

Science AMA Series: Hi this is Robert Morhard, Corrine Nief, Carlos Barrero Castedo and Jenna Mueller at Duke University, we're working on developing an ethanol-based treatment for tumor treatment in resource-limited settings. AUA!

Duke-TOSL ¹ and r/Science AMAs¹

¹Affiliation not available

April 17, 2023

Abstract

Our recent publication was recently posted here: https://www.reddit.com/r/science/comments/6xs76y/duke_university_scientists_have_created_a_lethal/. We've been working on this project for three years now and would love to answer any related questions. This project is a combination of global health and biomedical engineering. We're really excited by our most recent proof-of-concept and are planning more exciting experiments. Feel free to just generally ask about anything biology-related as well. Answering questions will be: Robert Morhard, Robert obtained a BS in Biomedical Engineering and Materials Science and Engineering from Carnegie Mellon University in 2012. In 2014 He received an MS in Biomedical Engineering from the Swiss Federal Institute of Technology - Zurich At Duke he works on developing a low-cost ablative tumor therapy for use in resource-limited settings. Corrine Nief Corrine obtained a BSc in Engineering with minors in Math and Chemistry from Baylor University. She was a summer researcher at Oak Ridge National Lab studying protein structure dynamics with super-computing. Later, she studied mitochondrial protein energetics at The National Institutes of Health. Now at Duke, her research is focused on developing low-cost cancer treatments for cervical and breast cancer. Carlos Barrero Castedo Undergraduate researcher, Duke University Jenna Mueller Jenna received a B.S. degree in bioengineering with a minor in global health technologies from Rice University, and completed both an M.S. and Ph.D. in biomedical engineering at Duke University. Currently, Jenna is a postdoctoral researcher, who is interested in the intersection of biomedical engineering and global health. Specifically, she is interested in developing low cost optical devices and therapies to diagnose and treat cervical cancer in resource limited settings. Here is a direct link to our paper: <https://www.nature.com/articles/s41598-017-09371-2> Here is a summary of the paper: <https://www.acsh.org/news/2017/09/03/ethanol-lethal-injection-tumors-11779> We will be back at 1 pm Et to answer your questions, ask us anything!

[REDDIT](#)

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DUKE-TOSL [R/SCIENCE](#)

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CORRESPONDENCE:

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ARCHIVED:

In layman's terms how does your treatment work?

What are the side effects?

How will this effect the industry?

How costly will this treatment be?

How long have you worked/been working on developing this treatment?

September 16, 2017

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[superboyk](#)

This is my first question to answer!

-How does this work - We directly inject a solution of ethyl cellulose (similar to the cellulose in plants) in ethanol. Ethyl cellulose is a unique material in that it dissolves in ethanol, but not in water. When you inject the liquid ethyl cellulose-ethanol solution into the water-rich environment of the tumor it undergoes a phase transition and forms a gel. This gel is a similar consistence to wet wood pulp. This is great for treatment because the gel has a very high ethanol concentration and gets retained well inside the tumor. This means that the tumor cells get a longer exposure to ethanol and are more likely to die.

-Side effects: We're not entirely sure. It seems as though there are minimal side effects according to studies done by other groups in the treatment of varicose veins and herniated discs. It'll take some more research to determine if this is true for tumor ablation as well. We hope it is!

-Effect on industry: We'll have to wait to find out!

-Costly: I can only speak to the current cost of the raw materials, and that's very, very cheap.

-Duration of project: About 2.5 years now. It started off with me spending half of my time on it and now it's turning into a pretty large group of brilliant, determined researchers. It's been a fun transition!

-Rob

First, congratulations, wonderful work!

What types of cancers does the treatment work with, and what kind of side effects can there be if the ethanol gel leaks to healthy tissue?

[turskamuikkunen](#)

-Types of cancers: There will definitely be some damage to surrounding tissue. The ethanol doesn't selectively kill tumor cells, it just kills any cells it touches. We just try to make sure it touches mainly tumor cells. When it leaks out to healthy tissue it will kill that as well. The types of cancer it will work best with is solid tumors that are not surrounded by "essential tissue" (so brain tumors are probably out, liver tumors are good).

