



**The efficacy of the Cook-Swartz implantable Doppler in the detection of free flap compromise: A systematic review protocol**

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# The efficacy of the Cook-Swartz implantable Doppler in the detection of free flap compromise: A systematic review protocol

## REVIEW INFORMATION

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## ABSTRACT

### Introduction

The Cook-Swartz implantable Doppler monitors venous blood flow from free flaps and can detect post-surgical free flap compromise. Previous studies have shown that the use of this Doppler can improve detection and salvage rates as it provides an earlier warning than the current method of clinical assessment. Such studies assert that the implantable Doppler is of great value in monitoring of free flaps in current microsurgical units. This systematic review aims to compare the efficacy of the Cook-Swartz implantable Doppler in monitoring free flap compromise against conventional clinical free flap monitoring techniques such as flap capillary refill or blanching time, skin temperature, turgor and flap skin colour.

### Methods and analysis

Various electronic databases will be systematically searched for studies which compare the use of Cook-Swartz implantable Doppler with clinical assessment in detecting the failure of free flaps. The selected studies will then have their titles and abstracts screened by two authors and any conflicts not resolvable between the two authors will be referred to the lead author for resolution. Articles selected after title and abstract screen will have full text downloaded and the complete article will be assessed for suitability. Once articles have been selected for inclusion, data extraction will take place. For the data analysis, the outcomes of the studies will be tabulated, with descriptive statistics performed as appropriate and the detection rate of the

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3 Doppler and clinical assessment will be compared and synthesised where  
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5 possible.  
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### 10 11 12 **Ethics and Dissemination** 13

14  
15 The authors hope to disseminate the findings as widely as possible,  
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17 irrespective of results as it will help to increase the knowledge base on  
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19 monitoring techniques of free flaps. This systematic review will be published in  
20  
21 a peer-reviewed journal and include a number of recommendations as its  
22  
23 conclusion based upon the evidence contained within. Given the wide range  
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25 of specialities now utilising flaps, it will be presented at a wide range of  
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27 national and international conferences.  
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32 **Protocol Registration: CRD42013005818**  
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## BACKGROUND

### Free flap reconstruction

Free flap reconstruction for large tissue defects is increasingly common and plays an important role in the field of plastic and reconstructive surgery.<sup>1</sup> Such surgery necessitates a microsurgical anastomosis from the harvested flap to the recipient using minute sutures. Data suggests that the commonest cause of failure is a problem with the venous anastomosis occurring within the first 24 to 48 hours postoperatively.<sup>2,3,4</sup> This problem affects up to 20% of all free flap reconstructions, depending upon their location and entails significant physical, psychological and emotional morbidity for patients.<sup>5,6,7</sup>

Flap failure often necessitates further general anaesthetics and operations. Due to the time critical nature of flap failure, reoperation may occur out of hours, which provides further logistical and practical challenges.<sup>7</sup> Initially, an attempt is made to salvage the flap, if this fails, then the flap is removed and an alternative reconstructive approach may be required. In some cases, venous congestion may require blood drainage; for example by use of medicinal leeches.<sup>8</sup> This is potentially highly unpleasant for patients and predisposes them to infection and anaemia.<sup>9</sup> Patients therefore require careful wound inspection, surveillance of haemoglobin and prophylactic antibiotics to protect them from further complications.<sup>8,10</sup>

### Monitoring of free flaps

Early recognition of flap compromise is the primary aim of every microsurgical unit. Prompt intervention and rescue is critical for ensuring flap survival.

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3 However, the complexities of free flap microcirculation are often difficult to  
4 assess.<sup>11</sup> At present, monitoring is carried out clinically and is based upon  
5 subjective clinical observations. These tests are carried out on an island of  
6 skin or 'skin paddle' – an area of skin considered to be indicative of the whole  
7 flap's arterial perfusion and venous drainage.<sup>12</sup> Such tests may include the  
8 colour, capillary refill or blanching time, skin temperature, turgor, and degree  
9 of bleeding in response to pin-prick and use of a handheld doppler device.<sup>1</sup>  
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13 Unlike solid organ transplantation, there is no objective assessment - such as  
14 decreased urine output in renal transplantation. Similarly, there are currently  
15 no suitable imaging modalities for assessing microvascular flow and  
16 specifically slow venous flow problems, though there are reports in the  
17 literature of the use of nuclear medicine techniques in successful  
18 monitoring.<sup>13</sup> A number of small studies have highlighted the use of Single-  
19 Positron Emission Computed Tomography (SPECT) in the determination of  
20 free flap compromise.<sup>14</sup> However, large comparative studies are required with  
21 standardised techniques to further define the role of this modality in the  
22 assessment of free flap compromise. Early compromise, which entails the  
23 large majority of flap failure, is often asymptomatic. Pain, bleeding and skin  
24 changes can take a while to develop, potentially increasing ischaemic times  
25 and reducing the possibility of successful salvage.<sup>15</sup>  
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49 Some free flaps are very challenging to monitor adequately, such as  
50 vascularised bone and muscle flaps; especially those that have been covered  
51 with a skin graft and cutaneous flaps in non-Caucasian skin. Some flaps, such  
52 as buried flaps within the head and neck are impossible to monitor by visual,  
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3 clinical assessment and in such circumstances, attempts have been made to  
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5 enhance clinical monitoring using microdialysis.<sup>11, 16</sup> However, this can take  
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7 up to 30 minutes to get a reading, necessitates training to learn a technique  
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9 and analyse results, does not directly measure flow and costs almost \$52,000  
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11 per monitor plus additional costs of up to \$570 per flap.<sup>11</sup>  
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### 14 15 16 **The Cook-Swartz Implantable Doppler**

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18 The Cook-Swartz implantable Doppler monitors the venous flow from free  
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20 flaps and obtained its CE mark in 2006.<sup>17</sup> Since then it has been distributed  
21  
22 widely in both Europe and the rest of the world.<sup>17</sup> It is the only device currently  
23  
24 on the market that allows this monitoring and is protected by patent. It  
25  
26 consists of a 20 MHz ultrasonic Doppler crystal, a silicone cuff and a monitor  
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28 unit.<sup>18, 19</sup> This cuff secures the Doppler to the flap's vein at the time of the  
29  
30 operation and is placed downstream of the microvascular anastomosis.<sup>19</sup> The  
31  
32 Doppler provides monitoring for 5-10 days postoperatively and is removed by  
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34 simple traction.<sup>17</sup> A number of studies have shown that use of this device  
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36 increases success and salvage rates as it provides an earlier warning that the  
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38 current method of clinical monitoring.<sup>12, 20-22</sup>  
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### 45 46 **The potential of the Cook-Swartz Doppler**

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48 The use of the Cook-Swartz Doppler in the assessment of such flaps has  
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50 demonstrated improved detection times.<sup>2, 12, 20, 22, 23</sup> This technology is needed  
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52 now more than ever as the indications for, and therefore absolute number of,  
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54 free flaps have increased. Indications for flaps include following resection of  
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56 breast tumours, head and neck cancers, skin cancers, major burns and  
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3 infections. Often these may be 'cross-speciality' flaps, for example with  
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5 orthopaedics to cover exposed metal work in lower limb fractures. Changes to  
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7 working practices mean that these patients may be returned to an orthopaedic  
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9 or general surgical ward where monitoring is performed by non-specialist  
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11 nurses who may not be used to monitoring flaps, let alone over night and in  
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13 challenging settings such as low light.  
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### 15 16 17 18 **Why is a systematic review of this required?** 19

