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EDITORIAL – BREAST ONCOLOGY

Intact Excision of Breast Lesions Using BLES^{TM}: Is There a Clinical Indication Yet?

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In this issue of *Annals of Surgical Oncology*, Whitworth et al.[1] report their data from their Intact Percutaneous Excision (IPEX) Registry. In a prospective study, 124 cancer patients (both invasive and noninvasive) and 160 patients with high-risk breast lesions (HRLs) underwent a minimally invasive (MI) resection of their lesions using the Intact Breast Lesion Excision System (BLES^{TM}; Medtronic Inc., Dublin, Ireland). BLES uses a 15 or 20 mm vacuum and radiofrequency biopsy device to remove mammographic lesions en masse. This is the second study by Whitworth et al. to examine the BLES device. In 2011,[2] 1170 patients at 25 institutions underwent IPEX with the BLES device. Eighty-three patients (7%) had an HRL and 191 (16%) had carcinoma. Only 32 patients had atypical ductal hyperplasia (ADH), of whom 9.4% were upgraded to carcinoma after surgical excision. None of the 51 patients with non-ADH HRL had an upgrade. In this current study, the authors examined their results with cancers < 20 mm and HRLs. The study examined the short-term goals of tumor upgrade or tumor-positive margins; follow-up was not long enough to establish the efficacy of BLES for cancer. Of 124 cancer patients, 55% had clear margins after undergoing a biopsy with the BLES device, 27% underwent another procedure with the BLES device to establish negative margins, and 18% underwent surgical excision of their cancer because they did not fulfill pathology and radiology criteria with IPEX. Therefore, amongst those who fulfilled IPEX criteria, 33% still had tumor positive margins and required another procedure to get negative margins. Of 88 HRLs, only two (2.4%) had subsequent upgrade to ductal carcinoma in situ (DCIS) on subsequent surgical excision. Furthermore, of 72 HRLs that fulfilled the criteria for MI resection, no further resection was performed, therefore tumor upgrade could not be assessed.

The BLES device was US FDA approved in 2001 for sampling biopsy and in 2005 for complete removal of an imaged abnormality. In 2015, the FDA approved the device for lesions 12–30 mm in size. The main advantage of the BLES device is that it removes the entire lesion as one specimen, thereby preserving the architecture and enabling more accurate tissue diagnosis. A smaller proportion of noninvasive lesions and HRLs are upgraded to invasive tumor or cancer, respectively. Indeed, previous studies have demonstrated that the biopsies with the BLES device resulted in a lower rate of lesion upgrade than a traditional vacuum-assisted core biopsy.[3,4] Because the BLES device removes the entire lesion, one might expect more complications, such as hematomas or wound issues; however, earlier studies[2,5,6] have reported hematoma rates of $< 3\%$, including the study included here. A study published last year reported a 6% complication rate,[7] while a more recent study reported that approximately 20% of patients had complications ranging from hematoma, delayed wound healing, skin burn, and infection.[8] Of note, 60% of these complications occurred days to months after the biopsy was performed, therefore this procedure is not without risk.[8] This study underscores the need for longer-term follow-up of these patients to determine the true rate of complications associated with the BLES device. Additionally, the impact of IPEX on future mammographic surveillance of cancer patients is not known and deserves future study.

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Studies of the BLES device, including the study by Whitworth et al., have shown rates of upgrade for HRLs of < 10%,[2] which compares favorably with upgrade rates in patients undergoing vacuum-assisted core biopsy, which range from 10 to 30%.[9–15] This study reports an upgrade rate of 2.4% for HRLs, while another recent study reported an upgrade rate of 3.0% in patients with HRLs who underwent the BLES procedure and surgical excision.[7] Lowering the upgrade rates with HRLs requires careful patient selection and the IPEX registry was careful to include certain patients. Cases must meet 'imaging and histologic criteria for definitive diagnosis', meaning complete removal of the imaged lesion, pathology correlation with imaging, and pathology evaluation to ensure no component of the lesion was at the margin of the specimen. In the former study by Whitworth et al.,[2] if these criteria were met, no lesions were upgraded to carcinoma; however, only one-third of the ADH cases actually met this criteria. In the current study, only 2.4% of all HRLs were upgraded if the criteria were met. It is not clear how many patients did not meet these criteria in the current study and what the upgrade rate would be if these patients were included. With these strict criteria, it is not surprising that the upgrade rate was so low. In fact, many recent studies have questioned the need for excision of all HRLs, particularly ADH and lobular neoplasia. Using strict radiologic and pathology criteria, upgrade rates have decreased to < 4%[16–19] for ADH and lobular neoplasia cases. These findings call into question whether a new device is really necessary if other clinical, radiologic and pathologic criteria, which do not require a new device per se, can be used to decrease the number of patients requiring surgical excision.

The role of the BLES device for small early-stage cancers is less well-studied. A recent study of the BLES device showed no upgrade rates for DCIS lesions that underwent surgical excision.[7] Another series reported that 21% of patients with DCIS on biopsy using the BLES device had invasive carcinoma on excision,[5] and 39% had complete excision. In the current study, 55% of cancerous lesions (DCIS and invasive carcinoma) had complete excision, with one procedure using the BLES device, and 45% of patients had to undergo another procedure, either with the BLES device or surgical excision. These data suggest that IPEX of smaller cancers is not decreasing the need for additional procedures to achieve negative margins. These findings should also be weighed with the lower tumor-positive margin rates (10–16%) now being reported with the publication of the Society of Surgical Oncology/American Society for Therapeutic Radiology and Oncology (SSO/ASTRO) margin guidelines.[20–25] Furthermore, the authors used a definition of 'no tumor at ink' for both DCIS and invasive cancer. Although the SSO/ASTRO guidelines[26] state clinical judgment can be used to determine if DCIS patients with margins < 2 mm require mastectomy or re-excision, a 2 mm margin for DCIS is still considered the 'standard' margin according to the guidelines. It is not clear from the current study what proportion of invasive and noninvasive cases had a tumor-positive margin and whether using a strict definition of 2 mm for DCIS cases would have changed the tumor-positive margin rate. Longer term follow-up of both DCIS and invasive lesions is needed to determine if BLES removal of lesions is equivalent to standard surgical excision for local recurrence.

In conclusion, while the concept of the BLES device is alluring, challenges remain for its implementation. If criteria for the excision of HRLs change over time, then low upgrade rates could be achieved without the need for another device. Re-excision rates may continue to decrease with growing adherence to the SSO/ASTRO guidelines,[25,26] making the BLES device less desirable or needed to decrease the number of procedures to establish negative margins. Long-term follow-up data for cancer patients is needed to establish efficacy in the cancer population. Cost effectiveness has not been established. Given that the device has been in use for over a decade, but not in widespread use across the country, makes it less likely that its utilization will change dramatically over the next decade.

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