The presence of sensation in a reconstructed breast has been shown to improve the patient-rated quality of life following mastectomy and reconstruction and is an important safety factor for prevention of burns and other flap injuries during postoperative care. Unfortunately, breast reinnervation is not considered a priority by most reconstructive surgeons because standard neurotization can be a lengthy process with variable results.

Methods: Fifty-seven deep inferior epigastric perforator (DIEP) flaps were performed on 35 patients. Neurotizations were performed to the third anterior intercostal nerve by directly coapting the flap donor nerve or coapting with a nerve conduit. Nine nonneurotized DIEP flaps served as controls and received no attempted neurotization. All patients were tested for breast sensibility in 9 areas of the flap skin-island and adjacent postmastectomy skin. Testing occurred at an average of 111 weeks (23–309) postoperatively.

Results: At a mean of 111 weeks after breast reconstruction, neurotization of the DIEP flap resulted in recovery of sensibility that was statistically significantly better (lower threshold) in the flap skin ($P < 0.01$) and statistically significantly better than in the native mastectomy skin into which the DIEP flap was inserted ($P < 0.01$). Sensibility recovered in DIEP flaps neurotized using the nerve conduit was significantly better (lower threshold) than that in the corresponding areas of the DIEP flaps neurotized by direct coaptation ($P < 0.01$).

Conclusion: DIEP flap neurotization using the third anterior intercostal nerve is an effective technique to provide a significant increase in sensory recovery for breast reconstruction patients, while adding minimal surgical time. Additionally, the use of a nerve conduit produces increased sensory recovery when compared direct coaptation. (Plast Reconstr Surg Glob Open 2013;1:e72; doi: 10.1097/GOX.0000000000000008; Published online 19 November 2013.)

Disclosure: Dr. Dellon has a proprietary interest in the Pressure-Specified Sensory Device, which he invented. He owns Sensory Management Services, LLC, the company that markets and sells this device. A small grant was received from Synovis to fund the research assistant who conducted the blinded sensory measurements. Neither of the other authors has any financial disclosures. The Article Processing Charge was paid for by the authors.
of nerves from the adjacent residual postmastectomy skin, the additional operative time required for neurotization has been considered difficult to justify. The traditional recipient nerve used for breast flap neurotization is the lateral cutaneous branch of the fourth intercostal nerve, which frequently is injured during mastectomy and lies in a separate microsurgical field, thereby increasing the flap inset complexity. The presence of a readily available, undamaged recipient nerve limited routine innervation. We propose that a new method of neurotization involving the anterior cutaneous branch of the third intercostal nerve will provide significant sensory benefit to the patient. This nerve is conveniently located within the microsurgical field when harvesting the internal mammary vessels and therefore adds minimal time to the surgery. The purpose of this article is to evaluate a new method of DIEP flap neurotization using a reliably located recipient nerve. Furthermore, we hypothesize that neurotization with this method (by means of either nerve conduit or direct nerve coaptation) will have a positive effect on sensory recovery.

PATIENTS AND METHODS
This study was approved by the institutional review board and included a retrospective review of patients who underwent free-flap breast reconstruction by senior author (A.J.S.) over a 5-year period. Only patients who had a unilateral or bilateral DIEP flap reconstruction who were able to return for sensory evaluation were included in the study. We had one case of DIEP flap failure that was converted to a latissimus dorsi flap, which was also excluded from the study. In total, there were 57 DIEP flaps performed on 35 patients which were included in the study. Thirty-three flaps had neurotization with the use of a polyglycolic acid nerve conduit (NeuroTube; Synovis, St. Paul, Minn.), 15 flaps had the donor and recipient nerves directly coapted, and 9 flaps had no neurotization and were therefore used as controls. These “controls” were identified intraoperatively when neurotization was not possible due to spatial relationships between the nerve and the vessels. To learn whether improvement in sensation continued to occur, we stratified the neurotized flaps into those ≤111 weeks and those >111 weeks after breast reconstruction. All surgical procedures and patient evaluations were performed at a single institution. The technique for routine neurotization of DIEP flaps using the third anterior intercostal nerve as the recipient has been previously described in detail by Spiegel et al. In earlier reconstructions, nerve conduits were only used when extra length was needed for nerve reconstruction; however, as research emerged displaying positive results with nerve conduit usage, all coaptations were attempted with the use of a nerve conduit. Weber et al described a clinical study of 136 nerve injury repairs over a 4-year period and reported 91% excellent sensory recovery from the nerve conduit repair group compared with 49% excellent results from the direct, end-to-end repair group, which was evidence enough for our group to investigate coaptation with a nerve conduit in our patient population. The majority of our mastectomies were skin sparing (43/57), and 22 of 35 patients had previous abdominal scars at the time of reconstruction.

