Discussion for 2021-1765

PROSPECTIVE EVALUATION OF RADAR LOCALIZED REFLECTOR DIRECTED TARGETED AXILLARY DISSECTION IN NODE-POSITIVE BREAST CANCER PATIENTS AFTER NEOADJUVANT SYSTEMIC THERAPY

**DR JULIE A MARGENTHALER** (St Louis, MO): De‑escalation in the surgical treatment of breast cancer has been a continuing trend for the past 2 decades. As targeted adjuvant therapies have been developed with increasing efficacy toward prevention of locoregional and distal recurrence, it is clear that surgical extirpation of all disease is no longer necessary for many patients with breast cancer as it does not impact overall survival or disease‑free recurrence rates. The key is determining which subset of patients can forego more extensive surgical resection with equivalent outcomes.

After the publication of Z1071, many of us sought ways to optimally identify biopsy‑proven axillary nodes in patients who had undergone neoadjuvant systemic therapy. The authors demonstrate that the use of the radar localization system is one feasible model with which to do this.

I have several questions related to the design of the study and potential future implications of your results. First, I question the inclusion of both neoadjuvant endocrine therapy and neoadjuvant chemotherapy patients. Previous studies have shown that the impact of systemic endocrine therapy versus chemotherapy on biopsy‑proven lymph nodes, lymphatic mapping, and the feasibility of lymph node mapping to be quite disparate. What was the breakdown in the numbers of patients in each of those neoadjuvant treatment groups? Further, how many patients in the chemotherapy group fell into the "high response" groups such as HER2 positive and triple negative phenotypes?

Based on the methods of the study, a formal sentinel lymph node procedure (and mapping) was not performed. Although there were only 3 patients where the biopsy‑proven node was not in the targeted dissection, I wonder if this number may have been zero had you performed a formal sentinel lymph node mapping procedure with targeted dissection, as described by others, such as Dr Caudle and her colleagues. Along those same lines, 35% of your patients had no residual disease in the axillary lymph node basin post‑neoadjuvant treatment. I would propose that this is a potential group that could have avoided axillary dissection altogether had a sentinel node procedure been combined with the targeted dissection.

Finally, I think the question that is most vital to answer pertains to the 65% of patients who did have residual disease post‑neoadjuvant treatment. The standard of care currently is completion axillary dissection as we await important clinical trial data. Whether we can further de‑escalate the surgical treatment and morbidity of our patients hinges on whether the residual axillary disease is truly "treatment resistant" in which case surgical dissection may be the only option.

**DR RONDA S HENRY‑TILLMAN** (Little Rock, AR): The surgical management of breast cancer has certainly evolved over time. We can all agree that improving the diagnostic and prognostic value of nodal evaluation, while minimizing the morbidity to patients, is an important goal in the ongoing improvement of breast cancer care. In particular, the management of the axilla has rapidly evolved as our understanding of tumor biology and behavior has improved. Targeted axillary dissection (TAD), with removal of the sentinel lymph node and any clipped nodes, is an example of balancing reduction of patient morbidity while obtaining the most accurate picture of a particular patient's tumor behavior. In that light, Dr Ollila and colleagues have taken the next step by evaluating the accuracy of using radar localization in conjunction with TAD, further aligning with patterns of de‑escalation in their cohort of 35% of patients who had no residual disease in the axilla after completion node dissection. Although complete axillary node dissection was performed, why was the axilla not staged with sentinel lymph node?

The authors did demonstrate a high accuracy, as shown by the low false‑negative rate of 4.7% and more importantly, defined the patient population prone to technical failure; patients who had radar localized reflector placement after neoadjuvant chemotherapy. One question of interest with this novel technique is what are the costs related to the device placement, both in the initial set‑up and in the ongoing reflector device use?

The current standard of care with clip placement requires minimal extra cost. High cost may be a barrier to widespread use of this technology. I have shown in numerous publications, that the placement of the clip, and finding it on ultrasound may also locate the lymph node. Additionally, how far in advance can the radar localized reflector (RLR) be placed without signal failure? The device manufacturers report use without issue with placement greater than 30 days, but is there a point where the device will no longer respond to the localizer, and does an alternative localizing device need to be used? This could be particularly important in patients whose chemotherapy is delayed due to side effects or illness. Finally, and most important, who is placing this device? Are these RLR placed by the radiologist as you indicated? We, as surgeons, should probably be placing them. From a training perspective, what is the learning curve in the placement of these devices? Will our fellows and surgeons who begin to implement this into their practice be adequately trained in the placement and use of these devices?

