Podcast Interview: Robert Langer and Steven Zeitels

PNAS: I’m your host Prashant Nair and welcome again to Science Sessions. For people whose livelihoods depend on their voices, damaged vocal cords are a pressing problem. Whether one’s a reporter for National Public Radio, an Academy Award-winning actress, or a world-renowned rock musician, losing voice can seem calamitous. Which is why, for many years now, physicians have used synthetic materials to restore the function of vocal cords damaged by a number of factors, such as accidents during surgery, laryngeal cancer, or even infections. At Harvard Medical School, laryngeal surgeon Steven Zeitels partnered with National Academy of Sciences Member Robert Langer, a bioengineer at MIT, to develop a polymer gel that can restore the function of scarred vocal cords. I recently sat down with the team to talk about the material that can help patients regain their normal voices. Here, Langer describes the voice-restoring gel.

Langer: The polymer gel is made out of a polymer called polyethylene glycol, which is a polymer that’s been used in a number of products in human beings, and we do what we call cross-linking, which is the same kind of thing that people do in tires. What we do is we make something that’s a little bit like gelatin, maybe a little bit stronger. We actually adjusted the properties so that it would be similar to that of the material in a vocal cord.

PNAS: Repairing scars on vocal cords is a devilishly difficult task, so there are two main approaches to helping patients regain vocal cord function. One is to develop a synthetic material that mimics the properties of vocal cords and another is to engineer artificial vocal cord tissue. That approach, Zeitels says, is much more technically challenging than the first.

Zeitels: We don’t personally believe that someone is going to alter scar to be soft. What they might do is place something like a type of cell between the scar and the basement membrane of the epithelium, and that may generate extracellular matrix proteins, which in turn may have the mechanical properties. But that’s a big leap. We then said, okay, we want to identify a material that is already acceptable in the human body and then try to find something that is tunable for different voices because different voices have different vibratory needs and characteristics.

PNAS: Zeitels and Langer tested their polymer gel formulation in dogs in which it appeared not to trigger adverse side effects. The formulation, Zeitels says, can be tailored to patients’ needs.

Zeitels: A material for a high-performing singer needs to do [mimes high-pitched croon]. Well, that’s a very different material than someone who has to talk fairly monotone and teach in a classroom. So the beauty of this is, if somebody needs to go on stage for a few days because they have a cold, they will have one formulation. In another formulation, it might be someone who doesn’t
have vocal cords at all, who uses their false cords to speak [mimes bass falsetto], and they’re going to always speak monotone, but the material may last for 8 months. So we wanted tunability to cater it to patients’ needs as well as the practicality of how many injections might you want to do in a specific period of time. We’re accepting the fact that it will dissolve, and the key for a lot of our work was to know that as this material dissolved, it did no harm because we knew the future would be reproducibility. Remember, the people that we’re treating...these are folks who sound like this [mimes feeble, breathy tone] because there’s no deformability of the tissue. In fact, one of the great populations to work on are people who don’t have vocal cord function at all.

PNAS: So, how did Zeitels determine that the polymer gel was indeed effective?

Zeitels: We knew if it worked in a normal environment and the vocal folds were still oscillating and deforming that the material had to be soft enough. With all these other materials that have been injected for years, whenever they go into this layer, it actually destroys the vibratory capabilities. And this did not.

PNAS: Zeitels reiterates that injecting synthetic substances into vocal cords to help restore voice is no novelty.

Zeitels: There is a long track record of unusual materials that have been put in vocal cords. In essence, what we’re doing is not a new procedure; it’s a 100-year-old procedure. It’s just most of the time implants were just put in different areas of the vocal cord. But no one that we know of has looked towards this approach with a synthetic material that is not designed just to be a volume expander. In that model, you’re moving the mass of the vocal cord over and assuming the surface has appropriate pliability. This is actually moving over the surface a little bit because you’re filling the mucosa, but primarily you’re altering the mechanical deformation, or its ability to do so with air flow.

PNAS: Zeitels plans to conduct clinical trials of the gel in a small number of patients. If the gel is approved, he estimates that a single injection of the gel, or less than a cc, might suffice for a few months and cost far less than medical devices like hearing aids. Langer’s former postdoc Sandeep Karajanagi, who helped develop the gel, says the team is poised for the trials.

Karajanagi: We have defined a lot of process parameters that the FDA mandates. We in fact showed our initial plan to the FDA as well, and they were pretty much on board on our plans, and we continue to work towards that right now. And we believe early 2013 we should be hopefully in clinical trials.

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