Clinical Data from the literature

Background

Vascular clips were first described in 1911 by Harvey Cushing for use in cerebral surgery (Cushing, 1911). The haemostatic clip in its current form was invented by Peter B. Samuels, M.D. in 1963, patented in 1966/67/68, and then marketed by Weck-Pilling. It has been developed since and is commonly used in the medical field as an alternative to other methods of haemostasis such as sutures and cauterization. Advantages of clip systems include rapid vascular closures and a non penetrating clip design, which may minimize intimal damage and ensuing arterial stricture (Findlay et al., 1998).

Review of similar products

Several manufacturers offer similar clips for the same application and have patented different clip holders and clip striation designs. In addition, both metal and resorbable polymer clips are now available (Hsu, 2004; Klein et al., 1994). Furthermore, a number of instruments have been developed for the rapid application of haemostatics clips to blood vessels (Findlay et al., 1998).

Are listed below the most significant patents regarding haemostatic clips. The first patents describe the medical purpose and use of the clip for surgical applications.

Assignee / Inventor	Date	Title / Document
Wood / Le Vaux, Samuels	June 1963	Hemostatic Clip Construction / US Patent #3,270,745 (Sep. 1966)
Wood / Le Vaux, Samuels	March 1964	Hemostatic Clip Construction / US Patent #3,326,216 (June 1967)
Wood / Le Vaux, Samuels	Sep. 1964	Hemostatic Clip / US Patent #3,363,628 (Jan. 1968)
Codman / Reimels	Apr. 1971	Hemostatic Clip Holder US Patent #3,713,533 (Jan. 1973)
Wood / Le Vaux, Samuels	Oct. 1972	Hemostatic Clip and Applicator / US Patent #3,867,944 (Feb. 1975)
Klieman	Aug. 1977	Hemostatic Clip / US Patent #4,188,953 (Feb. 1980)
Samuels	Mar. 1987	Hemostatic Clip Cartridge / US Patent #4,696,396 (Sep. 1987)
Horizon Surgical Inc. / Pfeiffer	Sep. 1989	Hemostatic Clip Holder US Patent #4,936,447 (June 1990)
Pilling Co. / Kulp	Jan. 1990	Hemostatic Clip Cartridge / US Patent #4,961,499 (Oct. 1990)
Horizon Surgical Inc. / Pfeiffer	Sep. 1989	Hemostatic Clip Holder / International Patent (Apr. 1991)

Literature Review

The literature review was aimed at demonstrating that the clinical data currently available in the scientific literature are sufficient in order to prove the safety and effectiveness of the SLS Clip device, based on the assessment of the risks and benefits associated with use of the device.

The review was carried out by entering the keywords "clip, ligation, haemostasis, MRI" in the PubMed database.

The articles were selected according to the below criteria :

- similarity of the devices with the SLS Clip
- relevance of the surgical speciality, patient population and surgical procedure, as compared with the intended use of the SLS Clip
- conditions of use (laparoscopy / endoscopy)

A critical evaluation of the scientific literature was then performed, taking into account the favorable and unfavorable articles.

They were subsequently organized in 4 sections:

- haemostatic clips and comparison with other techniques of haemostasis
- advantages of clip appliers
- compatibility of metal haemostatic clips with MRI
- adverse events involving haemostatic clips

Eventually, the review was completed with a search for adverse events involving hemostatic clips in the Safety Alerts letters published by the AFSSAPS (French Competent Authority) and in the MDR and MAUDE databases maintained by the FDA (USA).

Articles on haemostatic clips and comparison with other techniques for hemostasis :

Samuels PB et al. *(1966) A new hemostatic clip: 2-year review of 1007 cases. Annals of Surgery 163:427-431*

This report summarizes the use of and experience with a hemostatic clip system made from tantalum wire. Tantalum is used because it is inert and does not induce inflammation or necrosis. The clip system consists of two applying forceps, a plastic cartridge containing 25 hemostatic clips, a heavy base on which one or more of the cartridges may be mounted, and a clip-removing forceps. As with the SLS™ clip, the cross-section of the wire is triangular, and it is bent in the shape of a chevron, with the tips of the clip bent towards each other. The clip has a groove running down its center, crossed at intervals by transverse depressions. Furthermore, the system includes a forceps that prevents the loss of clips and simplifies clip loading. The report indicates that these design features, which are similar to those of the SLS™ clip, profoundly affect the ease of clip loading, the efficiency of applying forceps, and the security of hemostasis.

