

Safety and Performance Evaluation of Remanufactured Harmonic® Scalpels

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Abstract

Objective: To thoroughly evaluate the safety and performance of remanufactured harmonic® scalpels through extensive laboratory and animal evaluation.

Methods: Remanufactured harmonic® scalpels were evaluated in a series of laboratory and animal studies intended to determine their safety and performance characteristics as compared to new harmonic® scalpels. Included were evaluations assessing sterility, cleanliness, appearance, stability and performance following remanufacturing. In addition, evaluations were performed comparing remanufactured to new harmonic® scalpels in an animal model to assess time to transect tissues, as well as ability and time to achieve hemostasis.

Results: Remanufactured harmonic® scalpels consistently had no visible contamination, with insignificant levels of protein or hemoglobin (significantly below that required by consensus standard AAMI TIR 30 and that of reused metal instruments taken from the sterile inventory of a hospital) and were routinely shown to function for up to 300 activations without failure. This was observed for standard product, product subjected to worst-case contamination, storage, shipping, and cleaning, as well as product subjected to worst-case shipping and storage conditions followed by two years of accelerated and real-time aging. Remanufactured harmonic® scalpels withstood 300 activations without failure of Teflon pad while new scalpels failed 27% of the time. The process used to sterilize remanufactured harmonic® scalpels was effective at less than one third the normal cycle time, even in the most difficult to sterilize areas. In a simulated clinical application performed in a swine model, remanufactured and new harmonic® scalpels were equivalent in time to transect tissue, initial hemostasis and 10-minute hemostasis.

Conclusions: Remanufactured harmonic® scalpels are proven equivalent to new harmonic® scalpels in safety and performance.

Keywords

remanufactured, harmonic® scalpel, evaluation, laboratory, animal, cleanliness, performance, safety.

Introduction

In many cases, instruments labeled by the original manufacturer as disposable single use devices can be disassembled, thoroughly cleaned, refurbished, reassembled and sterilized, making them safely available for additional use¹. In most cases, instruments can be reprocessed or remanufactured 1-5 times and still function as intended. This practice began many years ago by hospitals that were interested in controlling costs of expensive medical instruments and reducing environmental waste. Initially, individual hospitals acted without much validation or evaluation of the efficacy of the process or the safety of the resulting instruments. Since those early days, several companies have developed specific detailed processes for reprocessing/remanufacturing, cleaning and sterilizing such instruments. In addition, the U.S. Food and Drug Administration (FDA) has developed regulations designed to control reprocessing and to assure adequate controlled evaluation and market

clearance processes^{2,3}. Based on FDA regulations, companies that reprocess/remanufacture instruments labeled by the original manufacturer as single use are required to have detailed processes and controls on their process. In addition, they are required to perform extensive evaluations to assure that reprocessed/remanufactured products are consistently clean, sterile and functionally equivalent to the new device. Finally, they are required to obtain FDA clearance to market based on stringent requirements similar to that of the original manufacturer.

This paper reports on extensive laboratory and animal evaluations that were performed using remanufactured harmonic® scalpels to evaluate their safety and performance as compared to new instruments. In this paper, emphasis is put on those factors which are most critical to the clinical application of remanufactured harmonic® scalpels – their consistent cleanliness (at both the macro and cellular level) and their function.

Methods

Materials

New harmonic® scalpels were those made by Ethicon Endo-Surgery (Cincinnati, OH). Remanufactured harmonic® scalpels used in these evaluations were produced by Ascent (Phoenix, AZ).

Sterilization Evaluation

The harmonic® scalpel was evaluated by microbiologists from an independent lab who are experts in the sterilization of medical devices to determine which areas of the design represented the greatest challenge to effective sterilization⁴. Five areas were chosen – 1) under inner blue sheath covering scalpel rod, 2) between inner blue sheath covering scalpel rod and actuating shaft, 3) between actuating shaft and external shaft, 4) inside handle and 5) under protective cap on tip. See Fig 1 below for an illustration of these locations. Each of these areas was inoculated, using either a mini spore strip or an inoculated suture, with 10⁶ CFU bacillus atrophaeus spores. The harmonic® scalpels were then ethylene oxide (EtO) sterilized per usual methods for shortened cycles of 20, 40, 60 and 90 minutes⁵. Following sterilization, the scalpels were assessed to determine sterility. This assessment was done by

aseptically immersing them into 20ml tubes of soybean casein digest broth, incubating them at 30-35°C for seven days and then evaluating them for growth of the bacillus atrophaeus organism.

