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A novel secure transfixing blood vessel occluder: comparison with the hemoclip in the porcine model

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ABSTRACT

Background: Secure vessel occlusion is critical to the success of all surgical and interventional procedures. The purpose of this study was to compare *in vivo* the use of the Amsel Vessel Occluder (AVO), a novel occlusion clip device for secure blood vessel closure, with one of the many commercially available hemoclips, the Ligaclip, in the porcine model.
Methods: Vessel closure of arteries and veins was performed on 10 swine to compare the ease of use, safety, and efficacy of the AVO with the Ligaclip as well as the tissue response at 7 and 30 d. After heparinization, the targeted vessels (carotid/femoral/brachial arteries and jugular/femoral/brachial veins) were occluded with two clips, either two AVO's or two Ligaclip's, and the vessels transected between the two clips. Any bleeding was recorded. At sacrifice, gross and histopathologic findings were examined for evidence of bleeding or injury to adjacent structures. The tissue response and healing were evaluated by a prospective randomized histopathologic study for the effects of any biological incompatibilities. At time of sacrifice, occluded vessel segments were subjected to nonphysiological pressures ("holding" pressures) to compare efficacy of occlusion in fresh, nonoccluded vessels, and the ability to dislodge the clips once applied.
Results: Twenty veins and 20 arteries between 2-mm and 7-mm outer diameter were occluded in 10 pigs. Each vessel was occluded with either AVO or Ligaclip. Our study confirmed easy and safe AVO application with no dislodgment of any AVO clips once deployed. The AVO showed no intraoperative or postoperative bleeding (AVO = 0/40), while one Ligaclip dislodged resulting in a fatal hemorrhage 16 h after surgery (Ligaclip = 1/40), and on two occasions where, with obvious slippage of the Ligaclip, immediately after deployment, additional clips were placed. The holding pressures for the two clips were similar but unlike the AVO, the Ligaclip was easily dislodged. Histopathologic examination showed no difference in the tissue response and healing of the two clips.
Conclusions: The AVO is simple to deploy and securely maintains occlusion by transfixing the targeted vessel, unlike the widely used, nontransfixing Ligaclip, that has a tendency to

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dislodge. As such, the Amsel secure vessel occluder opens up numerous treatment opportunities in both the venous and arterial systems to minimize open, laparoscopic, robotic surgical and interventional procedures, and reduce patient morbidity and its associated health care costs.

Introduction

Secure vessel occlusion that prevents hemorrhage is critical to the success of most surgical and interventional procedures. The first recorded attempt to control bleeding vessels by ligation was performed by Sushruta around 800-600 BCE, but it was Pare in the mid-16th century who reintroduced ligation and discouraged the use of cauterization with hot iron or boiling oils.[1] Ligation of blood vessels with various suture materials permitted the development of modern surgery. Mechanical vessel occlusion with clips and staplers was introduced in the latter half of the 20th century and remains a core occlusion method in current surgical practice. Electrical means of vessel occlusion have also gained traction. Electrosurgical methods were introduced in the early part of the 20th century mostly for neurosurgical procedures on the brain.[2] Today electrosurgery is widely used beyond the brain, and even to occlude medium sized blood vessels.[3] More recently, ultrasonic occlusion has been successfully introduced into surgical practice for occlusion of blood vessels.[4,5] While for many procedures electrosurgical or ultrasonic techniques are attractive, there are numerous procedures where due to contact area constraints or criticality of the occlusion, the security of permanent mechanical occlusion is a priority.

To advance the new minimally invasive methods, laparoscopy, robotic surgery, and interventional procedures small "foot print" devices to achieve secure and reliable vessel occlusion are required. In this regard, we have developed a novel mechanical occlusion device that is delivered through a fine hypodermic needle (18G) that transfixes the targeted vessel, delivers expandable proximal and distal elements on either side of the vessel wall which lock together for secure and reliable vessel occlusion.[6] This report presents the results of our preclinical *in vivo* studies where the Amsel Vessel Occluder (AVO) was compared with a commercially available hemoclip, the Ligaclip (Ethicon endo-surgery, LLC a Johnson and Johnson company) for the occlusion of both arteries and veins ranging in external diameter from 2 mm to 7 mm.

Materials and methods

Device description

The AVO consists of a delivery device and occluder clip. The AVO has received Food and Drug Administration 510 (k) clearance, similar to other metal clips (hemoclips) for the occlusion of vessels 2-7 mm in diameter, and for tubular structures such as the cystic duct or fallopian tube. The delivery device used in this study is of a prototypic design and can be easily modified to suite whatever the application, whether for interventional, percutaneous or surgical, laparoscopic or robotic use. The Amsel Occluder Clip is preloaded in the 18G needle of the AVO delivery device. The AVO is a mechanical occlusion clip that when deployed transfixes the target vessel while clamping it shut (Fig. 1A). The AVO consists of two "star"-shaped compression elements and a titanium fine strut which connects and locks the compression elements together. The proximal element, which compresses the near wall of the vessel, and distal element, which compresses the far wall of the vessel, are made of shape memory metal (nitinol), which once deployed, assumes its designated configuration closing off the vessel.