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21 To our knowledge, there has only been one systematic review involving the  
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23 Cook-Swartz Implantable Doppler. Poder and Fortier investigated the efficacy  
24  
25 and cost effectiveness of the implantable Doppler.<sup>24</sup> However, we aim to  
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27 investigate and further clarify the role of the Doppler as a monitoring  
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29 technique by comparing it to clinical assessment. Clinical assessment is the  
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31 most widely used technique and as such the standard against which the  
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33 Doppler should be compared. Further clarifying the role and possible benefit  
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35 of the Cook-Swartz Doppler in the detection of free flap compromise would  
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37 allow modification of practice and guidelines in line with the best evidence.  
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### 43 44 **OBJECTIVES** 45

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47 Our objective is to perform a comprehensive systematic review of the  
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49 implantable Doppler in the detection of free flap compromise.  
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### 52 53 **Primary objective:** 54

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56 To compare the efficacy of the Cook-Swartz implantable Doppler versus  
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58 clinical assessment in the detection of free flap compromise.  
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**Secondary objectives:**

To determine the absolute indications for use of the Doppler if any. Quantify the false positive and negative rates, salvage rates and number of associated complications.

**METHODS**

This systematic review will be conducted according to the recommendations outlined in the Cochrane Handbook for reviews and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.<sup>25</sup>

**Criteria for selecting studies:**

The following search criteria were specifically devised to locate studies specifically pertaining to the use of the Cook-Swartz Doppler and to provide evidence for the objectives previously stated.

**Types of studies**

Any study comparing the use of Cook-Swartz implantable doppler with clinical assessment in detecting the failure of free flaps will be included. Articles must describe use of the implantable doppler specifically and may be of any grade of evidence (1 to 5 as defined by the Oxford Centre for Evidence-Based Medicine).<sup>26</sup>

Any article where data is duplicated will be excluded, as will articles not describing original data; such as editorials, letters regarding other articles and

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3 discussion pieces. Unpublished reports will be included if the methodology  
4 and results are accessible in written form.  
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### 9 10 **Types of participants**

11 Human subjects of any age who have undergone free flap surgery. There will  
12 be no limitation on location of the flap or technique utilised.  
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### 15 16 17 18 **Types of interventions**

19 Any article describing use of the Cook-Swartz Doppler in the detection of free  
20 flap compromise would be considered. Ideally, this would be considered  
21 against a control group of clinical monitoring.  
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### 28 29 30 **Types of comparator**

31 Cook-Swartz implantable Doppler used on the venous pedicle of a free flap  
32 attached by any means and used to monitor free flaps post-operatively.  
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34 Clinical assessment of free flaps including, but not limited to; skin colour,  
35 turgor, surface temperature, capillary refill time or handheld  
36 Doppler.  
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## Types of outcome measures

### Primary outcome:

The rate of detection will be determined as the number of Doppler monitored flaps correctly identified as compromised divided by the total number of Doppler monitored flaps. This will be compared with clinical monitoring.

### Secondary outcomes:

The salvage rate will be the number of compromised flaps successfully salvaged divided by the total number of compromised flaps. The false positive rate is the number of flaps monitored by Doppler returned to theatre incorrectly divided by the total number of Doppler monitored flaps.

The false negative rate will be the number of flaps lost without any change in Doppler monitoring, divided by the total number of Doppler monitored flaps.

The true negative rates will be the number of flaps monitored without any change in Doppler and without any compromise divided by the total number of Doppler monitored flaps.

The rates for clinical assessment will be calculated as above and compared to that of the Doppler.

## Search methods for identification of studies

### Electronic Searches

The following electronic databases will be searched to 24<sup>th</sup> September 2013: PubMed, EMBASE, PsycINFO, Ebsco, Cochrane Database of Systematic Reviews, CINAHL, SCOPUS, SciELO, NHS evidence, [www.uptodate.com](http://www.uptodate.com),

<http://clinicaltrials.gov/>, <http://www.who.int/ictcp/en/>, <http://www.controlled-trials.com/>

### **Search terms and keywords**

The search strategy has been developed to locate papers related specifically to the Cook-Swartz implantable Doppler. This search will utilise the English language keywords combined with Boolean logical operators. Therefore the following terms will be utilised: “*Implantable doppler*” OR “*Cook-Swartz implantable doppler*” OR “*Cook-Swartz Implantable doppler*”.

The search will not be limited by language. Any non-English articles identified will proceed to title and abstract screening and the full text obtained if required. If full text is not available, then the authors will be contacted to obtain an English language copy of the full text. Failing this, colleagues speaking the language will be contacted to translate. Google Translate will be utilised as a last resort.

### **Other resources**

A hand search of the references of articles located by the search strategy will be used to identify any relevant citations within the grey literature. Active researchers will be contacted to identify any other published or unpublished work.

### **Identification and Selection of articles**

Studies identified by the electronic and manual search strategy will be listed. Results including citation, title and abstracts will be populated into EndNote®

(Thomson Reuters, New York, NY, USA) and duplicates removed. Titles and abstracts will be screened by two authors (BG and AJF), any conflicts not resolvable between the two will be referred to the lead author (RA) for resolution. Articles selected after title and abstract screen will have full text downloaded and a further assessment made. Once articles have been selected for inclusion, data extraction will take place.

### **Data extraction and management**

Data will be extracted independently by two authors (BG and AJF) utilising a standard extraction form where all data for each study will be collated (Appendix A). Any conflict of extraction will be resolved by discussion; where resolution this isn't possible, the lead author (RA) will have final say. This data will then be entered into a Microsoft Excel ® 2011 database (Microsoft, Redmond, WA, USA). Data collected will constitute three main areas:

#### **1) Article information**

- Title
- Authors
- PubMed ID
- Year of publication
- Journal

#### **2) Characteristics**

- Setting and Location of the study
- Number of patients
- Range of patient age
- Flap types included

- Clinical method of assessment
- Doppler method of assessment

### 3) Results (divided clinical and doppler)

- Number of patients per group
- Specific flaps in groups (where applicable)
- Detected
- Flap Salvage
- Needless theatre return
- Complications
- Lost flaps without any signs
- Flaps correctly monitored

### Assessment of study quality and bias in included studies

The quality of evidence included in this analysis needs to be established. Quality of evidence can be assessed based upon a number of criteria; we will be specifically utilising the Grading of Recommendation Assessment, Development and Evaluation (GRADE) system as proposed by Balshem et al.<sup>27</sup>

If we locate any Randomised Controlled Trials (RCTs) we will utilise the Cochrane risk of bias tool and compare outcomes to published trial protocols. Any information missing from studies will be documented and assessed to ascertain the risk of incomplete statistical sets.

### Assessment of publication bias

To ascertain if studies with negative outcomes are not being published (“publication bias”), we will assess funnel plot asymmetry.<sup>28, 29</sup> Where both positive and negative results are published, the plot should resemble a symmetrical, inverted funnel. The precision of the estimated intervention effect will increase as the size of the sample included in the study increases. Smaller studies will therefore scatter widely at the bottom, with larger, more powerful studies grouping more narrowly at the top. The asymmetrical distribution of standard error on analysis of the funnel plot would indicate publication bias.