Hi guys!! Bio student here.

The discussion says pain was significantly reduced when the injection was made manually. How did you measure that?

You used squamous cell carcinoma in this model, what other cancer models do you plan to test this on?

Isn't it still illegal to treat cancerous tumors in the US with anything other than chemo/radiation/surgery? Do you think this therapy could be used here in the (relatively) near future?

Thanks for doing this!! Congrats on your work and great job.

[sappyjewmovies](#)

Hmm can you send me the part of the discussion that says that?

This model was unique in that these tumors were chemically-induced. What this means is that we apply a carcinogen multiple times a week for many weeks (too many weeks...) and eventually tumors grow. I appreciate the fact that these tumors form "spontaneously" and will be more relevant to tumors we'd treat clinically. The downside of this model is that tumors are constantly forming and growing so it's hard to know if the tumor you treated really went away. We would like to use a different model moving forward to look at that aspect of the treatment.

It's not illegal to treat tumors in the US with things other than chemo/radiation/surgery. Those are just the most effective tools that we have. I think what we're working on now could add to that toolbox.
-Rob

So what you're saying is, "drinking kills cancer." I'm off to practice some preventative medicine!

On a more serious note, what do you think will be the challenges and timeline to getting your treatment out to the general population?

[arestheblue](#)

<http://i.imgur.com/GtRONZ1.gif>

The main challenges are generating the data to assess whether or not this is a safe technique. It's hard to know that until you try it, but you can't try that until you know it. You know?

How soon can human trials begin, and what's the process to get there from this point?

[username revoked](#)

So we first need to show proof of concept and safety in a larger animal model before we can even try it in human tissue. It would be a little longer until full blown human trials could begin. The process is ambiguous though and different for every drug that goes through it. -Corrine

Duke has been getting some decent press regarding cancer treatment lately, especially the group that that is developing the polio based brain tumor treatment theory. Do you guys collaborate at all or share ideas between groups?

[recks1](#)

That research is very interesting! I can't say I completely understand it though.. We don't collaborate with them, though I would love to pick their brain.

Ethanol in mouthwash has been linked to oral cancers. So now should we think of it as "ethanol gives you cancer, and takes it away" Or should we think of it as "ethanol kills everything it touches"?

[coolplate](#)

Ethanol can both give you cancer and kill cells. Overall the consumption of alcohol is a huge risk factor for cancer (either through drinking or through mouthwash).

-Rob

Hi everyone, and thank you for doing this AMA. Two questions for you:

1. What is the development workflow for this project? At some point it will need to be tested in humans, correct? What indications are you targeting, and what is standard of care for these indications? How do you design and enroll these trials, especially considering that the treatment is designed to be cheap, but not necessarily better than the standard of care in the US?
2. What is the advantage of designing a therapeutic specifically to be cheap vs. finding ways (subsidy, donation etc.) to bring currently approved, but often expensive drugs to poor countries?

[SirT6](#)

1. Development workflow: At this stage we've just proved to ourselves and others that this is a viable idea worth investigating. Now we're figuring out how one would go about investigating this. We're moving into other animal models to determine the tissue response to the specifics of the injection, as well as looking at building non-animal models to learn more about how injections work from a more general perspective. We're hoping the combined results from those studies will help us move into humans.
2. Wow, what a great question. And which way is more ethical? I'm not sure. What I can say is that I want to make it cheaper to provide healthcare. I think this can only happen when you start caring about the cost from the beginning of the process. Only time will tell if this is actually a good idea.
-Rob

What would you expect to be the initial skeptic's reaction and how do you plan to address them?

[chizzyman](#)

I think the skeptic would claim that this isn't a cure to cancer. And I agree, this is not a cure to cancer. This a low-cost procedure that can supplement existing therapies. It is especially attractive for use in resource-limited settings (like clinics in developing countries). We'll see how large of a role it ends up playing though. -Rob

Ethanol tumor treatment.

