), type of bone graft used for the anterior procedure (all will be bone morphogenic protein combined with local autograft), type of bone graft used for the posterior procedure.*

d. List the routine medical related costs for this research/project/trial.

1) **ROUTINE OR STANDARD MEDICAL CARE**: This <u>includes</u> items or services that are typically provided absent a clinical trial and those required for the provision of the investigational item or service, as well as appropriate monitoring, prevention of complications, and the diagnosis or treatment of complications arising from the provision of an investigational item or service.

   *The fusion surgery is considered standard of care. The costs of a single level lumbar fusion is information known to HealthEast as they are the entity that charges for this type of surgery. The charges and reimbursement for spinal surgery at HealthEast has not been shared with the investigator.*

2) **STUDY RELATED CARE**: List the additional items or services required for the provision of the investigational item or service

   *Additional items related to cost are limited CT scan at >9months postoperatively. This cost is $265 per patient and will be paid for by the principal investigator/Midwest Spine & Brain Institute.*

3) **STUDY SPECIFIC CARE**: List items or services furnished solely to satisfy data collection, analysis needs, or to determine trial eligibility.

   *Data will be collected by the PI on a personal password protected laptop computer. Statistical analysis will be obtained from a third party.*

## 5 Financial Information

a. Will this project by funded by, or supported by a center or cooperative group(s) that is funded by NIH, CDC, AHRQ, HCFA, or the VA?
☒ NO ☐ YES - Specify:

b. Will this project be funded through *other* outside granting agencies?
If yes, please list.
☒ NO ☐ YES - Source(s):

c. Do any of the investigators have a financial interest with the funding source/study sponsor, and if so, what type (e.g. shareholder, stock options, paid consultant or medical director, travel expense reimbursement, provision of office supplies or equipment)?
☒ NO ☐ YES - What Type?

d. Does this study have an IND number?
☒ NO ☐ YES - Number:

e. Does this study have an IDE number?
☒ NO ☐ YES - Number:

f. Is this trial exempt from having an IND under 21 CFR 312.2(b)(1)?
☒ NO ☐ YES ☐ NA

g. Inclusive Date of Project:
Start Date: October 1, 2015 End Date: January 1, 2020

h. Aspects of this study involving the use of human subjects will be conducted in:
☒ Hospital ☒ Physician's Office/Clinic ☐ Other (please identify):

## 6 Subject Population

a. Check all that apply:

☒ Inpatient ☐ Outpatient ☐ Healthy Volunteers ☐ Other

b. Describe criteria for inclusion and exclusion of subjects in this study:

- Inclusion Criteria:

  *Lumbar spinal fusion of a single segment for a degenerative condition; age 18 – 65*

- Exclusion Criteria:

  *Prior lumbar fusion surgery; prior abdominal surgery precluding access to the anterior spine; lytic spondylolisthesis; high grade stenosis requiring partial or complete facetectomy*

c. If the study includes use of clinical patients, will approval be obtained from the attending M.D.?
☐ NO ☒ YES - Describe how:

*Consent will be obtained at the time of preoperative discussion in patients who desire to proceed with fusion surgery after having failed non-operative treatment for their degenerative condition. Risk and benefits of surgery as well as specific risks related to bone graft products will be presented.*

d. How many subjects do you plan to enroll?

*100*

e. Please indicate the approximate number of subjects to be enrolled for each gender category:
40 Male 60 Female

f. Expected Age Range-please check all that apply:

☐ 0-7 (include parental consent form)

☐ 8-17 (include parental consent form and child assent form)

☒ 18-65

☐ 65 and older

Exact ages to be included:18-65

g. Protected Populations to be Studied-please check all that apply

☐ Pregnant women

☐ Embryos/Fetuses

☐ Prisoners

☐ Minors (under age 18)

☐ Mentally/Emotionally/Developmentally Disabled Persons

☒ NA

h. If this is a multi-center study, what is the total number of subjects to be enrolled from all centers:

*NA*

i. How will subjects be chosen? (e.g. records, classes, referral)

*Patients who are followed and treated for their spinal condition and who meet the entry criteria will be enrolled from the PI's clinical practice.*

j. Will subjects receive any inducements or rewards for participating in the study?
☒ NO ☐ YES - Please explain:

k. Will subjects be charged for any research-related procedures?
☒ NO ☐ YES - If amount is known, please list:

## 7 Risk

The purpose of this section is to determine whether the human subjects involved in the proposed research project will be placed at risk. In order to help determine what risk subjects will be exposed to, please answer the following questions:

| DOES THE RESEARCH PLAN IN THIS PROJECT INVOLVE: | YES | NO |
|---|---|---|
| a. Possible invasion of privacy of subject or family, including use of personal information or records? | ☒ | ☐ |
| b. The administration of physical stimuli other than auditory and visual stimuli associated with normal classroom situation? | ☐ | ☒ |
| c. Deprivation of physiological requirements such as nutrition or sleep; manipulation of psychological and/or social variables (e.g. sensory deprivation, social isolation, psychological stresses, etc.)? | ☐ | ☒ |
| d. Any probing for information in survey or interview that an individual might consider to be personal or sensitive? | ☐ | ☒ |
| e. The requirement of physical exertion beyond normal classroom situations? | ☐ | ☒ |
| f. The presentation to the subject of any materials which they might find to be offensive, threatening or degrading? | ☐ | ☒ |
| g. Deception as part of the experimental procedure? If the study involves the use of deception, the protocol must include a description of this fact and the "debriefing procedure" which will be used upon completion of the study. | ☐ | ☒ |
| h. The use of drugs? If yes, please comment on the preparation, dosage, toxicity, significant side effects, etc. | ☐ | ☒ |
| i. Any surgical processes? | ☒ | ☐ |
| j. Administration of approved/unapproved devices? | ☐ | ☒ |
| k. Blood drawing, marrow biopsy sampling, biopsy of other tissues, etc (if "yes", state the amount (volume measure) and frequency at which samples are taken. The consent form must include lay term equivalents for the amount, e.g. teaspoons. Please distinguish between procedures that are diagnostic from procedures performed solely for research | ☐ | ☒ |
| l. The use of radioisotopes, or other sources of ionizing radiation including X-rays? . | ☒ | ☐ |
| m. Use of controlled substances? | ☐ | ☒ |

n. Describe the nature and degree of risk or harm checked above:

