Hello and welcome to Behind the Breakthrough, the podcast all about groundbreaking medical research and the people behind it at Toronto's University Health Network, Canada's largest research and teaching hospital. I'm your host Christian Coté. Joining us on the podcast today, Dr. Jonathan Irish renowned head and neck cancer surgeon at UHN and award winning scientist at the Princess Margaret Cancer Center and Techna, the Institute for the Advancement of Technology for Health. Dr. Irish is a pioneer in the research of novel approaches to enhance cancer surgery outcomes, including the use of augmented reality to help make tumor removal more precise, and improve patient outcomes. Dr. Jonathan Irish, welcome to the podcast.

DR. JONATHAN IRISH

Oh, thanks, Christian, it's great to be here and share my experiences with both you and your audience.

BTB

So Jonathan, let's start with the clinical side of your work. Because I know that drives in many ways your research, cancer surgery is this really challenging, delicate balance of on the one hand getting all of the tumor versus not cutting healthy tissue. And because of the location of some tumors, that balance becomes all the more precipitous talk to us about this tension you face in the operating room?

DR. JONATHAN IRISH

Basically, you kind of described the balance that we face. On one hand, to ensure that we've completely removed the cancer that reflects our patients outcomes survival. And then on the other hand, to ensure that we are preserving as much normal tissue as possible in head neck cancer, that can mean the difference between a good swallowing, speech outcome cosmetic outcome, but in many other cancers, it can also be reflected on other types of quality of life, the ability to maintain one limb to maintain one's arteries supply to maintain one's nerve supply, and so on. So that concept and that balance, you described it as tension, that description of that balance or tension between ensuring that
we achieve a complete resection of cancer survival, and balance that with outcomes related to quality of life, which is so very much important for the longevity of our patients.

BTB

And I understand that follow up to cancer surgeries can be required, because that margin of delineation was not enough, the first time around, how common is that?

DR. JONATHAN IRISH

The failure to achieve an adequate removal can be impacted in many ways. Number one, it does increase the chances that the cancer will return. Number two, it increases the chances that other treatment modalities in the form of radiation treatment, or even radiation treatment and chemotherapy may be more likely to be required, and more importantly, at even a higher dose than you might have normally. So that concept of ensuring that you want to minimize the number of treatments the patient has. But you also want to obviously maximize the outcome of the patient for their spectrum of survival.

BTB

So up to now, again, I'm going back to this tension, I guess this relies really a lot in terms of this margin of error on imaging, correct in the OR?

DR. JONATHAN IRISH

Sure I mean, increasingly no question that surgical judgment, seeing the tumor, feeling the tumor, of course, important. But now increasingly over the last two to three decades, as our imaging modalities have become much more refined, much more advanced, and we've incorporated increasingly other tools to see the tumor.

BTB

This underscores certainly your drive in terms of your research to improve outcomes by improving your ability to see the tumor or be able to operate in a much more precise way. So let's get into your use of augmented reality or AR. First of all, take us back. What drew you to AR?

DR. JONATHAN IRISH

20 years ago, you brought out your map out of your glove box, and you opened it up and you looked to see where you wanted to go. Now I'm going to hazard a guess that you don't have a paper map in your glove box, but you have a GPS and you put in your parameters and your coordinates. And you're driving, as you do now, looking at the road, looking at the corridor that you want to go down, but periodically, especially in a unfamiliar area or a complex area, you're referring to that dashboard that is right beside you. And increasingly as you can probably appreciate, as we move forward, you're getting
a heads up display of not just you're now looking towards the road, but that heads up display is overlaid onto the road that you're actually seeing.

**DR. JONATHAN IRISH**

So you're not just having to look away now, and then look forward. But now you’re actually able to see what heads up display, where you should be going, where the dangers might be, and more importantly, where you want to go accurately. And yet avoid the areas the no fly zones or no drive zones that you want to avoid. And so if you think about augmented reality, it's not dissimilar. So we have very experienced surgeons, they could probably do the surgery very well in the way that they are doing it now. What we’re looking to though, is to move to the next level to increase our accuracy. Sure, maybe only a few millimeters or so. But when we talked about that tension or balance between survival and quality of life, that can mean the difference.