Once deployed and locked together the individual "arms" of the proximal occlusion component alternate with and interdigitate with the individual "arms" of the distal occlusion components. The "arms" thus pass below the plane of the distal occlusion component and vice versa. In effect, when fully deployed on an artery or vein, there is a circular occlusion around the central rod by the "arms" of the two occlusion components, and the proximal and distal wall of the occluded vessel are brought into apposition with one another regardless of vessel wall thickness (Fig. 2A-C).

Ligaclips are sterile, single-patient use clips produced from titanium (Fig. 1B). The clips are designed for ligation of tubular structures where a nonabsorbable ligating device is indicated. The ligating clips are positioned around a tubular structure and closed by applying pressure to the handles of the applier (Ligaclip; Ethicon endo-surgery, LLC a Johnson and Johnson company).

Hypothesis

The hypothesis being tested in this study in the porcine model is that the use of the transfixion AVO compared with the Ligaclip would be as easily applicable, while providing a more secure and safe vessel occlusion without injury to adjacent

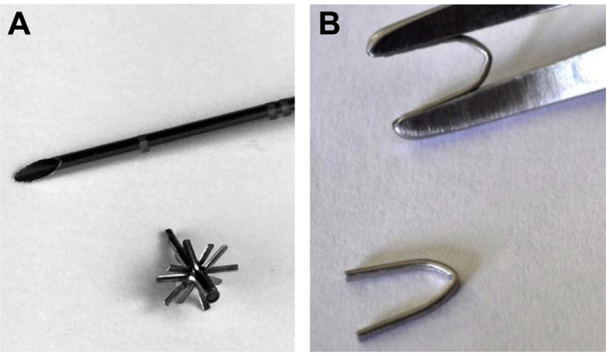

Fig. 1 – (A, B) A shows the 18G delivery needle and the Amsel Vessel Occluder after deployment. Note how the "arms" of the distal and proximal elements interweave to provide reliable clamping of the vessel. B shows a medium-large Ligaclip with its delivery device. (Color version of figure is available online.)

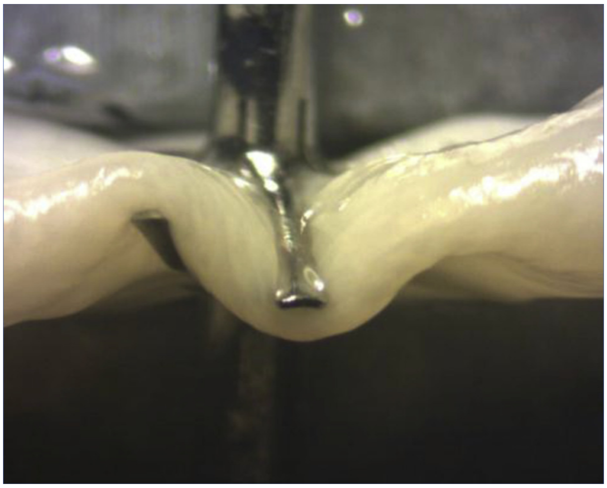

Fig. 2 – This figure shows the deployed device using a simulated vein (BioTissue "LifeLike" small saphenous vein) which shows how the "arms" of the proximal and distal occlusion components alternate and interdigitate with one another. In effect, when fully deployed on an artery or vein, there is a circular occlusion of the vessel around the central titanium rod made by the individual fingers of the two respective occlusion components. This circular occlusion resembles in some ways a "pie crust" pattern in which the proximal wall and distal wall of the vessel are brought into apposition with one another with the titanium rod at the center of the pie (also see Fig. 7B and D). (Color version of figure is available online.)

structures, and with no differences in the healing process, as evaluated by clinical and histopathologic study.

Methods and surgical technique

Clip insertion

A total of 10 female domestic pigs (Sus scrofa domestica) each weighing more than 60 kg at time of implantation underwent an open surgical procedure where selected veins and arteries between 2 mm and 7 mms in diameter were occluded. The study was performed at The Lahav Institute of Animal Research, Israel under the supervision of the veterinary surgeon U.W., the scientific manager at this institute. The studies were approved by the Institute of National Animal Care and Use Committee, Israel. Each animal was allowed to acclimate for at least 3 d before surgery. On the day of surgery, food was withdrawn, and only water was allowed.

All of the surgeries were open and performed under general anesthesia. Prophylactic antibiotic (cefazolin 30 mgs/kg IV) was administered concomitantly with induction of anesthesia. Arteries and veins between 2 mm and 7 mm were exposed in the groins, forelimb, and neck. For the large vessels (3.6-7 mm), the more proximal femoral arteries and veins and carotid arteries and jugular veins were exposed. For the small vessels (2-3.5 mm), the more distal femoral arteries and veins and forelimb brachial arteries and veins or their smaller tributaries were exposed and occluded.