The system allows complete occlusion of the lumen of vessels, but necrosis of the wall is minimized by the hypotraumatic surface, which avoids both immediate and delayed hemorrhage. Also, the occlusive action of the clip occurs in one plane. In contrast, it is sometimes difficult to tie at depth without pulling up or to one side, with subsequent avulsion of the tie or the vessel. The clip can be applied without any pull or tension of the vessel.

The article summarizes 1007 cases at four hospitals where the clip system was used. The clips were most frequently used in cholecystectomy, vagotomy, varicose vein surgery, and retroperiotoneal dissection. They were also used in vasectomy and a variety of types of surgery in the head and neck, chest, abdomen, and lower extremities. The article notes that the clips may be used for temporary occlusion of vessels such as small collaterals in arterial surgery and may be used as a radiopaque tag. Also, the clips are "unequalled" for the occlusion of deeply placed or inaccessible vessels. They may be placed prior to the division of a vessel or to secure a bleeding point. The visibility and precision of clip placement requires less exposure and minimizes the need for vigorous retraction. The clips may also be placed at any desired point on a vessel, which can be difficult with a ligature.

A major advantage noted by the authors is an improvement in the continuity of surgery because the preliminary clipping of small blood vessels and suspected small blood vessels allows work to be performed in a dry field without interruptions to clamp and tie bleeders or suction away blood. Finally, the authors state that, following 2 years of clinical use, there had been no intermediate or late complications due to the clips.

<u>Conclusion:</u> An inert metal hemostasis clip (with a design very similar to the SLS™ clip) was used to provide hemostasis in a wide variety of surgeries. The design of the clip profoundly affects the ease of clip loading and the security of hemostasis. Such clips are "unequalled" for the occlusion of deeply placed or inaccessible vessels. The clips are a substantial improvement over ligatures because (1) the clips can be placed at any desired point on a vessel, which can be

difficult with a ligature, and (2) the visibility and precision of clip placement requires less exposure and minimizes the need for vigorous retraction, whereas it is sometimes difficult to tie at depth without pulling up or to one side, with subsequent avulsion of the tie or the vessel.

***Dujovny M, Ressler EO, Kossovsky N, Tucker JB, Wackenhut N and Leff** L (1980) Vascular clip closure force meter. Surgical Neurology 14:107-109*

This report describes a portable device for measuring the static force exerted by an aneurysm clip. Measurement of the force exerted by aneurysm clips is important because the proper use of the clips depends on correlating the applied force with the diameter of the neck of the aneurysm, the blood pressure, and the width of the clip blade. Furthermore, excessive force on vascular clips causes the disruption of endothelial tissue, which may result in vascular thrombosis. Clip slippage is also related to the force applied, and excessive force can cause tears in the necks of aneurisms and clip breakage.

Conclusion: Application of the correct force on hemostatic clips is important to prevent damage to the tissue as well as clip slippage and breakage.

***Kossovsky N, Dujovny M, Perlin A, Gatti EF, Kossowsky R and Segal R** (1983) Vascular Clip Force Characterization. Vascular Surgery 17:9-24*

This report describes the measurement of clip forces for pivot-, alpha-, and mobile fulcrum-type clips. The SLS™ clip is of the latter type. This was tested because excessive force can cause damage to vessel walls, which can result in thrombi, and insufficient force can result in clip slippage. Twenty-one commonly used aneurysm and temporary surgical clips were evaluated for the amount of force exerted when opened and closed at a range of blade gaps. The results show that the forces exerted do not change in a uniform manner as the gap increases. Therefore, surgeons must take care to ascertain what the rate of change is for the particular clip that they are using.

Conclusion: Application of the correct force on hemostatic clips, which depends on the design and size of the clip, is important to prevent both damage to the tissue and clip slippage.

