TECHNOLOGY-ASSISTED AND SUTURELESS MICROVASCULAR ANASTOMOSES: EVIDENCE FOR CURRENT TECHNIQUES

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Background: Since the birth of reconstructive microvascular surgery, attempts have been made to shorten the operative time while maintaining patency and efficacy. Several devices have been developed to aid microsurgical anastomoses. This article investigates each of the currently available technologies and attempts to provide objective evidence supporting their use. *Methods*: Techniques of microvascular anastomosis were investigated by performing searches of the online databases Medline and Pubmed. Returned results were assessed according to the criteria for ranking medical evidence advocated by the Oxford Centre for Evidence Based Medicine. Emphasis was placed on publications with quantifiable endpoints such as unplanned return to theatre, flap salvage, and complication rates. *Results*: There is a relative paucity of high-level evidence supporting any form of assisted microvascular anastomosis. Specifically, there are no randomized prospective trials comparing outcomes using one method versus any other. However, comparative retrospective cohort studies do exist and have demonstrated convincing advantages of certain techniques. In particular, the Unilink™/3M™ coupler and the Autosuture™ Vessel Closure System® (VCS®) clip applicator have been shown to have level 2b evidence supporting their use, meaning that the body of evidence achieves a level of comparative cohort studies. *Conclusion*: Of the available forms of assisted microvascular anastomoses, there is level 2b evidence suggesting a positive outcome with the use of the Unilink™/3M™ coupler and the Autosuture™ VCS® clip applicator. Other techniques such as cyanoacrylates, fibrin glues, the Medtronic™ U-Clip®, and laser bonding have low levels of evidence supporting their use. Further research is required to establish any role for these techniques. © 2011 Wiley Periodicals, Inc. Microsurgery 32:68–76, 2012.

The French vascular surgeon Alexis Carrel challenged the widely held belief that vascular anastomosis was not possible in 1902. He pioneered new techniques such as the triangulation of vessels, the use of sharp round bodied needles to minimize intimal damage, and irrigation with crystalloid to perform the first successful anastomosis.[1] Many of his ideas are still used today, and he won a Nobel Prize in recognition of his work in 1912.

Reconstructive microvascular surgery as we understand it today—the anastomosis of vessels a few millimeters in diameter using microscopic assistance—was born in 1960 when Jules Jacobson, of the University of Vermont, carried out the first microvascular surgery, coupling vessels as small as 1.4 mm diameter. Since then, technical advances allowing anastomosis of successively smaller blood vessels and nerves have been central to the development of the microsurgical field.[2] Innovations in reconstructive microsurgery followed swiftly during the 1960s and 1970s. The first publication by Buncke[3] reported a successful rabbit ear replantation, requiring union of vessels of 1 mm in size. Then, in 1968, Cobbett[4] performed the first human microsurgical transplantation of the great toe to the thumb.

Microsurgery moved from the experimental to the mainstream with the development of specialized microsurgical instruments. These included fine-tipped toothed forceps designed to produce minimal intimal damage to the vessel, accurate sharp microsurgical scissors, fine vessel dilators, and an array of microclamps available in single and double configurations. Recently, the microsurgeons' tray has been supplemented with microvessel clips and suction pads. The goal of faster, more stable microvascular anastomoses continues to drive innovation and scientific progress in the field of microsurgery.

Modern microsurgical suturing techniques involve the use of fine (8/0-12/0) monofilament nylon sutures mounted on sharp round-bodied needles. The vessel is prepared under the microscope—clean perpendicular cuts are made to the ends for anastomosis using sharp microscissors and the adventitia is trimmed. The lumens are cleaned using heparinized crystalloid and if necessary gently dilated using vessel dilators. Often the vessels to be anastomosed are mounted in a double clamp such that the ends can be approximated under no tension. Suturing then proceeds with minimal luminal handling. This technique has been refined allowing successful anastomosis of vessels with significant size mismatch and also allowing end to side anastomosis.[5]

The development of reliable microanastomotic techniques facilitated a revolution in reconstructive surgery. The importation of remote tissue using the microvascular anastomosis provided a new solution where previous

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Institutional Ethical Approval was obtained prospectively for the studies reviewed in this article and conforms to the provisions of the Declaration of Helsinki in 1995.