Operative Technique
In the neurotized flap using the third anterior intercostal nerve, the DIEP flap harvest is performed in standard fashion by incising the inferior aspect of the abdominal flap and dissecting the superficial epigastric vein as a precaution in case of need for additional drainage of the flap. The dissection is carried down to the abdominal fascia, and then, microdissection is performed using loupe magnification to dissect out either the lateral or medial perforators of the flap, as warranted by the patient’s anatomy. The donor nerve is a cutaneous nerve that is identified with the most inferior lateral perforator vessels. These vessels are usually too small to use as perforators for the flap but generally are accompanied by branches of T11 or T12. The nerve is then dissected for neurotization and divided at the level of the fascia where it is a pure sensory nerve. This also allows for the preservation of the motor branches that are important for rectus muscle motor function while providing sensory neural input to a major portion of the flap.

The recipient intercostal nerve is usually easily identified in the third intercostal space during the dissection of the internal mammary artery and vein. Here, a small slip of the pectoralis muscle is elevated and excised. The underlying intercostal muscle is carefully resected to reveal the underlying internal mammary artery and vein. In most cases, the recipient vessels are dissected without resection of the rib. Our experience has shown that the anterior branch of the third intercostal nerve can usually be found at the junction of the inferior portion of the third rib and the sternum, approximately 80% of the time. The nerve, which courses across the superior portion of the vessels, is dissected and transected medially. It is then mobilized to give it the longest length possible in preparation for neurotization. Neurotization is performed by coapting the donor nerve to the third anterior intercostal nerve either directly with a 9-0 nylon suture in standard fashion or with the assistance of a 40-mm nerve conduit. When using the nerve conduit in the third intercostal space,
the donor and recipient nerves are anchored to opposite ends of the tube with 8-0 nylon suture (Fig. 1) (See Video 1, Supplemental Digital Content 1, which displays neurotization with the nerve conduit, available in the “Related Videos” section of the full-text article at http://www.PRSGO.com or, for Ovid users, http://links.lww.com/PRSGO/A13).

Evaluation of Sensibility

Evaluation occurred at an average of 111 weeks (23–309) postoperative. The touch perception threshold for pressure was assessed using a Pressure-Specified Sensory Device (Sensory Management Services, LLC, Baltimore, Md.) The Pressure-Specified Sensory Device (used to measure breast sensibility in this study) registers the amount of pressure required to generate a detectable stimulus for the patient expressed in g/mm². The range of the pressure applied was from 0 to 100 g/mm². Any measured area that required application of pressure above 100 g/mm² to elicit a response was considered to have loss of protective sensation. All patients were tested by a single investigator who was blinded as to the type of neurotization each patient received. Each patient was tested for pressure sensation in 9 predetermined areas of both breasts. Five of the measured areas were located on the skin that was transplanted with the flap and later reconstructed into the new nipple-areola complex. A single measurement was taken in the center of the flap skin (generally directly upon the reconstructed nipple), followed by one measurement in each of the 4 adjacent areas: superior, medial, inferior, and lateral to the nipple. The remaining 4 measurement areas were located on the residual, native, breast (mastectomy) skin surrounding the DIEP flap, and also in the superior, medial, inferior, and lateral position (Fig. 2).

