

“It’s a truly multidisciplinary enterprise,” says Dr. Matthias Schmidt, radiologist and director of research in the departments of Diagnostic Imaging (NSHA) and Diagnostic Radiology (Dalhousie Medical School). “On top of our work in radiology itself, we play a huge role in providing imaging services to researchers in other fields, such as oncology, neurology, urology and critical care. For example, we organize and conduct the imaging studies to monitor treatment effects in clinical trials for cancer drugs. Radiology provides that crucial window.”

Radiology is the essential bridge between technology and the patient. “Our research efforts are focused on advancing the technology and improving how we use the technology,” says Dr. David Barnes, clinical chief and academic head of diagnostic imaging and radiology. “But it’s really all about the patient and translating the value of that technology into better patient care.”

Radiology researchers are amplifying the diagnostic and risk-predicting power of existing imaging technologies (such as MRI and CT scans), while adding new depth and understanding to the interpretation of images. They’re also exploring new uses of existing technologies and validating their efficacy in patient populations. This includes new approaches to interventional radiology, in which imaging is used to guide the placement of a therapeutic device or procedure.

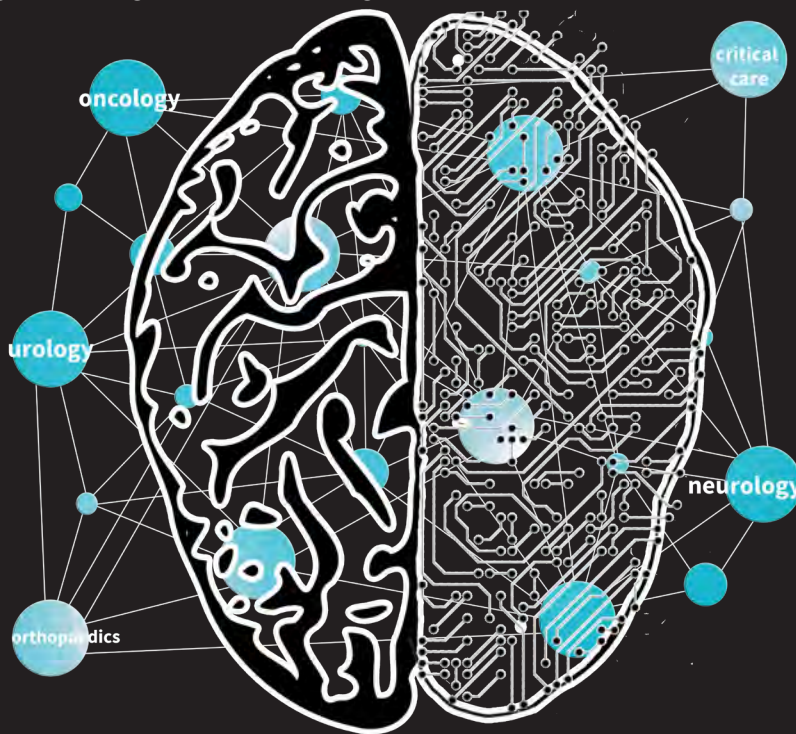
The researchers are involved in multiple commercial efforts, including joint ventures with industry partners to expand the capabilities of their imaging equipment and start-up companies that are launching innovative new products. These efforts are enhanced by a supportive R&D ecosystem that includes access to advanced facilities and expertise at BIOTIC (Biomedical Translational Imaging Centre), as well as significant support from the Nova Scotia Health Authority, Dalhousie University, InnovaCorp, the QEII Foundation, and the

department’s own Radiology Research Foundation. “We established the Radiology Research Foundation years ago, starting with contributions from our own department members,” notes Dr. Barnes. “It has grown since then, with gifts from industry and private individuals, so that we are able to provide

several grants and scholarships a year, along with seed funding for promising research projects and salary support for key members of our research staff.”

