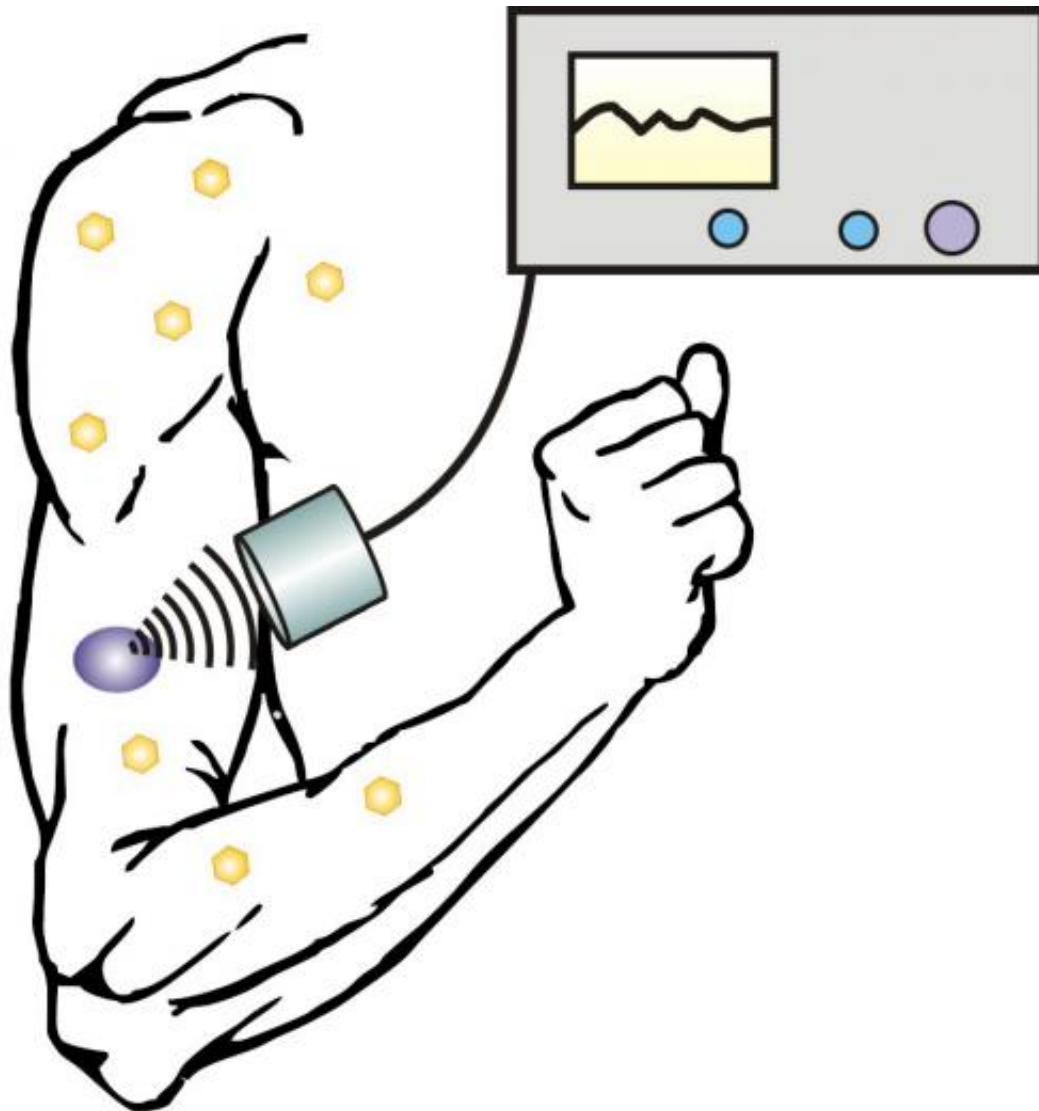


Ultrasound, nanoparticles may help diabetics avoid the needle

November 21 2013, by Matt Shipman



A new technique allows diabetics to control insulin release with an injectable nano-network and portable ultrasound device. Credit: Zhen Gu, North Carolina State University

A new nanotechnology-based technique for regulating blood sugar in diabetics may give patients the ability to release insulin painlessly using a small ultrasound device, allowing them to go days between injections – rather than using needles to give themselves multiple insulin injections each day. The technique was developed by researchers at North Carolina State University and the University of North Carolina at Chapel Hill.

"This is hopefully a big step toward giving diabetics a more painless method of maintaining healthy [blood sugar](#) levels," says Dr. Zhen Gu, senior author of a paper on the research and an assistant professor in the joint biomedical engineering program at NC State and UNC-Chapel Hill.