### Assessment of Heterogeneity

Heterogeneity between studies will be assessed using Higgins and Thompson’s  $I^2$ , which measures the percentage variability in result attributable to heterogeneity between studies rather than sampling error<sup>28</sup>. Variability in the intervention effects in studies will be tested for statistical heterogeneity utilising Tau-squared ( $T^2$ ),  $I^2$  and chi-squared ( $X^2$ ) with corresponding P-values calculated; the Cochrane tests.

The value of  $X^2$  statistics in the forest plot presents the assessment of whether the differences in results are compatible with chance alone. A large value of  $X^2$  test relative to its degree of freedom (df) or a low P-value indicates statistical variation (heterogeneity) beyond chance.

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3 The  $I^2$  percentage will be interpreted as follows:  
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- 5 • 0% - 30% may not be important.
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- 7 • 30% - 60% may represent moderate heterogeneity\*
- 8
- 9 • 50% - 90% may represent substantial heterogeneity\*
- 10
- 11 • 75% - 100% represents considerable heterogeneity\*
- 12
- 13
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15 [\*the importance of the observed  $I^2$  value depends on; magnitude and  
16 direction of effects and strength of evidence for heterogeneity such as P-value  
17 from  $X^2$  or a Confidence Interval for  $I^2$ ].  
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19 Generation of statistical heterogeneity can be a consequence of clinical  
20 (participants, interventions and outcomes) and/or methodological (study  
21 design and risk of bias) diversity or due to random error (chance) alone.  $T^2$   
22 represents the estimated standard deviation of underlying effects across  
23 studies. The exact model utilised for meta-analysis will be based upon the  
24 level of heterogeneity within our data; with a random effects model used if it is  
25 high and a fixed-effects analysis if moderate.  
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#### 40 **Data Synthesis and statistical analysis**

41 Outcomes will be tabulated, with descriptive statistics performed as  
42 appropriate. Similarly, the detection rate of each modality will be compared  
43 and synthesised where possible. Synthesis will be performed utilising Review  
44 Manager (RevMan 5.2.6) and an assessment of heterogeneity will be made.  
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46 Based upon this, meta-analysis will be carried out comparing Cook-Swartz  
47 Doppler to clinical monitoring; ideally utilising randomised controlled trials, but  
48 good quality observational studies will also be considered.  
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3 Rate of flap salvage will be compared between modalities of monitoring to  
4 establish any correlation. The false positive and negative rates of the Cook-  
5 Swartz Implantable Doppler will be calculated. If possible, the efficacy of the  
6 Cook-Swartz Implantable Doppler in different flap types and locations will be  
7 established.  
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### 13 14 15 16 **Dissemination**

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18 The number of free flaps that are compromised per year mean that  
19 improvements need to be made to monitoring protocols. It is possible that the  
20 Cook-Swartz Doppler may well represent a useful tool for such improvement.  
21 As such, the authors hope to disseminate the findings as widely as possible,  
22 irrespective of results as they add to wider corpora of information. The  
23 systematic review will be published in a peer-reviewed journal and include a  
24 number of recommendations as its conclusion based upon the evidence  
25 contained within. Given the wide range of specialities now utilising flaps, it will  
26 be presented at a wide range of national and international conferences.  
27 Updates of the review could be conducted as more information becomes  
28 available to guide best practice and further maintain the quality of evidence.  
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## Contributorship Statement

RAA - concept, initial drafting, critical revision, approval of manuscript to be submitted

BG - drafting, critical revision, approval of manuscript to be submitted

AJF - drafting, critical revision, approval of manuscript to be submitted

TWHB - concept, critical revision, approval of manuscript to be submitted

DO - concept, critical revision, approval of manuscript to be submitted

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**Conflicts of interest:** The authors declare no potential conflicts of interest

**Protocol Registration:** PROSPERO – National Institute of Health Research (NIHR) Prospective Register of Systematic Reviews CRD42013005818

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**The efficacy of the Cook-Swartz implantable Doppler in the detection of free flap compromise: A systematic review protocol**

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# The efficacy of the Cook-Swartz implantable Doppler in the detection of free flap compromise: A systematic review protocol

## REVIEW INFORMATION

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## ABSTRACT

### Introduction

The Cook-Swartz implantable Doppler monitors venous or arterial blood flow from free flaps and can detect free flap compromise. Previous studies have shown that the use of this Doppler can improve detection and salvage rates as it provides an earlier warning than the current method of clinical assessment. Such studies assert that the implantable Doppler is of great value in monitoring of free flaps in current microsurgical units. This systematic review aims to compare the efficacy of the Cook-Swartz implantable Doppler in monitoring free flap compromise against conventional clinical free flap monitoring techniques.

### Methods and analysis

Various electronic databases will be systematically searched for studies which compare the use of Cook-Swartz implantable Doppler with clinical assessment. The selected studies will then have their titles and abstracts screened by two authors. Articles selected after title and abstract screen will have full text downloaded and the complete article will be assessed for suitability. Once articles have been selected for inclusion, data extraction will take place. For the data analysis, the outcomes of the studies will be tabulated, with descriptive statistics performed as appropriate and the detection rate of the Doppler and clinical assessment will be compared and synthesised where possible.

## Ethics and Dissemination

The authors hope to disseminate the findings as widely as possible. This systematic review will be published in a peer-reviewed journal and include a number of recommendations as its conclusion based upon the evidence contained within. Given the wide range of specialities now utilising flaps, it will be presented at a wide range of national and international conferences.

## Protocol Registration in PROSPERO: CRD42013005818

By 28<sup>th</sup> January 2014, the literature search and data extraction had been ongoing for some time. These steps were revised in line with peer review comments.

## BACKGROUND

### Free flap reconstruction

Free flap reconstruction for large tissue defects is increasingly common and plays an important role in the field of plastic and reconstructive surgery.<sup>1</sup> Such surgery necessitates a microsurgical anastomosis from the harvested flap to



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3 the recipient using minute sutures. Data suggests that the commonest cause  
4 of failure is a problem with the venous anastomosis occurring within the first  
5 24 to 48 hours postoperatively.<sup>2,3,4</sup> This problem affects up to 20% of all free  
6 flap reconstructions, depending upon their location and entails significant  
7 physical, psychological and emotional morbidity for patients.<sup>5,6,7</sup>

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16 Flap failure often necessitates further general anaesthetics and operations.  
17 Due to the time critical nature of flap failure, reoperation may occur out of  
18 hours, which provides further logistical and practical challenges.<sup>7</sup> Initially, an  
19 attempt is made to salvage the flap, if this fails, then the flap is removed and  
20 an alternative reconstructive approach may be required. In some cases,  
21 venous congestion may require blood drainage; for example by use of  
22 medicinal leeches,<sup>8</sup> which is potentially highly unpleasant for patients and  
23 predisposes them to infection and anaemia.<sup>9</sup> Patients therefore require careful  
24 wound inspection, surveillance of haemoglobin and prophylactic antibiotics to  
25 protect them from further complications.<sup>8,10</sup>

