INTRODUCTION

Free tissue transfer (FTT) for breast reconstruction following mastectomy has become a standard procedure on account of its superior aesthetics and durability compared with implant reconstruction. Vascular microanastomosis is a critical step for tissue survival. Anastomosis failure causes a lack of oxygen and nutrients to be perfused within the FTT: thrombus or bleeding of either the recipient artery or donor vein may lead to ischemia and congestion, respectively, which may contribute to tissue necrosis. Studies have described that venous thrombosis is the most common microsurgical complication followed by arterial thrombosis and bleeding. Most microsurgical complications have been reported to happen within the first 24–48 hours following surgery with higher rates within the first 4 hours. Close monitoring is therefore necessary to detect signs of vascular complications to salvage the FTT and decrease the failure rate.

Use of Near-infrared Spectroscopy and Implantable Doppler for Postoperative Monitoring of Free Tissue Transfer for Breast Reconstruction: A Systematic Review and Meta-analysis

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Background: Failure to accurately assess the perfusion of free tissue transfer (FTT) in the early postoperative period may contribute to failure, which is a source of major patient morbidity and healthcare costs. This systematic review and meta-analysis aim to evaluate and appraise current evidence for the use of near-infrared spectroscopy (NIRS) and/or implantable Doppler (ID) devices compared with conventional clinical assessment (CCA) for postoperative monitoring of FTT in reconstructive breast surgery.

Methods: A systematic literature search was performed in accordance with the preferred reporting items for systematic reviews guidelines. Studies in human subjects published within the last decade relevant to the review question were identified. Meta-analysis using random-effects models of FTT failure rate and STARD scoring was then performed on the retrieved publications.

Results: Nineteen studies met the inclusions criteria. For NIRS and ID, the mean sensitivity for the detection of FTT failure is 99.36% and 100%, respectively, with average specificity of 99.36% and 97.63%, respectively. From studies with sufficient reported data, meta-analysis results demonstrated that both NIRS [OR = 0.09 (0.02–0.36); P < 0.001] and ID [OR = 0.39 (0.27–0.95); P = 0.04] were associated with significant reduction of FTT failure rates compared with CCA.

Conclusions: The use of ID and NIRS provided equivalent outcomes in detecting FTT failure and were superior to CCA. The ability to acquire continuous objective physiological data regarding tissue perfusion is a perceived advantage of these techniques. Reduced clinical staff workload and minimized hospital costs are also perceived as positive consequences of their use. (Plast Reconstr Surg Glob Open 2019;7:e2437; doi: 10.1097/GOX.0000000000002437; Published online 29 October 2019.)
evaluations of the FTT. As the final health status depends on the expertise of the clinical team, additional tools are often used. Hand-held acoustic Doppler sonography can also be used for assessment of the blood flow across pedicles. However, these assessments are discrete, prone to human error, and cannot provide prompt, real time and systematic detection of possible microanastomotic complications. Due to the shortcomings of CCA, devices based on the biophysical and biochemical tissue properties have been developed for continuous monitoring of the FTT. Specifically, near-infrared spectroscopy (NIRS) and implantable ultrasound Doppler (ID) devices have been commonly used for continuous and objective assessment of the tissue health.5–8

In the context of growing interest in the use of NIRS and ID to aid early detection of FTT complication and to prevent adverse patient outcomes, it is pertinent that current evidence in regard to these technologies is reviewed. The purpose of this systematic review is to compare the clinical outcomes of NIRS and/or ID and CCA for FTT monitoring.

METHODS

Systematic Review

A systematic search of the literature (title and abstract of full papers and conference abstracts) was performed using the guidelines described by the preferred reporting items for systematic reviews (http://www.prisma-statement.org/) and meta-analysis statement to identify publications between 2008 and October 2018 regarding the use of (1) ID, (2) NIRS, and (3) combined NIRS and ID in the postoperative monitoring of FTT for immediate or delayed breast reconstruction following mastectomy.

