Review

The Super Stent: a Stent Containing a Peristalsis Function and Capable of Delivering Heat for Hyperthermia

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Abstract: Surgery for esophageal cancer is a very difficult operation, even today with modern medical techniques. One of the most important aspects of such surgery is the difficulty of reconstructing the esophagus. In such a surgical procedure, the stomach and intestines are used to provide material to repair any esophageal damage, thus requiring a large and extensive operation which is difficult with elderly patients. Although an improvement in prognosis for the quality of life can be expected if the cancer is resectable, there are many cases which are diagnosed too late for effective surgery. To help these patients, a peristalsis stent with a hyperthermia function was developed for use with terminal esophageal cancer patients when surgery is not an option. The peristalsis stent with a hyperthermia function has three characteristics: 1) It is completely noninvasive; 2) hyperthermia can be delivered to the carcinoma tissue; and 3) it incorporates a peristalsis function. This stent is expected to provide an alternative tool for the treatment of terminal esophageal cancer.

Key Words: peristalsis stent, esophageal cancer, stent, shape memory alloy, electromagnetic induction

Introduction

The history of research and development of artificial internal organs is already decades old. In the development of artificial internal organs, reductions in size and weight of any implantable systems are very important problems. In a human body, if a foreign substance or object produces pressure on any organ or system, the body will attempt to eliminate the foreign object. Even in outpatient clinics, sutures are sometimes dissolved shortly after an operation. The pacemaker (PM) currently used widely in the clinic, is implanted after producing a pocket in the body. Since PM placement requires expansion of the skin, a reaction is stimulated. Producing a PM pocket is the equivalent of eliminating a foreign substance. Therefore, for any artificial internal organ, smaller is better. Nanotechnology or micromachining technology may provide medicine with key technologies to solve this problem.

The development of a complete implantable small and lightweight artificial esophagus segment is described here, and this device contains a peristalsis function when positioned in the body (Fig. 1). In
addition, attempts to regenerate the esophagus using tissue engineering with nano bioabsorbable technology are described.

Using these techniques, it was possible to develop a peristalsis stent with an integral hyperthermia function, thus making it possible to deliver a therapy for esophageal cancer, as well as providing a peristaltic function for the patient (Fig. 2). This system can thus provide a means to deliver targeted hyperthermia therapy to esophageal carcinoma tissue. Various investigators have noted the therapeutic effect of hyperthermia on esophageal cancer, providing the impetus to develop this device.\textsuperscript{2–0}

**Implantable artificial esophagus development using nanotechnology**

Among cancer operations, operations for esophageal cancer are one of the most difficult operations to perform along with pancreatic cancer operations.\textsuperscript{1–9} One of the reasons for this is the problem of reconstruction of a functional esophagus after resection. Even if the esophageal cancer can be resected, a patient cannot drink or eat easily, and nutrition is limited. For this reason, the stomach or intestinal tract is usually used to construct a substitute for a portion of an esophagus, and a laparotomy is required. Because of these additional abdominal operations, operation times are prolonged and the difficulty of the operation increases progressively, especially with elderly patients.

If there was an available “artificial esophagus”, which could be used to provide a substitute for a portion of the esophagus, the necessity for an incision in the abdomen could be eliminated, and the operation would be simplified. Furthermore, if such a small artificial esophagus could be implanted with a fiberscope, it could be used easily and frequently, and it could be used in increasing numbers of
patients in a cost effective manner.

However, to date, no functional artificial esophagus has been developed\textsuperscript{10-14}. An esophagus is not a simple pipe, but must also transport food to the stomach by peristalsis. Even if a person performs a handstand and remains in an upside down position, he can swallow food against gravity using peristalsis. An improperly working drinking function tends to be associated with the aspiration of food. In the case of elderly people, if food inadvertently goes into the trachea, it could easily lead to pneumonia. If there is no ability to function during drinking or for the intake of liquids, an “artificial esophagus” would not be a true replacement for a damaged esophagus. In the past, there was a simple pipe called a an artificial esophagus. However, an artificial esophagus which can be implanted and which permits the patient to swallow food has not been available to date. The work described here was undertaken to develop a functional artificial esophagus. The resulting system is so small that it can be implanted using only a fiberscope. In addition, the new implantable esophagus is also capable of peristaltic action.