Hearing these words brought in mind a House M.D episode where Dr. House injected ethanol into a tumor to make its size significantly smaller in order to trick the surgeon into believing that the operation would be safe.

I was wondering if your idea was inspired by this, or is it just a coincidence?

[RonitSarangi](#)

Lots of people have been injecting ethanol into tumors, not just House :-). We modified the procedure by reducing the injection rate and adding another component that makes an ethanol-based gel form within the tumor.

How long did it take for people to stop making fun of Robert because of his last name?

[XXX-XXX-XXX](#)

It still happens! -Rob

Do you think that we will ever see stuff like this be actively used over stuff like chemo and radiation? How many years would you say until cancer treatment centers use this?

This news makes me happy, my family has a history of cancer so this is great news

[kanyeBest11](#)

I'm not sure this will be a replacement to chemo and radiation. Those procedures are constantly getting better though.

-Rob

Why would this only be used in resource-limited settings? If it works, shouldn't it be applied in any setting where it's available?

[zycamzip](#)

Well, the unfortunate fact is that it will probably never be better than what we have in high-income countries. So if those resources are available, they should be used to save lives. But I do think it can be comparable and the low-cost and lack of specialized equipment means more people can use it. - Rob

Is there any strain-specific viability optimization? As in: does the treatment work better or worse with different types of tumors?

[901191](#)

Good question. I think it does depend on the type of tumor, but not in obvious ways. For instance, liver tumors generally form from excessive alcohol consumption. When this happens the liver tissue will become scarred and less permeable, but the tumor that forms within the liver is softer and more permeable. So when you inject a solution into the tumor, it basically gets trapped within the tumor, which is exactly what you wanted! In contrast, we tried conventional ethanol ablation (manual injection of pure ethanol into the tumor) on superficial tumors and it didn't work well at all. The fluid just leaked right out. Our "enhanced" version, on the other hand, worked well on these superficial tumors.

-Rob

What types of tumors are you thinking of trying them on ? I'm guessing pretty surface tumors like skin or something you'd be able to assess ultrasound guided without much worry or large complications? Eg thyroid, testicular, breast?

[lefttheovenon](#)

Good question! Initially we were thinking oral cancers and cervical cancer because these can be reached without needing ultrasound or x-ray. But there's no reason it couldn't be used on internal cancers if ultrasound is available. (Pure ethanol ablation has been used on liver cancer, thyroid cancer, adrenal cancer, lung cancer, and others) -Corrine

Hi im a high schooler in NC. I really want to get more involved in research.

I have emailed some professors but never get a response. I have really good extracurriculars and

grades.

Do you have any advice on how to get involved with research and working with duke professors in general.

If you know of any professors needing help or if your open to a high schooler working with you feel free to pm me. I would be happy to send my resume and any other relevant information

[AAL214](#)

I can probably answer this one best! If you live in the triangle area, I would definitely keep emailing professors to find someone that may be willing to take you on. If not, it can be really hard to do meaningful research for you or your PI if you're not physically present. I would look into schools closer to where you live and try to get involved there. It'll give you a look into research, and can help you decide if that's something you'd like to pursue further once you get into college!

-Carlos

Have you tried with human cancer cell lines in animals (instead of endogenous tumors) ?

[agumonkey](#)

We have shown that it kills human cancer cell lines in vitro, and we are currently doing a study with xenografts of HeLa cells in mice. We expect that the endogenous tumors are more similar to the clinical scenario though. -Corrine

Have you (or others) investigated using the ethanol gell as a vehicle for intratumour drug delivery, giving slow release of drug within the tumour?

[buttwarm](#)

Great idea, buttwarm! We haven't investigated it yet. It would be especially useful for hydrophobic drugs that are difficult to deliver otherwise. It would be a challenge because you'd also be inducing a lot of necrosis near the injection site. But maybe that's what you want? -Rob

So, why was there such a huge difference in results between the control group injected with only ethanol in comparison to the group injected with the ethanol gel. That is, what makes the ethanol gel so much more effective than pure ethanol?

