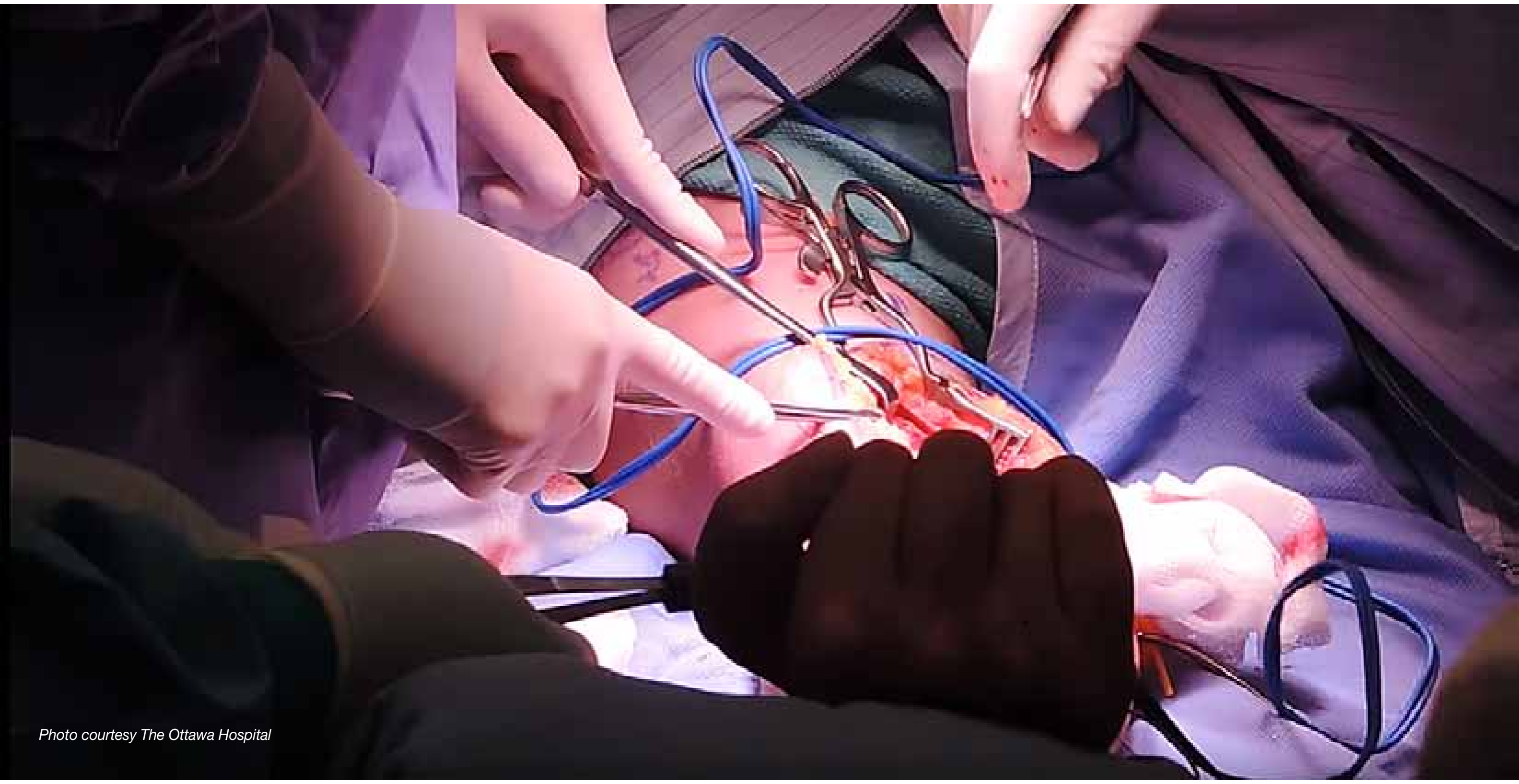

Photo courtesy The Ottawa Hospital

Getting Your Wires Crossed

A new study validates nerve transfer surgery as a way of improving hand function for some people with quadriplegia, just as the procedure debuts in Canada.

"Victory is won not in miles but in inches. Win a little now, hold your ground, and later, win a little more."

— Louis L'Amour

Cowboy fiction writer Louis L'Amour probably wasn't thinking about SCI when he wrote that iconic quote, but it's certainly appropriate.