Statistical Analysis

Inferential tests for equality of mean age and time to testing after date of surgery across surgical procedure (nerve conduit usage, direct coaptation, and no
innervation) were performed using the Kruskal-Wallis test (STATA V11, College Station, Tex.). Multiway chi-square contingency tables were also constructed to compare the proportion of procedures performed across immediate reconstruction (yes/no), tests made after the time of testing (yes/no), and abdominal scarring (yes/no), for which the Fisher’s exact test was used. Univariate tests were also performed using a linear mixed regression model (fixed and random subject effect) to identify significant differences in pressure required to generate a detectable stimulus at multiple DIEP flap and mastectomy locations for the following comparisons: nerve conduit vs no innervation, nerve conduit vs direct, and direct vs no innervation. The mixed model was used with a random subject effect to account for within-subject correlation of measurements due to varying bilateral procedures employed on both breasts. Under this approach, we assumed that measurement values obtained from different breasts within the same subject covaried and therefore had nonzero correlation, that is, were not independent. The univariate mixed models employed a within-treatment location-specific pressure measurement as the dependent variable and a single independent variable that was either nerve conduit (0—no, 1—yes), direct (0—no, 1—yes), or no innervation (0—no, 1—yes). Records were selected for only the pair of surgical procedures being considered. Multivariate linear mixed regression models were also used, where location-specific pressure was the dependent variable and age, nerve conduit usage (yes/no), direct coaptation (yes/no), immediate reconstruction (yes/no), time from surgery to sensory testing >95 weeks (yes/no), and abdominal scarring (yes/no) as the independent variables. Clustering on subjects was also used to account for within-subject correlation of responses. Separate regression models were used for the mastectomy and flap dependent variables. Specifically, the dependent variables for the mastectomy model were pressure required at the superior, medial, inferior, and lateral locations. The dependent variables for the flap model were pressure required at the superior, medial, inferior, lateral, and central nipple locations. All tests of hypotheses were based on two-tailed alternative hypothesis using a type I error rate of $\alpha = 0.05$, and therefore, any test with $P < 0.05$ was considered significant.

RESULTS

The mean age among the subjects ($n = 35$) was 47.7 (±7.1), and age ($P = 0.945$) and time from DOS to testing ($P = 0.069$) were not significantly different across the 3 procedures (Table 1). The average and median time from DOS to testing were 109.5 (±70.0) and 95 weeks. Table 1 also lists the frequency (%) of nerve conduit and direct and no innervation procedures and reveals that no significant proportions were observed for immediate vs delayed ($P = 0.376$), testing before or after the median test time of 95 weeks ($P = 0.228$), and abdominal scars ($P = 0.097$). Table 2 results indicate that when comparing nerve conduit and no innervation DIEP flap skin islands, thresholds were significantly lower at the superior ($P = 0.048$), lateral ($P = 0.008$), and nipple center ($P = 0.02$) sites. Whereas for nerve conduit vs direct innervation of the flap skin islands, the mean sensitivity threshold
was significantly lower at the lateral site ($P = 0.002$).

For mastectomy skin flaps (Table 3), the only significant univariate test for equality of mean sensitivity threshold was observed at the lateral site, for which nerve conduit results were approximately half the value of the no innervation results (34.0 vs 67.0, $P < 0.001$). Table 4 lists univariate test results for within-procedure equality of means for DIEP flap-based tests performed before and after the median time to testing of 95 weeks (Fig. 3). Nerve conduit test results after 95 weeks were significantly lower than test results measured before 95 weeks at the superior ($P = 0.038$), medial ($P = 0.11$), inferior ($P = 0.001$), lateral ($P = 0.002$), and nipple center sites ($P = 0.02$). For the direct procedures, we observed no significant differences between test results taken before and after 95 weeks. However, for control (no innervation) procedures, a significant difference was observed at the superior site ($P = 0.023$). For mastectomy skin flaps, significant univariate differences (Table 5) between tests measured before and after 95 weeks were observed for nerve conduit procedures (superior, $P = 0.006$) and control (superior, $P = 0.003$). Multivariate modeling results (Table 6) for DIEP flap data indicate that when adjusting for age, immediate vs delayed, and abdominal scarring (yes/no), a significant reduction in mean sensitivity was observed at all DIEP flap sites, which ranged from $-29.7$ to $-44.4$ ($P < 0.05$). Time to testing was also significant at the superior flap location ($P < 0.05$). At the nipple center location, the presence of abdominal scar-
ring was also related to an increase in mean sensitivity of 18.5 ($P < 0.05$). For mastectomy skin flaps, multivariate modeling indicates that nerve conduit technique resulted in mean reductions of 28.7 and 47.6 in the sensitivity thresholds at the inferior and lateral sites ($P < 0.05$). The direct technique also resulted in a significant mean reduction of 24.8 at the lateral location ($P < 0.05$). Finally, for mastectomy skin flaps, there was a significant mean reduction in sensitivity scores ranging from 0.12 to 0.19 per week after the DOS for the superior, medial, and inferior scores ($P < 0.05$) (Table 7).