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obstructions to local reconstruction might have existed. Today free tissue transfer is widely used in breast reconstruction, head and neck reconstruction, and lower limb trauma.

Despite the advances that resulted in reproducible microvascular anastomoses, the technique of sutured anastomosis necessarily involves an inherent degree of handling of the vessel including the intima. In addition, there remains intraluminal foreign material in the form of nylon sutures. These and other factors result in a persistent failure rate of sutured microvascular anastomoses in the order of 2–6%.[6,7] This is often as a result of thrombosis. Furthermore, even in experienced hands, microvascular anastomosis remains a challenging and time consuming procedure and has a steep learning curve for the training surgeon. For these reasons, alternatives to the traditional sutured microvascular anastomosis have been actively investigated in recent times. Forms of assisted microvascular anastomosis currently in use include coupling devices, clipping or stapling devices, various adhesives, and laser boding techniques.

The purpose of this article is to review all major publications regarding innovative methods of microsurgical anastomosis and to determine the level of evidence existing to support their use.

METHODS

The evidence for technology-assisted microvascular anastomoses to improve operative times and outcomes with safety was investigated by literature review. For inclusion in this review, papers were required to meet the following criteria: case series or higher in terms of construction, be published during the period 1991–2010 (inclusive), be within the field of reconstructive microvascular surgery, and be studies in humans.

Studies for inclusion were identified using the online databases PubMed and Medline. Boolean operators were used to link keywords such as "anastomosis AND coupler," "microsurgery AND coupler," "Unilink™ AND anastomosis," "VCS® clip," "clip AND microsurgery," "clip AND anastomosis," "staple AND microsurgery," "glue AND microsurgery," "glue AND anastomosis," "laser AND microsurgery," "laser AND anastomosis," and "photochemical AND anastomosis." This returned a very significant number of results ($n = 6{,}136$) including many from specialties such as neurosurgery, cardiac surgery, urology, and general surgery. This approach was made to ensure that no relevant papers were omitted from consideration. Secondary search was performed limiting this number to studies in the date from 1991 to 2010 and in English ($n = 3{,}143$). Article title search was performed within the citation manager to exclude papers clearly from other specialties. This was achieved by filtering by keywords such as ophthal or hepatic and removing the citations followed by manual filtering. The resulting 184 studies were assessed by abstract and cross-referencing resulting in 22 papers meeting inclusion criteria.[8–29] Figure 1 shows a citation attrition chart of the search process, and Tables 1 and 2 show an illustrative although not exhaustive sample of the reviewed papers. References to papers not meeting inclusion criteria (e.g., animal studies) are included for discussion purposes only. Although all series meeting inclusion criteria were assessed regardless of construction, emphasis was placed, in the discussion, on papers with control groups investigating quantifiable endpoints. These studies are assessed for gross errors of construction and subsequently attributed a CEBM (Centre for Evidence Based Medicine) evidence level. The CEBM (http://www.cebm.net) attributes levels of evidence ranging from levels 1 (randomized control trial [RCT] or meta-analysis of RCTs) to 5 (expert opinion) to any given research paper.

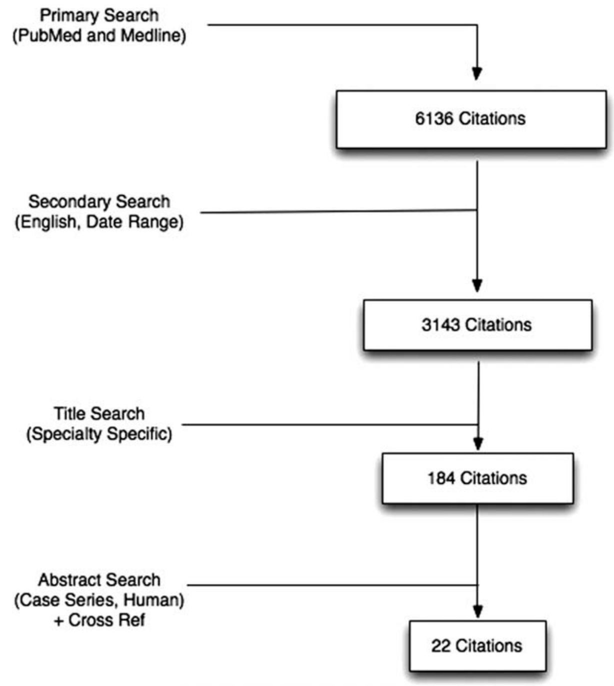

Figure 1. Citation attrition diagram documenting search process.