\textit{Structural development of the artificial esophagus using nanotechnology}

Patent information, published papers, and internet searches were used to look for existing reports describing an artificial esophagus. The search results found that some proposals had been made suggesting a methodology which could be used to construct an esophagus with peristaltic action. Various methods to transport food through an esophagus had been tried in the past. For example, one proposal suggested a method of putting a motor on the side of the pipe forming an artificial esophagus, allowing food to be drawn through. This proposal described using a screw-type device or worm drive type device to transport food through the esophagus\textsuperscript{14}. In a human body, the chest cavity contains few empty or available spaces. The thorax contains the lungs, trachea, heart, aorta, large arteries, etc., in addition to the esophagus. There is no available space in which to place a motor in the thorax, although the abdominal space does have some regions in which space could be utilized. Furthermore, it is unrealistic to use a device such as a screw-type drive\textsuperscript{10}.

In artificial heart research, since there is no space in which to place an actuator, methods of putting a motor in the abdominal space have been studied. In order to generate peristaltic action in the limited space available in the thorax, attention was given to a shape memory alloy (SMA) actuator using nanotechnology\textsuperscript{15-17}. SMA actuators are reported to have efficiencies 1,000 times higher than human muscle, making SMA actuators optimal candidates for an artificial organ. However, the problem of the durability was limiting until now, and this problem was solved by recent developments in nanotechnology. With shape memory alloys, the organization of molecular crystal structures are irregular and power is not absorbed efficiently during deformation. This is the one of the main factors, which limits durability. This problem was solved recently by improving the nano-level molecular crystal structure organization. If nano-level crystal arrangements are made with nanotechnology methods, the amount of deformation not only becomes larger, but SMA durability can increase by a factor of up to 1,000. To measure the durability of this new SMA, the small light weight actuators used in this system are tested by operating them a billion times or more.

After observations of peristalsis in the human esophagus, it was possible to simulate the observed movement and create a peristalsis like motion. Miniature ring-like peristalsis SMA actuators were
fabricated to produce a muscle-like peristaltic type motion, and peristalsis motion with the same speed as observed in the human esophagus was realized.

**Animal experiments with an artificial esophagus segment**

Animal experiments with the nano SMA actuator in an artificial esophagus were designed to test the new esophagus and its peristaltic action. After verifying that the peristalsis action in the model circuit was functional, animal experiments were done in order to check the esophagus performance in a live animal environment.

An artificial esophagus implanted in an animal is shown in Fig. 1. Since laboratory animals of the same size as humans were required for such an experiment, a healthy goat with approximately the same weight as an average Japanese adult was used for this experiment.

The neck of a goat was opened and the esophagus was approached behind the trachea, and about 30 cm the esophagus was removed and replaced with an artificial esophagus.

This experiment was intended to see if it was possible to generate a peristaltic like movement using electrically activated SMA actuators in the animal's body.

Since an esophagus is essentially a tube which transports food, the quality of the material used for the tube of the artificial esophagus is important. Trials of various biocompatible materials have been reported, and regenerative therapy is also being studied. Ideally, a replacement esophagus could grow from the ends like a regenerating tail in a lizard. However, at present, even though the regeneration of single structures like the skin or bone is possible, no successes have been reported for the reproduction or regeneration of an internal organ such as a liver or a heart. In several reports, the reproduction of a membrane was achieved in the alimentary canal, but there are limits for regeneration where a muscle or muscular layer must be regenerated. At Tohoku University, there have been successes in the regeneration of esophageal membranes in animal experiments using nano bioabsorbable material.

Ideally, a new artificial esophagus could be made with a combination of regenerative esophageal membrane tissue and peristalsis achieved using artificial muscles made using nanotechnology.

For every type of artificial internal organ, the supply of energy is a critical problem. Providing an energy supply by penetrating the skin, creates the possibility of generating an infection. Although methodologies for transcutaneous energy transmission have been tried at various institutions until now, efficient high transmission efficiency has not been achieved using electromagnetic induction. Tohoku University has developed a new delivery technology for electromagnetic energy using new nanotechnology. High levels of energy transmission were achieved using magnetic shielding with nanotechnology.

**Hyperthermia and the peristalsis stent**

In a case of esophageal cancer which could not be removed, a metallic stent for esophageal stenosis caused by carcinoma tissue was inserted for oral nutrition intake. However, at times, food aggregates obstructed the metallic stent after its insertion. If an esophagus stent is blocked by food aggregates, and peristalsis motion is blocked due to cancer, food aggregates cannot be removed unless an endoscope is used. In the patients with advanced esophageal cancer where surgery is not possible, the quality of life
(QOL) is very poor.