**DR. JONATHAN IRISH**

So in the head neck, for example, in the skull base, ie, that's the bone that separates the brain from the rest of the body, we have structures like the optic nerve going to the eye, the eye itself, the brain, the dura, and yet we have tumors of the sinus or sinus cavities that may be growing around those structures, you can appreciate that, we want to ensure that number one, we have a complete resection, and yet, we want to ensure that we preserve the optic nerve, the orbit, the eye, the brain, the dura. The second area that this can be incredibly helpful is in teaching and one of the major areas for UHN Princess Margaret is in teaching the oncologists or the surgeons of the future. Next Gen.

**DR. JONATHAN IRISH**

So the next gen imaging, teaching the next gen surgeons and the concept of being able to use these images to guide the surgeons of the future. So an experienced surgeon essentially as sitting in the passenger seat, but with his or her hands on the steering wheel. Well, the surgeon of the future, the next gen surgeon it might be driving the car, but yet you're able to see near real time what's going on. And so that is also a very useful and very strong advantage of this type of imaging as well.

**BTB**

What are we looking at physically, when you talk about AR in terms of the research you're doing?

**DR. JONATHAN IRISH**

Well, let's use an example. So you know, if I was to operate in a Sinus malignancy, for example, I could be using a small endoscope that's three or four millimeters in diameter going through the passage of a nose and removing a cancer around the optic nerve, eye, brain and dura. Obviously, a very experienced surgeon can do that and do it incredibly well, if I was to introduce augmented reality on top of the picture that I'm actually driving in. So again, getting back to the analogy of the car, I can nine
times out of 10. In fact, probably 98 times out of 100 Get to the right place, very accurately without crossing the yellow line without crossing the dotted white line and so on without hitting the curb.

**DR. JONATHAN IRISH**

But the fact of the matter is that in highly complex areas, or in areas that have been previously treated by other surgeons, or with previous radiation treatment where the anatomy has been distorted, or the anatomy has been distorted by the tumor, this kind of technology can augment not just the augmented reality picture, but augment the performance of the surgeon and therefore augment the outcome of our patients. Right now, these are purely dashboards that are overlaid on to the real world picture.

**BTB**

I'm just curious, they don't come out of a box. These are purpose built with your colleagues at Techna?

**DR. JONATHAN IRISH**

That's right. And there are take off the shelf models, but for our purposes, because we're at such a specialized institution and deal with highly complex specialized types of cancers we've developed in house technology and technological developers to actually do this work.

**BTB**

So what guides your decision making when you're collaborating with your colleagues at Techna in terms of what you're looking for, and then what they can deliver?

**DR. JONATHAN IRISH**

I think the cool thing about Techna is the fact that the engineers come to the operating room, and the surgeons go to the lab where the engineers are making the devices. So that's actually absolutely critical to the success I think of Techna, which, in my guide to therapeutics laboratory, for example, the GTX lab within Techna. We have five full time engineers, each one of them have operating room privileges, they don't operate, but they create the dotted lines and tell me where to where to cut and in some ways they're not operating, but they are giving me the parameters and the path. And really giving me in a sense the recipe for making the accurate cut either in bone or soft tissue around the tumor, and is my job basically to implement or to carry out the mission of the intervention. And you can appreciate that this becomes even more complex when we have moving targets.

**DR. JONATHAN IRISH**

So think of lung cancer, for example, where the lung is actually moving during the course of surgery or has or is deformable. So in the case of tongue cancer, a cancer that I treat, you know, with a large volume, the fact of the matter is, the tongue is not a stable organ, it moves, the lung is not a stable organ, it's deformable, it moves. And so you can appreciate how important that force dimension can
become over time, bone is easy in some ways. And that's why we chose some areas to target early in our interventions like Skull Base, where it is a fixed skull, and very fixed parameters are targets around critical structures like the optic nerve, eye, brain, dura, and so on carotid artery, for example, or the pelvis, where you have the pelvic bone itself and the hip bones itself. And that's why we've worked a lot with our sarcoma surgeons who deal with cancers within the pelvis and around the upper hip, and why we've chosen bone sarcoma as a good model to use this kind of technology in its early form.

BTB

So let's dive into a preclinical study you published late in 2021. First of all, could you frame for us like what you set out to do in that study?

