A Novel Noncontact Diffuse Correlation Spectroscopy Device for Assessing Blood Flow in Mastectomy Skin Flaps: A Prospective Study in Patients Undergoing Prosthesis-Based Reconstruction

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Summary: A new advanced technology, noncontact diffuse correlation spectroscopy, has been recently developed for the measurement of tissue blood flow through analyzing the motions of red blood cells in deep tissues. This technology is portable, inexpensive, and noninvasive, and can measure up to 1.5-cm tissue depth. In this prospective study, the authors aimed to explore the use of this novel device in the prediction of mastectomy skin flap necrosis. The noncontact diffuse correlation spectroscopy device was used to measure mastectomy skin flap flow in patients undergoing mastectomy and immediate implant-based breast reconstruction before and immediately after mastectomy, and after placement of the prosthesis. Patients were tracked for the development of complications, including skin necrosis and the need for further surgery. Nineteen patients were enrolled in the study. Four patients (21 percent) developed skin necrosis, one of which required additional surgery. The difference in relative blood flow levels immediately after mastectomy in patients with or without necrosis was statistically significant, with values of 0.27 ± 0.11 and 0.66 ± 0.22, respectively ($p = 0.0005$). Relative blood flow measurements immediately after mastectomy show a significant high accuracy in prediction of skin flap necrosis, with an area under the receiver operating characteristic curve of 0.95 (95 percent confidence interval, 0.81 to 1). The noncontact diffuse correlation spectroscopy device is a promising tool that provides objective information regarding mastectomy skin flap viability intraoperatively, allowing surgeons early identification of those compromised and ischemic flaps with the hope of potentially salvaging them. (*Plast. Reconstr. Surg.* 140: 26, 2017.)
CLINICAL QUESTION/LEVEL OF EVIDENCE: Diagnostic, IV.

Mastectomy skin flap necrosis, infection, and implant loss are all interlinked by a shortfall of blood flow/tissue perfusion at the microcirculatory level. Current approaches

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to detect mastectomy skin flap necrosis include clinical assessment, fluorescein dye angiography, and indocyanine green dye angiography. Clinical assessment has been shown to be inherently unreliable because of its lack of objectivity.[1] Fluorescence angiography involves an intravenous dye injection followed by wide-field illumination to map blood perfusion on the skin flap surface (1 to 2 mm deep).[1–5] This may not reflect blood flow in the deep tissues of the mastectomy skin flap. Furthermore, fluorescence angiography lacks feasibility for continuous use in the preoperative clinic and postoperative inpatient settings. In addition, both fluorescence dye angiography and indocyanine green have been shown to overpredict and underpredict mastectomy skin flap necrosis.[1,6]

Noninvasive, continuous, and quantitative methods are highly advantageous for assessing deep tissue hemodynamic states. Noncontact diffuse correlation spectroscopy is a novel, continuous, noninvasive technique that provides quantification of blood flow variations in deep tissues.[7] We hypothesized that noncontact diffuse correlation spectroscopy could provide intraoperative data to enable the prediction of mastectomy skin flap necrosis.

PATIENTS AND METHODS

Participants and Clinical Protocol

Institutional review board approval was obtained. Female patients more than 18 years old undergoing mastectomy and immediate implant-based breast reconstruction were included. Demographics were recorded.

Breast reconstruction was performed by a single plastic surgeon (L.W.), by placement of a tissue expander or implant into a subpectoral pocket with acellular dermal matrix, after mastectomy. The decision to proceed with direct-to-implant versus tissue expander placement was based on the patient's breast size preference and skin flap quantity, quality, and pliability for accommodation of an implant. For the mastectomy, neither tumescent nor vasoconstrictive agents such as epinephrine were used. Additional skin excision was performed if necessary, based solely on clinical judgment (e.g., color, capillary refill, skin turgor) after the mastectomy.

All patients were followed for at least 5 months for the development of complications, including mastectomy skin flap necrosis. Mastectomy skin flap necrosis was defined as any area of skin necrosis on the skin flap.

