K955064

OCT 17 1996

510(k) Summary of Safety and Effectiveness

SPETZLER Ti 100 TITANIUM ANEURYSM CLIP

A. LEGALLY MARKETED PREDICATE DEVICES

The **Spetzler Ti 100 Aneurysm Clip** is substantially equivalent to the Yasargil Aneurysm Clips as manufactured by Aesculap AG, Tutlingen, Germany (as cleared in K772200, K913765, and K922272), the Sugita Aneurysm Clips as manufactured by Mizuho Ikakogyo Co., Ltd., Japan (as cleared in K791978 and K881911), and the Sundt Slim Line Clip as manufactured by Codman and Shurtleff, Randolph, MA (as cleared in K912456).

B. DEVICE DESCRIPTION

Spetzler Ti 100 Aneurysm Clips are manufactured from titanium--Certified ASTM F67-89, "Unalloyed Titanium for Surgical Implant Applications, Grade IV" (see ASTM F67-89 specifications). This grade of titanium is often referred to as "Commercially Pure Titanium," or "C. P. Titanium." The basic models are distinguished by their surface finish: natural metallic color for clips intended for permanent implantation, and blue for temporary clips.

Aneurysm Clips, whether those proposed by Elekta or those manufactured or distributed by the sponsors of the predicate devices, are available in a wide variety of styles and sizes in order that all of the sizes and shapes of aneurysms can be treated. The clips are available for both temporary and permanent placement in the brain.

Spetzler Ti 100 Aneurysm Clips are applied with the **Elekta Titanium Nitride Coated Clip Appliers** to avoid foreign metal transfer. Clips are sterilized in the **Elekta Sterilization Tray**.

C. INTENDED USE

The **Spetzler Ti 100 Aneurysm Clips** are intended for:

- Temporary occlusion of intracranial blood vessels/aneurysms
- Permanent placement in the brain for occlusion of intracranial aneurysms

There are no differences with respect to the predicate devices for indications for use, target population, or mechanical properties.

The **Spetzler Ti 100 Aneurysm Clip** is safe for use with magnetic resonance (MR) devices, and produces only minimal image distortion, extending only slightly beyond the physical extent of the device. The demonstration of MR safety and compatibility is discussed below.

The **Spetzler Ti 100 Aneurysm Clip** is safe for use with CT imaging systems and produces significantly less image artifact than clips made from cobalt-chrome alloys such as Elgiloy (Sugita clip) or Phynox (Yasargil clip). The evaluation of the extent of clip induced artifact in CT imaging is discussed below.

The **Spetzler Ti 100 Aneurysm Clip** and other currently marketed clips such as the Sugita and Codman clips, are supplied to hospitals in a non-sterile package. Clips are selected for a given application and sterilized prior to use by the user. The validation of Elekta's recommended sterilization procedures is discussed below. No effect of repeated sterilization on the mechanical properties of the Elekta clips was found.

D. SUBSTANTIAL EQUIVALENCE SUMMARY

The Elekta device has the *same* intended use and target population as the predicate devices, and has *equivalent effectiveness* for its intended use. Furthermore, its new technological characteristic--the use of titanium--poses the same type of questions about safety and effectiveness as do the predicate devices.

E. NON-CLINICAL TESTING

This section summarizes the performance testing that Elekta carried out on the **Spetzler Ti 100 Aneurysm Clip**. This testing addressed the following issues:

(1) Mechanical and metallurgical tests to validate the structural integrity of the clips,

(2) Mechanical performance tests to demonstrate that the clips meet their specifications,

(3) Testing to validate sterilization recommendations

(4) Biocompatibility testing,

(5) MR safety testing, and

(6) Testing to determine image artifact size for MR and CT imaging.

1. Metallurgical/Structural Testing

Elekta's specifications and tight controls were validated by the following:

a. Destructive testing of a statistically determined number of clips by the independent metallurgical laboratory, Laboratory Testing, Inc., Dublin, PA. A metallographic examination of the surfaces and cross sections, at 100X and 400X, of all stressed, worked and critical areas showed the complete absences of imperfections and defects such as cracks, voids, etc. Such metallurgical examinations will be conducted on samples from each new titanium wire delivery and each clip production lot.

b. Elekta has confirmed that the relatively low temperature of the hospital sterilization process (270° F) has absolutely no effect on the metallurgical/operational properties of the titanium clip. As distributed today, aneurysm clips are provided to the hospital non-sterile (e.g. as by Sugita and Codman). Selected clips are placed in a sterilizing tray and sterilized prior to each procedure until used. In simulating these events, Elekta sterilized the titanium clips in excess of 100 times and after each ten cycles, opened the clips with the Elekta clip applier to the maximum recommended blade opening distance and then measured the closing force per the draft ASTM standard. The closing force remained consistent for all clips.

c. Though titanium is one of the most corrosion resistant metals, Elekta commissioned a corrosion test on the clips. The results confirm that these titanium clips do not corrode, even under stress. This is further confirmed by Elekta's review of literature concerning the effects of cerebral fluids on titanium.

d. A Vickers hardness was measured on the worked and unworked areas of the clip wire. The results demonstrated no statistically significant change in hardness.