RESULTS

Coupler

The Unilink/3M™ Microvascular Anastomotic Coupler[30] was developed in the 1960s.[31] Ring-type couplers use two rings with interlocking metal pins and reciprocal holes. Each end of the vessels for anastamosis is passed through the ring and reflected back over the pins. The two rings are then pressed together until a clip is engaged (Figs. 2–4). The rings were initially thought to

Table 1. Major Clinical Series Reporting Use of Microvascular Coupler

	Number of anastomoses	Veins and Arteries?	Failures	Salvage rate	Average anastomosis time	Notes	Case mix
Ahn et al.[13]	123	Yes	2 (1.6%)	100%	4 min	Only 24 arteries (the rest were sutured)	Breast, head/neck, limb trauma
Nishimoto et al. 2000[14]	121	Veins only	0	NA	'Most less than 5 min'	One take back for congestion but anastomosis was found to be patent	Head/neck
Spector et al.[16] (Senior Author Ahn)	? (80 flaps)	Yes	1 (1.3%)	100%	Not specified	Used elastic strip, able to successfully complete arterial anastomosis 80% of cases	Breast
Zeebregts et al.[8]	161	Veins only	7 (5%; failure rate for sutured veins was 6%)		9 min (significantly faster than sutures)	Compared sutures to coupler (and to VCS)	Breast, head/neck, limb trauma
Chernichenko et al.[17]	124 (out of 127, three were unable to be coupled)	Only **arteries** reported although suggests veins were anastomosed as well	4 (3.2%) arterial failures (overall flap failure 2.4%)	75%	Not reported	Able to successfully complete coupling of arteries in 98% of cases	Head and neck
Rozen et al.[11]	1,000 (of 2,500)	Veins and arteries	29 (2.9%)	Unclear	4 min (significantly faster than sutures)	Large studies comparing suture, coupled and clipped arms	Breast, head/neck, limb trauma
Jandali et al.[25]	1,000	Veins only	6 (0.6%)	Unclear	3 min (only measured in 20 cases)	Large series, however, no control arm	Breast

Table 2. Major Clinical Series Reporting Use of VCS® Clip Applicator

	Number of anastomoses	Veins & Arteries?	Failures	Salvage rate	Average anastomosis time	Notes	Case mix
Zeebregts et al.[8]	110	Yes	1 (2% of all clipped venous; failure rate for sutured veins was 6%)	58%	17 min (significantly faster than sutures)	Compared sutures to coupler (and to VCS)	Breast, head/neck, limb trauma
Cope et al.[9]	153	Yes	No failures	NA	Comment on l earning curve- as low as 5 minutes	Comment on need for trained assistant	Breast, head/neck, limb, trunk
Lorenzi et al.[9]	Not specified- 26 flaps	Yes	No failures	NA	Not specified-'quick'	Comment that in their experience VCS is superior to Unilink for size mismatch	Lower limb reconstruction
Rozen et al.[11]	400	Yes	20 (5%)	Unclear	15 min (significantly faster than sutures but slower than coupler)		Breast, head/neck, limb trauma

be only suitable for anastomosing pliable-walled vessels of equal size match (i.e., well matched veins).

As early as 1985, ring-type couplers were being used in small series[32] and over the last two decades their use has become progressively more common. Some prominent authors advocate their use for venous and arterial anastomoses.[13,16,17,19] There is a significant body of literature demonstrating faster and easier microanastomoses and a shorter learning curve when these devices are used.[8,11,13,14,16–18,20–22,25,33] Statistically similar patency rates have been found as compared to traditional sutured anastomoses.[8,11,13–18,20–24,34] Anastomotic strength has been tested in animal models and found to generally exceed that of traditional anastomoses.[35] One of the inherent benefits of anastomoses created using coupling devices is the absence of any intraluminal foreign material, which might be a nidus for thrombus formation. Critics of the coupler suggest that because of the penetrative nature of the device, the thrombogenic subendothelial collagen matrix may become exposed.