Inclusion and Exclusion Criteria

Only studies published in English before October 2018 containing original data where ID, NIRS, combined NIRS/ID, combined NIRS/CCA and combined ID/CCA were used to monitor FTT for breast reconstruction in humans were included. Review articles, oral or poster presentations, conference abstracts, letters, comments, any study describing the validation of animal or cadaveric simulation in surgical training, unpublished data, and any article using nonoriginal data (ie, previously published) were excluded.

Search

We conducted a systematic search strategy, which combined the following search terms and their variations with AND and OR operators using the OVID (EMBASE/ Medline) database: “reconstruction,” “autograft,” “surgical flap,” “implantable Doppler,” “monitoring,” “physical examination,” “near-infrared spectroscopy,” and “NIRS.” An additional search concerning specific devices (“Cook-Swartz,” “O2C,” “Synovis”) was performed. MeSH terms and truncation symbols were used where possible to widen the search.

Our systematic search strategy was applied the following online databases: Medline, Embase, PsycINFO, Global Health, HMIC, the Cochrane Libraries Database of Systematic Reviews, SCOPUS, NHS Evidence, the Transport Database. We used the OvidSP platform to search the Medline, EMBASE, PsychINFO, Global Health, and HMIC databases.

Selection Protocol and Data Extraction

Titles and abstracts of studies identified by the primary search were independently reviewed by M.B. and J.A. to identify potentially relevant articles. The full texts of potentially relevant articles were obtained to facilitate further review. In the cases were from the same patient population was presented in full or partially in separate publications either the most recent or relevant article was included. The reference lists of retrieved articles and relevant reviews were also hand-searched to identify other suitable publications. Any areas of disagreement between reviewers were resolved by P.B.

The articles satisfying the selection criteria were retrieved for independent data extraction by M.B. and J.A. Data include author, year of publication, country of design, patient number, characteristics of patient population, FTT overall survival rate, sensitivity, and, specificity of the monitoring method.

Statistical Analysis and Assessment of Quality Report

An additional meta-analysis is conducted using random effects, DerSimonian-Laird method (RevMan, Edition 5, Cochrane Library of Systematic Reviews) based on papers with adequate information to observe FTT failure results when respectively comparing ID and NIRS with CCA. Publication bias of included studies was assessed using funnel plots. The Egger test was used to assess funnel plot asymmetry. The I² value was used to assess heterogeneity between studies, to determine the degree of variation not attributable to chance alone. Low, moderate, and high degrees of heterogeneity were ascribed to I² values <25%, 25%–75%, and >75%, respectively. Statistical significance was assigned to P values <0.05. Methodological quality of the papers was independently assessed by M.B. and J.A. using the STARD checklist against 34 criteria (see appendices, Supplemental Digital Content 1, which displays STARD checklists for ID retrieved publications, http://links.lww.com/PRSGO/B226, and Supplemental Digital Content 2, which displays STARD checklists for NIRS retrieved publications, http://links.lww.com/PRSGO/B227).

RESULTS

The initial search identified 129 citations, of which 98 were excluded upon title and abstract screen. Thirty-one citations underwent further review, upon which 21 citations were removed. The remaining 15 citations were retrieved. An additional 4 citations were identified through hand searching of bibliographies (Fig. 1). Data were extracted from the 19 retrospective and prospective studies (Tables 1 and 2).
Assessment of reporting standards against the 34 criteria of the STARD checklist shows a mean of 17.1 (median: 18, range: 9–21) for ID and a mean of 19.2 (median: 17, range: 14–24) for NIRS. Tables 1 and 2 give the STARD score for each retrieved study.

### Implantable Doppler

Of the studies identified, 8 used ID to monitor FTT. The extracted data from these studies are presented in Table 1.

### Meta-analysis: FTT Failure Results

Comparisons between ID and clinical monitoring outcomes were made in 4 studies. Meta-analysis of outcomes presented within these studies identified that ID monitoring was associated with reduced odds of FTT failure ($OR = 0.39$ ($0.27–0.95$); $P = 0.04$) (Fig. 2).