Noncontact Diffuse Correlation Spectroscopy Device

Noncontact diffuse correlation spectroscopy is a noninvasive, continuous, portable, and easy-to-use technique for the measurement of tissue blood flow up to approximately 1.5 cm in depth/penetrance.[7] This technology has been tested and validated in computer simulations, tissue phantoms, and in vivo tissues.[7–10] We have successfully demonstrated its utility in perioperative monitoring of hemodynamic variations in local and free head and neck flaps.[10]

Noncontact diffuse correlation spectroscopy works by emitting near-infrared light (785 nm) into the tissue through the source path of the probe. [**See Figure, Supplemental Digital Content 1**, which shows a noncontact diffuse correlation spectroscopy flowmeter including *(1)* noncontact diffuse correlation spectroscopy optical probe, *(2)* motorized stage to drive the diffuse correlation spectroscopy probe, *(3)* diffuse correlation spectroscopy probe holder, *(4)* diffuse correlation spectroscopy control panel, and *(5)* diffuse correlation spectroscopy instrument. (*Above, right*) Optical paths of noncontact diffuse correlation spectroscopy probe. The source and detector fibers are projected through separated lens paths onto the tissue surface. Light paths through the tissue with different source-to-detector pairs ("banana shapes") are illustrated to demonstrate the coverages in different regions and depths of the measured tissue, ***http://links.lww.com/PRS/C189***.] The diffused/scattered light from the tissue is collected through the detector path by means of avalanche photodiodes. The light intensity fluctuations detected by the avalanche photodiodes are sensitive to the motion of moving red blood cells in the microvasculature.

Measurements were taken with the noncontact diffuse correlation spectroscopy device before mastectomy, after mastectomy, and after reconstruction (Figs. 1 and 2). Flow measurements were taken from two to three equidistant locations along both sides of the edge of the mastectomy incision at each period. Thirty frames of data were obtained per location at a sampling rate of 2 Hz. The total measurement time for each patient was less than 5 minutes.

Statistical Analysis

Statistical tests for averaged relative blood flow differences at different time points were performed using the Welch two-sample t test. The receiver operating characteristic curve was

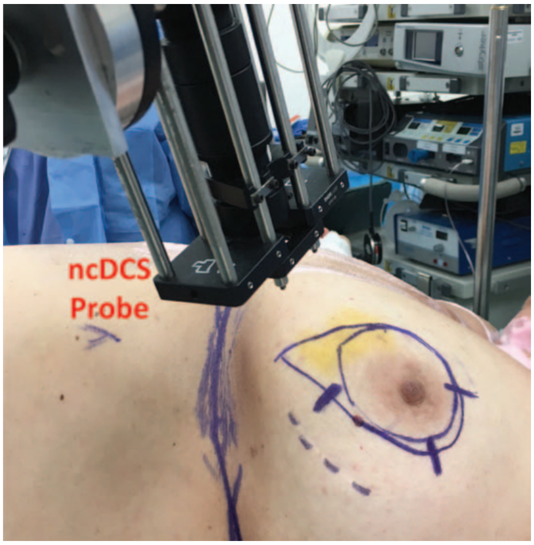

Fig. 1. Noncontact device setup demonstrating blood flow measurements being taken prior to mastectomy in a study patient. *ncDCS*, noncontact diffuse correlation spectroscopy.

constructed and the area under the receiver operating characteristic curve was calculated to evaluate the ability of relative blood flow measurements to discriminate necrosis and nonnecrosis groups.

RESULTS

This study has enrolled 19 patients (Table 1). Four of 19 patients developed mastectomy skin flap necrosis (patients 4, 7, 12, and 19). One patient (patient 4) required surgery (débridement, latissimus flap) (Fig. 2). Figures from Supplemental Digital Content 2 and 3 show results from one patient (patient 4) who developed, and one (patient 6) who did not develop mastectomy skin flap necrosis, respectively. [**See Figure, Supplemental Digital Content 2,** which shows (*above*) measurement setup before mastectomy, after mastectomy, and after reconstruction in a 48-year-old woman (patient 4) who developed skin flap necrosis. The *dashed circles* are flow measurement locations around the incision. (*Right*) Photograph of the reconstructed breast with development of mastectomy skin flap necrosis, taken at 3 weeks after surgery. This patient required a second surgical intervention because of postoperative necrosis. (*Below*) Relative blood flow (*rBF*) responses during surgery in a patient with left invasive lobular cancer. The four source-to-detector distances used in the noncontact diffuse correlation spectroscopy probe were 10.0, 14.2, 18.6, and 22.8 mm, respectively, resulting in light penetration depths of 5.0, 7.1, 9.3, and 11.4 mm. Data graph shows significant decreases in relative blood flow compared with baseline (*T1*), after mastectomy (*T2*), and after reconstruction (*T3*), ***http://links.lww.com/PRS/C190*****. See Figure, Supplemental Digital Content 3**, which shows (*above*) measurement setup before mastectomy, after mastectomy, and after reconstruction in a 41-year-old woman (patient 6) with ductal carcinoma in situ who did not develop skin flap necrosis. The *dashed circles* are flow measurement locations around the incision. The four source-to-detector distances used in the noncontact diffuse correlation spectroscopy probe were 10.0, 14.2, 18.6, and 22.8 mm, respectively, resulting in light penetration depths of 5.0, 7.1, 9.3, and 11.4 mm. Data graph shows relatively smaller variations in relative blood flow (*rBF*) compared with baseline (*T1*), after mastectomy (*T2*), and after reconstruction (*T3*), ***http://links.lww.com/PRS/C191*****.**]