Strong internal and local support for radiology research has enabled researchers to secure substantial external funding from the Canadian Institutes of Health Research, Canada Foundation for Innovation, the Atlantic Canada Opportunities

Agency (Atlantic Innovation Fund), and other agencies. In addition to radiologists, researchers in this field at NSHA include clinician scientists and PhD scientists in medical physics, a biostatistician and epidemiologist, and research associates and coordinators, residents, students and others.



Multiple departments doing research rely on Radiology for imaging services and some projects are teaching computers to detect certain cancers

Is it Epilepsy? MRI Triage After a First Seizure

When a person has a seizure for the first time, they have a 30 to 50 per cent chance of going on to have more seizures in the future. But how can a clinician predict who will and who won't develop epilepsy?

"We don't have reliable tools yet for predicting future risk," says Dr. Matthias Schmidt, Diagnostic Radiology's director of research. "In many cases, MRI can show us the lesion that triggered the seizure—in which case the patient might really benefit from surgery to remove the lesion. Patients without a resectable lesion can still benefit from medical treatment."

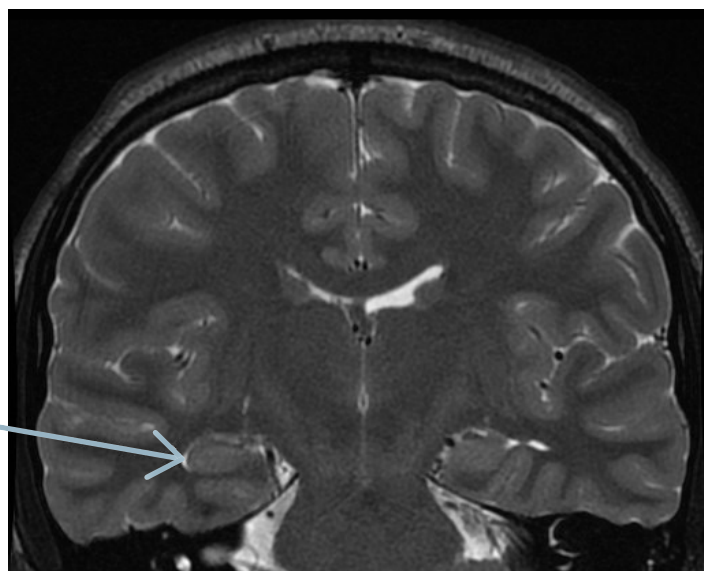
But what if the risk of a subsequent seizure is actually very low? Given the risks of brain surgery and the side effects of medication, it's crucially important

to quantify that risk. Dr. Schmidt, neuroscientist Dr. Candice Crocker and biostatistician Mohamed Abdoell have teamed up with neurologist Dr. Bernd Pohlmann-Eden, founder of NSHA's First Seizure Clinic, to advance the capabilities of MRI so it can do just that.

"When a person has a seizure for the first time, they have a 30 to 50 percent chance of more."

"We're doing MRI scans on patients when they present with a first seizure, to assess what's happening in the brain chemically, structurally and in terms of the diffusion of water molecules throughout the tissues," he says. "A year later, we do a second scan. As we gather data on more patients, we're identifying what MRI-measurable factors are most associated with subsequent seizures."

The goal of the research—funded by the Nova Scotia Health Research Foundation and NSHA Research Fund—is to create MRI protocols for assessing future seizure risk, so clinicians can provide the safest, most appropriate care.



This MR image is a T2-weighted image of the coronal section of the human brain and highlights the hippocampus, an important structure in the temporal lobe that helps regulate emotions and form memories. The hippocampus is commonly involved in the generation of seizures, which can often be alleviated with surgery or imaging-guided ablation procedures.

Contents

Neuroimaging.....	Page 2
Abdominal Imaging.....	Page 4
Earlier & Smarter Detection	Page 6
Commercializing Research	Back Cover

Radiology Research Office

The Radiology Research Office is the key link between departments requesting imaging procedures for research projects (such as: ultrasound, MRI, x-ray, CT, interventional radiology, nuclear medicine and PET) and the clinical radiology department. This important work would not be possible without the hardworking research staff: Melissa Butler, Jennifer Hiltz, Marlene Hudgins, Louise MacDonald, Mary McSweeney and Jane Slaunwhite.