***Dujovny M, Kossovsky N, Kossowsky R, Gatti EF, Segal R and Diaz FG** (1983) Mechanical and metallurgical properties of vascular clips designed for temporary use. Microsurgery 4:124-133.*

This report discusses the mechanical and metallurgical properties of metal vascular clips. Some problems include the use of metals that are not biocompatible are not designed to withstand the combined effects of stress and corrosion. Furthermore, some clips have different hardnesses than either their own specially designed appliers or other similar appliers. A mismatch between the two could produce metal shards that could evoke a foreign-body response. Studies of vascular tissue mechanics show that the force needed for vascular occlusion depends on vessel diameter, blood pressure, blade contact area, and vessel elasticity. The results of this study showed that the force exerted by a clip can differ greatly according to their design and size. In addition, the material properties of the metal define the range of forces that they may produce. X-ray diffraction, microhardness, passivation-reactivation, and scanning electron microscopy studies showed differences in the ability of the different clips to withstand stress and corrosion. The authors conclude that all of the clips examined in the study are suitable for temporary use because of their relative low closing forces. They also note that biocompatibility, elasticity, and resistance to stress and corrosion are key factors for choosing a material for vascular clips.

Conclusion: The metal used for clips should be biocompatible and its fracture toughness and corrosion resistance must be sufficiently high to withstand long-term implantation without undergoing a stress corrosion catastrophic failure.

Smith RC *(1988) Operative cholangiography using a modified disposable vascular clip. Surgery, Gynecology & Obstetrics 166:275-276*

This report describes the development of a method that is simple and less damaging to tissues than clamping or placing a ligature around a catheter for trancystic duct operative cholangiography. The authors note that the use of a vascular clip traumatizes the tissue very little and is easily removed or reapplied if a second cholangiogram is needed. The clip can be safely used through any incision and minimizes trauma to the tissues of the cystic duct.

Conclusion: The use of a metal hemostatic clip minimizes trauma to the tissues compared to other methods, such as clamping or placing a ligature around a catheter.

Grainger DA, Meyer WR, DeCherney AH and Diamod MP*. Laproscopic clips. Evaluation of absorbable and titanium with regard to hemostasis and tissue reactivity. Journal of Reproductive Medicine 36:493-495*

This study examined the ease of application of absorbable polymer and titanium surgical clips used for laparoscopy as well as their ability to provide hemostasis, and their tissue reactivity in a rabbit model. The clips were easily applied with the laproscopic applicator Hemostasis was achieved uniformly. There was no statistical difference in the adhesion formation between the two clip types. The authors conclude that hemostasis with clips may be preferable in some circumstances to electrocautery, such as in the ureter.

Conclusion: Titanium and absorbable polymer clips are equally effective and have equal tissue reactivity. They may be preferable to electrocautery in some circumstances.

Klein RD, Jessup G, Ahari F, Connolly RJ and Schwaitzberg *SD (1994) Comparison of titanium and absorbable polymeric surgical clips for use in laproscopic cholecystectomy. Surgical Endoscopy 8:753-758*

This article compares the use of titanium and absorbable polymeric surgical clips for use in laproscopic cholecystectomy. The article points out that metal-based clips have some disadvantages, including poor holding power, characterized by accidental dislodgement from a vessel or structure; induction of foreign body or inflammatory reactions; erosion into adjacent anatomic structures; and interference with roentologic studies including computerized tomography and magnetic resonance imaging. (However, these problems refer to earlier clips containing ferromagnetic materials.) Ligating clips made from absorbable polymers address these issues. The main drawback is that a latch mechanism is often used to secure them in place so that the structures to be ligated must be completely dissected free of surrounding tissues; however, the system used in this study does not rely on a latch mechanism.

The study showed that the force required to remove the polymer clips from canine cystic ducts was higher than for titanium clips. Also, the axial dislodgement force was significantly higher for the polymer clip. In addition, the polymer clip lost strength over time due to resorption, with 11% strength after 21 days. Both the polymer and the titanium clips were applied without difficulties, both provided hemostasis and prevented bile leakage, and there were no complications during the use of either type of clip. Dislodgement, postoperative bleeding, bile leakage, and dilation of the cystic duct were not detected for either of the clips.

Conclusion: Metal and polymeric clips are both effective for laproscopic cholecystectomy. Polymer clips may be more effective for situations where the clips may be subjected to axial and transverse traction. In addition, the polymer clips do not interfere with computer tomography and magnetic resonance imaging.