To expose the femoral and brachial vessels, incisions were made in the groins and forelimbs while in the neck, the carotid arteries, and jugular veins on both sides of the neck were exposed through a single midline incision. The targeted vessel was dissected free for an approximately 4-6 cm length, mobilized, and looped with vessel loops. Any branches or tributaries in the mobilized area of the vessels were ligated. After dissection of all of the targeted vessels was completed in a given animal, the vessels were bathed in a 2% solution of local anesthetic (lidocaine) to minimize any vessel spasm caused by the dissection.

Before vessel occlusion, the pig was given 5000 units (IU) of heparin intravenously. Following this the outer diameters of the exposed vessels were measured with calipers, and the measurement recorded.

For each of the pigs, one artery (either the carotid, femoral, or brachial) and one vein (either the jugular, femoral, or brachial) were occluded using either two Amsel Vessel Occluders or two Ligaclips (medium, medium–large, or large), consistent with the size of the vessel. In all cases, the pairs of occluders or clips were deployed between 1 cm and 3 cm apart.

The specific vessels and vessel sizes occluded in each animal are summarized in Table 1.

After occlusion with either the test AVO or control Ligaclips, the occluded vessel was severed approximately midway between the occluding clips, examined for bleeding, and the results recorded (Figs. 3 and 4).

Once it was determined that vessel occlusion was successful in all occluded vessels, the wounds were irrigated with saline, and the tissues closed in layers using Vicryl sutures. The skin was closed with intradermal sutures. Anesthesia was withdrawn, and the pigs were recovered and extubated before being taken to the recovery quarters.

Vessel harvest and sacrifice

The subject vessels were harvested from the animals at approximately 7 d ($n = 7$) and 30 d (27 d $n = 1$; 35 d $n = 2$) postimplantation. The procedures were carried out under general anesthesia and nonsterile conditions. First, the skin wounds of the previous surgery were examined for evidence of healing, swelling, and infection; and the results recorded. The wounds were then reopened, and the area of vessel implantation exposed noting the tissue reaction, tissue incorporation, evidence of bleeding or injury to the adjacent structure, and intactness of the occluding devices. Following this detailed examination, the pairs of occluded vessel segments (both proximal and distal segments) were dissected out and excised either separately as proximal and distal segments, or the two occluded segments of vessels were excised *en bloc*. The specimens were then fixed to cork boards to minimize contraction, and maintain orientation, and placed in formalin for histopathologic examination.

Fresh, nonoccluded vessel segments of similar sized arteries and veins, were excised, occluded with either a Ligaclip or AVO, and subjected to nonphysiological pressures of more than 300 mm Hg with infusion of saline to document the "holding pressure" and adequacy of the clip occlusion for both the AVO and Ligaclip. As a final step, an attempt was then made to dislodge or remove the clips using forceps.

Table 1 – Vessel size, vessel occluded, with either the Amsel Occluder or Ligaclip, and survival time for each pig.

Vessel sizes	Large vessels 3.5-7 mm			Small vessels 2-3.5 mm				Large vessels 3.5-7 mm		
Pig number	1	2*	3	4	5	6	7	8	9	10
Sacrifice (d)	7	7	7	7	7	30	30	7	30	30
Ligaclip (medium large)										
Brachial artery						3.5				
Brachial vein				3.2	2.4		2.9			
Femoral artery				3.0			3.0	6.0		5.0
Femoral vein	4.0	6.5	5		2.2	2.0			7.0†	
Carotid artery		7.0							6.5	
Jugular vein	4.5		7.0					4.0		4.2
Amsel Occluder										
Brachial artery				2.9	2.6		3.5			
Brachial vein						2.0				
Femoral artery		7.0			2.2	2.0			5.5	
Femoral vein	6.0		7.0	3.5			2.0	6.5		7.0
Carotid artery	5.5		6.0					5.0		7.0
Jugular vein		6.0							4.8	

*Expired on day 2 from exsanguination due to dislodgement of Ligaclip from the femoral vein.
†Proximal Ligaclip appeared to slip so a second M-L Ligaclip applied.

Results

Both the Amsel Vessel Occluder and Ligaclips occluded the targeted vessels without injury or tearing. The differences in vessel wall structure and thickness for both arteries and veins sized between 2 mm and 7 mm did not play a role in the simple, secure, and safe occlusion of these vessels with both types of occluding clips. Both the Amsel Occluders and the Ligaclips