### DISCUSSION

The results of this study demonstrate that the DIEP flap can be neurotized with the anterior branch of the third intercostal nerve and recover sensation that is significantly improved compared with the nonneurotized DIEP breast reconstruction. Although either a bioabsorbable (nerve) conduit or a directly coapted nerve can be used for neurotization, this study demonstrated the advantage of nerve conduit with significant improvement in sensory recovery. Over the course of the study, measured sensibility in the neurotized DIEP flap continued to improve significantly. Based on these results, and based on the relative ease of neurotization using the anterior branch of the third intercostal vs the lateral branch of the fourth intercostal, the opportunity to recover sensation may now be offered routinely to women seeking breast reconstruction.

The DIEP flap has, in recent years, become the flap of choice for autologous breast reconstruction at our high-volume center due to its reduced donor-site morbidity. The next step in the evolution of this flap, therefore, would be to improve upon its sensibility. The importance of sensibility following free-flap breast reconstruction has been debated at length in the literature. Although some authors have suggested that sensibility may not be a necessity, we propose that neurotization should be included in the goals for breast reconstruction for multiple reasons. First, sensory recovery is an important factor in flap protection, as several published articles describe injuries to a reconstructed breast due in part to the patient’s inability to sense the skin or tissue damage as it occurs. The presence of sensibility allows the patient to respond to nocuous events more rapidly and prevent prolonged exposure that could potentially harm the breast. Second, studies show that patient satisfaction increases directly with return of sensibility after reconstruction. Temple et al confirmed the results of this study using a multitude of universally accepted surveys and questionnaires. The increase in patient satisfaction associated with improved quality of life, particularly given the significant role of the breasts in a woman’s personal life, serves as the impetus behind the added effort to neurotize the flap.

Whereas previous methods of nerve reconstruction required significantly prolonged surgeries to harvest the fourth lateral cutaneous nerve at an additional microsurgical area, the described technique utilizes the third intercostal space in the vicinity of the internal mammary vessels’ dissection. As seen in Video 1 (Supplemental Digital Content 1, which displays neurotization with the nerve conduit, available in the “Related Videos” section of the full-text article at http://www.PRSGO.com or, for Ovid users, http://links.lww.com/PRSGO/A13), this technique...
is an easy alternative to traditional neurotization. This obviates the concerns over the risk vs benefits of a neurotized flap. Although the uncertainty of sensory recovery remains, as Blondeel et al. suggest, the opportunity for a higher quality of sensibility recovery outweighs the risk of additional operating time. We have demonstrated a higher quality of sensibility with neurorrhaphy and a minimal operative time increase of approximately 8–15 minutes using our harvest and nerve conduit technique. Use of the nerve conduit achieved better sensory recovery, with lower pressure threshold, than direct coaptation. The nerve conduit not only permits improved axonal regeneration but also tolerates the nerve size mismatch between the anterior branch of the third intercostal nerve and the intercostal
branch to the DIEP flap. This eliminates the scar formation inherent to direct anastomosis of the nerves and permits neurotrophic factors to guide the pathway of the sensory nerve toward a nerve of mixed sensory and motor composition for improved distal target recognition.

