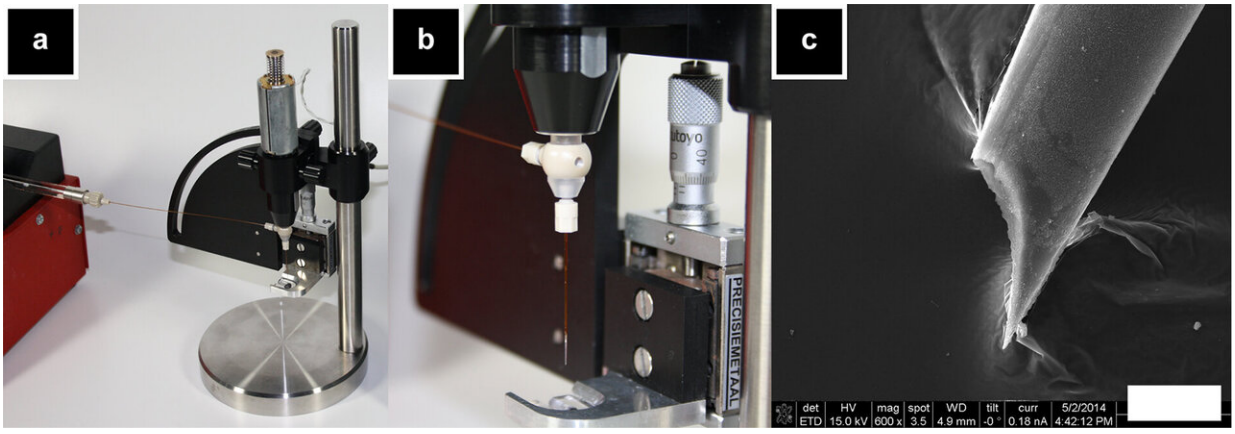
One step closer to pain-free vaccinations

June 20 2019, by Hilde Pracht



A hollow micro-needle and applicator. Credit: Pim Schipper

Micro-needles are a promising tool for the painless administration of vaccines through the skin. But, are these minuscule needles really effective? Ph.D. student Pim Schipper of the Leiden Academic Centre for Drug Research investigated various factors of vaccination via the skin and discovered, among other things, that the injection depth is not important and that it is better to spread the vaccine dose over several days.

Painless and effective?

Vaccination is normally performed by injection into the muscle. However, our skin contains many more immune cells than our muscles.

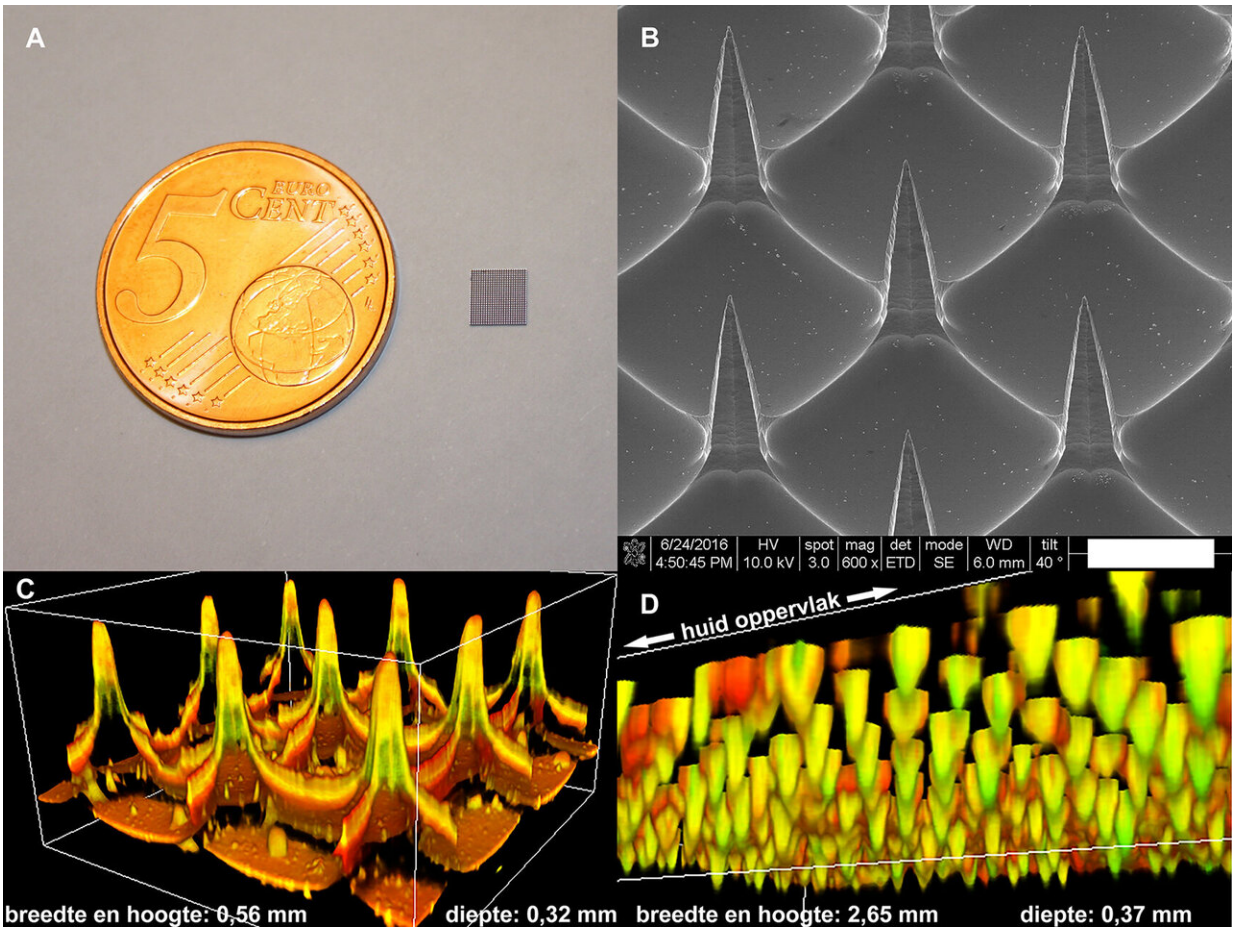
That is why researchers think that vaccination through the skin may be much more efficient than the traditional method. This new vaccination method uses micro-needles: tiny needles that only penetrate the upper layers of the skin. Therefore, this method is also painless.