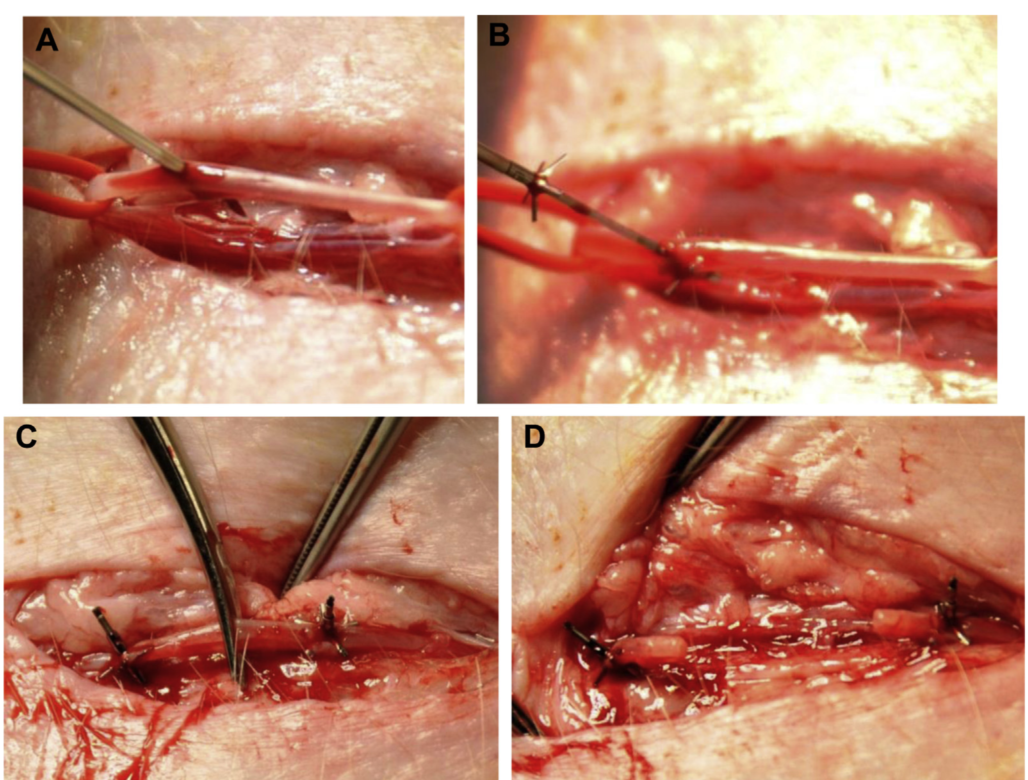

Fig. 3 – Shows in stepwise fashion the occlusion and division of a 2-mm femoral artery with the Amsel Vessel occluder. (A) Through and through penetration; (B) delivery of the proximal and distal occluders; (C) division of the femoral artery between the two Amsel Occluders; and (D) the retracted divided ends of the femoral artery with complete occlusion and no bleeding (Pig #6; Table 1). (Color version of figure is available online.)

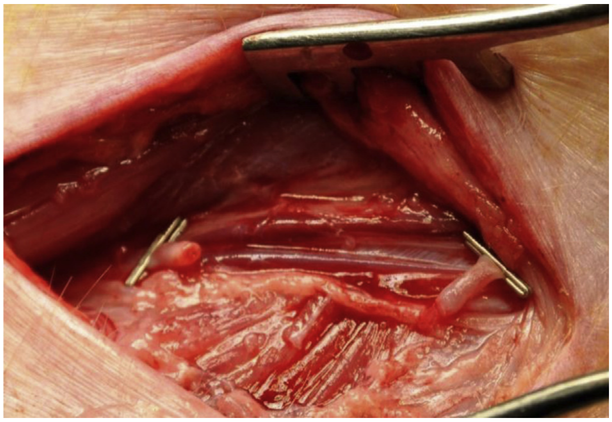

Fig. 4 – This figure shows the femoral artery, measured before occlusion at 3.0 mm, after division between 2 Ligaclips (medium–large) with complete occlusion and no bleeding (Pig #7; Table 1). (Color version of figure is available online.)

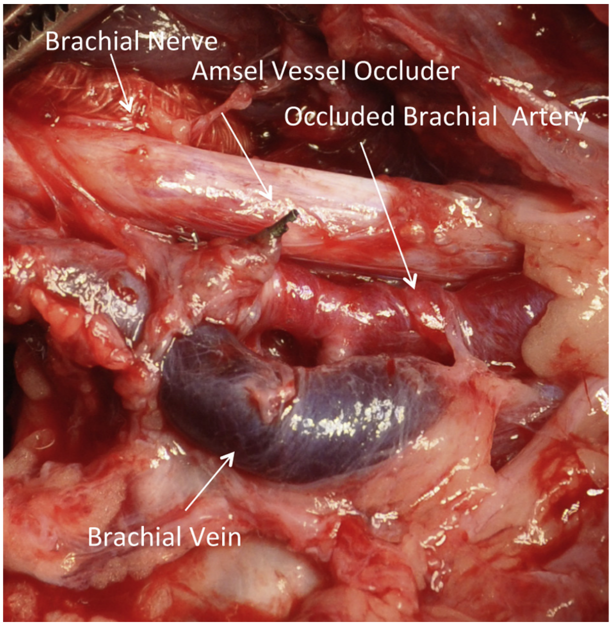

Fig. 5 – This figure shows a dissection of the occluded proximal segment of right brachial artery (3.5-mm diameter measured before occlusion) with the Amsel Vessel Occluder showing no injury to adjacent brachial vein and nerve at the time of harvest 30 d after insertion (Pig #4; Table 1). (Color version of figure is available online.)

were easily deployed from a technical view without any special preparation, dissection, or mobilization of the vessels.

