A pain-free window into painful neuropathies

December 5 2007

Scientists have demonstrated a new technique for detecting a painful nerve condition known as neuropathy, which affects millions of people with diabetes and many other patients as well.

The painless technique focuses on tiny structures in the skin known as Meissner corpuscles, which encapsulate the endings of microscopic nerves in our hands, feet, and other areas. When someone tickles your feet, or lightly brushes the palm of your hand, or gives you a kiss – it's Meissner corpuscles that are detecting the touch. The tiny structures act like little sensors, allowing us to feel light touch and pressure.

Now a neurologist at the University of Rochester Medical Center, working together with scientists from Lucid Technologies in Rochester, N.Y., has demonstrated a new way to monitor the structures, which offer a direct window into a condition known as peripheral neuropathy. The team showed that reflectance confocal microscopy, a technology for looking just beneath the surface of the skin, can be used to see and count the number of the structures in a person's fingers and hands. The work gives doctors a non-invasive way to detect and monitor the progression of nerve damage in patients.

The research appears in the December 4 issue of the journal *Neurology*.

Doctors have known that the number and density of Meissner corpuscles in a person's hands and feet offer a snapshot into the degree of a patient's nerve damage. As nerves degenerate and die, the corpuscles

disappear. The difficulty has been actually visualizing and counting them.

Currently, doctors take a small biopsy of the skin, freeze and stain the tissue, and then count the structures. Neurologist David Herrmann, MBBCh, the lead author of the Neurology paper, helped develop and popularize skin biopsy about 10 years ago as a way to keep close track of the condition of nerves in patients. At the time, for some forms of peripheral neuropathy, it was a big improvement over previous methods, which required a much larger biopsy of a large nerve.

Even so, “Taking a small piece of skin is not ideal,” said Herrmann, associate professor of Neurology and of Pathology and Laboratory Medicine. “It can be painful for the patient; the processing can be time-consuming; and it’s impossible to measure the exact same area of skin year to year to track the progression of the disease.”

A few years ago Herrmann met a scientist from Lucid, a medical device and information company that is creating tools for physicians based on innovative technologies such as confocal microscopy. The technology uses light to actually look beyond the surface of skin tissue into the layers of skin below. The technology is being used more and more to track skin cancers and to look at tissue samples in the operating room.

Herrmann and the Lucid team began a study of some of the tiniest nerves in our body, those that reach into the furthest reaches of our hands and feet. Damage to those nerves leads to a variety of troublesome symptoms for the millions of Americans who have some type of peripheral neuropathy. Symptoms in the feet and hands can include numbness, burning, tingling, weakness, and pain.

While diabetes is the most common cause of neuropathy, it’s caused by a variety of other conditions as well. Patients with HIV are prone to

getting it. Excess alcohol consumption can bring it on, as can some vitamin deficiencies, cancer treatments, and dozens of inherited disorders, most notably Charcot-Marie-Tooth disease.

“These patients are often dismissed, and many really suffer,” said Herrmann. “Diagnosis is often difficult. The small nerves in the skin are basically invisible to standard techniques for checking the function of a person’s nerves, such as conduction tests.”

So Herrmann lined up 15 little pinkies – well, 15 research subjects willing to put their little pinkies under the microscope. The group included 10 healthy people, and five who had neuropathies from various causes, such as diabetes or HIV.

The researchers found, as expected, that the healthy volunteers had many more Meissner corpuscles in the tip of the pinkie finger – about 12 such structures per square millimeter, compared to a mean of 2.8 in people with neuropathy. Patients with neuropathy also had fewer of the structures at the base of the thumb.

While the results were not surprising, attaining them so easily was. Volunteers simply held their pinkie finger under a microscope for a few minutes. No pain, no blood, no tissue preparation.

In an editorial about the research, Peter J. Dyck, M.D., of the Mayo Clinic wrote in the journal, “The approach may find use as the gold standard of tactile sensation and of large fiber sensorimotor polyneuropathy.” But he also pointed out some limitations of the work. Dyck said the technique needs to be tested in greater numbers of people, pointed out that the equipment needed for reflectance confocal microscopy is expensive, and mentioned the need to differentiate between healthy and abnormal Meissner corpuscles.

An advance in screening would be appreciated by millions of patients. More than half of people with diabetes will eventually develop neuropathy. Most of them won't feel pain – they'll simply lose sensation in their feet, making them vulnerable to wounds that can result in severe infections. Oftentimes sensation slips away so gradually that patients don't even notice. A new screening tool would help doctors monitor patients more closely so that both they and patients are aware of nerve damage and can do everything they can to prevent further damage.

"Neuropathy is very difficult to treat, and part of the reason is that currently, we usually identify it too late, after there has been significant damage," said Herrmann, director of the Peripheral Neuropathy Service at Strong Memorial Hospital. "Treatments might be more beneficial if we could detect the condition earlier.

"The idea is to move from an invasive biopsy for monitoring nerve endings, to non-invasive, painless approaches. A person could have this technique done as frequently as is necessary, for instance. That's an attractive notion for tracking the condition of nerves in patients," said Herrmann, who is now assessing the technique in 75 people, with funding from the National Institute of Neurological Disorders and Stroke.

Source: University of Rochester