Dye Penetrant Inspection Evaluation

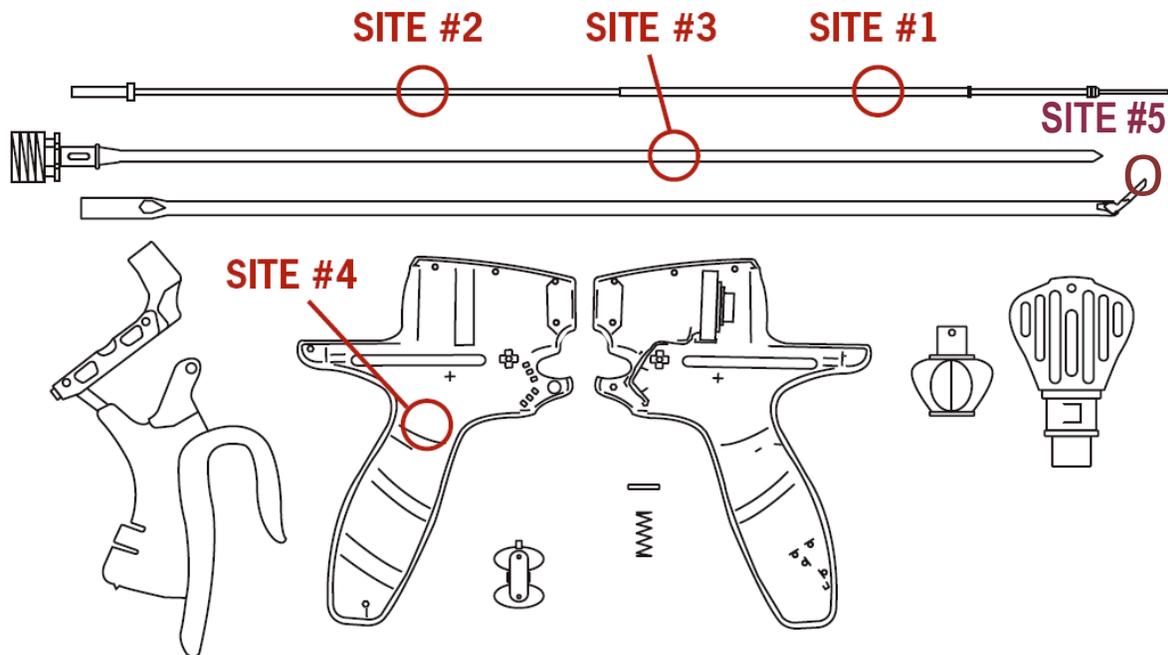
Twelve (12) remanufactured harmonic® scalpels were obtained. These devices were inspected for cracks in the blade using a sensitive inspection method called dye penetrant⁶. Scalpels were activated into bovine peritoneum for 270 ten-second activations with a five-second rest between each activation. The bovine peritoneum was selected as it most closely replicated human soft connective tissue. The 270 ten-second activations represented maximum use as determined from a survey of surgeons who are frequent users of harmonic® scalpels. Typical use is approximately 120 ten-second activations per procedure.

Cleaning Evaluation

To validate the cleaning process⁷, remanufactured harmonic® scalpels were subjected to the following to simulate worst case use, storage and shipment:

- Entire harmonic® scalpel manipulated with gloved hands covered with inoculum, composed of 1 part bovine serum, 2 parts ovine whole blood and 1 part 0.9% saline.

Fig 1. Areas of harmonic® scalpel representing greatest challenge to effective sterilization. Site #1: Under inner sheath covering scalpel rod; Site #2: Between inner sheath covering scalpel rod and actuating shaft; Site 3: Between actuating shaft and external shaft; Site 4: Inside handle and; Site 5: Under protective cap on tip.



