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Illuminating Innovations in Tumor Resection Surgery

Announcer:
Welcome to Medical Breakthroughs from Penn Medicine, Advancing Medicine Through Precision Diagnostics and Novel Therapy.

Dr. Caudle:
Even though surgery is one of the most common treatment options for patients diagnosed with cancer, it's not exactly synonymous with the word "cure," since many patients still experience recurrence following surgery, as undetected cells may still remain in the body. So, what research developments are being evaluated to improve the detection of cancer and treatment for these patients? This is Medical Breakthroughs from Penn Medicine on Reach MD. I'm your host, Dr. Jennifer Caudle, and here to discuss research being done using an illuminating new technology is Dr. Sunil Singhal, Director of the Thoracic Surgery Research Lab and Associate Professor in Research at Penn Medicine. His current surgical research program focuses upon evaluating TumorGlow, an investigational intraoperative imaging technique. Not yet FDA approved, TumorGlow employs fluorescent dyes that collect in cancer cells with the goal being to illuminate tumors and their margins. Dr. Singhal, thank you for joining us.

Dr. Singhal:
Thank you for having me.

Dr. Caudle:
Well, we're excited that you're here and to start us off, I'd like to do some level setting as to the current landscape of cancer care, specifically in terms of thoracic oncology. What can you tell us about this?

Dr. Singhal:
So thoracic oncology has really been evolving quite rapidly over the last decade or so. There's been several changes. We're having more adenocarcinoma than squamous cell carcinoma. There's also been a lot of changes in the epidemiology, although cigarette smoking is on a decline. It appears that the fifth largest population of cancer patients in this country now are nonsmokers. People who have never touched a cigarette and, quite frankly, haven't even been exposed to second-hand smoke. Within the field of thoracic oncology, there have been quite a few advances that I think we all have heard of – immunotherapies and PD1 inhibitors, which have changed the field. But what I've been most interested in is really what is going on in the world of surgical care for lung cancer patients.

Dr. Caudle:
Excellent. You know, now that we have that background, could you explain the development of TumorGlow and how it works in practice?

Dr. Singhal:
Yes. Sothere's roughly 100,000 people each year in the United States who go for lung cancer surgery. 40% of those patients will go on to develop a recurrence, A third of those patients were recurring within 2 cm of where the surgeon was working.

And that didn't make a whole lot of sense to me. I've done thousands of operations. So, I felt that we must be missing things – we must be missing cancer cells. And this is sort of the beginning of where my research got started.

And as I started to do my research, I found that the issue was we just couldn't see microscopic disease. because when we're in the operating room, the only things we have is our hands and our eyes. So, it was with that thought that I was thinking there's got to be a better way to highlight the tumors– some way for these cancer cells to glow so that they would become highlighted. And that's essentially the basis of the idea of TumorGlow. We were working on all sorts of dyes, fluorescent dyes. The dye that struck my interest

was something called indocyanine green. at the beginning of the 2000s in the 2005 era, this concept of nanotechnology was really emerging in medicine. The ability to take very, very small particles – very small dyes that are completely safe to humans because they attach right to the body. They can be excreted out. They really cause no toxicity and indocyanine green was one of those. And the beautiful thing about indocyanine green was it actually glows quite bright and so TumorGlow essentially became a decade-long project on how to inject indocyanine green into people to make tumors glow. And then the science behind that becomes a little bit more intricate. But that is essentially what TumorGlow is.

Dr. Caudle:
That's very, very interesting. And you've talked a little bit about how this technology is used, but from your observations, can you talk a little bit about where it's proved most useful, the technology, and also in your journeys with this, has there been anything unexpected that you've discovered from your research?

Dr. Singhal:
I don't think we ever stop finding unexpected things. I think it still shocks me how often we think we did a perfect case and then we turn on the camera that sees the glowing dye and we missed something. So, I would say that's always the biggest surprise.

In terms of – in terms of where I think we've made the most head – we're making headway in a lot of fields. I think one of the biggest areas is brain tumors. We're finding that our ability to see the borders of brain tumors is spectacular. I think within the chest– one of our biggest accomplishments is sarcomas that metastasize to the lungs and colon cancers that go through the lungs. We have been able to find nodules less than 1 mm, things that we never would've seen before. It's well below the detection of the CAT scan, which is sort of the traditional approach, or a PET scan. So, the ability to locate metastatic disease is very good.

Another cancer is thymomas, so the ability to see the borders of these tumors that start in the chest to see nerve – the phrenic nerve, which we want to preserve. Also, mesotheliomas, which is a cancer of asbestos, so the indications in the chest have become quite broad. I think the other area that we are starting to see some headway is in this concept of liver cancers where – well tumors that go to the liver, such as colon cancer, is another really big area. Cancers in the pancreas, especially in the distal pancreas, we can begin to see the borders of these cancers quite well, so I think the indications are quite broad. We're at the tip of the iceberg. It's only in the last two years that we've started to do larger clinical studies, so I think the future's exciting, and we'll find out.

