FOCUSED ON SCALPEL-FREE SURGERY

TARGETING MULTIPLE ULTRASOUND BEAMS DEEP INSIDE THE BODY MAY ONE DAY MAKE THE PHRASE GOING UNDER THE KNIFE OBSOLETE

BY MICHAEL MCKINNON
IF SUNNYBROOK RESEARCHERS HAVE THEIR WAY, THERE WILL BE A TIME WHEN PATIENTS ARE NO LONGER FORCED TO GO “UNDER THE KNIFE.”

There will be no such thing as an inoperable brain tumour, and uterine fibroids will be destroyed without incision. The brain’s natural defences will be safely bypassed to see medications delivered for a wide variety of brain diseases, and radiation doses will be cut by more than half.

And it will all be thanks to focused ultrasound. “It will be the tool of every surgeon,” says Dr. Kullervo Hynynen, director of imaging research at Sunnybrook Research Institute. “Think about 50 years from now: Nobody is going to cut a patient’s skin open if they have a tool that is non-invasive. It is definitely going to be the wave of the future.”

To be sure, high-intensity focused ultrasound (HIFU) is still in its infancy, but promises to someday lead to a standard of surgery without the scalpel. Based on traditional ultrasound, such as that used to create images of fetuses in utero, the procedure involves focusing ultrasound waves—beams that don’t individually cause tissue damage—into a target a few millimetres in diameter, producing enough heat to destroy tumours or tissue while leaving surrounding bone and tissue untouched. That target can be deep within the human body, leaving bone and tissue in the beam’s path unharmed—so no incision is needed. Magnetic resonance imaging is used both to pinpoint where the beams are to be focused and to monitor the procedure’s success.

“The fact that Dr. Hynynen’s team is able to take ultrasound waves and accurately focus them through a one-centimetre-thick skull to deliver thermal energy and be able to heat up and coagulate either a tumour or tissue in the brain is absolutely amazing,” says Dr. Todd Mainprize, a Sunnybrook neurosurgeon and principal investigator in an about-to-launch 10-patient study into the viability of HIFU’s treatment of brain tumours.

The study—Canada’s first and one of the world’s first—will see the procedure’s success.

“To do that, we have to divide the transducer by about a thousand small elements, and drive each of them separately to correct for the distortions,” says Dr. Hynynen.

Again, researchers are quick to point out that trials—those in brain tumours, as well as bone metastases, uterine fibroids and others—are in early phases or about to launch, and little is known with certainty about how well HIFU will work in a clinical setting. But they also say HIFU shows great promise in a wide variety of conditions.

Dr. Gregory Czaarota, director of the Odette Cancer Research program at the Sunnybrook Research Institute, says early results of a phase 1 trial of HIFU’s treatment of painful bone metastases at Sunnybrook are so promising that Sunnybrook researchers are leading the expansion of the Ipsenburg trial into a 30-patient study with sites in Canada, the U.S. and Europe this fall. This could be good news for patients suffering from the pain of cancers that have spread from their primary sites to bone.

“Of the seven patients enrolled so far, all had good-to-excellent pain response, related primarily to how much of the bone we can actually treat with the ultrasound—and some as soon as hours after the treatment,” says Dr. Czaarota. “Some patients had scored their initial pain at nine out of 10, and a day later it was down to a one or a zero, and then just pain free since.”

He says it’s possible HIFU is doing double-duty, targeting the metastases within the bone but also creating an anesthetic effect through the act of heating the bone. But while Dr. Czaarota says the possibility of treating bone disease without radiation is exciting—and the HIFU treatment takes half an hour, compared with up to five return trips for radiation—he says even more exciting focused ultrasound treatments may be on the horizon. Focused ultrasound shows promise in greatly improving radiation therapy’s effect on the tumour, which could lead to doses of radiotherapy being cut by more than half with the same results. As well, by making blood vessels “leakier,” low-intensity focused ultrasound could allow 20 to 50 times more chemotherapy into the tumour.

“HIFU has the power to introduce surgery without a scalpel, but also make chemotherapy and radiation therapy much more powerful,” says Dr. Czaarota. “And we’re talking hugely significant increases.”

Similarly positive results have been found in the treatment of uterine fibroids, which lead to pain, bleeding and infertility in one in four women at some point in their lives. Hysterecetomy is one traditional treatment, a procedure that leaves women infertile and can require up to two weeks of recovery time. Early results of uterine fibroid trials at Sunnybrook and Thunder Bay Regional Health Sciences Centre, though, suggest much-improved results. The procedure hasn’t reached the point where it’s equal to other treatments, but Dr. Elizabeth David, the study’s principle investigator, says she’s confident it will get there with the help of ongoing tweaks and adjustments.
“There is no incision, no scarring and very little post-operative care. It’s truly non-invasive, where everything else is really minimally invasive,” says Dr. David. “HIFU doesn’t even involve a needle.”

In fact, the greatest discomfort these patients experience is from lying face-down on the table for the required three hours. Sedation is “exceedingly light,” says Dr. David, and some have returned to work the following day.

“We have patients who went cycling the same day of their surgery,” points out Dr. Hynynen. “You cannot do that after a hysterectomy.”

But perhaps most exciting is HIFU’s ability to help scientists safely open up the blood-brain barrier, the brain’s natural defence against toxins that also prevents medications from reaching the brain. The HIFU technique is slightly different here; researchers are not heating or destroying tissue, but rather injecting microbubbles—tiny bubbles of gas—into the bloodstream. Once targeted by focused ultrasound, the bubbles expand to open the blood-brain barrier safely by temporarily pushing aside protective cells to allow the delivery of brain medication; the barrier closes on its own within about six hours.

“The brain is a privileged site—whatever is in your bloodstream does not get across the blood vessels into the neurons unless the brain wants it there,” explains Dr. Mainprize. “We can use focused ultrasound to reversibly and safely open up the blood-brain barrier to allow for the delivery of medications to these brain tumours, treatments that would otherwise not be possible or effective because they wouldn’t get to the tumour. That’s Dr. Hynynen’s team’s work, and that’s phenomenal. It’s a very exciting time.”

Dr. Mainprize says there are other methods of opening the barrier, but most are not very effective and many open the entire barrier, exposing the brain to the risk of toxins. HIFU’s precision allows just a small door in a specific area of the barrier to be opened, creating opportunities for designer drugs to target tumours, depression, Alzheimer’s disease, stroke and more.

“Almost everyone I speak with thinks it’s going to revolutionize brain treatments on many levels,” says Dr. Hynynen, adding that the potential hasn’t been proven yet in patients. “Suddenly we have all of these medicines that can be used in brain treatments and they haven’t been used before. Now we can use them and use the imaging to target where they are going in the brain so we can limit side-effects—and that can have a huge impact.”