- Distal end of harmonic® scalpel activated twice (10 seconds each) into a piece of fresh salt pork. Salt pork was used to simulate human tissue as it contains layers of skin, fatty tissue and muscle.
- Distal one-third of harmonic® scalpel inserted into a tube filled with inoculum and activated 10 times. This resulted in blood being drawn into the shaft of the harmonic® scalpel.
- Entire uncleaned harmonic® scalpel placed in incubator for at least 72 hours at a temperature of at least 60°C.

These harmonic® scalpels were then cleaned in 3 production lots, under worst-case conditions, using maximum lot sizes and minimum cleaning conditions of standard reprocessing steps. Cleaning steps included: 1) an enzymatic solution at 35°C for 40 minutes, 2) a disinfectant at ambient temperature for 12 minutes, 3) a base solution at 55°C for 25 minutes and 4) an alcohol wipe.

Following cleaning, ten harmonic® scalpels were randomly selected from each lot (for a total of 30 samples) and the harmonic® scalpels were evaluated for visible contamination and the level of remaining protein and hemoglobin^{8,9}. Protein and hemoglobin levels were evaluated from samples taken from 400 ml single extractions in physiological saline taken from fully disassembled scalpels. Coomassie Plus® and Hemastix® reagents were used to assess level of protein and hemoglobin, respectively.

To further support the above testing; an additional evaluation¹⁰ was performed in which 30 remanufactured scalpels, 10 each from 3 production lots, were randomly selected from product available for use. The packages of these units were visually inspected for any foreign material and the harmonic® scalpels were visually inspected for cracks, separation, damage, wear and deterioration. Each of these harmonic® scalpels were then subjected to 90 ten-second activations against bovine intestine with a 5 second cool-down between each activation. The level of any protein and hemoglobin on the harmonic® scalpels was also evaluated as described previously^{8,9}, except that testing was done with assembled harmonic® scalpels.

Performance Evaluation

Two performance evaluation tests were conducted. In the first test, thirty (30) fully remanufactured harmonic® scalpels and 30 new harmonic® scalpels were evaluated¹¹. All harmonic® scalpels (both new and remanufactured) were visually inspected for cracks, separation and damage. These same harmonic® scalpels were then activated against bovine intestine for 300 twenty-second activations

combined with 3-5 rotation cycles (right and left) at 180° of the external shaft. To prevent overheating, the harmonic® scalpels were allowed to air cool for 2 minutes after every 30 cycles. This activation methodology mimics the longest and most challenging operation using the harmonic® scalpel. After each activation cycle, the harmonic® scalpel was inspected to determine whether the Teflon pad remained attached and seated in the Teflon pad arm.

To validate performance of remanufactured harmonic® scalpels, 30 harmonic® scalpels were subjected to the following in a separate test to simulate worst-case use, storage, processing and shipment¹²:

- Inoculated with challenge contamination.
- Entire uncleaned harmonic® scalpel placed in incubator for at least 72 hours at a temperature of 60°C.
- Cleaned using standard procedures, but at maximum process conditions, i.e., greatest temperatures, times and chemical concentrations. Such parameters have the greatest potentially negative effect on the structural integrity and performance of the harmonic® scalpel.
- Packaged and sterilized per nominal process conditions.
- Subjected to thermal cycling environmental conditioning to simulate worst-case environmental conditions of storage and transit (40°C/ 90% humidity, -18°C/ 0% humidity and 60°C/ 15% humidity, each for 18 hours)¹³.
- Subjected to worst-case transit conditions (accelerations, compressive forces, pressures, temperatures and vibrations)^{14,15}.

Following the above preparation, these harmonic® scalpels were then visually inspected for structural damage including cracks, separation, damage, wear or deterioration. The harmonic® scalpels were then activated into bovine intestine for 270 ten-second activations with five-second rest between each activation.