Although early reports suggested that the use of the coupler (particularly for arterial anastomoses) may be suboptimal in irradiated fields in head and neck surgery,[22] more recent series[19] and animal studies[36] suggest otherwise.

At least two reports exist for a possible foreign body sensation associated with the use of the coupler in the digits, possibly requiring removal of the device,[37,38] and one report demonstrates the possibility of delayed removal of the device without negative consequences.[39]

Two very large series have been recently published, which provide further evidence for the use of the coupler. Rozen et al.[11] compared 1,000 coupled venous anastomoses to 1,100 sutured anastomoses in breast, head and neck, and lower limb reconstruction and showed a statistically significant reduction in time to anastomosis as well as excellent success rates. Jandali et al.[25] published a series of 1,000 consecutive venous anastomoses in breast reconstruction using the Synovis™ coupler. Although this series had no control arm, a venous thrombosis rate of 0.6% was reported.

The results regarding anastomotic coupling devices are summarized in Table 1.

Clips

Autosuture™ developed the second-generation anastomotic aid—the Vessel Closure System® (VCS®) in 1995. The proposed benefit of this system is a clipped anastomosis that results in the absence of intraluminal foreign material and has a theoretical lower rate of thrombosis.

The clip applicator is used by initially placing a variable number of "stay sutures" around the anastomosis in a conventional manner. The edges of the anastomosis are then everted using a specialized everting forceps and a variable number of clips are placed around the circumference. In the event of a clip being placed incorrectly, it is easily removed with the use of a specialized tool. As the clips are placed at variable distance, discrepancy in size match of the two vessels can be accommodated. Various sizes of clip are available, the selection determined by the thickness of the vessel wall rather than the diameter of the vessel.

A large body of animal experimental research exists which demonstrates that the VCS® clip applicator is fast and produces little histological reaction in the vessels anastomosed.[40–44] It has been shown to be effective in

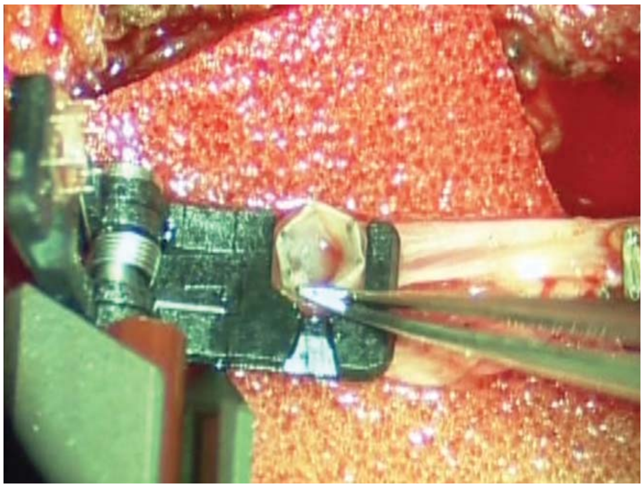

Figure 2. The vessel walls are reflected onto the prongs of the device. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

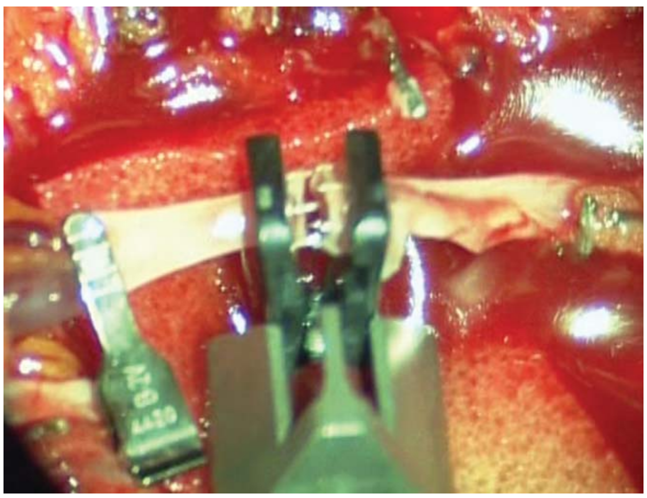

Figure 3. The two rings are approximated. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

both end-to-end and end-to-side anastomoses.[9,10,45–47] Large series by Zeebregts and Cope[8,9,46,48,49] and numerous review articles have established clipped anastomoses as faster and safe when compared with conventional sutured anastomoses. When compared with conventional anastomoses, patency rates have been shown to be at least equal, and some histological studies have demonstrated faster healing, attributed to the absence of intraluminal foreign material and better intima to intima contact. Rozen et al.[11] recently published a very large series in which the VCS® device was used in 400 anastomoses with excellent results in a variety of clinical applications.