Case in point: nerve transfer surgery to restore modest amounts of function and strength for people with C6 – C7 quadriplegia. It's far from being a cure for SCI, but that doesn't make any of its recipients any less enthusiastic about it—while the handful of people who have had the procedure report incremental improvements in function, they say those improvements have resulted in huge improvements in their quality of life.

Essentially, the surgery involves connecting a nerve in the arm that is healthy, but not functioning because it emerges from the spinal cord below the injury site, to another nerve in the arm that is fully functioning because it originates above the injury site in the spinal cord. The result in most cases is reestablishment of some communication between the brain and the paralyzed arm or hand muscle being targeted. (Note that this description is greatly simplified—please see page 31 for a detailed explanation of how this surgery is performed and why it's successful for some patients.)

The surgeons who helped pioneer the procedure published the promising results from nine patients with quadriplegia in the October 2015 issue of the American Society of Plastic Surgeons' journal *Plastic and Reconstructive Surgery*. Meanwhile, the procedure has recently been adopted by a surgeon in Canada, with others considering offering it in the future. So with compelling evidence and emerging availability, nerve transfer surgery may be an attractive option for some readers of *The Spin*.

It's fitting that the procedure has found a home in Canada, as it was actually developed by a Canadian. Dr. Susan Mackinnon is a graduate of Queen's University in Kingston who moved in 1982 to the USA, where she has earned a reputation as one of the country's leading plastic and reconstructive surgeons.

Now the Chief of Plastic and Reconstructive Surgery at the Washington University School of Medicine in St. Louis, Mackinnon started exploring nerve transfer surgery in 1988. For years, she and her colleagues used the procedure to restore movement in the foot or an arm of patients with injured peripheral nerves. But about five years ago, she and colleague Dr. Ida Fox began to employ the technique to restore some limited hand function in patients with SCI. Since then, a number of quadriplegics from across the USA have had the procedure.

One of those who have benefitted is a physician himself, and a colleague of Fox and Mackinnon at the Washington University School of Medicine. Dr. Michael Bavlsik was injured in a car crash in 2012. After the surgery, Bavlsik regained the ability to grip with his left hand—essential for his work as a doctor and assistant professor.

"Nerve-transfer surgery has been very successful in helping me because it restored triceps function and improvement in my grip," says Bavlsik. "I am extremely grateful for this surgery."

Bavlsik's surgery, along with that of eight other recipients, was reviewed in the *Plastic and Reconstructive Surgery* journal article. The other eight also reported various levels of improvement in hand and arm function. The conclusions, as summarized in the article's abstract, leave little doubt that the technique can provide significant benefits. "Nerve transfers can provide an alternative and consistent means of re-establishing volitional control of upper extremity function in people with cervical level spinal cord injury," wrote the authors. "Early outcomes provide evidence of substantial improvements in self-reported function despite relatively subtle objective gains in isolated muscle strength."

No doubt, the results of the study will create demand from more quadriplegics. Which brings us to you, the reader who is quadriplegic and might do just about anything to get enough grip or pinching strength to eat, self-cath, write, or button up clothes. No doubt you're wondering, "Well, when can I get this surgery?"

The answer is, perhaps you already can, providing you meet the criteria.

In February 2015, Dr. Kirsty Boyd, a plastic surgeon at The Ottawa Hospital, performed the surgery on two patients—44-year-old Tim Raglin, and 21-year-old Brett Nugent. Nugent and Raglin became the first Canadians to receive the operation, and it was also the first time the surgery had been performed in Canada.

Raglin, who became quadriplegic in a diving accident six years ago, can take credit for getting the ball rolling. When he learned about the procedure in 2013, he asked his physiatrist if he could get it done in Ottawa. In turn, his physiatrist referred him to Boyd. As it turned out, Boyd knew Mackinnon well—she had completed a year-long surgical fellowship with her in 2011, with the focus on nerve transfers. So she agreed to give it a try.

Boyd relied on Dr. Gerald Wolff, cofounder of Ottawa's Peripheral Nerve Trauma Clinic, to determine if Raglin was an ideal candidate. Wolff gave

NERVE TRANSFER PIONEERS: Brett Nugent (left) and Tim Raglin are Canada's first recipients of nerve transfer surgery to restore hand function in people with quadriplegia. After a year's wait, both are now beginning to experience some restoration of function.

the green light for Raglin, and also for Nugent, a quadriplegic as the result of a hockey accident who had been approached to see if he was also interested.