Hsu T *(2006) Comparison of holding power of metal and absorbable clips. American Journal of Surgery. 191:68-71.*

The article describes a clinical study comparing the holding power of metal clips and absorbable polymer clips in 74 patients undergoing cholectomy. The article notes that metal clips can interfere with computer tomography and magnetic resonance imaging. The study showed that the polymer clip can withstand much higher holding strength or pressure before slippage than the metal clip; however, two metal clips are equally as effective as one polymer clip.

Conclusion: Single polymer hemostatic clips have lower risks of slippage than single metal hemostatic clips; however, two metal clips are equally as effective as one polymer clip.

Articles on the advantages of clip appliers

Busch RF *(1992) A new vascular clip applier for internal maxillary and ethmoidal artery ligations. Otolaryngology and Head and Neck Surgery. 107:129-30.*

This report describes the use of a vascular clip applier manufactured by Ethicon, Inc. This instrument is a modification of a previous instrument called the Ligaclip applier. The instrument has a narrow tip that is not angled, which allows easier visualization during ligation procedures, especially where the surgical site is limited, such as in ethmoidal artery ligation. Previous instruments have been too bulky at the tip and provided distal angulation, which causes difficulty in confined spaces. Also, incomplete closure of the vascular clips has necessitated multiple reapplications within the same surgical setting.

Conclusion: The use of a clip applier with a fine and narrow tip that is not angled, which is similar to the SLS applier instrument, improves visualization and reduces operating time in the occlusion of blood vessels

Articles on the compatibility of metal hemostatic clips with magnetic resonance imaging (MRI)

Barrafato D (1984) *Magnetic resonance imaging and surgical clips. Canadian Journal of Surgery 27:509-512*

This article presents a study on the magnetic properties of 54 different metal surgical clips. The magnetic properties measured included (a) displacement in a magnetic field gradient, (b) rotation to align within a magnetic field, and (c) artifacts in a magnetic resonance image. All non-steel clips (i.e. titanium or silver) were not magnetic, whereas some of the stainless steel clips were magnetic. Because of the wide spectrum of proprietary steels used in the manufacture of surgical implants, the authors conclude that the use of ferromagnetic surgical implants be discontinued.

Conclusion: Nonferromagnetic surgical clips such as those made from titanium are compatible with MRI, but those made from ferromagnetic materials are not.

Brown MA, Carden JA, Coleman RE, McKinney R and Spicer LD *(1987) Magnetic field effects on surgical ligation clips. Magnetic resonance imaging 5:443-453*

This article presents the results of a study on the effects of ligation and aneurism clips on magnetic resonance images obtained at a field strength of 1.5 Tesla. Clips made from three types of stainless steel as well as titanium, tantalum and niobium metals were examined. The magnetic forces exerted on stainless steel clips of a given size were much larger than on the other types of clips, and those on tantalum clips were larger than on titanium clips. In addition, stainless steel clips distort the magnetic resonance images more than the other types of clips, and the niobium

clips cause an intermediate level of distortion. The authors recommend the selection of the smallest clip consistent with good surgical practice made from tantalum or titanium. They also recommend against magnetic resonance studies in patients with certain types of stainless steel implants.

Conclusions: The selection of the smallest clip consistent with good surgical practice made from tantalum or titanium is recommended.

***Shellock FG** (1988) MR imaging of metallic implants and materials: a compilation of the literature. American Journal of Roentgenology 151:811-814*

This review summarizes the literature on the ferromagnetic qualities of 127 different metallic implants and other materials, including aneurysm and hemostatic clips. The author points out that knowledge of the specific types of metallic implants or materials is essential for screening patients before MRI. Potential problems include movement, heating, induction of an electrical current, and misinterpretation of artifacts as an abnormality. Tantalum and silver alloy clips did not deflect in a magnetic field up to 1.5 Tesla, whereas some of those made from stainless steel or other alloys did show deflection.

Conclusion: The presence or degree of ferromagnetism in implants including hemostatic clips must be determined before performing MRI. MRI should only be carried out when nonferromagnetic clips have been used.