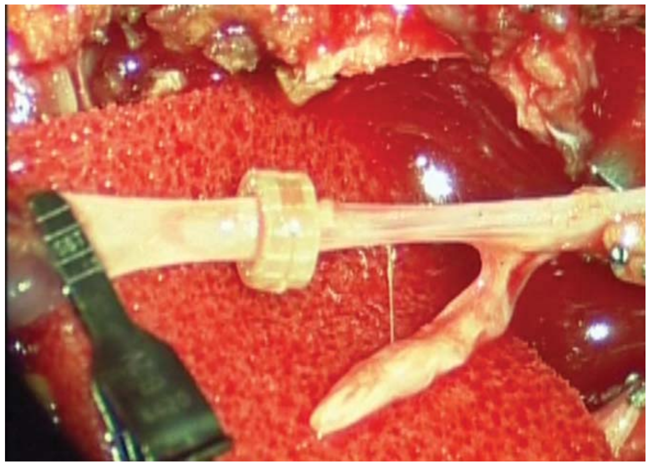

Figure 4. The completed anastomosis. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

A newer clipping device—the Medtronic™ U-Clip®—uses a clip mounted on a penetrating needle. As with sutures, this device results in foreign material within the lumen of the anastomosis and thus does not have the theoretical benefit of the VCS® with no intraluminal foreign material. Nonetheless, the U-Clip® is significantly faster to use when compared with traditional anastomoses. Although this device has shown promise in cardiac surgery, there exist few reports[50] of its use in reconstructive microsurgery. It has, however, been compared favorably to other mechanical anastomotic aides in a small series.[51] The results regarding the VCS clip applicator are summarized in Table 2.

Adhesives

The use of adhesives in surgery has gathered more interest in recent times. Currently available surgical adhesives can be broken into two groups—cyanoacrylates and the so-called "fibrin glues." Cyanoacrylates have long been used by emergency departments and general practitioners to close minor wounds, particularly in pediatric populations. Various other uses have been reported in the literature including roles in microvascular reconstructive surgery.

Thrombin-based fibrin glues such as Tisseel® and Tissucol® continue to generate interest in terms of novel surgical applications. In theory, these substances could be used for sutureless anastomoses and also for stabilizing anastomoses and plugging minor leaks after conventional anastomoses. Certainly the use of these products in anastomosing other structures such as vas deferens, nerves, and hollow viscus is well reported in the literature.[52–57] However, concerns regarding the inherent thrombogenicity of these products and the potential for triggering intraluminial thrombosis exist.[58] Although promising animal studies have been published,[59–64] few clinical series exist. At least one large series of free tissue transfers in breast reconstruction (n = 349) reports use of thrombin-based glues with no apparent increase in anastomotic failure.[65] A cohort study in 2009 compared sutured anastomoses with or without fibrin glue.[66] It was found that the fibrin glue group had faster anastomotic times and used reduced number of sutures. Outcomes were similar although the two groups were small. In addition, a series of 36 digital replants using reduced sutures and fibrin sealant was reported by Isogai et al.[28] This series used a reduced number of sutures and fibrin sealant was applied to the anastomoses. An overall failure rate of 11% was reported, consistent with other studies. A small series reporting the use of fibrin glues to stabilize pedicles and prevent kinking showed no increased rate of thrombotic anastomotic complications.[29]

Various potential uses of cyanoacrylate adhesives have been reported in animal studies ranging from completely sutureless anastomoses with glue only[67] or glue with absorbable biostents[67,68] to reduced suture anastomoses with adhesive and hemostasis.[69–72] Although these studies have gone some way to demonstrate safety and increased speed and reliability of anastomoses, some studies have shown significant histological foreign body reactions in vessels walls.[73]

One report in the literature advocates use of a coating of cyanoacrylate to give collapsed veins added rigidity thereby reducing the risks of suturing the back wall[74] and at least one report of using cyanoacrylates as haemostatic agent in anastomoses in humans exists.[75] Although some of these reports are letters referring to human surgical practices, there are no published series supporting the benefits or safety of cyanoacrylates in microvascular reconstructive surgery.