### 40 **Monitoring of free flaps**

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43 Early recognition of flap compromise is the primary aim of every microsurgical  
44 unit. Prompt intervention and rescue is critical for ensuring flap survival.  
45 However, the complexities of free flap microcirculation are often difficult to  
46 assess, and there are a wide array of possible monitoring modalities.<sup>11</sup> The  
47 commonest method of monitoring is carried out clinically and is based upon  
48 subjective clinical observations. These tests are carried out on an island of  
49 skin or 'skin paddle' – an area of skin considered to be indicative of the whole  
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3 flap's arterial perfusion and venous drainage.<sup>12</sup> Such tests may include the  
4 colour, capillary refill or blanching time, skin temperature, turgor, and degree  
5 of bleeding in response to pin-prick and use of a handheld doppler device.<sup>13</sup>  
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10 Unlike solid organ transplantation, there is no objective assessment - such as  
11 decreased urine output in renal transplantation. Similarly, there are currently  
12 no suitable imaging modalities for assessing microvascular flow and  
13 specifically slow venous flow problems, though there are reports in the  
14 literature of the use of nuclear medicine techniques in successful  
15 monitoring.<sup>14</sup> A number of small studies have highlighted the use of Single-  
16 Positron Emission Computed Tomography (SPECT) in the determination of  
17 free flap compromise.<sup>15</sup> However, large comparative studies are required with  
18 standardised techniques to further define the role of this modality in the  
19 assessment of free flap compromise. Early compromise, which entails the  
20 large majority of flap failure, is often asymptomatic. Pain, bleeding and skin  
21 changes can take a while to develop, potentially increasing ischaemic times  
22 and reducing the possibility of successful salvage.<sup>16</sup>  
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40 Some free flaps are very challenging to monitor adequately, such as  
41 vascularised bone and muscle flaps; especially those that have been covered  
42 with a skin graft and cutaneous flaps in non-Caucasian skin. Some flaps, such  
43 as buried flaps within the head and neck are impossible to monitor by visual,  
44 clinical assessment and in such circumstances, attempts have been made to  
45 enhance clinical monitoring using microdialysis.<sup>11, 17</sup> However, this can take  
46 up to 30 minutes to get a reading, necessitates training to learn a technique  
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3 and analyse results, does not directly measure flow and costs almost \$52,000  
4 per monitor plus additional costs of up to \$570 per flap.<sup>11</sup>  
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### 9 10 **The Cook-Swartz Implantable Doppler**

11 The Cook-Swartz implantable Doppler monitors the venous flow from free  
12 flaps and obtained its CE mark in 2006.<sup>18</sup> Since then it has been distributed  
13 widely in both Europe and the rest of the world.<sup>18</sup> It is the only device currently  
14 on the market that allows this monitoring and is protected by patent. It  
15 consists of a 20 MHz ultrasonic Doppler crystal, a silicone cuff and a monitor  
16 unit.<sup>19, 20</sup> This cuff secures the Doppler to the flap's vein at the time of the  
17 operation and is placed downstream of the microvascular anastomosis.<sup>20</sup> The  
18 Doppler provides monitoring for 5-10 days postoperatively and is removed by  
19 simple traction.<sup>18</sup> A number of studies have shown that use of this device  
20 increases success and salvage rates as it provides an earlier warning that the  
21 current method of clinical monitoring.<sup>12, 21, 22</sup>  
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### 43 **The potential of the Cook-Swartz Doppler**

44 The use of the Cook-Swartz Doppler in the assessment of such flaps has  
45 demonstrated improved detection times.<sup>2, 12, 22, 23</sup> This technology is needed  
46 now more than ever as the indications for, and therefore absolute number of,  
47 free flaps have increased. Indications for flaps include following resection of  
48 breast tumours, head and neck cancers, skin cancers, major burns and  
49 infections. Often these may be 'cross-speciality' flaps, for example with  
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3 orthopaedics to cover exposed metal work in lower limb fractures. Changes to  
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5 working practices mean that these patients may be returned to an orthopaedic  
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7 or general surgical ward where monitoring is performed by non-specialist  
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9 nurses who may not be used to monitoring flaps, let alone over night and in  
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11 challenging settings such as low light.  
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### 13 14 15 16 **Why is a systematic review of this required?** 17

18 To our knowledge, there has only been one systematic review involving the  
19  
20 Cook-Swartz Implantable Doppler. Poder and Fortier investigated the efficacy  
21  
22 and cost effectiveness of the implantable Doppler.<sup>24</sup> However, we aim to  
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24 investigate and further clarify the role of the Doppler as a monitoring  
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26 technique by comparing it to clinical assessment. Clinical assessment is the  
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28 most widely used technique and as such the standard against which the  
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30 Doppler should be compared. Further clarifying the role and possible benefit  
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32 of the Cook-Swartz Doppler in the detection of free flap compromise would  
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34 allow modification of practice and guidelines in line with the best evidence.  
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36 We realise that previous reviews were limited by the quality of evidence  
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38 available, but a number of studies have been published since the last review  
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40 and therefore an updated review is required.  
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### 50 51 **OBJECTIVES** 52

53 Our objective is to perform a comprehensive systematic review of the  
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55 implantable Doppler in the detection of free flap compromise.  
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**Primary objective:**

To compare the efficacy of the Cook-Swartz implantable Doppler versus clinical assessment in the detection of free flap compromise and flap salvage.

**Secondary objectives:**

To determine the absolute indications for use of the Doppler (if any). Quantify the sensitivity, specificity, positive and negative predictive values of the Doppler. To describe complications associated with Doppler use.

**METHODS**

This systematic review will be conducted according to the recommendations outlined in the Cochrane Handbook for reviews and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.<sup>25</sup>

**Criteria for selecting studies:**

The following search criteria were specifically devised to locate studies specifically pertaining to the use of the Cook-Swartz Doppler and to provide evidence for the objectives previously stated.

**Types of studies**

Any study comparing the use of Cook-Swartz implantable doppler with clinical assessment in detecting the failure of free flaps will be included. Articles must describe use of the implantable doppler specifically and may be of any grade of evidence (1 to 5 as defined by the Oxford Centre for Evidence-Based Medicine).<sup>26</sup>

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3 Any article where data is duplicated will be excluded, as will articles not  
4 describing original data; such as editorials, letters regarding other articles and  
5 discussion pieces. Unpublished reports will be included if the methodology  
6 and results are accessible in written form.  
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### 11 12 13 14 **Types of participants**

15 Human subjects of any age who have undergone free flap surgery. There will  
16 be no limitation on location of the flap or technique utilised.  
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### 21 22 23 **Types of interventions**

24 Any article describing use of the Cook-Swartz Doppler in the detection of free  
25 flap compromise would be considered, and articles won't be excluded based  
26 on type of flap. Articles will only be considered if they include a group  
27 monitored by clinical detection for comparison with the Cook-Swartz Doppler.  
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### 36 37 **Types of comparator**

38 Cook-Swartz implantable Doppler used on the venous or arterial pedicle of a  
39 free flap attached by any means and used to monitor free flaps post-  
40 operatively. Clinical assessment of free flaps including, but not limited to; skin  
41 colour, turgor, surface temperature, capillary refill time or handheld  
42 Doppler.  
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## Types of outcome measures

### Primary outcome:

Flap failure rate, defined as the number of free flaps lost divided by the total number of flaps. This outcome will be calculated for both doppler and clinically monitored flaps.