***Gold JP, Pulsnelli W, Winchester P, Brill PW, Jacewicz M and Isom W** (1989) Safety of metallic surgical clips in patients undergoing high-field-strength magnetic resonance imaging. Annals of Thoracic Surgery 48:643-645.*

This study examined the displacement of medium-sized titanium and tantalum metallic clips in vitro. Two clips made from highly ferromagnetic materials were used as controls. In a magnetic field of 1.5 Tesla, the titanium and tantalum clips did not show displacement, whereas the ferromagnetic clips showed marked displacement.

Conclusion: Clips made from titanium or tantalum do not displace in a magnetic field of up to 1.5 Tesla and should be compatible with MRI.

***Shellock FG and Crues JV** (1988) High-field-strength MR imaging and metallic biomedical implants: an ex vivo evaluation of deflection forces. American Journal of Roentgenology 151:389-392*

In this report, 36 different metallic biomedical implants were evaluated for deflection in a 1.5-Tesla magnetic field. Of the aneurysm and hemostatic clips evaluated, those made from tantalum did not show deflection, whereas some of those made from stainless steel did show deflection. The authors recommend that patients should be examined by MRI only if the exact type of aneurysm clip is known and demonstrated to be nonferromagnetic.

Conclusion: Only clips made from nonferromagnetic materials such as tantalum are compatible with MRI.

***Shellock FG** (1993) MR procedures and biomedical implants, materials, and devices: 1993 update. Radiology 189:587-599*

This review summarizes the literature on the ferromagnetic qualities of 338 different metallic implants and other materials, including aneurysm and hemostatic clips. The author points out that knowledge of the specific types of metallic implants or materials is essential for screening patients before MRI. Clips made from nonferromagnetic materials such as tantalum did not deflect in a magnetic field up to 1.5 Tesla, whereas some of those made from stainless steel or other alloys did show deflection.

Conclusion: The presence or degree of ferromagnetism in implants including hemostatic clips must be determined before performing MRI. MRI should only be carried out when nonferromagnetic clips have been used.

***Shellock FG** (2002) Biomedical implants and devices: assessment of biomagnetic field interactions with a 3.0-Tesla MR system. Journal of Magnetic Resonance Imaging 16:721-732*

This study examined the magnetic field interactions at 3.0 Tesla of 109 different biomedical implants and devices, including 32 different aneurysm clips. Of the 32 clips tested, 15 showed weak ferromagnetic qualities, but these should not be sufficient to consider them unsafe. Those made from titanium show no deflection in the 3.0-Tesla field.

Conclusion: For aneurysm clips, those made from nonferromagnetic materials, especially titanium, are unaffected by a 3.0-Tesla magnetic field and therefore should be compatible with MRI.

***Merkle EM, Dale MB, Thomas J and Paulson EK** (2006) MR liver imaging and cholangiography in the presence of surgical metallic clips at 1.5 and 3 Tesla. European Radiology 16: 2309-2316*

This study was carried out to evaluate whether clips from prior cholecystectomy impair image quality during magnetic resonance cholangiography at 3.0 and 1.5 Tesla. Image quality was examined using an in vitro system as well as in 42 patients post-cholecystectomy who underwent cholangiography at 3 or 1.5 Tesla. The in vitro study suggests that surgical metallic clips made from titanium may cause a pseudo-obstruction on magnetic resonance cholangiography at 1.5 Tesla if the clip is within 2 mm of the bilary tree. This distance increases to 4 mm at 3.0 Tesla, making the occurrence of pseudo-obstructions more likely. Susceptibility artifacts were not significantly more common at 1.5 Tesla than at 3.0 Tesla. The study showed that the presence of bilary pseudo-obstructions due to susceptibility artifacts from surgical clips was not more common but that they were larger in the 3.0-Tesla cholangiography. The authors conclude that patients with a history of prior cholecystectomy should not be excluded from 3.0-Tesla cholangiography.

Conclusions: Titanium clips are compatible with magnetic resonance cholangiography at 3.0 Tesla.

Articles on adverse events from haemostatic clips

***Edner GF, Ericson K, Forster DMC and Steiner L** (1978) The broken clip. Acta Nerochiurgica 40:145-149*

The report describes two cases of broken clips following surgery for subarachnoid hemorrhage. X-rays revealed that the clips had broken within 18 months in one case and 24 months in the other. The cause of the fracture was unclear but may have been to clip fatigue. (Note: it was not clear from this article what kind of clips had been used, but given the year of this article, they were probably not made from titanium.)