Product Stability Performance Evaluation

Thirty (30) remanufactured harmonic® scalpels were subjected to the following to simulate worst-case use, storage and shipment¹⁶:

- Remanufactured and cleaned using standard nominal process conditions.
- Packaged and sterilized per nominal process conditions.
- Subjected to thermal cycling environmental conditioning to simulate worst-case environmental conditions of storage and transit 40°C/ 90% humidity, -18°C/ 0% humidity and 60°C/ 15% humidity, each for 18 hours)¹³.

- Subjected to worst-case transit conditions (accelerations, compressive forces, pressures, temperatures and vibrations)^{14,15}.
- Subjected to accelerated and real-time aging for up to 2 years, to represent typical warehouse storage.

Following the above preparation, these harmonic® scalpels were visually inspected for structural damage including cracks, separation, damage, wear or deterioration. The harmonic® scalpels were then activated into bovine intestine for 270 ten-second activations with five-second rest between each activation.

Animal Efficacy Evaluation

Three (3) remanufactured and 3 new harmonic® scalpels were evaluated in a living swine model (female, 50kg) to determine comparative efficacy¹⁷. Swine were selected to provide vessels of similar size to those transected in typical human procedures. A veterinary surgeon experienced in using the harmonic® scalpel used each scalpel 3 times to transect mesenteric vessels (≤ 5mm diameter) and 3 times to transect liver tissue, in accordance with standard medical practice. To assure consistency, one new and one remanufactured scalpel were used per animal, for a total of 3 animals. For each cut, evaluations were made of the time to transect each tissue, the initial hemostasis score, 10 minute hemostasis score and overall amount of time to achieve hemostasis. Comparisons between remanufactured and new scalpels were made for each of the above values.

Results

Sterilization Evaluation

Following inoculation of those areas of the harmonic® scalpel that represented the greatest challenge to effective sterilization with 10⁶ CFU, all areas were sterile following a 60 minute cycle. This represents a sterility assurance level (SAL) of 10⁻⁶ achieved in approximately one-third the time of a usual cycle.

Dye Penetrant Inspection Evaluation

Ten of the 12 dye-penetrant inspected remanufactured harmonic® scalpels survived the 270 activations without failure. Two harmonic® scalpels failed by developing cracks during the test and ceased to function thereafter. Confirmation was made that the cracks did not exist prior to the test. However, it was noted that the cracks developed in locations where flaws in the surface of the blade existed. To confirm, testing was completed using

blades that had surface flaws buffed off. All ten survived the 270 activations without fail. In standard remanufacturing, all surface flaws are routinely buffed out. In cases where the flaws are too large, the blades are rejected.

Cleaning Evaluation

All 30 harmonic® scalpels which were the subject of cleaning validation were free of visible contamination. In addition, protein concentration was at least 33 times less, and hemoglobin concentration was at least 39 times less, than acceptable levels as specified in AAMI TIR 30⁹.

All 30 harmonic® scalpels evaluated following standard remanufacturing had packages free of foreign material and all harmonic® scalpels were free of visible contamination. All harmonic® scalpels were structurally sound, without any evidence of cracks, separation, damage, wear or deterioration. All 30 harmonic® scalpels also functioned through 90 activations without failure. In addition, protein concentration was at least 64 times less, and hemoglobin concentration was at least 36 times less, than acceptable levels as specified in AAMI TIR 30⁹.

Performance Evaluation

All new and remanufactured harmonic® scalpels were structurally sound. All remanufactured harmonic® scalpels completed the 300 activations, while only 73% of new scalpels completed the 300 activations, without failure of the Teflon pad. This was a statistically significant difference with a p-value of 0.005. The remaining 27% failed at an average of 128 cycles (range: 5-270).

Sample Number	Failure Cycle Number
3	206
4	195
6	5
8	51
12	50
17	40
22	270
30	210

In the separate performance validation test, all 30 harmonic® scalpels were structurally sound, without any cracks, separation, damage, wear or deterioration. In addition, all of the scalpels functioned through 270 activations without failure.