Brain Imaging in Critical Care

Dr. Jai Shankar is co-leading a Canada-wide study to confirm the earliest signs of brain stem death in CT perfusion scans of unconscious patients on life support. Dr. Shankar and his collaborators at 13 other centres have received approximately \$1 million from the Canadian Institutes of Health Research to gather and analyze CT perfusion scans of 300 patients on life support, who are later declared dead on the basis of the current gold standard—clinical exam.

“The brain stem is the common final pathway for all vital signals from the brain to the body,” notes Dr. Shankar, an interventional neuroradiologist. “If it is dead, the brain cannot support the body’s vital functions, even if the front brain is active.”

Dr. Shankar is pioneering CT perfusion to assess patients critically ill with cardiac arrest or severe traumatic brain injury. “The clinical exam is not a reliable indicator of brain function when patients are mechanically ventilated and sedated,” explains Dr. Shankar. “We want to identify an objective way to know, conclusively, when someone is

really dead and we must contemplate withdrawal of life support.” It’s critically important that clinicians get this right. “Families need to know, and so does the health care system,” Dr. Shankar says.

“We want to identify an objective way to know, conclusively, when someone is really dead...families need to know.”

“If the person wanted to donate their organs, for example, those organs need to be harvested while they’re still viable for transplant.”

Dr. Shankar is gaining international recognition for use of CT perfusion for stroke, brain tumours, brain hemorrhage and brain death. His pioneering work in interventional neuroradiology techniques helped establish EVT (the endovascular removal of a clot from a blood vessel in the brain) in Nova Scotia.

Preventing Disease After Traumatic Brain Injury

Traumatic brain injury can damage the fine blood vessels of the brain, compromising the blood-brain-barrier and allowing blood to leak into the white and gray matter. This in turn leads to inflammation and neural damage that can progress to epilepsy, Parkinson’s disease, chronic traumatic encephalopathy, depression and other diseases of the brain.

Dr. Schmidt, a radiologist, and Dr. Steven Beyea and Dr. Chris Bowen, medical physicists, have teamed up with neurosurgeon Dr. David Clarke, critical care physician Dr. Rob Greene, and Dalhousie neuroscientist Dr. Alon Friedman, to test new MRI sequences in brain-injured patients. They’re using the sequences, developed at BIOTIC, to assess damage to the blood-brain-barrier and then measure the ability of various medications to repair the damage, potentially preventing devastating long-term consequences of brain injury.

Push-Button Technologies for fMRI

Functional MRI (fMRI) scans generate thousands of images of the brain in action as it responds to stimuli. Dr. Beyea and his team at BIOTIC are creating algorithms to capture, analyze and present this data in a more meaningful, usable form that doesn’t require the expertise of a radiologist for interpretation.

“We’ve filed a patent for the algorithms, which allow clinicians to extract information about brain activity at the push of a button,” says Dr. Beyea. “This technology saves hours of time, removes subjectivity, and makes it possible for smaller centres to use fMRI effectively.”

GE Healthcare is the industrial partner in the project, which is part of a larger NSHA-ACOA Atlantic Innovation Fund-supported effort to develop and commercialize imaging technologies.

Abdominal Imaging

Tackling the Growing Epidemic of Fatty Liver Disease

“Fatty liver disease” doesn’t get much public attention, but it should. Fatty liver—when fat makes up more than five per cent of the liver—can lead to cirrhosis, cancer and liver failure. And, rates are on the rise.

“Fatty liver is the big disease of the coming century,” says radiologist Dr. Andreu Costa. “It’s the most common thing we see... we find excess fat in 40 to 50 per cent of the livers we scan.”