Conclusion: Clip breakage is an uncommon but important problem. (However, it may not apply to those made from titanium like the SLS™ clips.)

***Miedema EB and Redman JF** (1982) Case profile: radiolucent urethral calculus with hemostatic clip nidus. Urology 19:328.*

The report describes a case of a 53-year-old man that presented with a 6-month history of recurrent urinary tract infections, progressive dysuria, and a decreasing urinary stream 2 years after prostatectomy for adenocarcinoma of the prostate. Cytoscopy showed a calculus with a

metallic hemostatic clip protruding from its center. A few other reports in the literature have shown similar findings, which appears to be due to clip slippage, leading to clip migration into the bladder.

Conclusion: Clip slippage leading to clip migration can be a problem.

***Margolis JL** (1986) Recurrent choledocholithiasis due to hemostatic clip. Archives of Surgery 121:1212*

This report describes a case of the formation of a common bile duct stone following common bile duct exploration. The stone had formed around a hemostatic clip that was used in the surgery. The clip had apparently dislodged and migrated down the tract into the duct to acts as a nidus for stone formation. This is a common problem with surgical suture material. The authors suggested that absorbable suture be used for surgery of the bilary tract.

Conclusion: Clip slippage leading to clip migration can be a problem, especially in the bile duct, where it can lead to the formation of stones. This is also a problem for sutures.

Rationale/Analysis for Extrapolation of the Results to SLS CLIPS

- Collectively, these studies show that metal hemostatic clips are effective at providing hemostasis. Metal hemostatic clips are an improvement over the use of ligatures, which is the major alternative for hemostasis, because the clips can be placed at any desired point on a vessel, which can be difficult with a ligature. Also, the visibility and precision of clip placement requires less exposure and minimizes the need for vigorous retraction compared to ligatures. Thus, the use of clips minimizes trauma to the tissues compared to ligatures.

- The metal used for clips should be biocompatible, and its fracture toughness and corrosion resistance must be sufficiently high to withstand long-term implantation without undergoing a stress corrosion catastrophic failure. Titanium clips such as SLS™ clip provide a substantial benefit over other types of metals because they are biocompatible and resist corrosion and stress. They also do not interact with magnetic fields of up to 3.0 Tesla and therefore, unlike many other metal clips, are compatible with MRI. In addition, in most cases, titanium and resorbable polymer clips seem to provide equivalent results.

- Reported problems with metal hemostatic clips in the scientific literature include the following:
  1- Clip slippage leading to clip migration. In the bile duct or the urinary tract, this can lead to the generation of insoluble deposits. Although metal and resorbable polymeric clips are both effective at providing hemostasis, polymer clips may be more resistant to slippage and migration.
  2- Clip breakage. This seems to be a rare problem but could result in tissue damage. However, it may not apply to those made from titanium like the SLS™ clips. In fact, a literature search did not identify any articles on the breakage of titanium clips.

- Reported Adverse events are rare for manual Titanium clips as SLS clips.

  A search of the Safety Alerts letters published by Afssaps reported the recall of certain lots of an automatic clip applier due to a possibility to produce incorrect closure of vessels. This incident was link to a malfunction of the automatic applier and not to a non conformity of the clip.

The FDA MDR database also report adverse event during clip ligating with similar devices from the competition.
Most of the incident are :
1- Clip cut the vessel/arteries (usually due to clip scissoring), Clip scissored. The cause of failure identify was an applier malfunction : bent tip, misaligned jaw.These malfunctions were due to a lack of maintenance of the applier.
2- Clip dropped off the vessel, Bleeding – bad clip closing : FDA medical device reporting (MDR) database showed one case of death following cardiac artery bypass grafting due to metal clip slippage and resulting bleeding. The incident reported was isolated incident.
Overall, the problems of "Clip dropped off the vessel, Bleeding – bad clip closing" seems to be a relatively rare problem. Application of the correct force via hemostatic clips should help avoid these problems. This depends mostly on the dimensions of the clip when closed, and clip appliers are designed to reproducibly provide the proper dimensions.
Most of the time, the cause of failure identify was the selection of a clip that was not large enough for the vessel ligated, or the use of a non conform applier (jaws not jointed)
3- Clip do not hold or do not even stay in the applier : The cause of failure identify was due to a failure of the applier (jaws too open..) or a bad loading of the clip into the applier jaws by the nurse.