### ID versus Clinical Monitoring

Schmulder et al., Rozen et al., and Whitaker et al. investigated the impact of using the Cook-Swartz ID (Cook Medical; Cook Ireland Ltd., Limerick, Ireland) compared with that of CCA (Table 1). Schmulder et al. and Rozen et al. found that using ID significantly improved the success rate of FTT surgery for breast reconstruction. However, Whitaker et al. found similar success rate for both CCA and ID. In addition, although Rozen et al. found that there are no statistical differences in the false-positive and re-exploration rates, Whitaker et al. did in favor of ID. This difference might be due to the difference between the number of cases monitored with CCA and that with...
the ID. In Rozen et al study, about 3.5 times more FTT cases were monitored with CCA alone while about 2 and 1.1 times more in Whitaker et al and Schmulder et al studies, respectively. Additional differences can originate from CCA results which remain subjective and require expertise.

Sensitivity and Specificity of ID Probes

Focusing on the sensitivity and specificity of the use of Cook-Swartz ID, Chang et al found that they are both high despite 40.4% of negative findings on re-exploration. When looking at all types of surgery, Chang et al advocate that positioning the ID on the artery is recommended as sensitivity and specificity are greater than when placed on the vein (respectively, $N_{\text{patient}} = 267$ at 94.2% sensitivity and $N_{\text{patient}} = 101$ at 74.0% sensitivity). They also found no statistical difference in the results when an ID is placed only on the artery compared with the results when placing 2 ID probes on each the vein and artery ($N_{\text{patient}} = 71$).

ID Probe Placement

Unlike Chang et al, Swartz et al have demonstrated that when placed on the artery, while arterial occlusion is immediately detected, detection of venous occlusion is delayed for up to 6 hours due to persistent arterial pulse. Likewise, when placed on the vein, venous occlusion is immediately detected and arterial occlusion is detected after 6 minutes in average. The difference in the practical use of the probe might come from the characteristics of the FTT, such as the size of the pedicle, the patient’s vascular pattern, or the type and weight of the FTT.

Near-infrared Spectroscopy

Of the studies identified, 11 used NIRS devices to monitor FTT. The extracted data from these studies are in Table 2.

Meta-analysis: FTT Failure Results

Comparisons between NIRS and CCA were made in only 2 studies, with NIRS monitoring being greatly associated with reduced odds of FTT failure [OR = 0.09 (0.02–0.36); $P < 0.001$] (Fig. 3).

NIRS versus Conventional Monitoring

Lin et al and Koolen et al compared the outcomes of CCA with those of the T.Ox. (ViOptix Inc.). For Lin et al, the difference in the outcomes between the two methods is statistically significant, while it is not for Koolen et al. Similar studies were conducted by Fox et al with the T-Stat device (Spectros Corp., Portola Valley, Calif.), by Whitaker et al and by Repez et al with the InSpectra device (Novatech Resources Pte Ltd.), and Rothenberger et al using the O2C machine (LEA Medizintechnik GmbH). In general, results show an increase in the FTT salvage rate and an early detection of complications, even before clinical evidence. Differences in the results might come from subjectivity in CCA results as it requires expertise.

<table>
<thead>
<tr>
<th>Table 2. A Summary of Studies Using NIRS Devices for Postoperative Monitoring of FTT for Immediate or Delayed Breast Reconstruction following Mastectomy</th>
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<tbody>
<tr>
<td><strong>Study</strong></td>
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<tr>
<td>---</td>
</tr>
<tr>
<td>Repez et al 2008 Slovenia PCS 48 50 13</td>
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<tr>
<td>Keller 2009 United States RCS 145 208</td>
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<tr>
<td>Lin et al 2010 United States RCS 164 234</td>
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<tr>
<td>Pelletier et al 2011 United States PCS 25 25</td>
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<tr>
<td>Pelletier et al 2011 United States PCS 25 25</td>
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<tr>
<td>Whitaker et al 2012 United Kingdom PCS 10 10</td>
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<tr>
<td>Rothenberger et al 2013 Germany PCS 34 34</td>
</tr>
<tr>
<td>Koolen et al 2015 United States RCS 451 670</td>
</tr>
<tr>
<td>Vranken et al 2017 The Netherlands PCS 29 29</td>
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<tr>
<td>Ricci et al 2017 United States RCS 595 900</td>
</tr>
<tr>
<td>Fox et al 2013 United States PCS 27 32</td>
</tr>
<tr>
<td>Merlizli et al 2011 United States PCS 68 81</td>
</tr>
</tbody>
</table>