When the procedures were done last February, they were completed under the watchful eye of both Mackinnon and Fox, who travelled to Canada on their own dime to supervise Boyd's first two attempts at the procedure. By all accounts, both surgeries went flawlessly, and both Raglin and Nugent returned home to patiently wait for any signs of improvement—something that can take up to a year to show up.

Why so long? "The distance required for the nerve to regrow inside its new route and reach the new muscle is such that we would not have expected to see any changes within the first six months," says Boyd. "If the procedure is successful, then one may notice slow gains between six months and three years post-operatively."

Fast forward to February 2016, when we reached Nugent and Raglin in Ottawa to talk about their surgery, and their progress to date.

"It took about three hours and went perfectly," says Nugent. "I healed quickly and had no complications. I was wheeling around on my own in about three weeks, and was back to playing (rugby) in about a month."

Raglin's surgery also went smoothly.

But what about results? As predicted, both are showing signs of success.

"The first little things that I noticed that kind of tipped me off about the transfer beginning to work was the fact that my fingers began to tighten up," says Nugent, a university student who leads an active lifestyle. "Before they remained fairly loose and my hand stayed a little more open but now it tends to keep a more closed grip position. I'm not quite sure when this started since change is slow, but I would say around three months ago or so I noticed this. Now I notice I can tighten my grip in my hand a little more on my own, and it continues to get much stronger. Looking forward, I'm hoping to see more change in the opening of the hand as well."

For Raglin, the first sign happened during a therapy session just before Christmas when he noticed a slight twitch that he thought at first was simply a spasm. "It was only after sitting with the therapist that I realized it was actually me making my fingers move," he says. "From that point on, we've seen very small incremental movements that are controlled by me. Basically, I can open my fingers slightly more than I could before Christmas and I have

BC's Own Nerve Transfer Pioneer

If you're interested in having nerve transfer surgery, Dr. Sean Bristol and his team are likely your best (and only) option here in BC. Bristol is an Assistant Professor in UBC's Division of Plastic Surgery, and a clinical researcher conducting studies related to his plastic surgery clinical practice. Among his areas of interest and specialization is nerve and tendon surgery to restore hand function.

"I got into nerve transfer surgery generally because of the capabilities it provides over and above nerve grafts," says Bristol. "And we've never really had an option for tetraplegic patients before. The expansion of the nerve transfer into that field is exciting because it's about gaining more function where we never thought there could be any before."

Bristol and his colleagues have recently started a clinical trial to evaluate the impact of nerve transfer surgery for people with tetraplegia. But the specific surgery is somewhat different than the procedure that Dr. Boyd provided to Tim Raglin and Brett Nugent, as described in the main story. It involves transferring a nerve from the supinator muscle (the nerve is called a supinator motor branch) to the posterior interosseous nerve, or PIN, which is a nerve in the forearm that controls the muscles that allow us to extend or flex our fingers and thumb.

"The benefit is that (partipants) will be able to extend their fingers and thumb, in order to grasp some larger objects," explains Bristol. "The great difficulty getting fingers and thumb out of the way without having to use the wrist as a fulcrum is challenging for the tetraplegic patient, and that's one that (surgeons) can't do well for using tendon-based operations. That's why we decided to focus on this procedure."

The first of five participants in Bristol's trial had the surgery just after Christmas. As with all nerve transfer surgeries, it will be months before any benefits materialize. Bristol explains that the ultimate goal will be to determine the quality of life impact of the surgery, and adds that once a patient experiences some restoration of the finger and thumb extension, they could then be offered a tendon transplant to improve grip strength as well.

"I think we're approaching our study in a cautious and ethical way," he says. "We want to make sure we're going about it the right way, and not trying to just be the first one out of the gate."

While he's focused on the specific surgery employed in his study, Bristol has also performed several of the procedures that Dr. Boyd performed with Raglin and Nugent—but with patients who have a damaged brachial plexus nerve due to something other than SCI.

"I would offer those procedures now," he says. "Of course, we would like to enrol patients in our study. If they're interested in participating in the study, then we'll enrol them in the study. But if they're not, and they want to do other nerve transfers, then I'll talk to them about the risks and benefits of those other transfers. We can technically do those any time, and I'm happy to see patients in that regard."

Once again, there's the thorny issue of "who pays?" But just as Boyd has offered the procedure in Ottawa at no charge, Bristol is also adamant that there will be no cost here in BC.

"If they've got BC Health Care, it gets covered under BC HealthCare, as far as I'm concerned," he concludes.

If you think you're a candidate for either of the nerve transfer surgeries described above, speak with your own doctor or physiatrist about a referral.

slightly more control closing. Again, we're talking miniscule movement here—millimetres at the most."