- The studies summarized in this report can be extrapolated to the SLS Clip system because:
  - The SLS™ clips are similar in design to other inert metal hemostasis clips that have been used clinically and studied for security of hemostasis, ease of use, and safety. In fact, the SLS™ clips have already been in clinical use for 10 year
  - The SLS™ clips are similar to other titanium metal hemostasis clips that have been studied for biocompatibility, resistance to stress and corrosion, and compatibility with MRI.
  - The loading system is similar in design to other clip appliers that have been examined for ease of use and effectiveness.

- On this basis, the results from the studies in the literature suggest that the SLS CLIP will provide effective, reliable, and safe hemostasis in open surgery. Hemostasis using the SLS CLIP should be more effective than ligatures because (1) the clips can be placed at any desired point on a vessel, which can be difficult with a ligature, and (2) the visibility and precision of clip placement requires less exposure and minimizes the need for vigorous retraction. Furthermore, proper use of the SLS CLIP should minimize problems due to clip slippage and resulting clip migration.

- Risks reported in the scientific literature or identified by adverse event analysis has been take in account in the risk analysis.

Clinical Evaluation

Evaluation sheets have been created for surgeons who have used haemostatic SLS clips in order to have a feedback about its quality and efficacy (see attachment).

The evaluation is based on the quality of :

- ⇒ Adhesive backing : evaluation of the system with an adhesive contactsurface (which allows the cartridge to be sellotaped on the surgeon glove close to the patient = time saving)
- ⇒ Clip access : easiness of access to the clip in the cartridge
- ⇒ Clip extraction : easinesss of extraction of the clip from the cartridge
- ⇒ Clip grip (applier) : correct holding of the clip in the applier's jaw
- ⇒ Distal closure : correct distal closure of the clip on the tissues
- ⇒ Clip holding (tissue) : efficient holding of the clip on the ligated tissues

The evaluation compares the **competitive clips** (the usual clip reference used by the physician) with the haemostatic SLS clips.

- ***2000*** : Results were received from 6 surgeons operating in 2 different hospital centers on 15 operative cases.

	Quality level of SLS clips as compared with device usually in use		
	Superior quality	Equivalent quality	Inferior quality
Adhesive backing	87%	13%	0%
Clip access	40%	60%	0%
Clip extraction	40%	60%	0%
Clip holding in jaws	73%	27%	0%
Distal closure	100%	0%	0%
Clip holding (tissue)	87%	13%	0%

→ 100% of the results confirm that the quality of the haemostatic SLS clips is at least equivalent to that of the competitive clips.

- *2005* : results were received from 5 surgeons operating in 3 different hospital centers on 7 operative cases.

	Quality level of SLS clips as compared with device usually in use		
	Superior quality	Equivalent quality	Inferior quality
Adhesive backing	28.5%	57%	14.5%
Clip access	0%	100%	0%
Clip extraction	43%	57%	0%
Clip holding in jaws	71.5%	28.5%	0%
Distal closure	43%	57%	0%
Clip holding (tissue)	57%	43%	0%

→ almost all the results confirm that the quality of the haemostatic SLS clips is at least equivalent to that of the competitive clips.

- *2008* : results were received from 6 different surgeons on 4 different surgical procedures

	Quality level of SLS clips as compared with device usually in use		
	Superior quality	Equivalent quality	Inferior quality
Adhesive backing	0%	66%	17%
Clip access	33%	66%	0%
Clip extraction	66%	33%	0%
Clip holding in jaws	33%	33%	33%
Distal closure	33%	66%	0%
Clip holding (tissue)	17%	66%	0%

Note 1 : the total for each lign is not always 100%, since some surgeons did not evaluate every item.
Note 2 : the 2 surgeons who evaluated clip grip as inferior were nevertheless ready to use SLS Clips.

Conclusion : Overall, the feedback from surgeons operating in different hospital centers is most favorable.