Although we demonstrate sensory return, the extent of recovery did not reach the same level of sensibility as the normal breast. This is illustrated by a subgroup of patients (11) who underwent solely unilateral breast reconstruction, offering a self-control for comparison of sensory recovery. As a general conclusion from these small groups of patients, it can be estimated that the magnitude of sensation recovered in the areolar portion of the DIEP flap skin, neurotized with the nerve conduit, was only half as sensitive as the contralateral nonoperated breast, given that twice the pressure was required for the

Table 5. Mastectomy Data: Univariate Tests for Equality of Mean Sensitivity Scores before 95 Weeks vs after 95 Weeks

| Site      | ≤95 wk Mean (SD) | n | >95 wk Mean (SD) | n | P  |
|-----------|-----------------|---|-----------------|---|----|
| Nerve conduit |                 |   |                 |   |    |
| Superior  | 60.0 (27.3)     | 17| 35.6 (11.5)     | 11| 0.006 |
| Medial    | 42.2 (28.2)     | 21| 30.1 (20.0)     | 12| 0.264 |
| Inferior  | 43.6 (26.1)     | 21| 26.9 (14.6)     | 12| 0.053 |
| Lateral   | 38.8 (28.8)     | 21| 25.7 (18.7)     | 12| 0.263 |
| Direct innervation |     |   |                 |   |    |
| Superior  | 56.9 (26.7)     | 7 | 45.8 (12.5)     | 8 | 0.13 |
| Medial    | 45.3 (36.4)     | 7 | 29.6 (21.6)     | 8 | 0.088 |
| Inferior  | 46.9 (27.3)     | 7 | 35.6 (30.2)     | 8 | 0.416 |
| Lateral   | 56.7 (24.5)     | 7 | 45.5 (33.1)     | 8 | 0.428 |
| No innervation |       |   |                 |   |    |
| Superior  | 78.4 (14.7)     | 3 | 35.5 (28.9)     | 6 | 0.003 |
| Medial    | 54.0 (32.3)     | 3 | 27.7 (25.0)     | 6 | 0.094 |
| Inferior  | 70.8 (29.3)     | 3 | 41.6 (32.1)     | 6 | 0.219 |
| Lateral   | 88.3 (20.3)     | 3 | 56.4 (24.6)     | 6 | 0.126 |

P-values account for within-subject correlation among repeated measures.

Table 6. Flap Data: Multivariate Tests for Mean Change in Sensitivity due to Treatment (Nerve Conduit, Direct) Adjusted for Age, Time to Testing >95 Weeks (Yes/No), Immediate (Yes/No), Abdominal Scaring (Yes/No), and Interaction between Nerve Conduit (Yes/No) and Direct (Yes/No) with Time to Testing >95 Weeks

| Site         | Mean (SD) | n    | Mean (SD) | n    | P  |
|--------------|-----------|------|-----------|------|----|
| Superior     | -42.18*   |      | -33.64*   |      |    |
| Medial       | -18.10    | 7    | -9.33     | 7    | 0.13 |
| Inferior     | -19.19*   |      | -12.12    |      |    |
| Lateral      | 10.28     | 8.92 | 7.43      | 10.22| 18.5*|

Nerve conduit and direct effects are compared with no innervation (control) group. *P<0.05.
same sensory perception. However, the areolar portion of the DIEP flap skin neurotized by direct coaptation required a pressure stimulus of 4 times that of the contralateral breast.

With the positive results that we achieved, further investigation into other measurements of sensation is warranted. Although this study was not designed to assess recovery of hot, cold, or erogenous sensation, it serves as a good pilot study to examine the efficacy of the third intercostal nerve as a possibility for free-flap innervation. At the time of this study, there was no validated quality of life measurement specifically for breast reconstruction patients. For future studies, we plan to employ the Breast Q questionnaire. Using its psychometric benchmarks, we will be able to augment our current results with better quantification of the impact and effectiveness of breast surgery from the patient’s perspective with respect to both satisfaction and important aspects of health-related quality of life.15

CONCLUSION

Neural coaptation using the anterior cutaneous third intercostal nerve as the recipient is an effective technique for providing sensation. With its conveniently located position within the microsurgical field, the nerve is easily incorporated into the flap inset, as seen in Video 1 (Supplemental Digital Content 1, which displays neurotization with the nerve conduit, available in the “Related Videos” section of the full-text article at http://www.PRSGO.com or, for Ovid users, http://links.lww.com/PRSGO/A13). However, in our effort to further enhance sensory recovery, we now introduce superior results using a nerve conduit. This provides a significant increase in sensory recovery for the reconstructive patient. We continue to strive for the best modality to recover function, form and quality for the reconstructive breast cancer patient, and feel that this method attains an additional benefit in their recovery.

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