### Secondary outcomes:

Sensitivity, specificity, positive predictive value and negative predictive value.

Time to detection will be reported where possible and compared between clinically monitored and Doppler monitored flaps.

Any complications associated with flap use will be described

## Search methods for identification of studies

### Electronic Searches

The following electronic databases will be searched to 24<sup>th</sup> September 2013: MEDLINE, EMBASE, PsycINFO, Ebsco, Cochrane Database of Systematic Reviews, CINAHL, SCOPUS, SciELO, NHS evidence, [www.uptodate.com](http://www.uptodate.com), <http://clinicaltrials.gov/>, <http://www.who.int/ictrp/en/>, <http://www.controlled-trials.com/>

### Search terms and keywords

The search strategy has been developed to locate papers related specifically to the Cook-Swartz implantable Doppler. This search will utilise the English language keywords combined with Boolean logical operators. Therefore the

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3 following terms will be utilised: “*Implantable doppler*” OR “*Cook-Swartz*  
4 *implantable doppler*” OR “*Cook-Swartz Implantable doppler*”.  
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7 The search will not be limited by language. Any non-English articles identified  
8 will proceed to title and abstract screening and the full text obtained if  
9 required. If full text is not available, then the authors will be contacted to  
10 obtain an English language copy of the full text. Failing this, colleagues  
11 speaking the language will be contacted to translate. Google Translate will be  
12 utilised as a last resort.  
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### 20 21 22 23 **Other resources**

24 A hand search of the references of articles located by the search strategy will  
25 be used to identify any relevant citations within the grey literature. Active  
26 researchers will be contacted to identify any other published or unpublished  
27 work. An active researcher is defined as one who has published more than  
28 three articles in the field in the last five years, or one in the last two.  
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### 40 41 42 43 **Identification and Selection of articles**

44 Studies identified by the electronic and manual search strategy will be listed.  
45 Results including citation, title and abstracts will be populated into EndNote®  
46 (Thomson Reuters, New York, NY, USA) and duplicates removed. Titles and  
47 abstracts will be screened by two authors (BG and AJF), any conflicts not  
48 resolvable between the two will be referred to the lead author (RA) for  
49 resolution. Articles selected after title and abstract screen will have full text  
50 downloaded and a further assessment made. Once articles have been  
51 selected for inclusion, data extraction will take place.  
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## Data extraction and management

Data will be extracted independently by two authors (BG and AJF) utilising a standard extraction form where all data for each study will be collated (Appendix A). Any conflict of extraction will be resolved by discussion; where resolution this isn't possible, the lead author (RA) will make a final decision. This data will then be entered into a Microsoft Excel ® 2011 database (Microsoft, Redmond, WA, USA). Data collected will constitute three main areas:

### 1) Article information

- Title
- Authors
- Year of publication
- Journal

### 2) Characteristics

- Setting and Location of the study
- Number of patients
- Range of patient age
- Flap types included
- Clinical method of assessment
- Doppler method of assessment (Arterial vs. Venous)

### 3) Results (divided clinical and doppler)

- Number of patients per group
- Specific flaps in groups (where applicable)
- Detected

- Flap Salvage
- Needless theatre return
- Complications
- Lost flaps without any signs
- Flaps correctly monitored

### **Assessment of study quality and bias in included studies**

Quality of evidence can be assessed based upon a number of criteria; we will be specifically utilising the Grading of Recommendation Assessment, Development and Evaluation (GRADE) system as proposed by Balshem et al.<sup>27</sup> This will allow us to determine the quality of the evidence that is being utilised in the data analysis of this topic.

If we locate any Randomised Controlled Trials (RCTs) we will utilise the Cochrane risk of bias tool and compare outcomes to published trial protocols. Any information missing from studies will be documented and assessed to ascertain the risk of incomplete statistical sets.

### **Assessment of publication bias**

To ascertain if studies with negative outcomes are not being published (“publication bias”), we will visually assess funnel plot asymmetry.<sup>28, 29</sup> Where both positive and negative results are published, the plot should resemble a symmetrical, inverted funnel. The precision of the estimated intervention effect will increase as the size of the sample included in the study increases. Smaller studies will therefore scatter widely at the bottom, with larger, more powerful studies grouping more narrowly at the top. The asymmetrical

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3 distribution of standard error on analysis of the funnel plot would indicate  
4 publication bias.  
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### 9 10 **Assessment of Heterogeneity**

11 Heterogeneity between studies will be assessed using Higgins and  
12 Thompson's  $I^2$ , which measures the percentage variability in result attributable  
13 to heterogeneity between studies rather than sampling error<sup>28</sup>. Variability in  
14 the intervention effects in studies will be tested for statistical heterogeneity  
15 utilising Tau-squared ( $T^2$ ),  $I^2$  and chi-squared ( $X^2$ ) with corresponding P-  
16 values calculated; the Cochran tests.  
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19 The value of  $X^2$  statistics in the forest plot presents the assessment of  
20 whether the differences in results are compatible with chance alone. A large  
21 value of  $X^2$  test relative to its degree of freedom (df) or a low P-value indicates  
22 statistical variation (heterogeneity) beyond chance.  
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36 The  $I^2$  percentage will be interpreted as follows:

- 37 • 0% - 30% may not be important.
- 38 • 30% - 60% may represent moderate heterogeneity\*
- 39 • 50% - 90% may represent substantial heterogeneity\*
- 40 • 75% - 100% represents considerable heterogeneity\*
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48 [\*the importance of the observed  $I^2$  value depends on; magnitude and  
49 direction of effects and strength of evidence for heterogeneity such as P-value  
50 from  $X^2$  or a Confidence Interval for  $I^2$ ].<sup>28</sup>  
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53 Generation of statistical heterogeneity can be a consequence of clinical  
54 (participants, interventions and outcomes) and/or methodological (study  
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3 design and risk of bias) diversity or due to random error (chance) alone.  $T^2$   
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5 represents the estimated standard deviation of underlying effects across  
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7 studies. The exact model utilised for meta-analysis will be based upon the  
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9 level of heterogeneity within our data; with a random effects model used if it is  
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11 high and a fixed-effects analysis if moderate.  
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### 14 15 16 **Data Synthesis and statistical analysis**

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18 Outcomes will be tabulated, with descriptive statistics performed as  
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20 appropriate. Similarly, the detection rate of each modality will be compared  
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22 and synthesised where possible. Synthesis will be performed utilising Review  
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24 Manager (RevMan 5.2.6) and an assessment of heterogeneity will be made.  
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26 Based upon this, meta-analysis will be carried out comparing Cook-Swartz  
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28 Doppler to clinical monitoring; ideally utilising randomised controlled trials, but  
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30 good quality observational studies will also be considered.  
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34 Rate of flap salvage will be compared between modalities of monitoring to  
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36 establish any correlation. The false positive and negative rates of the Cook-  
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38 Swartz Implantable Doppler will be calculated. If possible, the efficacy of the  
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40 Cook-Swartz Implantable Doppler in different flap types and locations will be  
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42 established.  
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### 45 **Sub Group Analysis**

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47 Subgroup analyses will be undertaken of the following groups where  
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49 available:  
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- 51 • Different flap type (if >3 studies describing specific flap types)
- 52 • Venous vs. Arterial Doppler probe placement
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- Different anatomic locations (if >3 studies describe the same anatomic locations)

### Dissemination

The number of free flaps that are compromised per year mean that improvements need to be made to monitoring protocols. It is possible that the Cook-Swartz Doppler may well represent a useful tool for such improvement. As such, the authors hope to disseminate the findings as widely as possible, irrespective of results as they add to wider corpora of information. The systematic review will be published in a peer-reviewed journal and include a number of recommendations as its conclusion based upon the evidence contained within. Given the wide range of specialities now utilising flaps, it will be presented at a wide range of national and international conferences. Updates of the review could be conducted as more information becomes available to guide best practice and further maintain the quality of evidence.