However, there is still a lot of discussion as to whether vaccination with micro-needles is truly more efficient than the traditional routes, and about the best way to administer vaccine via micro-needles. "We investigated various factors of vaccination through the skin in order to be able to answer this question," says Schipper.

Micro-needles

micro-needles are tiny needles of only hundreds of micro-metres in length; they are smaller than a millimetre and (almost) not visible to the naked eye. There are two types of micro-needles: hollow and massive. A hollow micro-needle resembles a normal injection needle with a pointy tip and a hollow tube through which liquids can flow. Using an applicator, you can insert the hollow micro-needle into the skin at a precise depth. A pump then initiates the injection.

Solid micro-n needles are placed in rows on a plate, called an array. The needles protrude from this plate. The length of the micro-needles and thus the injection depth is determined during production. Solid micro-ns are coated with a vaccine. After they have been inserted into the skin, the coating is released and the vaccine remains in the skin upon removal.



Upperleft: array with solid micro-needles and a nickel. Upperright: an enlarged picture of the micro-needles. Lower left: the same micro-needles but coated. Lower right: an image of the skin after the application and removal of coated micro-needles. Credit: Pim Schipper

Depth doesn't matter

"First of all, we discovered that there is no connection between the injection depth in the skin and the immune response that follows," says Schipper. "In short: for vaccination through the skin, it does not matter how deep you insert the needles." As a result, there are no strict requirements for the design of the micro-needles. That's good news: it

simplifies the design and ultimately reduces costs. "Until now, this had never been investigated. But the device we have developed can insert our hollow micro-needles into the skin at a precise depth and then accurately inject a fixed volume," explains Schipper.

Imitating infection

In addition, Schipper and his colleagues also discovered that the vaccine is more efficient if you spread the dose over several days. "In this way, you simulate a natural infection during vaccination," he explains. The technique proved to be very efficient: "The immune responses increased to such an extent that a so-called adjuvant was no longer necessary. An adjuvant helps the immune system to process the vaccine. Omitting this addition saves costs and simplifies the formulation of the vaccine." Moreover, some adjuvants are not suitable for vaccination through the skin. A method that makes adjuvants redundant, would therefore be very beneficial for the development of injections in the skin.

New method

In addition to testing various injection techniques, Schipper and his colleagues also developed a new technique for the coating of solid micro- needles. They applied a vaccine for diphtheria layer by layer to a set of needles. "By choosing how many layers you apply, you can determine exactly how much diphtheria vaccine is ultimately released to the skin," explains Schipper. Due to the limited surface area of the micro-needles, only a limited dose of vaccine can normally be applied and administered. Thanks to the layer-by-layer method, it is now possible to apply enough vaccine to vaccinate not only animals but also people with coated solid micro-n needles. This makes it possible to test the micro-n needles in clinical studies.

Vaccination against diphtheria through the skin turned out to be even more effective than via the traditional route. "With this vaccine, we can therefore save dose—and therefore costs and scarce vaccine material—by vaccinating through the skin. In this way, painless vaccinations by means of micro-needles are one step closer."

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