*N = 11, P = 0.09 (OR = 0.09, 95% CI: 0.02–0.36).*
Sensitivity and Specificity of NIRS: Clinical Use

Keller and Mericli et al. compared NIRS monitoring to CCA for early detection of FTT complications. Results show higher sensitivity and specificity with a detection of complications before clinical evidence using the NIRS device.

Ricci et al. investigated the potential use of NIRS device as a mean to reduce intensive monitoring and lower consequent care costs. As high sensitivity and specificity were found using the T.Ox device, they advocate that the use of a NIRS device for postoperative monitoring can reduce the time patients spend in an intensive monitoring setting while saving hospital cost for similar outcomes compared with CCA. Similarly, Pelletier et al. found concurring results and suggest that a NIRS device can completely replace specialized clinical staff for postoperative monitoring.

NIRS Placement

Vranken et al. investigated the use of NIRS devices as a reliable mean for postoperative FTT monitoring and can provide early detection of a complication. Using the Invos 5000C (MedTronic Ltd.), which is primary designed for cerebral/somatic use, results were conclusive and the authors advocate that the use of a NIRS device for postoperative monitoring can reduce the time patients spend in an intensive monitoring setting while saving hospital cost for similar outcomes compared with CCA. Similarly, Pelletier et al. found concurring results and suggest that a NIRS device can completely replace specialized clinical staff for postoperative monitoring.

DISCUSSION

The main limitation of the ID lies in its positioning. Improper positioning can result in (1) false-positive alerts, especially if the probe has moved, which may induce negative re-explorations; (2) hematoma following anastomosis rupture, sometimes due to inadvertent pulling or removal of the wire; (3) blood vessel thrombosis, if the probe is too tightly secured onto the blood vessel. With experience, the number of complications due to the use of the ID generally reduces. Also, by combining the ID outcomes with CCA and other monitoring methods, false-positive alarms can be backed up to avoid negative re-explorations.

NIRS devices have limitations that are intrinsic to (1) the device’s hardware, (2) the device’s algorithm for the analysis of the measurements, and (3) the patient’s demographic details. Components (light emitter and light detector) placement and light wavelengths induce hardware limitations which result in a specific range of penetration depth and a relative measurement of the concentration of blood compound or tissue components. Hardware limitations can be overcome with the design of a specific algorithm for the analysis of the measurements, for signal amplification and adjustment when investigating a given compound. Ozturk et al. showed that surgical and clinical parameters, such as blood pressure, supplemental oxygen saturation, FTT type, perforator’s size and number, patient’s demographic details (such as skin tone and age), and the environment’s characteristics into which measurements are taken (such as ambient light) can also affect the final outcome of the NIRS device.

To directly compare ID and NIRS devices, it is necessary to acknowledge their differences: (1) between what is measured, respectively blood flow perfusion, and, StO₂ and its related parameters; (2) between their positions, respectively, implanted at the entrance/exit of the FTT (onto the pedicles) and at an external localized area. Although these differences are related because a change...
in blood flow perfusion will affect the overall StO₂ independently to where the measurement is taken, they can affect the minimum time taken to detect a complication. To compensate for autonomic denervation, inflammatory reaction, and ischemia, which are normal reactions following FTT harvest, StO₂ consumption increases. This induces an increased blood flow perfusion and a decreased vascular resistance that dilates the microcirculation within the tissue, which facilitate the dissolution of possible microthrombosis and the repair of micronecrosis.50–52 These physical responses can vary according to the vascular pattern, nicotine or alcohol abuse, demographics, and comorbidities of the patient.45,49,51 Raittinen et al32 argued that although the readings might vary across patients, the StO₂ trend remains the same. This trend has been described as a sharp increase followed by a decrease and ultimately a stabilization within the first 3 days following surgery.25,55