DR. JONATHAN IRISH

So essentially, what we did is we compared using near real time on the table imaging with and without augmented reality and compared the outcomes. We compare the outcomes between experienced surgeons, and we were better. We compared the outcomes between novice or less experienced surgeons, and we were way better. So experience means a lot. None of this technology replaces a good surgeon, it makes a good surgeon better, and it can help teach and I've already alluded to this, the novice or less experienced surgeon during the course of his or her learning experience. What we found basically to completely answer your question is that the imaging helped, it made us more accurate, it made us more accurate with regards to ensuring resectability. Again getting back to that concept that we've first started with that tension, that concept of the balance between ensuring resectability. But preserving normal structure.

BTB

And another benefit you discovered I understand is the actual physical setup of the augmented reality system. And the OR actually helps the surgeons focus, talk to us about what you found?

DR. JONATHAN IRISH

First of all, we measured eye movement, we were able to determine that we were able to achieve nearly 100% focus on the operative field without eye gaze disturbance, as opposed to having the display to the side, where we achieved around 80% focus on the operative field. So a significant improvement. In addition, we measured something called the NASA workflow or workload index, which is a work load index, which was devised by NASA to determine the impact physically, emotionally, mentally, on astronauts when they were performing tasks in orbit in space, which can obviously be quite arduous undertaking under stress and so on. And we had a significant improvement in workload reduction by putting the imaging and integrating the imaging into what the surgeon is doing.

BTB

What does this augmented reality look like when you're using in the OR?
DR. JONATHAN IRISH

You know, basically, a large computer monitor divided into four quadrants, and in one quadrant is what we call the axial plane, which is kind of the flat plane. The next plane is a coronal plane, which is if you cut your head in half right through your nose, splitting your head right in two. And then the third pane or picture is the coronal plane, which is as if you cut your head in two by dividing it between the two ears. And then finally, the augmented reality plane, which is the ability to basically superimpose the really avatar like structures on to the image, the real time image, but project have our engineers who have created the software to project images that are behind walls. So as I am approaching a wall to resect, the tumor, I can see behind that wall, because of the imaging and integration and Avatar, conceptualization of the carotid artery, or optic nerve, so that I know if I open that door, this case, take down that bone, I will be seeing the carotid artery.

DR. JONATHAN IRISH

That dashboard isn't just me driving along the road, but it's me driving along the road and looking at down from above, looking from the side, looking from behind, but also that gives me X ray glasses, so that I can see that behind a wall coming up is something else and critical structure, we can create no fly zones. So for example, if you think of the road is two curbs on either side, it's not unlike the lane, warning signs or alarms that you get in some cars now that if you hit go outside the corridor, the alarm will go, well, as you're approaching, let's say we come within two or three millimeters of the carotid artery behind that wall that I talked about, you might get a signal, you might get a pulsatile signal because our engineers can create all sorts of different sounds that approach that signal, we can create no fly zones of two millimeters, three millimeters, five millimeters, depending on the side and what you want, you can dial in the parameter. And basically, as you approach a critical structure, you're basically creating a signal, hey, you're getting close, you need to slow down, or you need to stop. And so there's a safety element there, of course, and obviously, that's an important part in education as well.

BTB

That's amazing. How are they generating these images for you?

DR. JONATHAN IRISH

Well they do it, because they are basically taking the images that were created before surgery, and loading them onto a computer platform and grading software that basically creates those avatar images.

BTB

So you've talked about in your study last year, that it was definitely a benefit in terms of the margin of delineation, it was a benefit to the actual surgeon themselves in terms of less distraction, that kind of thing. What will it take, do you think for this AR System to be ready for primetime?
DR. JONATHAN IRISH

Well, it really is already ready for primetime. And we're using it now. But I think it really gets back to the sum greater than its parts because the story doesn't stop there. Because this story was started, I don't know 20 years ago, probably in our laboratory. And really, over the last 10 years, we've kind of been using it. But really what's taken it to the different level is to create the ability to see the tumor in a using some new tools that I haven't yet described. So the most interesting one of those is to create chemicals, nanoparticles that are created and engineered on our laboratories, by our nanoparticle engineers, by our scientists that are manmade, injectable into humans, and go to tumors and fluoresce. So let's think about that. So this has opened up a whole new pillar of cancer treatment. And when we think of the traditional pillars of radiation treatment, medical oncology, or systemic therapy or chemotherapy, surgery, and the fourth pillar, of course, immunotherapy, but the fifth pillar, which I think we're into now, and it certainly well into is the concept of theranostics.