Figures 3 and 4 shows relative blood flow data distribution of all patients after mastectomy

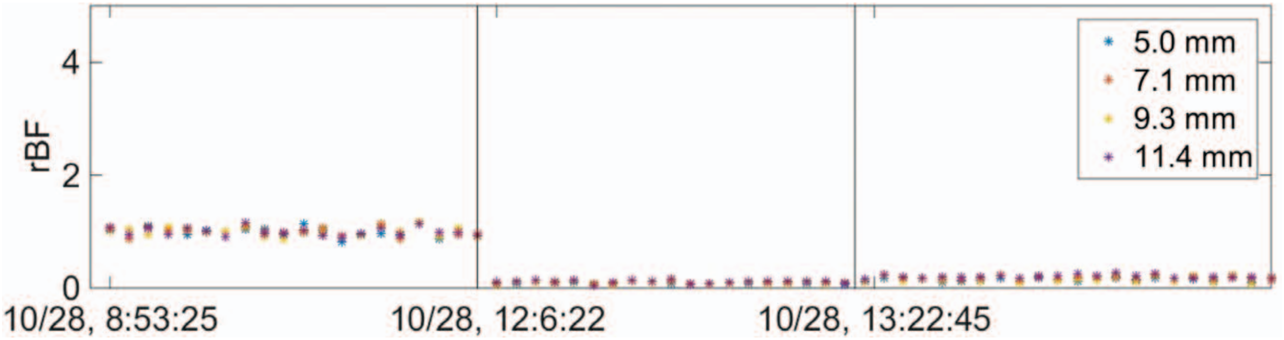

Fig. 2. Relative blood flow (*rBF*) responses during surgery in a 48-year-old woman with left invasive lobular cancer who developed mastectomy skin flap necrosis. The four source-to-detector distances used in the noncontact diffuse correlation spectroscopy probe were 10.0, 14.2, 18.6, and 22.8 mm, respectively, resulting in light penetration depths of 5.0, 7.1, 9.3, and 11.4 mm. Data graph shows significant decreases in relative blood flow compared with baseline (time 1- left box), after mastectomy (time 2 - center box), and after reconstruction (time 3 - right box).

Table 1. Patient Demographic and Relative Blood Flow Responses

					rBF		
Patient	Age (yr)	Type of Mastectomy	TS vs. SS/FF	Skin Flap Necrosis?	Before Mastectomy	After Mastectomy	After Reconstruction
1	35	Skin sparing	TS/100	N	1	0.51	1.07
2	41	Nipple sparing	TS/100	N	1	0.51	1.39
3	53	Skin sparing	TS/200	N	1	0.81	1.36
4*	48	Skin sparing	TS/50	Y	1	0.12	0.35
5	60	Skin sparing	TS/100	N	1	0.80	0.45
6	41	Skin sparing	TS/100	N	1	1.05	0.39
7	36	Amputation	TS/100	Y	1	0.37	0.60
8	32	Skin sparing	TS/60	N	1	0.81	0.58
9	68	Skin sparing	TS/100	N	1	0.52	0.97
10	55	Amputation	TS/100	N	1	0.24	0.50
11	66	Skin sparing	TS/100	N	1	0.53	0.72
12	75	Skin sparing	TS/100	Y	1	0.29	1.16
13	49	Skin sparing	SS/445†	N	1	1.07	0.91
14	66	Skin sparing	TS/100	N	1	0.76	0.85
15	49	Amputation	TS/100	N	1	0.72	1.04
16	45	Skin sparing	TS/50	N	1	0.66	1.26
17	45	Skin sparing	TS/100	N	1	0.52	0.52
18	44	Skin sparing	TS/100	N	1	0.46	0.29
19	59	Skin sparing	TS/100	Y	1	0.31	0.27

rBF, relative blood flow; TS, two-stage reconstruction (expander followed by implant); SS, single-stage reconstruction (direct-to-implant reconstruction); FF, final intraoperative fill of tissue expander (at the time of reconstruction for patients who underwent two-stage reconstruction); N, no; Y, yes.
*This patient required reoperation (latissimus flap) because of severity of mastectomy skin flap necrosis.
†Implant size is written next to the single patient who had a single-stage reconstruction.