In order to treat patients in this situation, a newly invented esophageal stent with an integral peristalsis function was developed. This system is positioned with an endoscope, and is inserted in a noninvasive manner. Energy for its operation is supplied with a transcutaneous energy transmission unit attached to the internal side of the stomach with clips.

Hyperthermia therapy has been used for the patients with carcinoma worldwide, and several reports have noted the usefulness of hyperthermia therapy for esophageal carcinoma tissue. Kochevarov et al. reported on a combination therapy with hyperthermia and surgery, radiation and chemotherapy. They reported that Local hyperthermia potentiated the effect of radiation treatments\(^5\). Matsufuji et al. reported on a case of spreading esophageal cancer which was controlled with hyperthermochemoradiotherapy\(^5\). Sugimachi et al. reported the feasibility of hyperthermochemoradiotherapy for esophageal carcinoma\(^4\). Thus, thermotherapy is one of the established methodologies in this situation.

However, it is very difficult to heat cancer tissue deep inside of the body, and the esophagus is located far from the surface of the body. To solve this problem, a stent with an integral heating element was designed, which could deliver heat to the carcinoma tissue from the interior of the esophagus. The stent is heated by electromagnetic induction via a power source located outside of the body (Fig. 3).

The first coil is placed outside of the body and is a pocket size compact device which is managed with a small electric controller (Fig. 4). This coil is designed to be about the same size as a standard business card, and can be easily contained in a pocket. The second coil is attached to the inner surface of the stomach as shown in Fig. 2 and Fig. 4. The second coil is designed to be almost same size as a pencil, and can easily be inserted with fiberscope and attached to the internal surface of the stomach with a clip. This is apparently the first artificial internal functional organ. When peristaltic motion is needed, the first coil can be attached to the stomach, and an electric current can lead to the induction of and the peristaltic motion.

All previous artificial internal organs were systems designed to be implanted with surgery through the skin. However, this newly developed Super Stent which was designed to have a peristaltic action and an integral heat delivery system for hyperthermia, can be delivered through the alimentary canal. This

![Fig. 3. Thermography of the Hyperthermia Drinking Stent.](image)

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may be the first artificial internal organ which can be implanted without first making an incision. The internal alimentary canal is anatomically on the outside of the body. This means that the peristalsis stent has an advantage in controlling infection, because there in no external invasion of tissue. In the past, temporary hyperthermia applicators were developed to be used with a fiber scope, and were not implantable systems, and this led to patient discomfort during therapy. Furthermore, repeated insertion of a fiber scope is not completely free from a risk of infection. The newly developed Super Stent system is designed to be an implantable system, so, patients should not experience discomfort during therapy. The quality of life of the patients will hopefully be improved by the Super Stent system.

Unfortunately, in many cases of esophageal carcinoma, it is too late to use surgery when the cases are diagnosed. For this reason, he Super Stent system was developed to aid with peristaltic functions and to deliver hyperthermia therapy. Although medical treatments using hyperthermia for esophageal cancer have been reported by previous investigators, it was difficult to heat the esophagus in the interior of the body. Because this new stent system is designed to be in direct contact with the interior surface of the carcinoma tissue, a hyperthermic therapeutic effect is expected.

Moreover, a therapeutic treatment’s effect can be reinforced by combining it with another therapy such anti-neoplastic drugs, radiotherapy, etc., and such combined treatments are planned for use with this stent. By experimenting with therapeutic combinations, it is hoped that an effective therapy for esophageal carcinoma will be developed. Such new treatment combinations are expected to lead to treatment plans for esophageal carcinomas in accord with patient pathophysiological findings.

After the insertion of the super stent system, patients will have to visit outpatient hyperthermia clinics once a week, where an electromagnetic power device will be attached to the body surface. The internal stent can be heated with electromagnetic induction to generate a planned hyperthermia therapy temperature of 42-44°C. This temperature can be easily controlled with an exterior device. Radiation or chemotherapy can also be delivered in conjunction with hyperthermia in an optimal manner, leading to a combined therapy for esophageal cancer.

Other applications for this stent can also be considered, such as for like Gastro-esophageal Reflux Disease, or other parts of the digestive tract, the urinary tract, the biliary tract, etc. It is hoped that this
Super Stent system may also provide new therapeutic tools for other types of patients in the future.

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