Complete occlusion of all arteries and veins was immediately achieved with no bleeding after division of the vessel for the 40 consecutive deployments of the Amsel Occluder. It was observed that no dislodgment of any Amsel Occluder clips occurred either immediately after their deployment during the implantation surgery or during the postoperative follow-up period.

For the Ligaclip, complete occlusion of all arteries and veins was also immediately achieved with no bleeding after division of the vessel for the 40 consecutive deployments. However, on one occasion following division of the vessel between the two occluding Ligaclips, one of the clips was observed to slip from the site of occlusion to the edge of the divided vessel. A second Ligaclip was immediately deployed more proximally on the vessel to prevent dislodgment and bleeding. In the postoperative follow-up period, one of the pigs, where complete occlusion was observed immediately after implantation and division of the vessel, suffered a massive hemorrhage from a groin vessel (proximal femoral vein) occlusion site approximately 16 h after surgery and exsanguinated. Postmortem examination revealed that the Ligaclip from the proximal occluded segment of the divided femoral vein had dislodged, causing a massive hematoma and hemorrhage (Pig #2, Table 1).

All other vessels segments occluded with either AVO or Ligaclip were intact at the time of vessel harvest.

Sacrifice and vessel harvest

Before sacrifice all sites of vessel occlusion were exposed and examined. Tissue incorporation and inflammatory response was similar for both the Ligaclip and AVO with variation for both. It was observed that irrespective of the type of clips, the tissue response was more severe in some wounds than in others. However, in none of the wounds was the tissue response so severe that the occluded segments could not be excised. Only one vessel occlusion site, a brachial artery occluded with a Ligaclip (Pig #01 Table 1), was the occlusion site not harvested due to difficulty in identifying the occluded vessel. Subsequently, X-rays were used to identify any occlusion sites which were not immediately apparent.

For both the Amsel Occluder and Ligaclip, there was no evidence of bleeding, hematoma formation, or infection. In addition, the integrity of the clips was maintained with no migration. No injury to adjacent structures, nerves, or vessels in close proximity to either type of the occluding clips was evident (Fig. 5).

Studies of "holding" pressures and resistance to mechanical dislodgment

The magnitude of the holding pressures generated in each of the selected fresh vessels is summarized in Table 2. The variations in pressures observed for both occlusion clips were due to leakage through the vessel wall or small vasa vasorum, with no leakage at the site of the occlusion clip themselves.

The robustness of the two types of occlusions clips was also evaluated by using forceps to try to dislodge the clips by tugging. Whereas the Amsel Occluder could not be dislodged or removed without tearing the vessel, the Ligaclips could all be easily dislodged and removed from all tested vessels with rather weak tugs with the forceps (Fig. 6).

Histopathologic technique and findings

In our initial studies (Pigs 1-3, Table 1), only a few samples were subjected to histopathologic study. Because the inflammatory response was found to be variable, it was decided to

Table 2 – Holding pressures and attempted dislodgement of the occluding clips performed *ex vivo* on previously nonoccluded vessels harvested at time of sacrifice.

Pig# (see Table 1)	Amsel/ Ligaclip	Vessel size mms	Vessel occluded (segment)	Burst pressure (mm Hg) sustained	Maximum pressure (mm Hg)	Comment	Dislodgement evaluation
6	Amsel	7.2	Carotid artery (proximal segment)	600	600	No leak	No (or would tear vessel)
	Ligaclip	7.2	Carotid artery (distal segment)	700	700	No leak	Yes (easily removed)
7	Amsel	5.5	Carotid artery (proximal segment)	760	760	No leak	No (or would tear vessel)
	Ligaclip	5.5	Carotid artery(distal segment)	730	730	No leak	Yes (easily removed)
	Amsel	4.0	Jugular vein (proximal segment)	680	680	No leak	No (or would tear vessel)
	Ligaclip	4.0	Jugular vein (distal segment)	700	700	No leak	Yes (easily removed)
8	Amsel	6.0	Carotid artery (distal segment)	760	760	No leak	No (or would tear vessel)
	Ligaclip	6.0	Carotid artery (proximal segment)	730	730	No leak	Yes (easily removed)
9	Amsel	2.6	Distal femoral vein	550	550	No leak	No (or would tear vessel)
	Ligaclip	2.6	Distal femoral vein	150	200	Leak (through wall of vein)	Yes (easily removed)
10	Amsel	3.0	Distal femoral artery	760	760	No leak	No (or would tear vessel

excise all the occluded vessel segments from the remaining seven pigs (Pigs 4-10, Table 1) and subject them to a comparative histopathologic study. The harvested occluded vessels were thus divided into two groups by size, small vessels 2 mm-3.5 mm, and large vessels 3.6 mm-7 mm. These two groups were then further subdivided with respect to the time of sacrifice, 7 d and approximately 30 d.