(Fig. 3) and after reconstruction (Fig. 4) compared with baseline values. The average relative blood flow after mastectomy was 0.27 ± 0.11 (mean ± SD) in patients who developed necrosis ($n = 4$) and 0.66 ± 0.22 in patients who did not develop necrosis ($n = 15$). This difference was statistically significant ($p = 0.0005$). The average relative blood flow after reconstruction was 0.58 ± 0.40 in patients who developed necrosis and 0.82 ± 0.36 in patients who did not develop necrosis. This difference was not statistically significant ($p = 0.35$).

Relative blood flow measurements after mastectomy show a significant high accuracy in discriminating necrosis and nonnecrosis patients, with an area under the receiver operating characteristic curve of 0.95 (95 percent CI, 0.81 to 1) (Fig. 3). In contrast, relative blood flow measurements after reconstruction demonstrated poor discriminating ability, with an area under the receiver operating characteristic curve of 0.68 (95 percent CI, 0.17 to 1) (Fig. 4).

DISCUSSION

Our pilot study demonstrates the feasibility of a novel, noncontact device (noncontact diffuse correlation spectroscopy) for the prediction of mastectomy skin flap necrosis. The noncontact diffuse correlation spectroscopy device has a negligible risk profile, because of the lack of an intravenous dye injection and lack of direct contact with the patient. Although this device has the ability to detect continuous relative blood flow, the measurements in this study were done in a noncontinuous fashion.

Patients who developed mastectomy skin flap necrosis demonstrated significantly lower blood flow values immediately after mastectomy compared with patients who did not develop mastectomy skin flap necrosis (Fig. 3). Interestingly, the patient who required reoperation had the lowest relative blood flow value (only 12 percent of its baseline flow value) immediately after mastectomy (Table 1), a value likely associated with the severity and extent of the mastectomy skin flap necrosis.

Although average relative blood flow after reconstruction was also lower in patients who developed mastectomy skin flap necrosis when compared to those who did not develop mastectomy skin flap necrosis (Fig. 3), this difference did not reach statistical significance. Furthermore, relative blood flow measurements after reconstruction demonstrated poor ability to predict mastectomy skin flap necrosis (Fig. 4). Relative blood flow values after reconstruction also demonstrated larger variations compared with those after mastectomy (Table 1 and Figs. 3 and 4). Congestion caused by the presence of the tissue expander or implant after reconstruction may lead to larger flow variations in the overlying tissues. In addition, the relatively large change in tissue geometry and volume