Product Stability Performance Evaluation

All harmonic® scalpels that were part of the stability performance evaluation test were structurally sound, without any cracks, separation, damage, wear or deterioration. In addition, all of the harmonic® scalpels functioned through 270 activations without failure.

Animal Efficacy Evaluation

Based on the animal studies conducted, time to transect tissues, initial hemostasis score, ten minute hemostasis score and overall amount of time to achieve hemostasis were equivalent between the new and remanufactured harmonic® scalpels.

Table 2. Comparative Efficacy Measures Between New and Remanufactured Harmonic® Scalpels

Efficacy Measure	New Scalpel	Remanufactured Scalpel	p-value
Mesenteric Vessels			
Time to Transect Tissue (secs)	2.7	2.2	0.182
Initial Hemostasis Score	1.0	1.0	1.000
Ten Minute Hemostasis Score	1.0	1.0	1.000
Time to Achieve Hemostasis (secs)	0	0	1.000
Liver			
Time to Transect Tissue (secs)	3.4	4.1	0.398
Initial Hemostasis Score	1.1	1.2	0.539
Ten Minute Hemostasis Score	1.0	1.0	1.000
Time to Achieve Hemostasis (secs)	43.8	88.1	0.541

Discussion

Historically, concern has been raised regarding the safety and performance of reprocessed/remanufactured instruments labeled by the original manufacturer as single use. These concerns typically focus on whether the instrument is adequately cleaned and whether the reprocessed/remanufactured instrument functions as well as new instruments. Many of these concerns come from early experiences, when much of the reprocessing took place in an unregulated or uncontrolled hospital environment and little validation of the reprocessed/remanufactured product was done. Since that time, however, companies that specialize in reprocessing/remanufacturing instruments have become established. In addition, the FDA has developed requirements for validating, controlling and clearing the process. As a result, such reprocessing companies are required to have controlled processes, and to validate cleanliness, performance and sterility of their

reprocessed/remanufactured products in a rigorous manner.

Since 2006, Ascent has remanufactured over 220,000 harmonic® scalpels. The remanufacturing of harmonic® scalpels is done in a specific, documented, validated and controlled manner by well-trained individuals. Key remanufacturing steps include careful disassembly of the harmonic® scalpel to its component parts, thorough cleaning, buffing out any minor surface flaws from blade (visible at 25X magnification), replacement of used Teflon pads with new ones, placement of internal labeling to allow tracking of prior reprocessing, and careful reassembly back into final product.

Throughout the remanufacturing process, all parts are inspected at 20-25X magnification for cleanliness, cosmetic defects, damage or missing parts. Parts that do not meet strict criteria are diverted out of the remanufacturing stream. Whenever possible, plastics and metals are recycled into other products within the stream of commerce. Following visual inspection for minor surface defects and polishing to remove them, dye penetrant testing is used to identify and remove any with possible cracks in the blade. Once fully re-assembled, each remanufactured unit is individually tested for function.

This report unequivocally demonstrates that remanufactured harmonic® scalpels from Ascent function at least as well as new scalpels. This report provided data from a large number of (150) remanufactured harmonic® scalpels. Based on this testing data, remanufactured harmonic® scalpels consistently had no visible contamination, with insignificant levels of protein or hemoglobin. These remanufactured scalpels were also cosmetically and functionally sound, without any foreign material, cracks, separation, damage or wear. In addition, remanufactured scalpels functioned for up to 300 activations without failure. This was demonstrated for:

1. Product remanufactured using standard production processes
2. Product subjected to worst-case contamination, storage, shipping, and cleaning, as well as
3. Product subjected to worst-case shipping and storage conditions followed by two years of accelerated and real-time aging.

Finally, remanufactured harmonic® scalpels routinely withstood 300 activations without failure of the Teflon pad while new scalpels failed 27% of the time.

This report demonstrated that the remanufactured harmonic® scalpels were cleaned such that they consistently had levels of protein and hemoglobin which were at least 33 and 36 times less, respectively than acceptable levels specified in a consensus standard (AAMI TIR 30) for cleaning of reusable medical devices. Although minimal, one could potentially still be concerned with even this level of remaining protein and hemoglobin. It must be understood however, that these remanufactured harmonic® scalpels were also subjected to biocompatibility testing (cytotoxicity, sensitization and irritation) in compliance with the ISO-10993¹⁸ standards and successfully passed.