The histologic evaluation focused on the tissue reaction to the particular device. After fixation of the vessels, the occlusion device was carefully removed, to minimize any artifacts due to tearing. Samples were taken from both the normal vessel and from areas located at the immediate sites of the occlusions. Evaluation was focused on the reaction to the device rather than the scarring from the surgical procedure and a semiquantitative method of scoring the samples was used which was based on a modified version of the international Standard for the Biological Evaluation of Medical Devices.[7] Semiquantitative assessments were done of the field with the largest numbers of leukocytes, rather than the actual count in 10 fields; and the accurate measurement of fibrosis surrounding the device was used rather than scoring the fibrous area as “thin” or “thick.”

Irrespective of which clips had been used, the findings were very similar for all samples, although with mild variations in intensity of fibrosis and mononuclear cell infiltration (Fig. 7A-D, Table 3). Both necrosis and fibrosis was observed in the collapsed occluded vessel, and in general, a band-like region of fibrous tissue surrounding the device of variable thickness was noted. This tissue was well vascularized and organized, infiltrated by variable numbers of polymorphonuclear leukocytes, lymphocytes, macrophages, and few multinucleated giant cells. For most samples, multinucleated giant cells and macrophages were usually found to form a rim about the device, in turn surrounded by the fibrous tissue, infiltrated by lymphocytes, and smaller numbers of granulocytes. The concentrations of granulocytes were found to have increased in the 7-d samples and decreased in the 30-d samples. In addition, in a few of the 30-d samples for both the Amsel Occluder and the Ligaclip, lymphocytes were found to be forming small aggregations. In one of the pigs at 7 d, rare mineralization was observed for both the Amsel Occluders and the Ligaclips.

In general, the vessels were usually collapsed, necrotic and, with evidence of thrombus formation adjacent to the area of occlusion. Necrosis in all samples was restricted to the vessel wall. In a few samples of small blood vessels (one Ligaclip and three Amsel Occluders), foci of mineralization surrounded by multinucleated giant cells were observed in the area of fibrosis.

Under the conditions of this study, all test samples for the AVO were considered nonirritant when compared with the Ligaclip and did not provoke any undue tissue response.

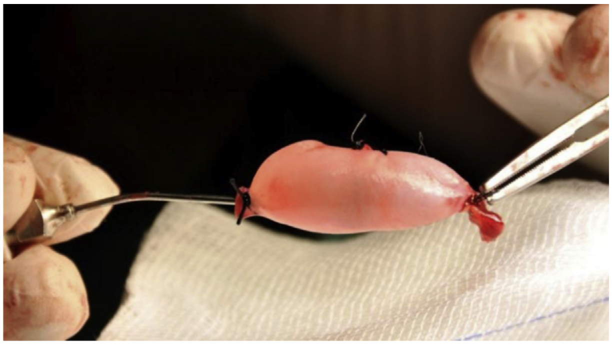

Fig. 6 – This figure shows a segment of freshly harvested of femoral vein occluded with the Amsel clip and pressurized to 700 mm Hg, distending to 9 mm diameter (external measurement) with no leakage through the occluding clip. The Amsel clip could not be dislodged or removed despite vigorous attempts with a forceps. (Color version of figure is available online.)

Discussion

This study, comparing the Amsel Vessel Occluder with the Ligaclips, confirms that the Amsel Vessel Occluder is more secure than the Ligaclip or similar metal clips, for the occlusion of both arteries and veins. In fact, it emphasizes the advantages and opportunities provided by this novel occlusion device. The study shows that deployment of the Amsel Occluder is intuitive, easy to learn, and effective for its intended use. Specifically, it provides a reliable, secure, and safe method for vessel occlusion.

Despite having a more complex structure than the Ligaclip, as confirmed by the prospective comparative histopathologic study of all the specimens, it does not provoke any different and undue tissue response. The ability of the Amsel Occluder to readily transfix and ligate a vessel provides a significant advantage over the externally applied Ligaclip. Dislodgment of metal and polymer occluding clips or hemoclips, of which the Ligaclip is one iteration, is well known and a recognized risk for these occluding devices.[8,9]

Many prior attempts to improve the security of externally placed clips have been made with a number of different iterations by different companies. However, despite these improvements and extra care taken by the operating surgeon, all of whom well aware of the dislodgment problems, there continue to be frequent reports of dislodgment of these types of hemoclips, often with catastrophic results. In fact, the Food and Drug Administration has issued a warning in this regard and contraindicated the use of such clips for some procedures, such as occlusion of the renal vessels for donor kidney harvest for renal transplantation.[10,11]

With the advent and the universal application of laparoscopy and more recently, robotic or robot-assisted surgery achieving simple, secure ligation of vessels during such

Table 3 – Average of score per parameter and tests, and comparison between tests.

