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The Evolving Role of Radiation Oncology in Breast Cancer Care

Announcer:
You're listening to a special focus on breast cancer from *Advances in Women's Health,* sponsored by Lilly.

Dr. Birhnolz:
Coming to you from the Lynn Sage Breast Cancer Symposium in Chicago, Illinois, this is Reach MD. I'm Dr. Matt Birnholz. Joining me is Dr. Jonathan Strauss, Associate Professor of Radiation Oncology at the Robert H. Lurie Comprehensive Cancer Center of Northwestern University. Dr. Strauss has delivered multiple talks at this year's symposium, reflecting on the evolution of radiation oncology as a field, tackling challenging breast cancer cases, and most recently examining some of the emerging factors supporting the emission of radiotherapy in invasive cancers, which I imagine in some ways is a taboo subject among some in your field – the idea of maybe we should not do it at all. I imagine it would be antithetical to some, from a distant standpoint, in the radiation oncology field. So, Dr. Strauss, welcome to you.

Dr. Strauss:
Well, thank you. I'm glad to be here.

Dr. Birhnolz:
So, why don't we get right into that. As far as the most recent topic of discussion that you maybe came in and spoke about, what kind of factors from a general standpoint – we can't get this done in a 5-minute kind of conversation, but what kind of factors play into your mind as considerations for when to omit radiotherapy in invasive cancers? Because that's not intuitive to many people I think.

Dr. Strauss:
I think that's a great question. And let's start with the fact that when we began to do breast conservation, we learned that radiotherapy was an integral component of the overall treatment. That with surgery alone, we found high rates of recurrence in the breast, but then after radiotherapy, we found much lower rates of recurrence in the breast. And on meta-analysis of these trials, we saw that radiation improved survival. So we've seen for a long time that radiation has been a valuable component of the overall cancer care. At the same time, our rates of in-breast recurrence have been slowly and steadily declining, which is great news, and it's been happening for a whole variety of reasons. Most notably, improvements in systemic therapy – things like chemo and endocrine therapy, but also improvements in surgical technique and imaging and pathologic assessment. And all of that has led us to ask the question again – are there subsets of women who maybe don't require radiation, or maybe the risk of recurrence in the breast gets low enough that we feel comfortable with that level of risk without radiation? And so we have a series of trials that have asked this question, slightly different, but overlapping populations. The clearest answer is that, for women who are over the age of 70 and have a very wimpy breast cancer – so small and node-negative, estrogen-positive, planning to take an anti-estrogen pill, especially when HER-2 negative, that these women have a relatively low risk of in-breast recurrence with estrogen – with an anti-estrogen alone. Often at 10 years in the range of 8 to 10%. Now, does radiation still work? It sure does. It pushes that risk of recurrence even lower, but there isn't that much for radiation to do. Those women have a very modest risk of recurrence already, although it can get extremely low with radiotherapy.

Dr. Birhnolz:
Were you looking at some rates between comparative and 1% versus 5%?

Dr. Strauss:
That's right. At five years, we would compare about 5% with endocrine therapy alone, pushed down to 1% with radiation. Those rates double at 10 years to be about 10% versus 2%, but it's very unlikely that would bring with it any change in survival. In other words, these

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women are very unlikely to have their life shortened by breast cancer. No matter what we do with radiation. So we can do radiation and sometimes a woman will really want it because her main goal is to minimize the risk of recurrence, and that's very reasonable. But it's also very reasonable to think about leaving it out. And for that woman to have a modest risk of recurrence in the breast that likely won't compromise her survival. And then the question is, we're starting to leave out radiation for women with wimpy breast cancers over 70, but what about for those women under 70ho have that same wimpy breast cancer? And maybe, are there emerging ways to refine this population even further to find women with an exceptionally low risk of recurrence without radiation? And here we have some ongoing trials that are using newer biomarkers to try to identify women at very low risk for recurrence even without radiation. And they're using tests like the Ki-67, which is a proliferative index. They're using tests like the Oncotype recurrence score or the PAM50 test, or just a combination of known factors like estrogen-progesterone receptor status, HER-2, Ki-67. And a whole variety of trials are looking to omit radiation on the basis of using these tests in combination with clinical factors to find a very low-risk women – population of women. I'll say at Northwestern, we have a similar trial that's about to get up and running using circulating tumor cell status in addition to other clinical variables to try to identify a very low risk of women where it's safe to leave out radiation. From the point of view of a radiation oncologist, I think we always want to help people. And to the extent that we can better identify who really needs our treatment and who doesn't, that's even better.

Dr. Birhnolz:
In effect, it sounds a little bit like something, if not just short of it, right around the market of the Holy Grail of your area just to be able to accurately, predictively identify patients who would not need, even with invasive cancers, who would not need radiotherapy.

Dr. Strauss:
I completely agree. Right now, essentially what we're seeing is we find women who have enough risk as a population that they deserve radiation or they would benefit as a population from radiation. But if I could pick from that group who really needs it and who would be safe to have omission, that would be even better. And as a radiation oncologist what would be great is if I knew absolutely that the women I was treating needed my treatment and knew absolutely which women would be safe to omit, that would be the best. Historically, we've simply had to treat everyone because we couldn't differentiate who needed the treatment and who didn't. But we're hoping going forward to be more selective, and to treat only those women with a very high likelihood of benefit.

