Title: Comparison of traditional back-loaded fiducial needles with preloaded fiducial needles in EUS-guided fiducial marker placement for image-guided radiation therapy in patients with pancreatic cancer: A multicenter randomized controlled trial.

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Study Title: Comparison of traditional back-loaded fiducial needles with preloaded fiducial needles in EUS-guided fiducial marker placement for image-guided radiation therapy in patients with pancreatic cancer: A multicenter randomized controlled trial.

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.

Why is this study being done?

This study plans to learn more about the duration of time needed and effectiveness of a new model for fiducial marker delivery in patients with pancreatic cancer needing image guided radiation therapy.

For certain patients with pancreatic cancer, radiation therapy is performed prior to attempts at surgical resection of the cancer and/or chemotherapy. Radiation therapy to a soft tissue organ such as the pancreas can be difficult, as it is not easily seen on XRAY/CAT Scans. A process known as image guided radiation therapy (IGRT) helps better target the pancreas for radiation therapy. In order to perform IGRT, fiducials, which are non-active radiographic markers typically made from gold or carbon, are placed in and around the tumor to mark tumor margins. This allows for the delivery of high doses of radiation directed at cancer tissue, while reducing unnecessary damage to nearby healthy tissue.

Currently, the placement of fiducials involves endoscopic ultrasound (EUS) to identify target areas in the pancreas to receive radiation therapy. Fiducial marker placement is usually performed using a certain sized needle (known as a 22-guage fine needle aspiration (FNA) needle). To prepare the needle for fiducial placement, one to two fiducials are manually back-loaded into the tip of the needle, secured using sterile lubrication or wax, and once the pancreatic mass has been targeted, fiducial injection is manually accomplished by the endoscopist using a stream of sterile water a stylet. This technique is the only option for preparing delivery of fiducials via the EUS approach. Difficulties associated with fiducial loading and deployment can increase procedure duration due to awkward and inefficient fiducial

back-loading, fiducial misplacement & migration, as well as inability to pass the fidicual marker through the needle due to EUS angulation.

A new mode of fiducial delivery has recently been developed that hopes to avoid some of the technical issues seen with traditional fiducial marker loading and deployment. A 22-Gauge EUS needle preloaded with four fiducials has been tested in animal models, and has showed promising results that may yield improvements in ease of deployment, technical success, accuracy of marker placement, as well as time for placement, reducing overall procedure time.

To date, there is no randomized controlled trials comparing total duration of time needed or effectiveness for placement of fiducials using the traditional back-loading technique of fiducial markers to the new preloaded needles in regards to EUS based fiducial marker placement for IGRT in pancreatic cancer.

You are being asked to be in this research study because you will need fiducial marker placement into your pancreatic tumor prior to receiving IGRT.

Other people in this study

This is a multicenter study involving several academic hospitals around the country. At least 40 people around the country will be in this study.

What happens if I join this study?

If you join the study, you will be randomized to 1 of 2 groups; either the standard of care traditional back-loaded group or the experimental preloaded group.

You will be consented for EUS and have fiducial marker placement performed based on your randomly assigned group. Multiple data will be recorded, including total length of the procedure, how many markers are successfully deployed, and technical success (ease of passage of delivery system, ease of deployment of fiducials, EUS visualization of delivery system needle, EUS visual appearance of fiducials, and time for fiducial placement defined as starting time of removing the needle from its packaging and ending time as removal of needle after final marker deployment). Fiducial marker location will be confirmed via XRAY at time of placement during your EUS.

You will be observed in the post procedure recovery unit and once you have recovered will be discharged home. In the event that you experience and post procedure related adverse events, such as severe abdominal pain, your treating physician will discuss potential admission to the hospital for further observation. You will be contacted at home by a research coordinator or endoscopy staff member 24-48 hours after your procedure, as well as 7-10 days after your procedure to document any immediate or delayed complications from your procedure. Regardless of which treatment group you are assigned to (standard of care or experimental), you will return to the hospital for

your previously scheduled IGRT visit, and any evidence of fiducial marker migration will be recorded by the radiation oncologist. After your IGRT visit, this will conclude your study participation.