Laser and Photochemical-Assisted Anastomoses

Interest began to develop in the use of lasers in microsurgical anastomoses in the early 1980s.[76] Since then many studies investigating various lasers (e.g., carbon dioxide, argon, thulium–holmium–chromium) for thermal bonding of microvascular anastomoses have been reported,[77–90] although descriptions of use in clinical practice remain limited. Most recently, interests in Excimer® laser-assisted nonocclusive anastomoses in neurosurgery[91–95] and the use of the KTP-532 laser for microsurgical anastomoses[96] have emerged. Laser-assisted thermal bonding for neural reconstruction[97,98] and the use of photochemical bonding using visible spectrum light and photoactive dyes[99] have been described.

A solitary clinical paper by Leclère et al.[27] reports perhaps the first use of laser microanastomoses in clinical use in reconstructive surgery. In this series, 27 patients underwent 58 anastomosis with the use of a 1.9 micron diode laser to perform welded reduced suture anastomoses. Generally, four sutures were still applied to achieve apposed edges. This study included arteries and veins and both end-to-end and end-to-side anstomoses. A single case of anastomosis failure was reported (1.7%) in which an arterial anastomosis “ruptured,” possibly due to the anastomosis being in irradiated tissue. Anastomotic time was not measured but was considered anecdotally to be reduced. There was no control arm in this study.

DISCUSSION

While a meticulously sutured microvascular anastomosis remains a standard practice, there is a growing body of evidence supporting the use of coupling and clipping devices. Many units have adopted the use of these devices and report significant advantages in terms of speed and ease of use over traditional anastomoses. Where previously these devices were thought to have applications limited to certain situations such as easier venous anastomoses, innovators in the field have challenged these ideas and shown potential use in arterial anastomoses, end-to-side anastomoses, and even in irradiated tissue. Detractors of these devices have supported that reducing the surgeon’s exposure to traditional satured anastomoses could result in dangerous de-skilling, pointing out that particularly challenging anastomoses are often not amenable to the current devices anyway. In addition, issues of potential selection bias in many of the series is invoked—namely that the device is often used on easier anastomoses and then compared to sutured anastomoses which were the remaining more technically challenging vessels. Despite these concerns it is likely that there is a genuine role for these devices in accelerating microsurgery. As the cost of couplers and clipping systems falls, the cost savings associated with speedier surgeries will make the cost benefit ratio increasingly favorable. Currently, the evidence supporting the use of both the Unilink™ Coupler and the VCS® clip applicator has achieved level 2b as defined by the Oxford CEBM. This implies that well-constructed, cohort-controlled studies demonstrating a benefit for these techniques exist.

Currently, there is little evidence beyond small series supporting glues and laser-assisted bonding in microsurgery save for one small sample cohort study by Cho et al.[66] However, advances in either of these fields could in the future see completely sutureless anastomoses with little or no handling of the vessels. In addition, recent interest in robotics in other branches of surgery has spilled over into microsurgery with proof of concept papers reporting successful use of robots in experimental microsurgical models.[100,101] Other completely sutureless techniques using bioabsorbable stents and glues are also being investigated.[102] Until such time as these technologies are established, the humble sutured microvascular anastomosis, with or without the use of couplers and clipping devices will remain the norm.

CONCLUSIONS

There is level 2b evidence supporting the use of the Unilink™/3M™ anastomotic coupler and the Autosuture™ VCS® clip applicator in a wide variety of microvascular anastomoses including end-to-side, arterial anastomoses, and anastomoses in irradiated fields. Glues including cyanoacrylates and fibrin glues have scant evidence associated with their use in any capacity be it sutureless anastomoses or adjuncts to reduced suture anastomoses. Laser and photochemical bonded anastomoses have virtually no clinical evidence associated with their use in microvascular anastomoses save for one small series. All the above technologies would benefit from further high quality research to definitively establish their role in the microsurgeon's armamentarium.

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