Now that Raglin and Nugent are showing signs of improvement, they'll have to work hard to maximize any benefits.

"Patients are initially given some guidance on what they should be doing on their own for the first six months," explains Boyd. "After that, they start working with a hand therapist. The frequency of visits will depend on what gains the patient makes, how quickly the patient learns to perform new exercises, and what supports the patient has at home to work on the rehabilitation program. Therapy will likely continue for up to two years."

This therapy is necessary to train the brain to recognize the new nerve signals. "In a nutshell, therapy involves loosening up my hand as the muscle is slightly tight, and then practicing triggering the muscles that move my fingers through various exercises," says Raglin. "As it stands now, therapy is scheduled to be pretty intense over the next couple of months and then slow down in spring and summer. I have plenty of exercises to

Nerve Transfer Surgery: The Fine Print

Who is it for?

This surgery is only appropriate for those with a specific level of injury—C6/C7. It typically does not help people who have lost all arm function due to higher injury levels. Although younger candidates may respond better, there is no age limit, nor are there any restrictions about time from injury. Candidates go through a rigorous evaluation to determine suitability. They must have movement in their upper extremities, which signals that there are nerves in their arms that still communicate with the brain. Arm and hand muscles must be well-preserved. Other factors include functional goals, neurological deficits, contractures and spasticity.

How does it work?

The technique restores some communication between the brain and the paralyzed muscles of the hand by rerouting healthy nerves that emerge from the spinal cord above the injury site and connecting them with the target nerves in the hand and arm that are damaged where they emerge from the spinal cord below the injury site. The benefits are not immediate—after the surgery, it takes six months or more for the nerves to merge and restore communication between brain and hand. Once a connection is established, patients undergo extensive physical therapy to train the brain to recognize the new nerve signals, a process that takes up to two years.

What does it entail?

Prior to the procedure, the surgeons determine which nerves they are targeting—both a donor nerve, and the recipient nerve.

Since the primary goal is to improve grip or pinch function, the recipient nerve is almost always the anterior interosseous, or AIN. Although it no longer carries signals, the AIN looks like any other healthy nerve, since it still receives blood and nutrients.

The donor nerve, meanwhile, must be redundant—in other words, it will be expendable because other nerves are present that perform the same task. In most cases, the donor nerve is the brachialis—a nerve that triggers flexing in the elbow. It's expendable because there are two other nerves that perform the same job.

Once the targets have been determined, the surgeons create a long incision on the inside of the arm and begin to unpack its muscles, arteries, tendons and nerves. They then search for the appropriate peripheral nerves, which look like cooked spaghetti. The peripheral nerves are essentially nerve bundles—they consist of a bundle of smaller nerves that control specific functions. Once identified, the covering of the peripheral nerve is cut back to reveal the smaller nerves inside. Then, using a tiny electric current, each of the smaller nerves are activated to see which function they perform.

Once the donor and recipient nerve are isolated, they're cut and attached to each other. Again, however, there is no immediate connection—in fact, the interior of the recipient (the AIN) starts to die and disintegrate. However, the empty nerve tube remains intact, and the rerouted donor nerve slowly grows down to the muscles of the thumb and finger. That's a distance of about 20 centimetres, and the donor nerve only grows about one millimetre a day, which is why benefits of the surgery don't appear until months down the road.

With the new connections made, the surgeons return all the arm's components back to their original position and state, and the incision is carefully sutured.

What happens next?

The patient has to do intense physical therapy to relearn how to trigger hand movement. That process is more difficult than it sounds because the individual will be using a nerve that used to bend the elbow to move the thumb and index finger. It takes time for the brain to adapt to this new reality.

What are the limitations?

Right now, the surgery has a number of limitations. First, it is limited by the number of redundant nerves in the body that surgeons can "borrow" to put to use elsewhere. Second, it is limited by the rate of nerve growth following a peripheral nerve injury, which is essentially what the surgeons create when they cut the brachialis nerve and join it to the anterior interosseus nerve. The nerve must regrow to the target muscle within 12 to 18 months or else that muscle will become damaged. It means, for instance, that a nerve transfer in the leg is unworkable because of the required distance: by the time the nerve fibre reached its target, the muscle would no longer be responsive.

Researchers, however, are working to speed nerve growth and to preserve unconnected muscles so that they remain receptive to nerve growth for a longer period of time.

do at home—this will help move things along faster than just relying on the sessions with the therapist."