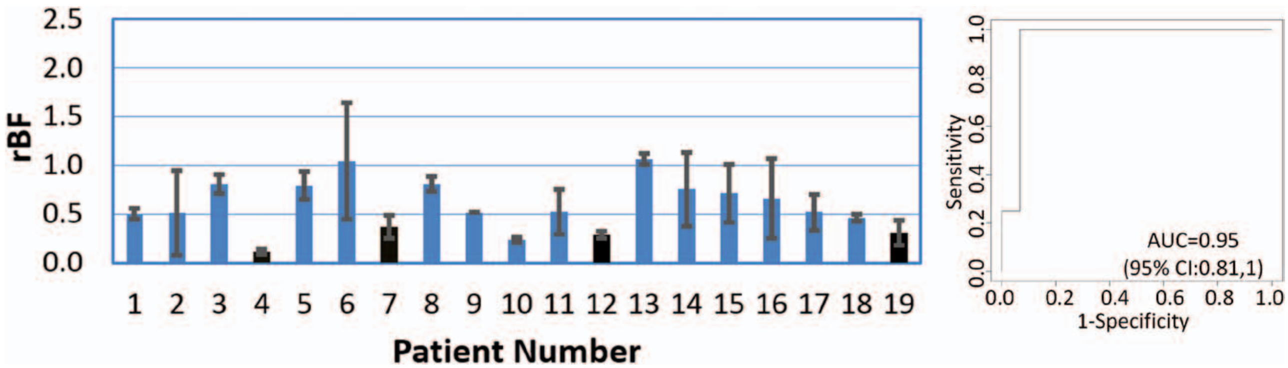

Fig. 3. (*Left*) Relative blood flow (*rBF*) data measured immediately after mastectomy compared with baseline values from 19 patients, four with mastectomy skin flap necrosis (patients 4, 7, 12, and 19, *black bars*). *Error bars* represent relative blood flow variations (standard deviations) at different measurement depths of the mastectomy skin flap. (*Right*) Area under the receiver operating characteristic curve (*AUC*) data immediately after mastectomy for discriminating mastectomy skin flaps with necrosis (*n* = 4) and without necrosis (*n* = 15).

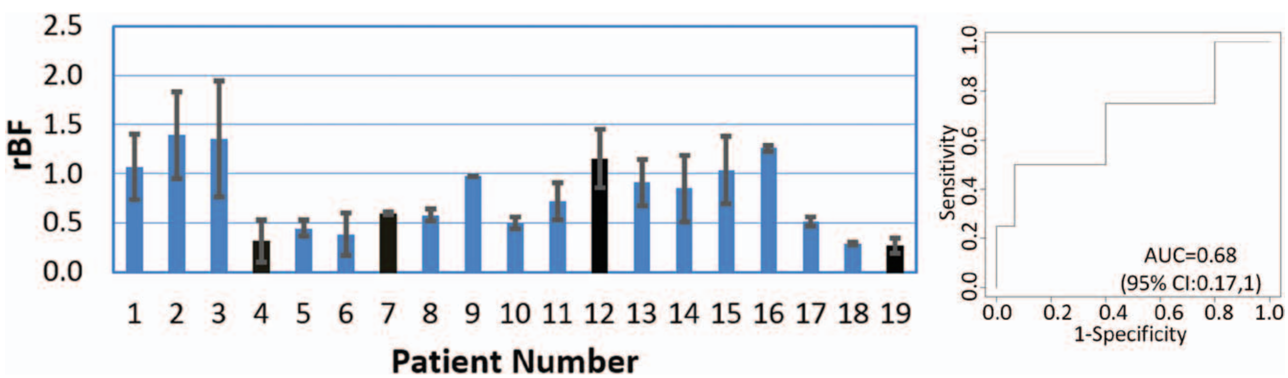

Fig. 4. (*Left*) Relative blood flow (*rBF*) data measured immediately after reconstruction compared with baseline values from 19 patients, four with mastectomy skin flap necrosis (patients 4, 7, 12, and 19, *black bars*). *Error bars* represent relative blood flow variations (standard deviations) at different measurement depths of the mastectomy skin flap. (*Right*) Area under the receiver operating characteristic curve (*AUC*) data immediately after reconstruction for discriminating mastectomy skin flaps with necrosis (*n* = 4) and without necrosis (*n* = 15).

before and after reconstruction may also impact the optical measurements. Also, we have noted variations/changes in the patient's temperature at these time points which may have an effect on relative blood flow. We have begun to monitor surface and core temperatures prospectively.

A trend toward lower relative blood flow was observed in smokers and patients who had an amputation style/inframammary fold incision. These values did not show statistical significance.

Limitations of this study include the relatively low number of patients and the inability of noncontact diffuse correlation spectroscopy to measure the entire mastectomy skin flap (**See Figures, Supplemental Digital Content 2, *http://links.lww.com/PRS/C190***; and **Supplemental Digital Content 3**, ***http://links.lww.com/PRS/C191***). We are currently developing novel prototypical noncontact diffuse correlation tomographic systems that provide three-dimensional imaging of global blood flow distributions in the entire mastectomy flap.[7,11–13] These systems are more user-friendly and less cumbersome than the current device. We are currently attempting to translate these novel imaging techniques to the clinical and intraoperative settings. With more investigation, we envision determination of a quantitative threshold and cutoff value of relative blood flow to precisely predict mastectomy skin flap necrosis.

CONCLUSIONS

Our pilot study has demonstrated the feasibility of noncontact diffuse correlation spectroscopy for the perioperative monitoring of blood flow variations in mastectomy skin flaps and prediction of mastectomy skin flap necrosis. Further studies will provide the rationale and framework needed for designing optical image-guided clinical trials of breast reconstruction and the application of this technology to other clinical uses, including wound care and burns.

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