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21 **Funding:** No funding was received for this systematic review  
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24 **Contributorsip Statement:**

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27 RAA - concept, intial drafting, critical revision, approval of manuscript to be  
28 submitted  
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33 BG - drafting, critical revision, approval of manuscript to be submitted  
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36 AJF - drafting, critical revision, approval of manuscript to be submitted  
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39 TWHB - concept, critical revision, approval of manuscript to be submitted  
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42 DO - concept, critical revision, approval of manuscript to be submitted  
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45 **Conflicts of interest:** The authors declare no potential conflicts of  
46 interest  
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50 **Protocol Registration:** PROSPERO – National Institute of Health Research  
51 (NIHR) Prospective Register of Systematic Reviews CRD42013005818  
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# The efficacy of the Cook-Swartz implantable Doppler in the detection of free flap compromise: A systematic review protocol

## REVIEW INFORMATION

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**Protocol Registration:** PROSPERO – National Institute of Health Research (NIHR) Prospective Register of Systematic Reviews CRD42013005818

## ABSTRACT

### Introduction

The Cook-Swartz implantable Doppler monitors venous or arterial blood flow from free flaps and can detect free flap compromise. Previous studies have shown that the use of this Doppler can improve detection and salvage rates as it provides an earlier warning than the current method of clinical assessment. Such studies assert that the implantable Doppler is of great value in monitoring of free flaps in current microsurgical units. This systematic review aims to compare the efficacy of the Cook-Swartz implantable Doppler in monitoring free flap compromise against conventional clinical free flap monitoring techniques.

### Methods and analysis

Various electronic databases will be systematically searched for studies which compare the use of Cook-Swartz implantable Doppler with clinical assessment. The selected studies will then have their titles and abstracts screened by two authors. Articles selected after title and abstract screen will have full text downloaded and the complete article will be assessed for suitability. Once articles have been selected for inclusion, data extraction will take place. For the data analysis, the outcomes of the studies will be tabulated, with descriptive statistics performed as appropriate and the detection rate of the Doppler and clinical assessment will be compared and synthesised where possible.

## Ethics and Dissemination

The authors hope to disseminate the findings as widely as possible. This systematic review will be published in a peer-reviewed journal and include a number of recommendations as its conclusion based upon the evidence contained within. Given the wide range of specialities now utilising flaps, it will be presented at a wide range of national and international conferences.

### Protocol Registration in PROSPERO: CRD42013005818

By 28<sup>th</sup> January 2014, the literature search and data extraction had been ongoing for some time. These steps were revised in line with peer review comments.

## BACKGROUND

### Free flap reconstruction

Free flap reconstruction for large tissue defects is increasingly common and plays an important role in the field of plastic and reconstructive surgery.<sup>1</sup> Such surgery necessitates a microsurgical anastomosis from the harvested flap to

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6 the recipient using minute sutures. Data suggests that the commonest cause  
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8 of failure is a problem with the venous anastomosis occurring within the first  
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10 24 to 48 hours postoperatively.<sup>2,3,4</sup> This problem affects up to 20% of all free  
11  
12 flap reconstructions, depending upon their location and entails significant  
13  
14 physical, psychological and emotional morbidity for patients.<sup>5,6,7</sup>  
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18 Flap failure often necessitates further general anaesthetics and operations.  
19  
20 Due to the time critical nature of flap failure, reoperation may occur out of  
21  
22 hours, which provides further logistical and practical challenges.<sup>7</sup> Initially, an  
23  
24 attempt is made to salvage the flap, if this fails, then the flap is removed and  
25  
26 an alternative reconstructive approach may be required. In some cases,  
27  
28 venous congestion may require blood drainage; for example by use of  
29  
30 medicinal leeches,<sup>8</sup> ~~which~~ ~~This~~ is potentially highly unpleasant for patients  
31  
32 and predisposes them to infection and anaemia.<sup>9</sup> Patients therefore require  
33  
34 careful wound inspection, surveillance of haemoglobin and prophylactic  
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36 antibiotics to protect them from further complications.<sup>8,10</sup>  
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### 39 **Monitoring of free flaps**

40  
41 Early recognition of flap compromise is the primary aim of every microsurgical  
42  
43 unit. Prompt intervention and rescue is critical for ensuring flap survival.  
44  
45 However, the complexities of free flap microcirculation are often difficult to  
46  
47 assess, and there are a wide array of possible monitoring modalities.<sup>11</sup> ~~At~~  
48  
49 ~~present, m~~ The commonest method of monitoring is carried out clinically and is  
50  
51 based upon subjective clinical observations. These tests are carried out on an  
52  
53 island of skin or 'skin paddle' – an area of skin considered to be indicative of  
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6 the whole flap's arterial perfusion and venous drainage.<sup>12</sup> Such tests may  
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8 include the colour, capillary refill or blanching time, skin temperature, turgor,  
9  
10 and degree of bleeding in response to pin-prick and use of a handheld  
11  
12 doppler device.<sup>13</sup>  
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15 Unlike solid organ transplantation, there is no objective assessment - such as  
16  
17 decreased urine output in renal transplantation. Similarly, there are currently  
18  
19 no suitable imaging modalities for assessing microvascular flow and  
20  
21 specifically slow venous flow problems, though there are reports in the  
22  
23 literature of the use of nuclear medicine techniques in successful  
24  
25 monitoring.<sup>14</sup> A number of small studies have highlighted the use of Single-  
26  
27 Positron Emission Computed Tomography (SPECT) in the determination of  
28  
29 free flap compromise.<sup>15</sup> However, large comparative studies are required with  
30  
31 standardised techniques to further define the role of this modality in the  
32  
33 assessment of free flap compromise. Early compromise, which entails the  
34  
35 large majority of flap failure, is often asymptomatic. Pain, bleeding and skin  
36  
37 changes can take a while to develop, potentially increasing ischaemic times  
38  
39 and reducing the possibility of successful salvage.<sup>16</sup>  
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41  
42 Some free flaps are very challenging to monitor adequately, such as  
43  
44 vascularised bone and muscle flaps; especially those that have been covered  
45  
46 with a skin graft and cutaneous flaps in non-Caucasian skin. Some flaps, such  
47  
48 as buried flaps within the head and neck are impossible to monitor by visual,  
49  
50 clinical assessment and in such circumstances, attempts have been made to  
51  
52 enhance clinical monitoring using microdialysis.<sup>11, 17</sup> However, this can take  
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54 up to 30 minutes to get a reading, necessitates training to learn a technique  
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6 and analyse results, does not directly measure flow and costs almost \$52,000  
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8 per monitor plus additional costs of up to \$570 per flap.<sup>11</sup>  
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### 11 **The Cook-Swartz Implantable Doppler**