DR. JONATHAN IRISH

So what does that mean the development of theranostic molecules? Well, theranostic molecules are manmade, they are both diagnostic and therapeutic. Theranostic, so they are created and are tumor specific. They preferentially go to a tumor. They can be laden with other types of molecules or other parts, other structures to make them fluoresce, or they can be naturally fluorescent, such that when you shine a light, they're green. And so think of all of the things I've talked about and think of the fact that we've used traditional imaging CT, MRI, PET scan our eyes, and we inject a molecule that goes to a tumor. And we introduce a light, a fiber optic three millimeter light that lights up the extent of the tumor. So we can see, not just traditionally how we used to see a cancer, but we can see a cancer because it's fluorescing. It's glowing. Well, that certainly is augmented how we see a cancer.

DR. JONATHAN IRISH

But think of it if that same molecule can be laden with other chemicals, iodine, copper, or other modalities that allow it to be seen near real time with CT scan, or MRI scans or PET scans. So not only is it fluorescing, but it also contains chemicals or modalities that allow it to be seen by near real time on the table on the operating table imaging, but doesn't even stop there. So now remember I said it was theranostic. Theranostic the therapeutic part. So fluorescence is all about heat. That's what fluorescence is. It's low grade heat, but think of that same molecule being heated up to an extensive degree with that laser that excited that level of particles. Remember I said that laser is exciting the particles within the tumor that were taken up by the nanoparticle, well think if we instead of just fluorescing at a low grade, we start to really superheat it.

DR. JONATHAN IRISH

So that becomes photothermal or photodynamic or it changes its structure because photodynamic is in other words, it's not only just diagnostic, and it starts to become therapeutic because it's become superheated and destroys, destroys the cells that it's sitting in.
What's next for you?

DR. JONATHAN IRISH

For me, I think it'll be all about we got to ride this nanoparticle train, right? This is a very exciting time for us. We built this program. The imaging program is 20 years old, but I'd say we really took on or took off. I think when we started to integrate into the nanoparticle and imaging program and started to bring them all together, we want to bring it to first in human I mean, this alone is this is an enormously exciting period of time for us.

BTB

You're listening to behind the breakthrough, the podcast all about groundbreaking medical research and the people behind it at Toronto's University Health Network, Canada's largest research and teaching hospital. I'm your host Christian Coté. Joining us on the podcast today, Dr. Jonathan Irish, a pioneer in the research of using augmented reality in the operating room to help make the removal of cancer tumors more precise, and to improve patient outcomes. Dr. Irish is research is funded, in part with generous help from both Princess Margaret Cancer Foundation, and the UHN Foundation.

Jonathan, you're born in Toronto, raised in Burlington, and in grade school, you were drawn to the life sciences in the pursuit of discovery. While at the same time I understand you're also heavily drawn to sports and one of them being canoeing where you were actually on a path to the Olympic Games. Talk to us about that amount of your passion?

DR. JONATHAN IRISH

I was happened to be a five time provincial champion and Canadian champion as well. So I had an important decision to make in the early 1980s. And I obviously couldn't become a full time occupation, but I went on to medical school and that was a great choice for me.

BTB

I'm curious if the rigor of training to be an elite athlete and understanding you know, dynamics of team, the commitment, all those attributes to be an elite athlete, did you find those skills transferable to your career in medicine?

DR. JONATHAN IRISH

Oh, yeah, absolutely perseverance. I would say dedication, concentration, and surgery, repetition, to become better, style and form incredibly important. Paddling is a great example for that. There is an element there of teamwork, too, I think throughout my clinical life, the reason that and quite frankly, the reason I've enjoyed the work that I do in head neck cancer is that it is all about teamwork.
You've talked in the past about your gravitation towards surgery and research. It wasn't a lightning bolt or aha moment, it was more of a journey. And it was informed by and shaped by mentors. Talk to us about how important those voices were in your career progression.

**DR. JONATHAN IRISH**

A good example for me on the clinical side would be someone like Pat Gullane, who is a surgeon here at UHN and Princess Margaret who instilled the excitement, I think, and probably the best word is enthusiasm, of both clinical care and discovery. And then on the basic science side, I was lucky enough to work in Dr. Alan Bernstein's lab at the Mount Sinai Hospital, a world, a national leader in research, and obviously, set the path for discovery and how to appropriately experimentally discover.

On the research side, you know, it often involves roadblocks, challenges, failure. I'm interested to hear how you navigate failure, because it's not like it's something that we're taught in school?