[fightmeee](#)

Great question. Without the gel, the injected solution doesn't cover as much of the tumor because it leaks out of the tumor and won't be as effective. The gel reduces how much of the injected solution leaks out and increases the number of cells it contacts. This makes it more effective.

-Rob

From the discussion section:

...there are several limitations to this study. First, the use of a chemically-induced tumor model (in which spontaneous tumors arising in sites adjacent to a treated site would be indistinguishable from the original tumor) precluded the possibility of any long-term monitoring of tumor recurrence.

What kind of model would allow you to monitor long-term recurrence?

Thanks for the work you do!

[snOrthway](#)

Good question, monitoring long term recurrence is difficult in animal models. Ideally, you find animals that already have tumors and you treat them and wait for recurrence. It's like clinical trials for pets. Or you can do a tumor graft into animals and monitor for recurrence. This is done much more often because it's easier to control for tumor type and location. -Corrine

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[snOrthway](#)

Good question! The challenge is that we want to use a model with an intact immune system and it should have a large enough body mass that we can treat larger tumors (that therefore require more ethanol). Corrine is in charge of that part of the project :-)

-Rob

Does your treatment have any plans to cooperate with radiation therapy or chemotherapy as a sensitizer to tumors or anything like that? I work in rad onc and I'm curious if there could be any cooperation between the treatments.

Edit- I see above you talk about replacing surgery, but what about other Non-invasive techniques like I'm suggesting?

[buckeyebandguy](#)

That's an awesome idea that we'd love to investigate further. For now we're focused on cervical precancer treatment in resource-limited settings. By focusing on one specific clinical indication I think we maximize our chances of making the transition to the clinic. There are lots of details to work out.

What effect does the alcohol gel have on the vasculature? If you had to hazard a guess, would it work in tandem with liposome-delivered chemotherapy agents to enhance the enhanced permeability and retention effect (EPR)?

[HolyPotato](#)

I think it damages endothelial cells in the vasculature and would basically shut down blood flow to the tumor. Since liposomes are generally injected systemically, shutting down access to the tumor would not be ideal.

What is the layman's understanding of how the gel goes about 'curing' the tumors?

[BBBelmont](#)

Ethanol kills cells that it touches. Adding ethyl cellulose to the ethanol makes the gel form within the tumor. The gel keeps the ethanol from leaking away and makes it touch more cells. Since it touches more cells, it kills more of the tumor. The more of the tumor it kills, the more likely the tumor is to die completely.

-Rob

It seems many cancer treatments must be paired with surgery to have a chance of a cure. Is this true if your treatment?

[ThetaThetaTheta](#)

I'd actually imagine this more as a replacement for surgery rather than something we'd pair with it. But we'll have to wait and see.

Given the pain associated with an ethanol injection, could a local anesthetic be added to the formula to mitigate this?

[Hydropos](#)

Great idea! You might want to inject the anesthetic before the ethyl cellulose-ethanol to give it time to kick in.

How many undergraduates are you working with?

[seven_ensi](#)

We currently only have one undergraduate that's willing to put up with how crazy we are. -Rob

Congratulations! How would one be able to join in this research? Lend a helping hand, be a research assistant? I am genuinely curious as I am a medical student and finding research opportunities is not that easy.

[Pleasebeunique27](#)

I'm a PhD student, so this project started off from lots of reading and discussions with my PI (Dr. Ramanujam, she runs my lab). I pitch her lots of bad ideas, but we agreed that we should try ethanol ablation. We've been working on the project for 2.5 years now and our team has gotten much larger, it's been a lot of fun!

As a Med Student I'd imagine there are opportunities within the medical school. I'm sure you could spend a year or two doing research after you get your MD. Just email professors who's work you're interested in and ask if they have any space for you in their lab. You'll get lots of no's, but just keep asking! -Rob

Awesome stuff to see this idea getting tested!

I'm a grain inspector who deals with a fairly large ethanol production facility in east-central Illinois. If this

proves more effective than initially anticipated, do you believe it could be adopted for mainstream use, even in areas where other methods are readily available? Would this require enough ethanol to change the market or necessitate a specialised ethanol variant as opposed to petroleum-blended ethanol?