Dr. Costa, fellow radiologist Dr. Sharon Clarke, and colleagues at NSHA and BIOTIC—including Dr. Magnus MacLeod, Dr. Steven Beyea and Dr. James Rioux—are developing new MRI methods of detecting, measuring and analyzing fatty liver disease. They want to identify an imaging biomarker that accurately predicts risk.

“Not everyone with a fatty liver will develop serious disease, but we need to identify who’s at risk,” says Dr. Clarke. “If fatty liver is identified early, it can be reversed with diet, exercise and medication.”

A Canada Foundation for Innovation equipment award has allowed Dr. Clarke to purchase an MRI elastography system for measuring stiffness of the liver, and a radio-frequency coil that detects phosphorus as an indicator of energy metabolism. “We’re one of only a handful of centres in the world looking at phosphorus as a predictive biomarker of fatty liver disease,” notes Dr. Clarke.

MRI yields many gigabytes of data for every scan—enough to occupy a radiologist for hours. The researchers aim to develop algorithms that collapse and interpret this data into more rapidly accessible and powerful information. Drs. Clarke and Beyea are currently co-leading an ACOA Atlantic Innovation Fund project to develop a means of quantifying the amount and types of fat in the liver.

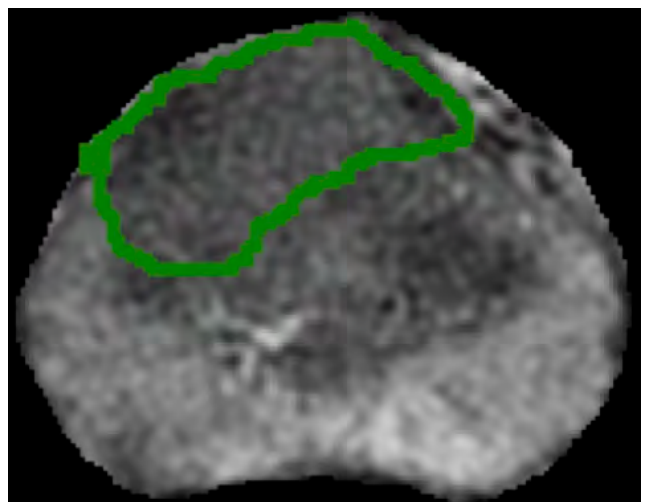


Dr. Sharon Clarke is pioneering new methods of investigating with a \$214,000 Canada Foundation for Innovation award

Piecing Together Prostate Cancer

In prostate cancer, it’s vitally important to know which tumours need to be removed swiftly, and which can be left alone with careful monitoring. NSHA radiologists, urologists and pathologists are working together to “train” MRI systems to recognize the difference in an artificial intelligence process known as “machine learning.” This involves comparing large volumes of patient’s diagnostic MRI data to the pathology slides of their resected prostate cancers. The pathology slides must be pieced back together digitally, like a puzzle, in order to match the MRI data.

Images left to right: MRI of cancer (circled in green), “map” of cancer as output by the machine learning algorithm (red cancer, green not cancer) and corresponding pathology slides (cancer outlined in black)



Non-invasive Detection of Chronic Pancreatitis



chronic liver disease, thanks to equipment she purchased

NSHA research scientist Dr. James Rioux is developing new MRI methods of precisely measuring changes in the pancreas that could herald the onset of chronic pancreatitis. This inflammation of the pancreas causes significant pain and increases the risk of pancreatic cancer—one of the deadliest cancers—by 12 to 15-fold.