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13  
14 The Cook-Swartz implantable Doppler monitors the venous flow from free  
15 flaps and obtained its CE mark in 2006.<sup>18</sup> Since then it has been distributed  
16 widely in both Europe and the rest of the world.<sup>18</sup> It is the only device currently  
17 on the market that allows this monitoring and is protected by patent. It  
18 consists of a 20 MHz ultrasonic Doppler crystal, a silicone cuff and a monitor  
19 unit.<sup>19, 20</sup> This cuff secures the Doppler to the flap's vein at the time of the  
20 operation and is placed downstream of the microvascular anastomosis.<sup>20</sup> The  
21 Doppler provides monitoring for 5-10 days postoperatively and is removed by  
22 simple traction.<sup>18</sup> A number of studies have shown that use of this device  
23 increases success and salvage rates as it provides an earlier warning that the  
24 current method of clinical monitoring.<sup>12, 21, 22</sup>  
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### 42 **The potential of the Cook-Swartz Doppler**

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44 The use of the Cook-Swartz Doppler in the assessment of such flaps has  
45 demonstrated improved detection times.<sup>2, 12, 22, 23</sup> This technology is needed  
46 now more than ever as the indications for, and therefore absolute number of,  
47 free flaps have increased. Indications for flaps include following resection of  
48 breast tumours, head and neck cancers, skin cancers, major burns and  
49 infections. Often these may be 'cross-speciality' flaps, for example with  
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6 orthopaedics to cover exposed metal work in lower limb fractures. Changes to  
7  
8 working practices mean that these patients may be returned to an orthopaedic  
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10 or general surgical ward where monitoring is performed by non-specialist  
11  
12 nurses who may not be used to monitoring flaps, let alone over night and in  
13  
14 challenging settings such as low light.

### 15 16 17 18 **Why is a systematic review of this required?**

19  
20 To our knowledge, there has only been one systematic review involving the  
21  
22 Cook-Swartz Implantable Doppler. Poder and Fortier investigated the efficacy  
23  
24 and cost effectiveness of the implantable Doppler.<sup>24</sup> However, we aim to  
25  
26 investigate and further clarify the role of the Doppler as a monitoring  
27  
28 technique by comparing it to clinical assessment. Clinical assessment is the  
29  
30 most widely used technique and as such the standard against which the  
31  
32 Doppler should be compared. Further clarifying the role and possible benefit  
33  
34 of the Cook-Swartz Doppler in the detection of free flap compromise would  
35  
36 allow modification of practice and guidelines in line with the best evidence.

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38 We realise that previous reviews were limited by the quality of evidence  
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40 available, but a number of studies have been published since the last review  
41  
42 and therefore an updated review is required.

### 43 44 45 46 47 48 **OBJECTIVES**

49  
50 Our objective is to perform a comprehensive systematic review of the  
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52 implantable Doppler in the detection of free flap compromise.  
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**Primary objective:**

To compare the efficacy of the Cook-Swartz implantable Doppler versus clinical assessment in the detection of free flap compromise and flap salvage.

**Secondary objectives:**

To determine the absolute indications for use of the Doppler (if any). Quantify the sensitivity, specificity, false positive and negative rates, salvage rates and number of associated complications positive and negative predictive values of the Doppler. To describe complications associated with Doppler use.

**METHODS**

This systematic review will be conducted according to the recommendations outlined in the Cochrane Handbook for reviews and reported in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.<sup>25</sup>

**Criteria for selecting studies:**

The following search criteria were specifically devised to locate studies specifically pertaining to the use of the Cook-Swartz Doppler and to provide evidence for the objectives previously stated.

**Types of studies**

Any study comparing the use of Cook-Swartz implantable doppler with clinical assessment in detecting the failure of free flaps will be included. Articles must describe use of the implantable doppler specifically and may be of any grade



of evidence (1 to 5 as defined by the Oxford Centre for Evidence-Based Medicine).<sup>26</sup>

Any article where data is duplicated will be excluded, as will articles not describing original data; such as editorials, letters regarding other articles and discussion pieces. Unpublished reports will be included if the methodology and results are accessible in written form.

### Types of participants

Human subjects of any age who have undergone free flap surgery. There will be no limitation on location of the flap or technique utilised.

### Types of interventions

Any article describing use of the Cook-Swartz Doppler in the detection of free flap compromise would be considered, and articles won't be excluded based on type of flap. Ideally, Articles will only be considered if they include a group monitored by clinical detection for comparison with the Cook-Swartz Doppler. ~~his would be considered against a control group of clinical monitoring.~~

### Types of comparator

Cook-Swartz implantable Doppler used on the venous or arterial pedicle of a free flap attached by any means and used to monitor free flaps post-operatively. Clinical assessment of free flaps including, but not limited to; skin colour, turgor, surface temperature, capillary refill time or handheld Doppler.

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For peer review only

Types of outcome measures

**Primary outcome:**

Flap failure rate, defined as the number of free flaps lost divided by the total number of flaps~~The rate of detection will be determined as the number of Doppler monitored flaps correctly identified as compromised divided by the total number of Doppler monitored flaps.~~ This outcome will be compared calculated for both doppler and with clinically monitored flaps~~ing.~~

**Secondary outcomes:**

Sensitivity, specificity, positive predictive value and negative predictive value.  
~~The salvage rate will be the number of compromised flaps successfully salvaged divided by the total number of compromised flaps. The false positive rate is the number of flaps monitored by Doppler returned to theatre incorrectly divided by the total number of Doppler monitored flaps.~~

~~The false negative rate will be the number of flaps lost without any change in Doppler monitoring, divided by the total number of Doppler monitored flaps.~~

~~The true negative rates will be the number of flaps monitored without any change in Doppler and without any compromise divided by the total number of Doppler monitored flaps.~~

~~The rates for clinical assessment will be calculated as above and compared to that of the Doppler.~~ Time to detection will be reported where possible and compared between clinically monitored and Doppler monitored flaps.

Any complications associated with flap use will be described

**Search methods for identification of studies****Electronic Searches**

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6 The following electronic databases will be searched to 24<sup>th</sup> September 2013:  
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8 MEDLINE, EMBASE, PsycINFO, Ebsco, Cochrane Database of Systematic  
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10 Reviews, CINAHL, SCOPUS, SciELO, NHS evidence, [www.uptodate.com](http://www.uptodate.com),  
11  
12 <http://clinicaltrials.gov/>, <http://www.who.int/ictrp/en/>, <http://www.controlled->  
13  
14 [trials.com/](http://www.controlled-trials.com/)

### 15 16 17 18 **Search terms and keywords**

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20 The search strategy has been developed to locate papers related specifically  
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22 to the Cook-Swartz implantable Doppler. This search will utilise the English  
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24 language keywords combined with Boolean logical operators. Therefore the  
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26 following terms will be utilised: “*Implantable doppler*” OR “*Cook-Swartz*  
27  
28 *implantable doppler*” OR “*Cook-Swartz Implantable doppler*”.