*The risks associated with obtaining iliac bone autograft and include pain, infection (<5%), pelvic fracture (very rare).*

*The limited post-procedure CT scan results in approximately 2.88mSv of radiation exposure, which is equivalent to one year's worth of background radiation.*

o. List any anticipated direct and/or societal benefits to participating in this research project. If none, state that fact here and in the consent form:

*The benefits are for future spinal fusion patients who may be able to avoid the morbidity related to harvesting iliac bone autograft yet still reliably obtain a solid posterior fusion using one of the alternative bone graft products evaluated in this study.*

p. Do the benefits of this study outweigh the risks? ..... Yes ☒ No ☐

## 8 Confidentiality of Data

a. Will any data from this study be a part of permanent record (identifiable to the subject) that will be made available to physician, employer, supervisor, student, FDA, etc.?
☐ NO ☒ YES - Please explain:

*Both the patient and their physician can access their medical record including the operative report which indicates the type of bone graft used in their fusion.*

b. Where, how long, and in what format (paper, electronic, digital) will the data be kept?

*The data will be kept electronically for approximately 10 years.*

c. Describe what security precautions (locked cabinet, password protected, encryption, etc.) that will be taken to protect the data.

*The data will be stored on a password protected computer.*

## 9 Informed Consent

Informed consent is necessary for all research and other activities which involve humans as subjects. It may be secured in several ways, but usually must be documented in some manner. The investigator may determine what method he/she believes would best serve the interest of the subject population. However, the Committee reserves the right, upon review of the research and its attendant risks, to require alternate and/or more stringent means of securing consent. Use of subjects not able to give personal consent for reason of age, mental status, legal or other such status, require that consent be secured from the parents(s) or legal guardian. If it appears necessary to use consent procedures which differ from those normally required, please define and justify their use.

At the top of the Informed Consent form, the study/trial name, the sponsor of the study, and the sponsor-assigned protocol number **MUST** be clearly identified.

In addition, the section on the Informed Consent dealing with problems, questions, etc., must include the following statement:

***"You may also contact Dean Huska, Chair, HealthEast Institutional Review Board (651-232-3234 or dhuska@HealthEast.org) with questions regarding your rights as a patient in research studies".***

The Informed Consent must also document the individual who reviewed the informed consent with the subject.

***I confirm that I have personally explained the nature, purpose, duration, and foreseeable benefits and risks of the trial to the participant (or if applicable, the participant's legal representative) named above.***

_____
Person who administered the consent

_____ _____
Signature Date

Please describe procedures used to obtain informed consent and attach a copy of the informed consent document. These procedures should include an explanation of the following:

a. In relation to actual data gathering, when will consent be discussed and documentation obtained?

*Consent for this study will be reviewed, discussed, and obtained from the patient preoperatively. The assessment of fusion status occurs post-operatively.*

Will the investigator(s) be securing all informed consent?

☒ Yes ☐ No – If no, please list the name(s) job title(s) and credentials of the individual(s) responsible for obtaining informed consent

b. What is the reading level of the informed consent? How was this level measured?

10th grade-Flesch-Kincaid readability statistics

*Please be prepared to discuss with the Institutional Review Board how you and/or your research team will assure subjects' understanding of the consent process.

You may refer to the HealthEast consent template (Appendix A) when drafting the informed consent document. Do ***not*** submit sponsored prepared consent forms without editing the form to include HealthEast IRB standard language and all essential elements of informed consent.

*Under specific conditions, when justifiable, documentation of informed consent can be waived or altered. These limited conditions are described in 45CRF46.116 and 45 CRF 46.117. If you believe that this research qualifies for waived or altered consent, please complete Appendix B and include this form with the completed application.*

## 10 VERIFICATION OF APPLICATION

I certify that the information furnished concerning the procedures to be taken for the protection of human subjects is correct. I will seek to obtain prior approval for any substantive modification to the proposal and will report promptly any unexpected or otherwise significant adverse effect in the course of the study

_____

Signature of Principal Investigator Date

**11 How will the proposed research protocol impact HealthEast facilities, staff, or resources?** (Provide assessment of the project's impact to resources and staff workload by answering the following questions.)

a. Will this project require additional resources from HealthEast?
☒ NO ☐ YES - Specify:

b. Will this project increase the staff workload?
☒ NO ☐ YES - Specify:

**12 How will the results of the study be reported? Who will the results be reported to?**

*Study results may be presented at a spine conference or in a peer-reviewed professional journal.*

**13 Budget:** Attach a budget. If applicable, also include a detailed list of medical related services/procedures and associated costs for this research/project/trial (as outlined on Question 4d).

*The only study-related cost is the follow-up CT scan, which will be paid for by the principal investigator/Midwest Spine & Brain Institute.*

***You have reached the end of this form. Please make sure that you have responded to every question on this application, even if your response is "not applicable".***