The technique involves injecting biocompatible and biodegradable nanoparticles into a patient's skin. The nanoparticles are made out of poly(lactic-co-glycolic) acid (PLGA) and are filled with [insulin](#).

Each of the PLGA nanoparticles is given either a positively charged coating made of chitosan (a biocompatible material normally found in shrimp shells), or a negatively charged coating made of alginate (a biocompatible material normally found in seaweed). When the solution of coated nanoparticles is mixed together, the positively and negatively charged coatings are attracted to each other by electrostatic force to form a "nano-network." Once injected into the subcutaneous layer of the skin, that nano-network holds the nanoparticles together and prevents them from dispersing throughout the body.

The coated PLGA nanoparticles are also porous. Once in the body, the insulin begins to diffuse from the nanoparticles. But the bulk of the insulin doesn't stray far – it is suspended in a de facto reservoir in the subcutaneous layer of the skin by the electrostatic force of the nano-

network. This essentially creates a dose of insulin that is simply waiting to be delivered into the bloodstream.

When a patient has type 1 or advanced type 2 diabetes, his or her body needs additional insulin, a hormone that transports glucose – or blood sugar – from the bloodstream into the body's cells. These diabetes patients must inject insulin as needed to ensure their [blood sugar levels](#) are in the "normal" range. However, these injections can be painful.

Using the new technology developed by Gu's team, a diabetes patient doesn't have to inject a dose of insulin – it's already there. Instead, patients can use a small, hand-held device to apply focused [ultrasound waves](#) to the site of the nano-network, painlessly releasing the insulin from its de facto reservoir into the bloodstream.

The researchers believe the technique works because the ultrasound waves excite microscopic gas bubbles in the tissue, temporarily disrupting nano-network in the subcutaneous layer of the skin. That disruption pushes the nanoparticles apart, relaxing the electrostatic force being exerted on the insulin in the reservoir. This allows the insulin to begin entering the bloodstream – a process hastened by the effect of the ultrasound waves pushing on the insulin.

"We know this technique works, and we think this is how it works, but we are still trying to determine the precise details," says Dr. Yun Jing, an assistant professor of mechanical engineering at NC State and co-corresponding author of the paper.

When the ultrasound is removed, the [electrostatic force](#) reasserts itself and pulls the nanoparticles in the nano-network back together. The [nanoparticles](#) then diffuse more insulin, refilling the reservoir.

"We've done proof-of-concept testing in laboratory mice with type 1

diabetes," Gu says. "We found that this technique achieves a quick release of insulin into the bloodstream, and that the nano-networks contain enough insulin to regulate blood glucose levels for up to 10 days."

"When the insulin runs out, you have to inject a new nano-network," says Jin Di, lead author of the paper and a Ph.D. student in Gu's research lab. "The previous nano-network is dissolved and fully absorbed into the body in a few weeks."

"This advance will certainly give millions of people with diabetes worldwide hope that better days are ahead," says Dr. John Buse, director of UNC-Chapel Hill's Diabetes Care Center and deputy director of UNC-Chapel Hill's NIH Clinical and Translational Sciences Award. "We must work to translate these exciting studies in the lab to clinical practice."

More information: The paper, "Ultrasound-Triggered Regulation of Blood Glucose Levels Using Injectable Nano-Network," is published online in *Advanced Healthcare Materials* and was selected as a cover article. [onlinelibrary.wiley.com/doi/10 ... m.201300490/abstract](http://onlinelibrary.wiley.com/doi/10.1002/adhm.201300490/abstract)

Abstract

An on demand, non-invasive and portable insulin delivery method that can achieve pulsatile insulin release and effective regulation of blood glucose is highly desirable for type 1 and advanced type 2 diabetes administration. We report that integration of an injectable nano-network with a focused ultrasound system (FUS) can remotely regulate insulin release both in vitro and in vivo. Serving as a synthetic insulin reservoir, the nano-network consisting of adhesive poly(lactic-co-glycolic acid) nanoparticles significantly promoted insulin release upon intermittent FUS triggers. Remarkably, a maximum of 80-fold increase in the insulin release rate was observed when the nano-network was exposed to the irradiation of ultrasound for 30 sec. In vivo studies validated that this

method provided repeatable and spatiotemporal regulation of blood glucose levels in Type 1 diabetic mice. A single subcutaneous injection of the nano-network with intermittent FUS administration facilitated reduction of the blood glucose levels for up to 10 days.

Provided by North Carolina State University

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