Treatment name	Test number							
	7 d SV-AVO	7 d SV-Liga	7 d LV-AVO	30 d SV-AVO	30 d SV-AVO	30 d SV-Liga	30 d LV-AVO	30 d LV-Liga
Number samples evaluated	8	6	4	4	8	8	8	7
Polymorphonuclear	1.38	1.50	1.00	1.50	0.88	1.13	1.00	1.29
Lymphocytes	1.38	1.00	1.50	1.25	1.38	0.88	2.13	1.43
Plasma cells	0.13	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Macrophages	1.13	1.67	0.75	1.75	1.50	1.25	1.88	1.86
Giant cells	0.60	0.60	0.50	1.00	1.13	1.25	0.88	1.29
Necrosis, extent	2.00	2.00	2.00	2.00	1.88	2.00	2.13	2.00
Neovascularization	2.50	2.67	1.75	2.00	2.38	1.25	2.63	2.43
Fibrosis	2.38	1.83	2.25	1.25	1.38	1.13	2.00	1.14
Fatty infiltrate	0.00	0.00	1.00	0.25	0.00	0.00	0.00	0.00
Total	11.48	11.27	10.75	11.00	10.50	8.88	12.63	11.43
Average	1.28	1.25	1.19	1.22	1.17	0.99	1.40	1.27
Test control	1.28-1.25		1.19-1.22		1.17-0.99		1.40-1.27	
Results	0.02		0.03		0.18		0.13	

AVO = Amsel Vessel Occluder; SV = small vessels (2-3.5 mm); LV = large vessels (3.5-7 mm).
The average of all score was calculated per treatment, e.g., AVO *versus* Ligaclip at 7 and at 30 d separately.
Results key.
Nonirritant: 0.0-2.9.
Slight irritant: 3-8.9.
Moderate irritant: 9-15.
Severe irritant: >15.
Negative difference is recorded as 0.

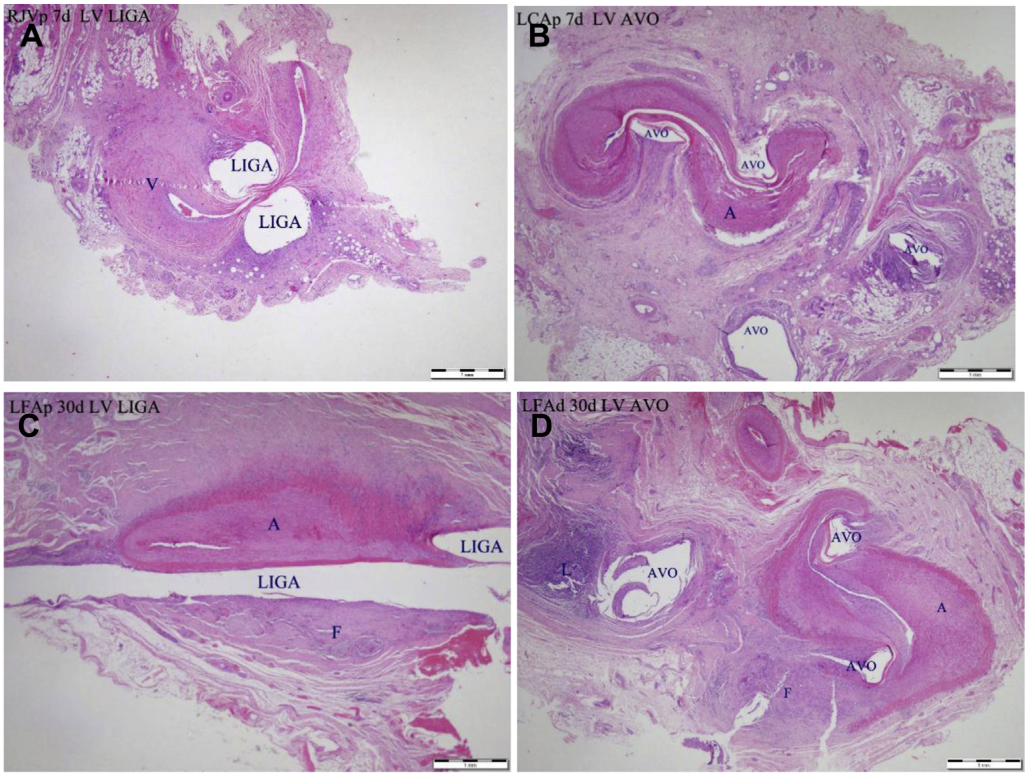

Fig. 7 – Histologic sections of occluded vessels at 7 d. H&E, 2× magnification. Scale bar: 1 mm. (A) Ligaclip, note collapsed vein (V) and the spaces where the Ligaclip was compressing the vein wall (LIGA). There is mild fibrosis and leukocyte infiltration surrounding the device. (B) AVO (Amsel Vessel Occluder), collapsed undulating artery (A) by interdigitating arms (AVO). There is similar mild tissue reaction as for the Ligaclip. (C, D) This shows the histologic sections of occluded vessels at 30 days. H&E, 2× magnification. Scale bar: 1 mm. (C) Ligaclip, note collapsed artery (A) and the spaces where the Ligaclip was compressing it (LIGA). There is mild surrounding fibrosis. (D) AVO, collapsed undulating artery (A) by interdigitating arms (AVO). The mild tissue response is similar to that of the Ligaclip. (Color version of figure is available online.)

procedures remains an issue. Although the technique of laparoscopic suture ligation is well established, it remains quite time consuming; hence, the popularity of the use of hemoclips for vessel occlusion and vascular staplers for occlusion of the larger vessels during such procedures. Radiofrequency occluders have become a useful tool in these minimally invasive procedures but still remain limited by vessel size.