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30 The search will not be limited by language. Any non-English articles identified  
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32 will proceed to title and abstract screening and the full text obtained if  
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34 required. If full text is not available, then the authors will be contacted to  
35  
36 obtain an English language copy of the full text. Failing this, colleagues  
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38 speaking the language will be contacted to translate. Google Translate will be  
39  
40 utilised as a last resort.

### 41 42 43 44 **Other resources**

45  
46 A hand search of the references of articles located by the search strategy will  
47  
48 be used to identify any relevant citations within the grey literature. Active  
49  
50 researchers will be contacted to identify any other published or unpublished  
51  
52 work. An active researcher is defined as one who has published more than  
53  
54 three articles in the field in the last five years, or one in the last two.

## Identification and Selection of articles

Studies identified by the electronic and manual search strategy will be listed. Results including citation, title and abstracts will be populated into EndNote® (Thomson Reuters, New York, NY, USA) and duplicates removed. Titles and abstracts will be screened by two authors (BG and AJF), any conflicts not resolvable between the two will be referred to the lead author (RA) for resolution. Articles selected after title and abstract screen will have full text downloaded and a further assessment made. Once articles have been selected for inclusion, data extraction will take place.

## Data extraction and management

Data will be extracted independently by two authors (BG and AJF) utilising a standard extraction form where all data for each study will be collated (Appendix A). Any conflict of extraction will be resolved by discussion; where resolution this isn't possible, the lead author (RA) will ~~have final say~~ make a final decision. This data will then be entered into a Microsoft Excel® 2011 database (Microsoft, Redmond, WA, USA). Data collected will constitute three main areas:

### 1) Article information

- Title
- Authors
- Year of publication
- Journal

### 2) Characteristics

- Setting and Location of the study
- Number of patients
- Range of patient age
- Flap types included
- Clinical method of assessment
- Doppler method of assessment (Arterial vs. Venous)

### 3) Results (divided clinical and doppler)

- Number of patients per group
- Specific flaps in groups (where applicable)
- Detected
- Flap Salvage
- Needless theatre return
- Complications
- Lost flaps without any signs
- Flaps correctly monitored

#### Assessment of study quality and bias in included studies

~~The quality of evidence included in this analysis needs to be established.~~

Quality of evidence can be assessed based upon a number of criteria; we will be specifically utilising the Grading of Recommendation Assessment, Development and Evaluation (GRADE) system as proposed by Balshem et

al.<sup>27</sup> This will allow us to determine the quality of the evidence that is being utilised in the data analysis of this topic.

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6 If we locate any Randomised Controlled Trials (RCTs) we will utilise the  
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8 Cochrane risk of bias tool and compare outcomes to published trial protocols.  
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10 Any information missing from studies will be documented and assessed to  
11  
12 ascertain the risk of incomplete statistical sets.  
13

### 14 15 16 17 18 19 20 21 22 **Assessment of publication bias**

23  
24 To ascertain if studies with negative outcomes are not being published  
25  
26 (“publication bias”), we will visually assess funnel plot asymmetry.<sup>28, 29</sup> Where  
27  
28 both positive and negative results are published, the plot should resemble a  
29  
30 symmetrical, inverted funnel. The precision of the estimated intervention effect  
31  
32 will increase as the size of the sample included in the study increases.  
33  
34 Smaller studies will therefore scatter widely at the bottom, with larger, more  
35  
36 powerful studies grouping more narrowly at the top. The asymmetrical  
37  
38 distribution of standard error on analysis of the funnel plot would indicate  
39  
40 publication bias.  
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### 43 44 **Assessment of Heterogeneity**

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46 Heterogeneity between studies will be assessed using Higgins and  
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48 Thompson’s  $I^2$ , which measures the percentage variability in result attributable  
49  
50 to heterogeneity between studies rather than sampling error<sup>28</sup>. Variability in  
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52 the intervention effects in studies will be tested for statistical heterogeneity  
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6 utilising Tau-squared ( $T^2$ ),  $I^2$  and chi-squared ( $X^2$ ) with corresponding P-  
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8 values calculated; the Cochran tests.

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10 The value of  $X^2$  statistics in the forest plot presents the assessment of  
11  
12 whether the differences in results are compatible with chance alone. A large  
13  
14 value of  $X^2$  test relative to its degree of freedom (df) or a low P-value indicates  
15  
16 statistical variation (heterogeneity) beyond chance.

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20 The  $I^2$  percentage will be interpreted as follows:

- 21 • 0% - 30% may not be important.
- 22 • 30% - 60% may represent moderate heterogeneity\*
- 23 • 50% - 90% may represent substantial heterogeneity\*
- 24 • 75% - 100% represents considerable heterogeneity\*
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31 [\*the importance of the observed  $I^2$  value depends on; magnitude and  
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33 direction of effects and strength of evidence for heterogeneity such as P-value  
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35 from  $X^2$  or a Confidence Interval for  $I^2$ ].<sup>28</sup>

36  
37 Generation of statistical heterogeneity can be a consequence of clinical  
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39 (participants, interventions and outcomes) and/or methodological (study  
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41 design and risk of bias) diversity or due to random error (chance) alone.  $T^2$   
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43 represents the estimated standard deviation of underlying effects across  
44  
45 studies. The exact model utilised for meta-analysis will be based upon the  
46  
47 level of heterogeneity within our data; with a random effects model used if it is  
48  
49 high and a fixed-effects analysis if moderate.

## 50 51 52 **Data Synthesis and statistical analysis** 53 54



Outcomes will be tabulated, with descriptive statistics performed as appropriate. Similarly, the detection rate of each modality will be compared and synthesised where possible. Synthesis will be performed utilising Review Manager (RevMan 5.2.6) and an assessment of heterogeneity will be made. Based upon this, meta-analysis will be carried out comparing Cook-Swartz Doppler to clinical monitoring; ideally utilising randomised controlled trials, but good quality observational studies will also be considered.

Rate of flap salvage will be compared between modalities of monitoring to establish any correlation. The false positive and negative rates of the Cook-Swartz Implantable Doppler will be calculated. If possible, the efficacy of the Cook-Swartz Implantable Doppler in different flap types and locations will be established.

### **Sub Group Analysis**

Subgroup analyses will be undertaken of the following groups where available:

- Different flap type (if >3 studies describing specific flap types)
- Venous vs. Arterial Doppler probe placement
- Different anatomic locations (if >3 studies describe the same anatomic locations)

### **Dissemination**

The number of free flaps that are compromised per year mean that improvements need to be made to monitoring protocols. It is possible that the Cook-Swartz Doppler may well represent a useful tool for such improvement. As such, the authors hope to disseminate the findings as widely as possible,

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6 irrespective of results as they add to wider corpora of information. The  
7  
8 systematic review will be published in a peer-reviewed journal and include a  
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10 number of recommendations as its conclusion based upon the evidence  
11  
12 contained within. Given the wide range of specialities now utilising flaps, it will  
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14 be presented at a wide range of national and international conferences.  
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16 Updates of the review could be conducted as more information becomes  
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18 available to guide best practice and further maintain the quality of evidence.  
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