**CONCLUSIONS**

Most studies found the ID as an effective, efficient, and safe monitoring system that is a valuable adjunct to CCA. Specifically, Rozen et al.13 Schmulder et al.29 and Whitaker et al.28 have reported that the system can improve salvage rates. However, Smit et al30 reported no such improvement in salvage rates, but encourage its use as it reduces the workload of the clinical staff and interruptions on the patients. Chang et al.31 suggest that CCA should remain the gold standard for postoperative FTT monitoring, especially when a cutaneous paddle on the FTT is available. Using a weighted average analysis, based on the total number of FTT cases, the overall re-exploration rate, survival rate, sensitivity, and specificity were calculated. Overall studies investigating the results of the Cook-Swartz placed at the venous pedicle,10,13,18,27,29 with a total number of 509 FTT cases, results demonstrate a 10.41% re-exploration rate, 97.20% survival rate, 100% sensitivity, and 99.00% specificity. Similarly, with the Synovis Flow Coupler placed at the venous pedicle,14,18 with a total number of 196 FTT cases, results show 5.63% re-exploration rate, 97.39% survival rate, 100% sensitivity, and 96.26% specificity.

Most studies reported that NIRS is a highly sensitive, specific, and reliable technique that can improve the FTT salvage rate. Most studies have a 0% false-positive rate.26,27,32–34 Ricci et al30 and Koolen et al37 studies have a false-positive rate of 0.1% and 0.15%, respectively. In these studies, no particular definition of a false-positive result was given. Vranken et al38 and Rothenberg et al.36 did not define false-positive rate at 0.1% and 0.15%, respectively. In these studies, a sharp increase followed by a decrease and ultimately a stabilization within the first 3 days following surgery.25,55

Specific studies investigating either implantable or NIRS methods, compared with or without CCA have been conducted. With the included studies, the weighted average results show that NIRS, using the T.Ox machine, gives better outcomes than when using the Cook-Swartz or Synovis ID, with, respectively, 4 and 10.5 times more FTT cases recruited. However, large studies aiming to compare NIRS and ID on the same patients under the same clinical conditions would need to be conducted for a more rigorous comparison. Table 3 shows the prices of the most common devices used in the presented clinical studies.

Many studies have demonstrated that both methods are useful and reliable as they reduce the staff burden and improve the overall FTT salvage rate. However, few studies have tried to decipher which method is the most appropriate taking into consideration the multiple variables across the range of microsurgical applications. In addition to high accuracy and robustness, wider and systematic use of such methods lies into their (1) ease of use, with a relatively short learning curve, (2) acceptance (based on the medical relevance, learning curve, and large studies outcomes), and (3) relative costs.

### Table 3. Costs of the NIRS and ID Devices Which Are Currently Available and Used in the Reviewed Studies

<table>
<thead>
<tr>
<th>Company</th>
<th>Name</th>
<th>Controller</th>
<th>Machine Price</th>
<th>Disposable Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cook Medical</td>
<td>Cook-Swartz</td>
<td></td>
<td>2,494.00 GBP</td>
<td>380.00 GBP</td>
</tr>
<tr>
<td>Synovis Micro</td>
<td>Flow Coupler</td>
<td></td>
<td>2,305.00 GBP</td>
<td>714.00 GBP</td>
</tr>
<tr>
<td>ViOptix</td>
<td>T.Ox</td>
<td></td>
<td>25,000.00 USD</td>
<td>1,450.00 USD</td>
</tr>
<tr>
<td>Spectros</td>
<td>T-Stat</td>
<td></td>
<td>32,000.00 USD</td>
<td>629.00 USD</td>
</tr>
</tbody>
</table>

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**REFERENCES**