Numerous trocars and mechanical laparoscopic devices, such as scissors and graspers, are generally accepted as reusable devices and are routinely cleaned and autoclaved multiple times by hospitals without safety concerns. An assessment of the protein and hemoglobin level on 17 such devices taken from the sterile inventory of a JCAHO approved hospital demonstrated hemoglobin levels averaging 150.9 µg/device and protein levels averaging 639.8 µg/device¹⁹. These levels are significantly higher than those observed with remanufactured harmonic® scalpels in this report (not able to be detected and 48.2 µg/device for hemoglobin and protein respectively).

Some level of organic material is to be expected on any product, whether they are new, reprocessed/remanufactured or reused. This fact led to the establishment of an expert consensus standard for what levels are acceptable⁹. Testing of new harmonic® scalpels demonstrated total organic carbon levels of 137 µg/device²⁰ or 0.2µg/cm². Although less than that of remanufactured devices, both new and remanufactured harmonic® scalpels are in the range established as safe for medical devices.

As noted above, one concern often raised regarding the use of reprocessed/remanufactured instruments is whether they are consistently sterile or not. All medical products which are labeled as sterile are required to undergo validation testing using a large number of product and multiple production runs to show that there is only a 10⁻⁶ (one in one million) chance for non-sterility⁵. The remanufactured harmonic® scalpels were subjected to the same set of tests required for new harmonic® scalpels and the standard sterilization process was found to be effective in assuring sterile product at a one in one million chance even at less than one third the standard production cycle time, even in the most difficult to sterilize areas. These results thereby

assure sterility in a typical full production sterilization cycle.

Although bench studies are important for understanding the safety and efficacy of a device, clinical use remains the ultimate test. As shown in this report, using a simulated clinical application performed in a swine model, remanufactured and new harmonic® scalpels were equivalent in the critical parameters of time to transect tissue, initial hemostasis and 10-minute hemostasis.

The FDA maintains a database of serious adverse events reported with medical devices. In a summary of adverse events from this database associated with harmonic® scalpels covering the time period of January 1, 2008 to February 4, 2009, 53 such adverse events were reported²¹. The majority of these (49) were from new product. Table 3 presents a summary of these reported events.

Table 3. Summary of MedSun Adverse Event Reports with Harmonic® Scalpels

Adverse Event	New Scalpel	Remanufactured Scalpel
Didn't Function	20	3
Piece Came Off	16	1
Overheat	6	0
Broke	5	0
Snagging	1	0
Stuck in Trocar	1	0
	49	4

As can be seen from the above table, the types of adverse events are similar between the new and remanufactured scalpels.

Conclusions

Remanufactured harmonic® scalpels are proven equivalent to new scalpels in safety and performance, based on an extensive series of bench and animal evaluations. This is proven primarily through their consistent cleanliness (at both the macro and cellular level) and their function through even the most lengthy of typical uses.

The minimal risks of remanufactured harmonic® scalpels do not exceed those of new harmonic® scalpels and apparently do not include any potential risks beyond those inherent in new harmonic® scalpels from the original manufacturer.

The first FDA cleared remanufactured harmonic® scalpel was clinically used in 2004. Since 2006, Ascent has remanufactured more than 220,000 harmonic® scalpels. No adverse patient events have been confirmed. The science of this study supports the safety record already validated in clinical use.

Key Points

1. Remanufactured harmonic® scalpels are thoroughly clean, even from protein and hemoglobin.
2. Remanufactured harmonic® scalpels can be consistently activated up to 300 times without failure of any component part.
3. Remanufactured harmonic® scalpels consistently demonstrate cosmetically and structurally sound devices, without cracks, separation, damage or cosmetic deficiencies.
4. In a head to head animal efficacy comparison, remanufactured harmonic® scalpels functioned in an equivalent manner to new harmonic® scalpels.

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