2. Mechanical Performance Testing

In evaluating the measure of closing force, Elekta has followed FDA's recommendation to use the ASTM proposed test protocol to measure each clip, prior to release for distribution. The closing force is recorded on the clip label and in the history file, by serial number.

To confirm that the **Spetzler Ti 100 Aneurysm Clips** retain their mechanical performance in simulated use conditions, the following study was carried out:

Clips placed on tubing filled with a 98.6° saline solution were pulsed in excess of twenty million cycles at a pressure in excess of 300 mm Hg. Using colored liquid in the tubing, the results confirm no leakage through the clip, no loss of blade alignment, and the changes in closing forces measured (double blind) never went below the release specifications of competitive clips.

3. Sterilization

Elekta has validated its recommended steam sterilization cycles. Furthermore, Elekta has demonstrated that repeated sterilization has no effect on the mechanical properties of the clips.

4. Biocompatibility

Because titanium has not been previously cleared for use in the brain in an aneurysm clip, it was incumbent upon Elekta to demonstrate that titanium is not significantly different with respect to biocompatibility properties from the cobalt-chrome alloys currently utilized in the predicate devices. This demonstration of biocompatibility includes the following studies commissioned by Elekta:

A study of the **Spetzler Ti 100 Aneurysm Clip** implanted in the brains of rabbits addresses the concern that titanium might increase the susceptibility to seizure activity. Elekta commissioned a six-month intra-cranial, pre-clinical implant study of 30 rabbits, divided into three groups, including 12 implanted with titanium clips, 12 implanted with the presently marketed Yasargil Phynox (cobalt chrome alloy) clips and 6 non-implanted controls. These animals were maintained and monitored for one month (six of both groups) and six months (six of both groups) and the six negative controls. The study evaluated the substantial equivalence of the Elekta titanium clip as compared to the presently marketed Yasargil (Aesculap) clip through daily monitoring, monthly EEG evaluations and Time-to-Induced-Seizure. The results of this evaluation demonstrated the substantial equivalence of the **Spetzler Ti 100 Aneurysm Clip** as there was no difference in the three groups in function and behavior (as recorded in daily observations), no difference in EEG recordings (30 minutes each), and no statistically significant differences in seizure latency.

The study by von Holst, et al. [Acta Neurochirurgica 56:239-242 (1981)] found that clips made of titanium, silver, and tantalum, and implanted in

the brains of rabbits, were tolerated quite differently. The implant of titanium showed no evidence of any reaction, while the others showed cytoplasmic pigmentation and reactive gliosis (silver) and local limited pigmentation (tantalum).

The report by A. Ammar, "Tissue Compatibility of Different Intracranial Implant Materials: In-vivo and In-Vitro Studies" [Acta Neurochirurgica 72:45-59 (1984)], compared brain implants of alumina ceramics, hydroxy apatite ceramics, titanium, methylmethacrylate, Surgita aneurysm clip, silicon shunt tube, and lyophilized human dura mater (Lyo-dura). While the non-metalic implants had varying degrees of compatibility, the titanium showed excellent compatibility, while the Surgita showed fair compatibility. The report noted for the titanium implant, "No reaction of brain tissue was observed."

Elekta commissioned a major review of the titanium toxicological literature which concluded that:

- Titanium's lack of inflammatory potential is supported by many studies. The available literature indicates that titanium does not act as an immunotoxicant.

- The scientific literature, which indicates that titanium dioxide is non-mutagenic, and the lack of reported tumors in patients with titanium implants, support the position that titanium is not genotoxic.

- The scientific literature and titanium's satisfactory use in many craniofacial implants suggest that titanium will unlikely cause adverse effects in soft tissue.

- The literature and lack of relevant observations among patients with titanium implants demonstrate that titanium dioxide does not cause adverse effects with chronic exposure and suggest that titanium will not elicit systemic effects.

- The available evidence strongly supports titanium's non-carcinogenicity.

- The limited information available on brain implantation shows that titanium does not elicit histopathology and is not associated with dissolution of the oxide layer.