**DR. JONATHAN IRISH**

You learn a lot from your failures too. Research and clinical care, we all have losses, and you learn, and you learn from your mistakes, you learn of how you could have done it better, how the team might have done it better, what you might have done better to do better. And we have that in research all the time. That's the re in research. And we do, and we relook, and we repurpose, and we recover, and we do it again. And we think of how we could have done it again and get to success.

And what if you have a must have list of qualities, that someone needs to be a success in medical research?

**DR. JONATHAN IRISH**

I would say passion, because in passion comes, you gotta want to do it. And you got to have that stick to itiveness. And so I think the passion kind of describes is one word that kind of describes that.

You see patients most every day, you see the need for better treatments, how do you reconcile their urgency and their need with the fact that science takes time?

**DR. JONATHAN IRISH**
The clinical problem we are faced with regards to speed, and to those who must be external observers of the research process. And having seen so much money being raised and invested in to research and the perception, I guess, that we're moving so slowly. And it's a complicated problem, right? I mean, let's think back 40 years to Terry Fox's Marathon of Hope. When you walk through the doors of the Princess Margaret, and your chances of survival, putting all cancers together and your chances of survival were in the order of around less than 40%. And now, we're between 65 and 70%. So somewhere along that 40 years, we've made advances. Was there a eureka moment? Was there a switch turned on was there? You know, one thing that moved that? No, we moved the dial slowly, but surely.

DR. JONATHAN IRISH

And that's the problem, right? And that their perception is that, oh, we got to find the cure for cancer. The fact of the matter is, there is no one cure for cancer. It'll be many, many steps, built one on another, that achieves a slow but incremental improvement over time. I really emphasize the fact that this is an investment in time, investment in research and investment in that slow, incremental building block of achievements built one on another to achieve and improve.

BTB

And what do you think of the patients who step up and say, I'll be a part of your trial?

DR. JONATHAN IRISH

I think, number one, they're brave. And number two, they want to be part of it. They want to be part of that discovery. And I really applaud that. And they also want to do something for others. And I think that is incredible, incredibly brave, incredibly meritorious, and is fundamentally at the end of the day as part of their character.

BTB

There's a great saying people don't buy what you do. They buy why you do it. Why do you do what you do?

DR. JONATHAN IRISH

Well, I guess it gets back to that. You asked about the quality I think passion, right? And I do it because I really enjoy it. It really turns me on. I like discovery. I like science. I like teaching others. I like to create. I like to translate that to care for others. I like to innovate. And I like to educate so there's a lot of cates in there, but somehow the Create, the innovate, the Translate, and the Educate are what I like to do.

BTB
You’re entering a phase where I think many of us would be putting the finishing touches on their career and contemplating retirement. Does slowing down ever enter your thinking at this point?

DR. JONATHAN IRISH

Not yet. I really have not thought about slowing down. But you know, obviously at the end of the day, when you hit the age of 60. The fact of the matter is that you’re closer to the end of your career than you are to the beginning and that’s sad for me. But at the end of the day, I will do what I do as long as I’m passionate about it, number one. And number two that I’m doing it well. And once those two boxes are not checked, then I’m out of here.

BTB

When you get to that point of those check boxes checking you out, so to speak, and then you reflect, do you think at all of your legacy?

DR. JONATHAN IRISH

Well, I think the legacy that I will have will be the fact that there will be no interruption in what we do, because I will have been part of a great team. And I'll reflect back to my canoeing days, we will have lost, you know, one of one member of the boat, but there'll be another stronger, smarter and very good replacement for me. That is the legacy that I think our program will have built is the fact that we have a machine and it's an inner many interdigitated gears, cogs in the wheel of that machine. But each member, each cog can be replaced, and I have no illusions to think that I can't be replaced.

BTB

Well, Dr. Jonathan Irish, pioneer in the research of novel approaches to enhance cancer surgery outcomes. Thanks for sharing your groundbreaking research with us and continued success.

DR. JONATHAN IRISH

Hey, Christian it's been great and I hope your audiences enjoyed it. Take Care.

BTB

For more on Dr. Irish’s work and on the podcast, go to uhn.ca or www.behindthebreakthrough.ca. And please let us know what you think we'd love your feedback. That's a wrap for this edition of Behind the breakthrough, the podcast all about groundbreaking medical research and the people behind it, at the University Health Network in Toronto, Canada’s largest research and teaching hospital. I'm your host, Christian Coté. Thanks for listening.