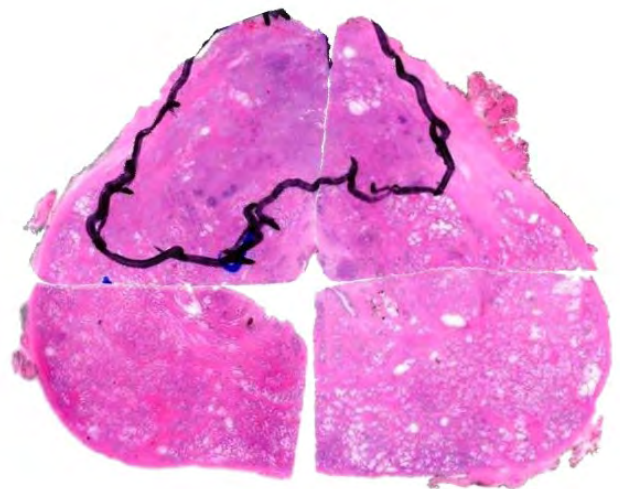
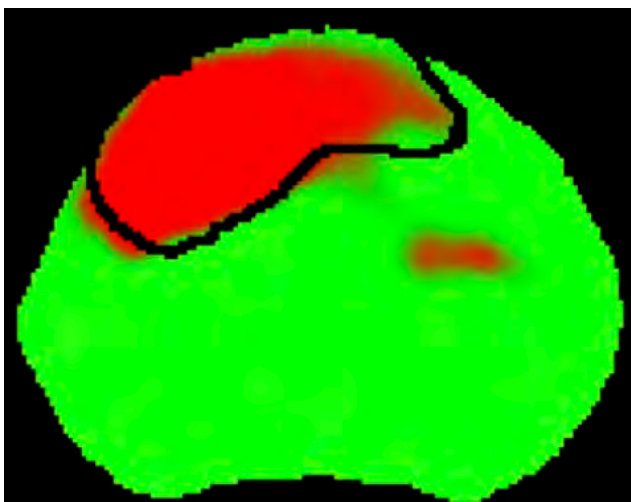
The NSHA Research Fund has awarded Dr. Rioux \$25,000 to test the accuracy of his new methods, while the Radiology Research Fund has contributed an additional \$9,700 to his work. Dr. Rioux is collaborating with gastroenterologist Dr. Geoff Williams on the study, which involves patients with chronic pancreatitis as well as healthy volunteers for comparison.

“...we’re developing analytical algorithms so radiologists and physicians receive the most useful, objective data possible.”

“We’re precisely defining and measuring the changes this disease causes in the pancreas over time,” explains Dr. Rioux. “For example, we’re quantifying the diffusion of water molecules throughout the organ. This becomes less and less as inflammation makes the pancreas more fibrotic.”

information, plus it is highly invasive and can make the condition worse in some instances,” notes Dr. Rioux. “In addition to quantifying the pathological changes, we’re developing analytical algorithms so radiologists and physicians receive the most useful, objective data possible.”

The gold standard for detecting chronic pancreatitis is endoscopy, which involves threading a tube with a tiny camera on the end from the mouth to the pancreas. “This provides subjective, qualitative



Earlier & Smarter Detection

Using CT Scans to Identify Liver & Lung Cancer



Dr. Daria Manos reviews images for tiny lesions on the lungs

Classifying Suspicious Lung Lesions

Radiologist Dr. Daria Manos is on a mission to develop reliable ways to tell when suspicious lesions in the lungs are likely to become cancerous.

As she explains, it's common for tiny shadows to show up in the lungs in CT scans. This usually happens when a person is getting a CT scan for some other reason. The question becomes, what to do about that spot?

Lung cancer is the #1 cancer killer in Nova Scotia—more than colon, breast and prostate cancer combined...When it's caught early, the cure rate is 90 per cent.

"Most lesions in the lungs will be old scar tissue from a previous lung infection," Dr. Manos explains. "The problem is, they look the same as a precancerous growth. You can't just go in and surgically remove it—that's risky—and many of these lesions just go away on their own."

Patients with suspicious spots are monitored with regular CT scans. Dr. Manos and her colleagues, Dr. Joy Borgaonkar and Dr. Robert Miller, are examining these scans, looking for subtle clues that distinguish normal changes from malignant ones, or signal the nodule may resolve on its own. Thanks to advances in CT technology, they're able to visualize an incredibly fine level of detail.