5. MR Safety and Compatibility

In response to the risks involved in more powerful MRI systems and the continuing concern for image quality in both MRI and CT, Elekta has completed an extensive, performance evaluation of the titanium aneurysm clips:

a. MR Safety

A study carried out at a university included characterization, mechanical testing and magnetic evaluation of the Elekta titanium, Codman, Aesculap and Sugita clips.

The direct measurement of magnetic susceptibility for these clips showed that the MP35N alloy (Codman) was 5.2 times larger than for Elekta's clip, Phynox alloy (Aesculap) was 17.2 times larger, and Elgiloy (Sugita) was 15.7 times larger. The magnetic force measured in a 2 Tesla magnetic field showed that the force was 14, 35, and 36 times larger for MP35N, Phyunox, and Elgiloy, respectively, than for the Elekta clip. The results of this study demonstrate a significantly lower interaction with the magnetic field for titanium over the other clips, some of which are presently promoted as MRI safe.

Furthermore, this study evaluated the magnetization over a cycle of applied magnetic field from 4 Tesla (T) to 0 T to -4 T to 0 T and finally back to 4 T, with measurements every 0.5 T. The resulting **M** vs **B** hysteresis loop would show the extent of ferromagnetism, if any. For the Elekta clip the "hysteresis loop" was a shallow straight line through the origin, indicating no detectable ferromagnetism, only paramagnetism. Since the magnetic susceptibility of the Elekta clip is so small and paramagnetic in nature, the magnetic torque on the Elekta clip would be expected to be very small.

Another study used 1.5, 2.0 and 7.0 Tesla fields to evaluate clip displacement/deflection and image quality of the Sugita, Yasargil (Aesculap) and Elekta titanium clips. The results of this study confirm that in 1.5 and 2.0 Tesla fields the forces applied are not significant but in higher fields the Sugita and Aesculap clips show what is presently considered an unacceptable deflection (in excess of 45°) as compared to the titanium clip. In image quality the Elekta titanium clip was found to be "considerably superior in the vicinity of the clip."

b. Image artifact in MR and CT Imaging

A study carried out at a university showed significantly reduced artifact, for the titanium clip, in MRI and CT scans. In the MR image, the artifact is a signal void with a thin rim of hyperintensity. This artifact was found to be 7.5 times larger for Elgiloy than Elekta and 6 times larger for Phynox. In CT imaging clips cause a streak artifact or starburst pattern. The relative sizes of these artifacts for Elgiloy, Phynox, and C. P. Titanium (Elekta) were in the ratios, 4:3:1.

The ACTA Neurochirurgica paper, "Titanium Clips in Neurosurgery for the Elimination of Artifacts in Computer Tomography (CT)," H. von Holst, et. al., compares the artifacts caused by various intracranial implant materials with titanium (99% pure) and finds that the titanium is highly resistant to corrosion and does not cause artifacts on CT images.

Observations at St. Vincent's Hospital in Dublin, Ireland of artifacts produced by Elekta (titanium), Sugita and Aesculap clips as seen in various MRI fields, were summarized. In this paper, significant artifacts are seen consistently, in various protocols, in both the Sugita and Aesculap clips. In comparison, only a "slight" artifact is seen in the Elekta titanium clip which gives almost no degradation to the surrounding structures.

"Titanium Aneurysm Clip-Decreased Image Degradation in MRI and CT," Michael J. Carron, M.D., et al., presents Dr. Carron's (Southwest Regional Hospital, Florida) imaging evaluations of the Sugita, Aesculap and the Elekta titanium clips in both CT and MRI which were done with regard to three areas: type of artifact, relative size of artifact, degree of degradation of image. The results indicate MRI artifact size 600% to 700% greater for Sugita and Aesculap clips, with significant image degradation, as compared to the Elekta titanium clip. CT artifact is 300% to 400% greater for the Sugita and Aesculap clips with equivalent image degradation while the titanium clip was noted as having no image degradation.

Another study commissioned by Elekta studied image artifact in a dog model, comparing the **Spetzler Ti 100 Aneurysm Clip** with a Yasargil Phynox alloy clip (Aesculap) of the same size. The main findings were:

- **Computed Tomography:** Artifact radius of titanium clip measured at 1 cm versus 3 cm for conventional clip.

- **Magnetic Resonance:** Artifact dimension in T1, T2 and intermediate weighted images were measured at 0.4 to 1.2 cm^2 for titanium while conventional clips were at 1.0 to 3.6 cm^2.

F. CONCLUSIONS

Elekta has demonstrated that its testing of the **Spetzler Ti 100 Aneurysm Clip** and its review of the literature on the biocompatibility of titanium shows equivalent safety and effectiveness with respect to mechanical performance and biocompatibility issues, and superior performance with respect to the ancillary issues of safety and compatibility with MR and CT imaging systems.