Dr. Birhnolz:
Fascinating. And, Dr. Strauss, looking at that theme of emerging data, we talked a little but about the work that you and your colleagues are trying to do to better identify patients who would not need radiation therapy and still have very positive outcomes. We talked about the work that has been done to be able to better position patients. There are scores of other areas that I'm sure you're very excited about that are improving the work that you're doing in the clinical practice and, by extension, the outcomes for your patients. As we look ahead, beyond this Lynn Sage Symposium, beyond ESMO, which happened just a week or two before, what's getting you most excited in your area and giving you the most hope on the horizon?

Dr. Strauss:
Sure. I do think there are a lot of things going on. I think we are really trying to understand which populations benefit from which treatments. And so I think these emerging ideas of biomarkers or other indicators, which patients need treatment and which don't. I think I'm quite excited about the idea that our treatments are not only getting safer, they're getting shorter, which is to say fewer treatments. That is more convenient for patients, and it is surprisingly cheaper for the healthcare system. It's interesting, the treatments that I deliver today are not only more effective or at least as effective as they were a few years ago, they're safer than they were a few years ago, and they are less expensive to the healthcare system than they were a few years ago.

There's almost nothing else in medicine that can make that claim. Going forward, I think we're going to continue to push the envelope on how quickly, how conveniently, how safely we can deliver this treatment. And then I want to talk a little bit about some exciting work that our group has been working on, and what we hope to continue on in the future. As we get so good at achieving very high rates of local regional control in breast cancer, we start to shift our focus away from just eliminating the cancer in the breast and lymph nodes and towards doing that safer than ever before, but also with better quality of life than ever before. One of our big considerations is this awful side effect called lymphedema, where a woman can have an arm that swells after breast cancer treatment. And we know there are some key drivers of this treatment.

We know that extent of the surgery in her axilla, her lymph node surgery. We know that BMI or weight plays a role. And we know that radiation to the draining lymph nodes plays a role. My group has been working on understanding what it is that is driving this radiation-related risk, and how we can minimize it. And so our studies looked first at a Northwestern population, and we went back to several hundred women who got regional nodal radiation and compared their radiation fields. And we found that a woman treated with a more

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limited field, one that excluded the dissected axilla, had a lower rate of lymphedema than women with the entire axilla, including the dissected axilla, was treated. We went to the MA-20 randomized trial, which had 2,000 women randomized between radiation to the breast or breast plus lymph nodes, and we looked at women on that trial who were treated with either more limited or more extensive axillary radiation and replicated those findings. Again, we found that extent of axillary surgery and BMI played a role, but also the extent of axillary radiation played a role.

And so now we're really advocating for the idea that when it's oncologically safe, and a patient has had an axillary dissection, we should be carefully omitting that dissected axilla from the radiation field, sparing the arm lymphatics that are traversing that space, and reducing the risk of lymphedema. And going forward, we have a few multidisciplinary efforts in my institution, collaborations between surgery, plastic surgery, physical therapy, and radiation oncology to try to further refine our techniques and continue to push the envelope, and hopefully eliminating this dreaded side effect.

Dr. Birhnolz:
Well, you've given us a lot to think about obviously, and something to look forward to in terms of being able to follow up with you and see how that work is doing. What kind of time course are you anticipating for the length of the trial itself?

Dr. Strauss:
For the different work that we're doing, we actually expect we'll probably have some data over about a two-year period. And we hope to incorporate a variety of techniques, including things like lymphovenous bypass after an axillary dissection, so hooking up lymphatics back to the blood system to drain lymphatic fluid that might be trapped other places. We're hoping to think about how radiation could coordinate with that bypass. We're hoping to look at understanding better body composition and its role as a risk factor. As well as understanding who might be at higher risk and how a screening program might be implemented and whether early detection might limit the development of lymphedema. We hope to get started on each of these projects over the next couple of years, and we'll have some real interesting data for you then.

Dr. Birhnolz:
Well, I'm glad you said that because we're definitely going to want to be on the other side to ask you about that and see how it's going. I very much want to thank my guest, Dr. Jonathan Strauss, from Northwestern University, talking to us about the latest and greatest updates in his field and the work that his team and other colleagues at this conference are doing to advance patient care. Dr. Strauss, it's been great talking to you today.

Dr. Strauss:
Thank you.

Dr. Birhnolz:
For access to this and other episodes, visit ReachMd.com, where you can join the conversation and be part of the knowledge. I'm Dr. Matt Birnholz. Thanks so much for listening.

Dr. Strauss:
That's great.

Dr. Birhnolz:
Thanks so much for sharing your thoughts.

Announcer:
You've been listening to this special focus on breast cancer from *Advances in Women's Health*. To revisit any part of this discussion and to access other episodes in this series, visit ReachMD.com/Advances-in-Women's-Health, where you can join the conversation and Be Part of the Knowledge. Thank you for listening.

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