"We can scan spots as small as one millimetre, a thousand images per patient. Twenty years ago, the smallest we could scan was one centimetre, with fifty images per patient," remarks Dr. Manos. "We're learning to detect precancerous changes when the spots are so small, they can't even be biopsied yet."

Dr. Manos led a task force to develop a national system for classifying the cancer risk of lung lesions, based on subtle changes in CT scans over time. The system, known as LU-RADS (Lung Reporting and Data System), provides radiologists with guidelines for identifying the level of risk and recommending appropriate follow-up.

As a radiologist who diagnoses lung cancer at least once a day, Dr. Manos is a passionate advocate of early detection. "There are often no early warning signs of lung cancer; by the time it's diagnosed, it may be inoperable," she says. "When it's caught early, the cure rate is 90 per cent."

Lung cancer is the #1 cancer killer in Nova Scotia—more than colon, breast and prostate cancer combined. A particularly aggressive form of lung cancer is showing up with increasing frequency in younger people who have never smoked; about half of all new diagnoses are in ex-smokers or people who never smoked.

Detecting Liver Cancer

Liver cancer as a primary cancer is on the rise in Canada. The best prognosis is achieved when the cancer is detected early and surgically removed. In Nova Scotia, Dr. Andreu Costa's research has led to improvements in the detection and diagnosis of liver cancer using CT scans.

"We changed the technical parameters of our CT scans—for example, we increased the dose of the contrast agent," says Dr. Costa. "This reduced the proportion of scans that were suboptimal or not diagnostic... so we're identifying liver cancer at an earlier stage, with more confidence in our diagnoses."

Fatty liver disease, hepatitis and cirrhosis all increase the risk of primary liver cancer. "We do an ultrasound every six months in patients with chronic liver disease to look for signs of cancer," Dr. Costa says. "If we see anything suspicious, we do a CT scan."

Improving Quality & Accuracy of Breast Imaging

Between the two of them, NSHA affiliated scientists Mohamed Abdoell and Dr. Jennifer Payne have the quality and accuracy of breast screening and diagnosis in Nova Scotia covered.

As an epidemiologist, Dr. Payne evaluates the accessibility and quality of breast screening services across N.S.

“We need to know that all women in the province have equal access to the same standard of breast screening care, regardless of geographic location,” explains Dr. Payne, who also works to support performance measurement through the Nova Scotia Breast Screening Program. “We want to ensure that women receive the same care at every site, and that the overall service is being delivered in a standardized and high-quality manner.”

Abdoell, on the other hand, is a biostatistician. While Payne mines the health system data, he analyzes the mammograms themselves—alongside the clinical information about the patients they belong to—in order to develop computer algorithms that combine all of this data to produce tailored patient-specific risk estimates.

“Ultimately, we need to be able to identify each patient’s degree of breast cancer risk,” Abdoell explains. “This way, we can tailor follow-up screening protocols driven by a woman’s risk. Those with the highest risk will be screened most often, and vice versa, so we provide better, more efficient care.”

As the researchers are learning, the density of the breast tissue is the crucial factor—not only is cancer more likely to develop in dense breast tissue, but cancer is harder to find in dense breasts.

Abdoell has formed a company called Densitas to develop the algorithms into a mammography-analysis and risk-prediction software suite. Abdoell and his team are using “machine learning” to train software algorithms to assess breast density and other breast screening and mammography-related outcomes, by feeding them a decade’s worth of digital mammograms and clinical data.



Mohamed Abdoell and Dr. Jennifer Payne hold Abdoell’s Discovery award. He received the Discovery Award for Innovation in 2017 for his work with Densitas