Thanks!

[ledzepp3](#)

Great question! I'm not sure the volume would high enough to drastically change the market. It requires very little ethanol per treatment.

Hello. Have you considered the impacts of alcohol detoxification on the DNA damage repair mechanism when using alcohols to treat solid tumors?

For example, have you done any research on the effect of treating FA patients who develop solid tumors?

[potatorunner](#)

Hmm we haven't looked into that but it might be interesting.

So how exactly does this differ from older ethanol treatments? I haven't found any explanation as to the differences. I've known at least one individual receiving ethanol treatments at least as far back as 2007.

[The-link-is-a-cock](#)

We added ethyl cellulose and reduced the injection rate. This modifications increased efficacy in the hamster oral tumor model.

Has anyone made the joke to you yet that the right alcohol can solve anything? Because if not use that joke when you meet someone who asks what you do for a living.

[sowhiteithurts](#)

Haha sorta like this: <http://i.imgur.com/GtRONZ1.gif> ?

What barriers, if any, will there be to performing clinical trials? Any problems that you foresee preventing the treatment from going to clinical trials/market?

[theuberchemist](#)

I tried to articulate this in a previous post, but we just need to get more evidence that this is safe. That evidence is hard to get because we try to minimize our use of research animals. It's a difficult process to figure out! -Rob

What do you do to the tumor after you kill it? Do you leave the ethanol gel in the body? Or do you remove it dead tumor and gel afterwards?

[Lowestprimate](#)

We don't plan on removing it afterwards. After the tumor becomes necrotic, it somehow gets cleared by the immune system. We're not really sure how the ethyl cellulose is metabolized.

What is the worst case scenario for using this treatment, i.e. could the cancer worsen due to an mistake in the preparation or procedure?

[ALSX3](#)

Worst case is the ethyl cellulose gets into the blood and causes issues in other organs. Seems like that doesn't happen based on previous studies that treated venous malformations and herniated discs, but more research is necessary.

How do you deal with people who dismiss your research, saying "ethanol is not patentable, 'Big Pharma' is going to bury your results?"

[mrhoof](#)

I try to just focus on the details of how to best design this procedure to maximize efficacy and hope that we can just worry about those details later. Too much to think about all at once!

Does this work in all kinds of tumor in people or in animals? Is this just pure ethanol or any chemicals are involved?

[lenvastra](#)

We'll need to do more studies to determine whether this works in humans, though I think it will. We add a cellulose-derivative called ethyl cellulose to the ethanol. This is why it forms a gel in the tumor. Ethyl cellulose is currently used as a food additive.

-Rob

Hasn't it been proved that ethanol only shrinks tumors temporarily?

[DocLevi](#)

I don't think that's true.

Hi Corrine!

You and your team are awesome, and sic'em bears!

[cjoyful](#)

Thanks! :)

have you thought about using hydrogen dioxide as a tool?

[PrinceParadox](#)

Great question, maybe that would work as well. Ethanol is exciting because it means we can use ethyl cellulose with it. When you combine the two it forms an ethanol-based gel within the tumor, which makes it much more effective.

Does this work for solid tumors only?

[TheNewAges1](#)

We have only tried our method on solid tumors. Pure ethanol ablation has been used successfully on liver and thyroid tumors so there is no reason it couldn't be used on these as well. It's just an injection so anywhere that a needle could deliver the ethanol to is a possibility.

Where does the ethanol come from?

[StripperStank](#)

We inject the ethanol along with ethyl cellulose directly into the tumor.

What influenced you to make it??

[captinepicfail1](#)

Our lab had been working on developing screening technology for cervical cancer. Our PI (Dr. Ramanujam, she leads our lab) wanted to develop a low-cost treatment mechanism because what's the point in expanding access to screening if you can't adequately treat those people? So we started investigating and doing lots and lots of reading. After many bad ideas we started down the path of ethanol ablation. After lots of failures we ended up with "enhanced" ethanol ablation, which seems to work thus far!