What are the possible discomforts or risks?

Discomforts you may experience while in this study include discomforts inherent to the EUS, including abdominal discomfort, nausea, and vomiting.

Other possible risks include risks associated with EUS and fiducial marker placement. Major risks include pancreatitis (inflammation of the pancreas, which can be minor or severe), bleeding, requirement for transfusion due to major bleeding, aspiration, arrhythmia, low blood pressure, organ perforation, infection, or death.

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 can not be guaranteed.

If you become pregnant, the particular treatment or procedures involved in the study may involve risks to the embryo or fetus which are currently unclear and would preclude you from continuing participation in the study.

There may be other risks that are unknown at this time.

What are the possible benefits of the study?

This study is designed for the researcher to learn more about the effectiveness of preloaded needles versus traditional back-loaded needles for fiducial marker placement in patients with pancreatic cancer. You may have the potential of benefiting from shorter duration of your endoscopic procedure (EUS), and possibly subjected to less risk of adverse events if randomized to the treatment arm, although the inverse is also possible. This study aims to answer these questions.

This study is not designed to treat any illness or to improve your health. Also, there may be risks, as discussed in the section describing the discomforts or risks.

Are there alternative treatments?

If you decline participation in the study, you will receive the standard of care for fiducial marker placement via EUS guided placement using back-loaded technique to load the needle.

You should talk to your doctor about your choices. Make sure you understand all of your choices before you decide to take part in this study. You may leave this study and still have these other choices available to you.

Who is paying for this study?

- Wilson Cook Medical INC (Bloomington, IN) is the manufacturer of the preloaded needle used in the experimental group. This company will be supplying the needles and fiducial markers for the procedures in both the experimental and standard of care group at no cost to the patient.
- For all other portions of your procedures, your insurance will be billed.

Other information that needs to be disclosed

The University of Colorado Denver and Dr. Raj Shah, have a financial interest in the success of the study because they hold Inventor/Intellectual Property Rights Ownership with Wilson Cook Medical. Dr. Raj Shah is a Consultant with Wilson Cook Medical and also a co-investigator in this study.

Will I be paid for being in the study?

You will not be paid to be in the study.

Will I have to pay for anything?

You will need to pay for your medicinal procedures through your insurer, such as costs associated with the EUS as well as IGRT.

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?

If you have an injury while you are in this study, you should call Sachin Wani, MD immediately. His phone number is 720-848-2775

We will arrange to get you medical care if you have any 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 researchers carrying out this study are Dr. Sachin Wani and Dr. Joshua Obuch. You may ask any questions you have now. If you have questions, concerns, or complaints later, you may call Dr. Wani or Dr. Obuch at 720-848-2775. 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. Wani or Dr. Obuch 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.

Who will see my research information?

The University of Colorado Denver (UCD) and its affiliated hospital(s) 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 Hospital

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 UCD 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 Investigators (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.

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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.
- People at the Colorado Multiple Institutional Review Board (COMIRB)
- The study doctor and the rest of the study team.
- 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 your information for the research outlined in this consent form. They will also make *all or some* **of the following health information about you collected in this study available to :**

Jason Klapman, MD and Cynthia Harris, MD
Moffitt Cancer Center

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

- Name and Demographic Information (age, sex, ethnicity).
- 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
- Tissue samples and the data with the samples.
- Billing or financial information

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

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

- The data, tissue, blood, or other 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, tissue, blood, or other specimens collected from you.
- If data, tissue, blood, or other specimens are in a form that identifies you, UCD or the hospitals 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 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:_____

Print Name:_____

Consent form explained by:_____ Date:_____

Print Name: _____

Investigator: _____ Date: _____
Investigator must sign within___30 days

Print Name:_____Date:_____

Witness of Signature

Witness of consent process