Despite the long wait for results, both Nugent and Raglin have never second-guessed having the procedure. "Waiting was never difficult, since I had already learned how to manage everything using the amount of function I had, which was very little," says Nugent. "I never really gave up hope as I was pretty optimistic and so were my doctors. Right now, the impact is pretty minimal in my life, since it's still in the early stages. But I'm optimistic that it will make daily routines and functions a little easier. Right now it's really still just a waiting game as things continue to progress."

"I didn't lose confidence at any time that something would happen," adds Raglin. "Again the definition of what that is has yet to be determined, whether it be a small pinch or an actual grasp. I'm pretty confident something between those two extremes will happen."

The surgeries for Raglin and Nugent were well-publicized, particularly in Ottawa-area media, and Boyd says that initially sparked interest from other quadriplegics in Ontario. But up to this point, no suitable candidates have been identified. Boyd says that's likely to change, particularly since Raglin and Nugent are now experiencing some improvements. And she adds that at least three of her Canadian colleagues are interested in learning the procedure.

"Dr. Chris Doherty and Dr. Tom Miller have evaluated patients in London, Ontario, and are planning to perform these surgeries in the near future," she says. "In Vancouver, Dr. Sean Bristol and his team have expressed an interest in doing this procedure (see sidebar on page 30). And there are a handful of surgeons across the country who are performing nerve transfers in the peripheral nerve injury population, and it's possible that these surgeons will apply the technique to patients with SCI in the future."

So it seems likely that the surgery may be an option for readers who meet the criteria. That, of course, leads to the million dollar question: who pays?

Here's how Boyd describes that particular issue: "In the Canadian health care system, these surgeries are performed with no cost to the patient. There is no expensive equipment or implantable device that need to be covered. The only costs are the operating room time, the surgical materials, and post-operative rehabilitation. Unfortunately, given the unique nature of the procedure, there are no billing codes in the Ontario Ministry of Health Schedule of Benefits for Physicians that accurately reflect the complexity of the surgery and the time involved. Therefore, the procedure requires a surgeon who is willing to make a fraction of what they might otherwise make during a normal operative day."

If you have the stomach to view it, The Ottawa Hospital has posted an excellent (but somewhat graphic) video of the surgery on YouTube—search for "first nerve transfer surgery in Canada" at www.youtube.com. ■

Botulinum Toxin & SCI Neuropathic Pain

Botulinum toxin type A, or BTX-A, is quickly becoming a common tool for treating several secondary complications of SCI. Today, BTX-A (also commonly know Botox, which is Allergan's trade name for its form of BTX-A) is being safely and successfully used to treat neurogenic or overactive bladder, as well as spasticity, for many people with SCI. Neuropathic pain could soon be added to the list.

In a study published in the February issue of *Annals of Neurology*, Dr. Zee-A Han and other researchers at the National Rehabilitation Center in Seoul, South Korea, outlined their apparent success in using BTX-A as a treatment for SCI neuropathic pain. The study, titled *Botox May Reduce Neuropathic Pain in Spinal Cord Injury*, enrolled 40 participants with SCI-associated neuropathic pain. The participants were randomly chosen to receive either a one-time subcutaneous BTX-A (200 units) injection or a placebo injection at the painful area. The study was double blind, meaning that neither the participants nor the researchers knew whether the participant was receiving BTX-A or the placebo.

Each participant was evaluated for pain before the injections, and then at four and eight weeks after the injections. Widely accepted methods of evaluating pain were used, including the short-form McGill Pain Questionnaire, developed by Dr. Melzack at McGill University in Montreal.

The researchers determined that those who received the BTX-A injection reported significantly more pain relief than those who were given the placebo. At four weeks after injection, 55 percent reported pain relief of 20 percent or greater, compared with 15 percent of those given the placebo. The result was similar at the eight week mark—45 percent versus 10 percent.

"These results indicate that BTX-A may reduce intractable chronic neuropathic pain in patients with spinal cord injury," the authors wrote. They also made it clear that the treatment did not reduce motor or sensory function below the injury.

BTX-A is Botulinum toxin, one of the most poisonous biological substances known, is a neurotoxin produced by the bacterium Clostridium botulinum. It works by interfering with transmission of nerve signals by blocking the release of acetylcholine, the principal neurotransmitter at the neuromuscular junction, leading to muscle paralysis.

Please note that this was an industry-supported study—Medytox, a maker of botulinum toxin products, supported the researchers' work.