Dr. Caudle:
Absolutely. Definitely. For those of you who are just tuning in, this is Medial Breakthroughs from Penn Medicine on Reach MD. I'm your host, Dr. Jennifer Caudle, and today I'm speaking with Dr. Sunil Singhal from Penn Medicine on the new innovation, TumorGlow, and how it's advancing care for thoracic oncology. So, continuing, Dr. Singhal. How is TumorGlow benefitting surgeons and patients, and are there any challenges that you've encountered in clinical practice?

Dr. Singhal:
I would say, for example, for lung cancer, we're finding three things that have been particularly useful with TumorGlow. The first is when we go into the chest to operate on the patient with a cancer, how often the patient may have a second cancer. Now, it's been known in the literature – it's been very hard to prove – that when you operate on a patient with lung cancer that in a percentage of them – a small percentage, 8-10% - will go on to get another cancer within 3-5 years.

But there was no way to detect this before, and so the patient 3-5 years later, would get a second operation for another cancer. What we're finding is that since our TumorGlow is so sensitive, we can begin to find these second cancers at the time of the initial operation.

So, that's the one big benefit. The second big advantage of TumorGlow is we can see the margins or the edges of the cancer as we're operating, and this allows us to have wider margins or essentially an opportunity to make sure that we're avoiding cutting through the cancer.

The third benefit that we've discovered over the last four or five years is for these small lesions, it's very hard to find them, even if you have a good CAT scan and a PET scan,

The one advantage of TumorGlow is, since it makes the tumor fluoresce, or glow, we can really pinpoint the location of the cancer and be much more precise in how much of the lung we cut out. And this has been also – although it's not necessarily improving long-term survival rates, it does improve the morbidity or the trauma the patient goes through. So, I would say those are the three biggest categories of help that TumorGlow is doing during our surgeries.

Dr. Caudle:
Excellent. Excellent. You know, in talking about the patient side, how might a physician refer a patient whom they feel might be a candidate to have this process done. You know, what's the availability of TumorGlow? Is it widely available?

Dr. Singhal:
No, so right now, we are conducting a clinical trial at University of Pennsylvania. We have – our initial studies are complete. So, we've done all the safety and toxicity. We're now moving into – we're up to about 1,000 patients. We are now starting a cooperative group trial, which is a multi-institutional call to the alliance which is a large umbrella organization in this country. So, that will be 10 sites. That hasn't started yet. Right now, it's – it's still available really at Penn through clinical trials that we hope – I'm hoping in the next six months we are going to get our cooperative group trial going. That will be 10 sites around the country. And then we'll go from there.

Dr. Caudle:
Excellent. And lastly, Dr. Singhal, how do you think TumorGlow will ultimately change the future of surgery for cancer?

Dr. Singhal:
Wow, it's been an – I can't imagine how it's not going to change the field. You're going to have the ability to have tumors glowing. You're going to now find cancers easier. You can do more directed operations. You can be a bit more selective in the lymph nodes you have to take out and not take out. You're going to solve all sorts of problems, whether you have breast cancer and you don't want to get lymphedema and do larger axillary node dissections. If you are in lung cancer and need to find smaller – small lesions, or you want to do – especially for patients who don't have very good lung function, so you can do smaller procedures. If you're in brain cancer and you need to be very careful about taking excessive areas of the brain because of affecting patient's normal functions. Whether you're doing ovarian cancer, and we're finding that we can do debulking operations better, especially for women who have metastases. So, I think that the field is going to be dramatically changed. I think what is going to happen, if I had to sort of think about this, where we're going to be in a decade, I do think that the first generation of dye – the TumorGlow dye that we're developing at Penn – are going to get better. I think that if we were to fast forward, the dyes are going to be brighter. We're going to be able to see deeper into organs with the fluorescence. I think that we are going to also have dyes which will have the ability to see more types of cancers because one of the issues, as we all know, is different types of cancers are very different. They're heterogeneous, and so we're going to have dye which will be able to tackle the heterogeneity of cancers. So I think we're at the tip of the iceberg. It's an exciting time and the field is going to be dramatically evolving over the next decade.

Dr. Caudle:
Excellent and I do agree with you. I do think this is a very exciting time. You know, with these hopes on the horizon, I'd like to thank our guest, Dr. Sunil Singhal, for sharing his insights on TumorGlow, and how this technology is impacting the field of oncological surgery. It was a pleasure speaking with you, Dr. Singhal. Thanks so much for being with us.

Dr. Singhal:
Thank you for having me.

Dr. Caudle:
And I'm your host, Dr. Jennifer Caudle, with ReachMD and thank you for listening.

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