**DR V SUZANNE KLIMBERG** (Galveston, TX): We use FIND, or Fluoroscopic Intraoperative Node Detection, which our surgeons know has very little added cost, and we find the clip every time. Considering value‑based care, we should be thinking of things such as this. It is also easy for the patient; they do not need an additional procedure. A needle localization or any kind of core base on the axilla is painful. I believe we can find easier and less costly ways to find a clip.

I also want to reiterate that leaving off the axilla is not the standard of care yet. We are awaiting Alliance trials to determine if it is safe to do, because this is resistant disease we leave behind when we have a false negative. It is not the same as Z11, and we need to wait to make that standard of care. The other problem is radiation therapists want to radiate the axilla now because there is an undissected axilla. So, we are replacing a one‑time surgery with radiation.

I want to reiterate that we can do better surgery. We are surgeons and should be figuring out how to better perform surgery. Please put patients on my trial, which is the Axillary Reverse Mapping 221702 Alliance trial. I have published a large series with over 600 patients showing we can decrease the lymphedema rate to 6%, which is lower than the sentinel lymph node trial, the Z11 for sentinel lymph node.

**DR KELLY McMASTERS** (Louisville, KY): I guess I am looking at this philosophically. We do the same thing. No matter how you decide to localize the lymph nodes prior to neoadjuvant therapy, we have now set the expectation in breast cancer and melanoma patients that axillary dissection is the most evil thing we can do to a patient, and that every patient and every oncologist thinks it is a horrible, horrendous procedure. So, every time I am in the clinic with my residents, and I have a patient who has been 10, 15, 20 or more years cured of their cancer after having a lymph node dissection, and has a fully functioning extremity without lymphedema, I make a point of showing the trainees that the risk/reward ratio of this procedure may not be so bad.

I do the same thing that you do, but I struggle with the expectation that every patient can have axillary nodal preservation even in the setting of having palpable nodal disease prior to therapy. There are some patients for whom we know that this is a bad idea. What if they have a cancer that is not exquisitely sensitive to neoadjuvant therapy? What if it is a patient who has a triple positive cancer getting chemotherapy and not a HER2 positive or a triple negative cancer where the pathologic complete response rate is going to be higher? What if you know the patient has not had a complete response in the primary breast tumor, and you know that it is very unlikely they are going to have a complete response in the axilla? Is there a way we can be more selective about the patients to whom we offer the potential for axillary nodal preservation? Can we just tell some patients that they need an axillary lymph node dissection?

**DR DAVID W OLLILA** (Chapel Hill, NC): I may group these a bit so we do not repeat, I would like to start with this: At UNC, if your TAD specimen is negative, we do no other surgery. We believe the results of our trial. We are not dissecting those patients any longer.

I completely agree with the concept that if there is disease in the TAD specimen after you have given all your systemic therapy, you have resistant disease, and I put these patients on Suzanne's ARM trial. I had to do that before the TAD, but there are some logistics. I completely support the ARM trial for these patients.

So, that dovetails into Dr McMasters’ question. I agree there are patients that we completely help in the cure of their disease. I am advocating that we are more selective of which patients we do this on, and I believe the TAD specimen directs us in doing what is needed.

Back to the top with Dr Margenthaler; I knew there would be a phenotype question. Fifty percent of our patients were HER2 negative, hormone receptor positive, and we have a bias at our institution that infiltrating lobulars, because of the very low response rate to systemic therapy, are more likely to receive endocrine therapy. So, your point is well taken. Half of the patients were hormone receptor positive, HER2 negative, and there was a bend towards endocrine therapy. One quarter of our patients were triple negative, 15% of our patients were triple positive, and the remaining seven patients, or 8%, were hormone receptor negative and HER2 positive. That brings up the question, to which patients are we going to add the sentinel? I think this is a back‑room discussion because I am still unclear on it. So, I am not dodging the question; I think it is very valid, but what more do we add in these patients to try and decrease the false negative rate? It is a fair question. Surgical therapy to overcome systemic resistance is a real property. I would like to leave with the thought that we must, as surgeons, intervene.

Back to the cost aspect. Placing a clip, then placing the reflector, we go straight to reflector, correct? So, these patients do not have two procedures. If their biopsy is positive, they have a reflector placed. That is our way of getting around this. This way there is nothing else, and we have a console in the operating room that we use, and the only disposable is a single hand‑held piece that is used.

In Radiology, the radiologists place them, and we can discuss, but that is a political issue at our institution. The radiologists place all clips. The radiologists place all SAVIs, so that is what we need to do at our institution. Your point is well made about what we are doing for our trainees. Unfortunately, that has been a hurdle we have been unable to overcome at our institution.