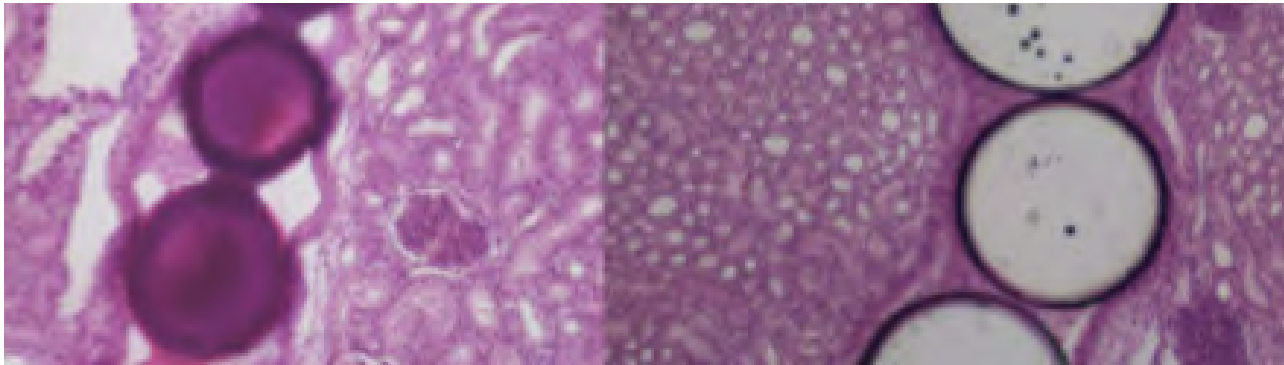
Health centres in Europe are helping to test and refine the algorithms that are being developed here in Nova Scotia and which Abdoell intends to market around the world. The Atlantic Canada Opportunities Agency, National Research Council’s Industrial Research Assistance Program and InnovaCorp have all been instrumental in the company’s progress.

“We want to ensure that women receive the same care at every site, and that the overall service is being delivered in a standardized and high-quality manner.”

“The support from the local community is phenomenal,” says Abdoell, who received the 2017 Discovery Award for Innovation for his work with Densitas. “People recognize how important it is to leverage our wealth of clinical data to improve breast health outcomes for women. We are arming radiologists with the tools to be highly confident in their recommendations.”

Commercializing Research

ABK Biomedical Develops Traceable Beads for Safer, More Effective Tumour Treatment & Global Investors are Lining Up



Triscaryl gelatin microspheres (left) versus ABK Biomedical's OccluRad embolization microspheres (right)

For years, interventional radiologists have injected tiny polymer beads into blood vessels to starve uterine fibroids of blood supply, and into the liver to kill cancer directly. The challenge has been to safely and accurately place the beads, in the absence of a way to see them as they're being injected.

This is all changing, thanks to NSHA interventional radiologist Dr. Bob Abraham and his collaborator, Dr. Daniel Boyd, a materials scientist in Dalhousie's Faculty of Dentistry. They have invented a compound that makes the beads show up on X-ray and CT scans. They are commercializing these beads through a rapidly growing company, ABK Biomedical.

"The beads contain radiopaque material that lights up on x-rays," Dr. Abraham explains. "This allows us to use imaging equipment in our interventional radiology suites to see exactly where the beads are going as we place them." This is particularly valuable in the treatment of liver cancer with radioactive beads, which destroy tissues within three millimetres of each bead. "Because we can see both the cancer and the beads, we can minimize damage in healthy liver tissue, while ensuring we treat the whole tumour."

ABK begins manufacturing "bland embolic beads" in its Halifax facility in 2018. These are purely for blocking blood supply—they do not contain radioactive materials and they don't break down over time. The company is seeking FDA clearance later this year, with Health Canada to follow in 2019. Its radioactive product is slated to undergo clinical trials within three years.

"Interventional radiologists are extremely keen on this technology for the precision it provides," says Dr. Abraham. "There is a huge market for this technology." Investors and venture capitalists in Canada, United States and Japan agree. Local support—provided by Innovacorp and the Atlantic Canada Opportunities Agency's Atlantic Innovation Fund, among others—has been pivotal. "Our investors have been extremely impressed by the government support here," says Dr. Abraham "It has really helped us establish our foundation and grow."

These revolutionary products—and others the company will no doubt develop in the future—will put safe and effective treatments in the hands of interventional radiologists around the world.