All currently used occlusion modalities require a fairly large access port for their delivery systems and clip deployment. The Amsel Occluder, with its small "foot" print, since the occluder is delivered through a fine hypodermic needle, offers a significant advantage. In addition, the Amsel Occluder allows for percutaneous interventions under ultrasound or other imaging guidance systems such as CT, simplifying vessel occlusion. This new type of mechanical occlusion device could simplify the treatment in such areas as varicose veins, where currently large segments of vein are ablated with expensive high-energy techniques, lasers and radiofrequency, or various chemicals, sclerosants, or glues are injected intraluminally to treat the underlying venous reflux, or in those situation where vessel occlusion is currently achieved via selective catheterization and the placement of intraluminal embolic materials or sclerosants, biological occluders, and occlusion devices.

For many applications, minimal modification of the occluding clips is required since simply choosing the optimum size of the clips and their "arms" would allow occlusion of vessels of different sizes, even much larger than those occluded in this study. We estimate that with minimal changes, the range of vessels which can be occluded with the new technique could be easily expanded. For these multiple different applications, appropriate delivery systems, with single-clip or multiclip delivery systems, also need to be developed. These, however, are simple engineering challenges.

Conclusions

In this study, we have used a porcine model to show that the use of the transfixion Amsel Vessel Occluder, which provides an occlusion similar to a transfixion suture, for the secure occlusion of blood vessels, is easy to use on both arteries and veins, and creates an occlusion which is not only more secure but also as safe with respect to the health of the surrounding tissues as that of the widely used Ligaclip. In addition to the ease of deployment, its most attractive feature is that it provides a more secure and safer occlusion by eliminating the risk of dislodgment from the occluded vessel and the associated complications.

The Amsel Vessel Occluder opens up numerous opportunities in both the arterial and venous systems to minimize open, laparoscopic, robotic surgical, and interventional procedures, and thus reduce patient morbidity and their associated health care costs.

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Disclosure

A.M., MD, is the President and founder of Amsel Medical Corporation. N.L., IED, is a Consultant Engineer (Eliachar Technologies Development Ltd, Haifa, Israel). A-M.B-A., DVM, DVSc, is a Consultant Pathologist (Pathovet, Rechovot, Israel). U.W., DVM, is a Scientific Manager, The Institute of Animal Research, Kibbutz Lahav. D.N. Negev 85,335, Israel. R.M., PhD, MBA, is the Founder and C.E.O. of Amsel Medical Corporation.

REFERENCES

1. Friedman SG. *A history of vascular surgery*. New York: Futura Publishing Company, Inc; 1989:1–14.
2. Bovie WT, Cushing H. Electrosurgery as an aid to the removal of intracranial tumors with a preliminary note on a new surgical-current generator. *Surg Gynecol Obstet*. 1928;47:751–784.
3. Massarweh NN, Cosgripp N, Slakey DP. Electrosurgery: history, principles and current and future uses. *J Am Coll Surg*. 2006;202:520–530.
4. Newcomb WL, Hope WW, Schmelzer TM, et al. Comparison of blood vessel sealing among new electrosurgical and ultrasonic devices. *Surg Endosc*. 2009;23:90–96.
5. Hruby GW, Marruffo FC, Durak E, et al. Evaluation of surgical energy devices for vessel sealing and peripheral energy spread in a porcine model. *J Urol*. 2007;178:2689–2693.
6. Miller A, Lilach N, Miller R. PS234. A novel secure vessel occluder for minimally invasive and percutaneous treatments. *J Vasc Surg*. 2014;59:89S.
7. *I.S. EN ISO 10993-6 (English): biological evaluation of medical devices - Part 6: tests for local effects after implantation*. 2009. Authority: The European Union Per Directive 90/385/EEC, Annex E,17-18. Available at: http://www.iso.org/iso/catalogue_detail.htm?csnumber=44789.
8. Maartense S, Heintjes RJ, Idu M, Bemelman FJ, Bemelman WA. Renal artery clip dislodgement during hand-assisted laparoscopic living donor nephrectomy. *Surg Endosc*. 2003;17:1851.
9. Friedman AL, Peters TH, Jones KW, et al. Fatal and nonfatal hemorrhagic complications of living kidney donation. *Ann Surg*. 2006;243:126–130.
10. U.S. Food and Drug Administration [internet]. Fda and HRSA Joint safety Communication: Weck Hem-o-Lok ligating clips contraindicated for ligation of renal artery during laparoscopic Living-donor Nephrectomy. Available at: http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm253237.htm. Accessed May 5, 2011.
11. Hsi RS, Ojogho ON, Baldwin DD. Analysis of techniques to secure the renal hilum during laparoscopic donor nephrectomy: review of the FDA database. *Urology*. 2009;74:142–147.